PUBLIC HEALTH
LAW CENTER

Tobacco Control Legal Consortium

July 19, 2018

Commissioner Scott Gottlieb, MD
c/o Division of Dockets Management
HFA-305
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20825

Re: Regulation of Flavors in Tobacco Products

Docket No. FDA-2017-N-6565

Dear Commissioner Gottlieb:

The Public Health Law Center is pleased to submit these comments to the U.S. Food and Drug Administration (FDA) on the regulation of flavors in tobacco products. The Public Health Law Center is the coordinating center of the Tobacco Control Legal Consortium, a national network of nonprofit legal centers providing legal technical assistance to public health professionals and advocates concerning legal issues related to tobacco and public health.[1]

Tobacco use is the leading cause of preventable death and disease in the United States. Approximately one in seven adults are current users of tobacco and nearly half of high school students have ever tried a tobacco product. One of the key drivers of tobacco use in the United States is the availability of flavored tobacco products. According to recent PATH data, for ever-users of all tobacco products, initiation with a flavored product was more likely in every age group, including an astonishing 81% of youth, 86% of young adults, and 55% of adults.[2] While the public health community's tireless efforts have significantly reduced cigarette use over the last

[1] The Tobacco Control Legal Consortium's activities are coordinated by the Public Health Law Center, at Mitchell Hamline School of Law in St. Paul, Minnesota. The Consortium's affiliated legal centers include: ChangeLab Solutions, Oakland, California; Legal Resource Center for Tobacco Regulation, Litigation & Advocacy, at University of Maryland Francis King Carey School of Law, Baltimore, Maryland; Public Health Advocacy Institute and the Center for Public Health and Tobacco Policy, both at Northeastern University School of Law, Boston, Massachusetts; Smoke-Free Environments Law Project, at the University of Michigan, Ann Arbor, Michigan; and Tobacco Control Policy and Legal Resource Center at New Jersey GASP, Summit, New Jersey.
[2] Andrea C. Villanti et al., *Flavored Tobacco Product Use in Youth and Adults: Findings from the First Wave of the PATH Study (2013–2014)*, 53 AM. J. PREVENTIVE MED. 139 (2017), https://www.ncbi.nlm.nih.gov/pubmed/28318902.

fifty years, those benefits have been undermined by the introduction and marketing of other tobacco products, many of which are flavored. These flavored products have flourished in the absence of significant regulation, exposing new tobacco users to health harms and starting them on the path of nicotine addiction.

As the FDA has noted in its Advance Notice of Proposed Rulemaking (ANPRM), there are many ways that flavored tobacco products create harm: they attract youth and adult never-users to initiate tobacco product use; they ease the palatability and reduce the harshness of inhaling tobacco smoke or nicotine aerosol; they make it harder to quit using tobacco products; some flavors have analgesic or numbing effects making tobacco products more palatable; and some flavors are toxic and create unique health harms when inhaled.

The FDA has broad authority to establish product standards for all tobacco products and has a duty to uphold the public health standard of the Family Smoking and Tobacco Control Act (Tobacco Control Act) by promulgating rules focused on reducing youth initiation and encouraging cessation. The Act clearly anticipates that the FDA would assess and address the impacts of flavors. The law prohibits flavors other than menthol in cigarettes and requires a commissioned report on the evidence to support regulation of menthol.

We urge the FDA to use its broad authority to maximize the protection of public health in proposing a final rule. Any such rule must prohibit menthol in cigarettes. The agency must also prohibit all flavors in all products and prohibit all chemicals or additives that may serve as a substitute for flavors in mitigating the taste of tobacco. The FDA must also take steps to ensure that any federal action does not jeopardize the cutting-edge tobacco control policies being advanced at the state and local level.

I. The FDA Must Prohibit Menthol In Tobacco Products.

Any FDA action addressing flavors in tobacco products must include a complete prohibition on the addition of menthol to tobacco products. The weight of the tremendous amount of evidence showing the extensive harms to public health caused by menthol in tobacco products requires immediate action by the FDA. The elimination of menthol is of grave importance because of its role in initiating and sustaining tobacco addiction and its prevalence in many targeted communities who already bear a disproportionate burden of health harms related to commercial tobacco product use.

For several years, the FDA has had abundant evidence that the elimination of menthol would save hundreds of thousands of lives and yet there has been no rule prohibiting menthol. The evidence at the FDA's disposal includes: 1) the FDA's commissioned scientific review from the Tobacco Products Scientific Advisory Committee (TPSAC) concluding that the "[r]emoval of menthol cigarettes from the marketplace would benefit public health in the United States";[3] 2) the FDA's own internal scientific review of menthol, which concludes that menthol plays a key role in youth and young adult initiation, that mentholated tobacco use is associated with a deeper level of addiction, and that these factors point to a greater overall health risk when compared to non-menthol cigarettes;[4] 3) a Citizen Petition from nineteen public health groups demonstrating tremendous support for the elimination of menthol to address the health harms imposed by mentholated cigarettes and to address the historic targeting of particular vulnerable populations by the tobacco industry;[5] and 4) a previous ANPRM, with over 170,000 submitted comments establishing overwhelming support for a prohibition on menthol in cigarettes.[6] The FDA's latest compilation of scientific research completed by the agency's Tobacco Regulatory Science Research Program also echoes these past conclusions: that menthol increases initiation, facilitates addiction through suppressing the irritation of cigarette smoke, decreases cessation, and affects vulnerable populations at higher rates.[7]

Because most public health policies, including those in commercial tobacco control, benefit the population as a whole, it is often challenging to address the disproportionate health harms for certain targeted and vulnerable populations. However, prohibiting menthol in cigarettes presents a unique opportunity for the FDA to advance health equity. Several studies have found that of the thousands of lives that could be saved with a menthol prohibition, one-third to one-half of those would be African American lives.[8] However, African Americans are not the only

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[3] TOBACCO PROD. SCI. ADVISORY COMM., FDA, *Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations* (2011) https://wayback.archive-it.org/7993/20170405201731/https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.

[4] FDA, *Preliminary Scientific Evaluation of the Possible Public Health Effects of Menthol Versus Nonmenthol Cigarettes* (2013), https://www.fda.gov/downloads/ucm361598.pdf.

[5] TOBACCO CONTROL LEGAL CONSORTIUM, *Citizen Petition to Food & Drug Administration: Prohibiting Menthol as a Characterizing Flavor in Cigarettes* (Apr. 12, 2013), http://www.publichealthlawcenter.org/sites/default/files/resources/tclc-fdacitizenpetition-menthol-2013.pdf; *see also* FDA, Prohibit Menthol as a Characterizing Flavoring of Cigarettes and Cigarette Smoke (2013), https://www.regulations.gov/docket?D=FDA-2013-P-0435.

[6] FDA, *Menthol in Cigarettes, Tobacco Products; Request for Comments* (2014), https://www.regulations.gov/docket?D=FDA-2013-N-0521.

[7] CTR. FOR TOBACCO PROD., FDA, *Tobacco Regulatory Science Research Program at FDA s Center for Tobacco Products: Summary and Highlights,* https://www.fda.gov/downloads/TobaccoProducts/PublicHealthScienceResearch/UCM613046.pdf.

[8] David T. Levy et al., *Modeling the Future Effects of a Menthol Ban on Smoking Prevalence and Smoking-Attributable Deaths in the United States*, 101 Am. J. Pub. Health 1236 (2011), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3110235/pdf/1236.pdf; TOBACCO PROD. SCI. ADVISORY COMM., FDA, *Menthol Cigarettes and Public Health: Review of the Scientific Evidence and Recommendations* (2011) https://wayback.archive-

minority population that use menthol tobacco products at a disproportionately high rate. As reflected in Table 1, research shows that menthol use is highest among those from racial minorities, youth users, LGBTQ communities, those with serious mental illnesses, and those of low socio-economic statuses (SES). Women have also been targeted by the industry, as demonstrated by their disproportionate menthol product use.

Table 1. Prevalence of menthol cigarette users among current users of combustible cigarettes focusing on vulnerable populations.[9]

Current Smokers	**Menthol Cigarette Smoking Prevalence (%)**
Female	43.5
Male	34.8
African American	84.6
Hispanic	46.9
White	28.9
Age	
12-17	53.9
18-25	50.0
26-34	43.9
35-49	32.3
50+	32.9
LGBTQ	36.3
Heterosexual	29.3
Serious mental illness	57.1
Household income (US$)	
< $10,000 - $29,999	43.7
$30,000 - $74,999	37.2
$75,000 or more	32.1

it.org/7993/20170405201731/https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/UCM269697.pdf.

[9] *See* Andrea C. Villanti et al., *Changes in the Prevalence and Correlates of Menthol Cigarette Use in the USA, 2004-2014,* 25 TOBACCO CONTROL ii14 (2016); Amanda Fallin et al., *Menthol Cigarette Smoking among Lesbian, Gay, Bisexual, and Transgender Adults*, 48 AM. J. PREVENTIVE MED. 93 (2015); Kelly C. Young-Wolff et al., *Correlates and Prevalence of Menthol Cigarette Use Among Adults with Serious Mental Illness,* 17 NICOTINE & TOBACCO RES. 285 (2015).

An FDA product standard prohibiting menthol in all tobacco products would do more to advance health equity than any other regulatory option currently under consideration.

The industry's tenacious lobbying and efforts to prevent a menthol prohibition at all levels of government indicate how valuable mentholated products are to its bottom line. For example, menthol is so important to the tobacco industry's portfolio, it is the only flavor that was exempted from the Tobacco Control Act's general prohibition on flavors in combustible tobacco products, despite evidence of its harmful effects. When local jurisdictions have considered ordinances restricting the sale of menthol tobacco products, the industry has threatened lawsuits,[10] lobbied the communities[11] and city councils,[12] launched ballot measures to repeal,[13] and actually sued.[14] Additionally, the tobacco industry has spent billions of dollars tailoring its messaging and targeting minority communities with marketing, advertising, sponsorships, and campaign contributions. Several studies demonstrate that the tobacco industry targets African-American communities more heavily by advertising in black owned newspapers, magazines, and media and in point-of-sale advertising.[15]

That the tobacco industry fights restrictions on menthol so aggressively demonstrates the value of menthol in facilitating nicotine addiction. Profits of

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[10] Letter from Ryan J. Watson, Partner at Jones Day, to Peter Lindstrom, Mayor of Falcon Heights, MN (May 9, 2018).

[11] J. Patrick Coolican, *Tobacco Industry Looks for Political Wins in Minnesota*, STAR TRIB. (Feb. 12, 2017), http://www.startribune.com/tobacco-industry-looks-for-political-wins-in-minnesota-usually-unfriendly-turf/413548993/.

[12] Emma Nelson, *Lobbyists Descend on Minneapolis to Fight Menthol Restriction*, STAR TRIB. (July 20, 2017), http://www.startribune.com/lobbyists-descend-on-minneapolis-to-fight-menthol-restriction/435699533/.

[13] Jan Hoffman, *San Francisco Voters Uphold Ban on Flavored Vaping Products,* N.Y. TIMES (June 6, 2018), https://www.nytimes.com/2018/06/06/health/vaping-ban-san-francisco.html.

f[14] Indep. Gas & Serv. Stations Ass'ns. v. City of Chicago/5827, Inc. v. City of Chicago, No. 14 C 7536 & No. 14 C 8860 (N.D. Ill. June 29, 2015).

[15] *See* Stacey J. Anderson, *Marketing of Menthol Cigarettes and Consumer Perceptions: A Review of Tobacco Industry Documents*, 20 TOBACCO CONTROL ii20 (2011); Valerie B. Yerger et al., *Racialized Geography, Corporate Activity, and Health Disparities: Tobacco Industry Targeting of Inner Cities,* 18 J. HEALTH CARE FOR POOR & UNDERSERVED 10 (2007); Rachel Widome et al., *The Relationship of Neighborhood Demographic Characteristics to Point-of-Sale Tobacco Advertising and Marketing*, 18 ETHNICITY & HEALTH 136 (2013); Lisa Henriksen et al., *Targeted Advertising, Promotion, and Price for Menthol Cigarettes in California High School Neighborhoods,* 14 NICOTINE & TOBACCO RES. 116 (2012); Andrew B. Seidenberg et al., *Storefront Cigarette Advertising Differs by Community Demographic Profile*, 24 AM. J. HEALTH PROMOTION e26 (2010); Jennifer Pearson et al., *Lorillard Brands' Availability, Price and Advertising: Association with Neighborhood Characteristics at the Point of Sale in Washington, DC,* Society for Research on Nicotine and Tobacco 2013 International Meeting (March 13, 2013).

cigarette manufacturers are driven by cigarette sales and those sales are driven by addiction. Clearly, menthol is one of the most valuable additives for creating and sustaining addiction to deadly tobacco products and the tobacco industry will do anything to prevent meaningful action that will lead to fewer people buying its products.

Finally, to best advance public health, rather than prohibit menthol as a characterizing flavor in tobacco products, as the Tobacco Control Act does with other flavors of cigarettes, the FDA must completely restrict menthol as an additive at any level. Menthol increases the palatability of tobacco through both adding flavor to minimize the harshness of tobacco and producing a numbing or analgesic effect to make smoking more palatable. Although cigarettes marketed as menthol cigarettes comprise 32% of the market, 90% of all cigarettes contain menthol at some level.[16] Because permitting menthol as an additive at subliminal levels makes those tobacco products more palatable, all menthol, whether a characterizing flavor or not, should be prohibited in tobacco products.

A complete prohibition on menthol as an additive in tobacco products has the added benefit of making enforcement easier. Rather than determining the exact level of menthol that rises to the level of a "characterizing flavor," a complete prohibition will simplify the enforcement of a final rule.

II. FDA Action on Flavored Tobacco Products Must Be Comprehensive.

In its notice, the FDA seeks comment on whether it should: (1) only prohibit flavors in certain tobacco products; (2) only prohibit certain exceptionally harmful flavors; or (3) only prohibit the advertising or marketing of flavors. To maximize the public health benefits of a rule, the FDA must prohibit all flavor additives in all tobacco products. As the ANPRM itself demonstrates, there is a multitude of evidence demonstrating that flavors are attractive to youth and adult non-users and that users of flavored tobacco products have a deeper level of addiction and more difficulty quitting tobacco use. The scope of this problem warrants comprehensive action by the FDA.

A. Comprehensive FDA Action Must Prohibit All Flavors at All Levels.

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[16] FTC, *Federal Trade Commission Cigarette Report for 2011* (2013), https://www.ftc.gov/sites/default/files/documents/reports/federal-trade-commission-cigarette-report-2011/130521cigarettereport.pdf; Gary A. Giovino et al., *Epidemiology of Menthol Cigarette Use*, 6 Nicotine & Tobacco Res. S67 (2004), https://academic.oup.com/ntr/article-abstract/6/Suppl_1/S67/1124563?redirectedFrom=fulltext#.

As the ANPRM acknowledges, some opponents of a restriction on flavors in tobacco products argue that the presence of flavors is important to help adult combustible tobacco users transition to less harmful products. Proponents of this view have often taken the position that some flavors in products only appeal to adults and that the presence of such flavors in non-combustible products facilitates the transitioning of smokers to less harmful products.[17] Although there is some research in this area, there is not sufficient evidence to establish that this is true.[18]

To maximize the public health benefits of a rule, the FDA should not just focus on transitioning tobacco product users to less harmful but still addictive and harmful products.[19] Instead, the agency must remove all flavors from all products so that youth and adults alike have less incentive to use the deadly products. In addition to making tobacco products more attractive to youth, flavors also contribute to palatability and the ease of using the product. Tobacco and nicotine are inherently harsh flavors that the industry has attempted to mask over the years through the addition of many additives, including flavors. To best protect public health, the FDA must establish product standards that are focused on making all tobacco and nicotine products less desirable and appetizing by prohibiting all flavors at all levels. All artificial and natural flavors that are added to tobacco products are added to adjust the way that a user experiences a product. Removing all flavor additives would drastically decrease the attractiveness and palatability of the products, making them significantly harder for youth to initiate with and making it significantly easier for adults to quit.

Additionally, to be most effective, prohibiting all flavors at all levels must include all additives that mimic the role of flavors. The FDA should consider a prohibition on the addition of sugar or other sweeteners to tobacco. While sugar is not a specific

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[17] NOT BLOWING SMOKE, http://adultslikeflavors.org/, (last visited July 19, 2018).

[18] Melissa B. Harrell et al., *Flavored E-cigarette Use: Characterizing Youth, Young Adult, and Adult Users*, 5 PREVENTIVE MED. REP. 33 (2017), https://www.sciencedirect.com/science/article/pii/S2211335516301346.

[19] U.S. DEP'T OF HEALTH AND HUMAN SERV., E-CIGARETTE USE AMONG YOUTH AND YOUNG ADULTS: A REPORT OF THE SURGEON GENERAL (2016); Samir S. Soneji et al., *Quantifying Population-Level Health Benefits and Harms of E-cigarette Use in the United States*, 13 PLOS ONE 1 (2018), https://www.ncbi.nlm.nih.gov/pubmed/29538396; Hyun-Wook Lee et al., *E-cigarette Smoke Damages DNA and Reduces Repair Activity in Mouse Lung, Heart, and Bladder as Well as in Human Lung and Bladder Cells*, PNAS 1 (2017), http://www.pnas.org/content/early/2018/01/25/1718185115; Nardos Temesgen et al., *A Cross Sectional Study Reveals an Association Between Electronic Cigarette Use and Myocardial Infarction*, Poster Presented at GW Annual Research Days (2017), https://hsrc.himmelfarb.gwu.edu/gw_research_days/2017/SMHS/85/; Stanton A. Glantz and David W. Bareham, *E-Cigarettes: Use, Effects on Smoking, Risks, and Policy Implications*, 39 ANN. REV. OF PUB. HEALTH 215 (2018), https://www.annualreviews.org/doi/10.1146/annurev-publhealth-040617-013757.

flavor, it is the most common tobacco additive.[20] Sugar additives increase the natural sugar content of tobacco to make the product more palatable by reducing the harshness of tobacco smoke and acidic compounds to reduce throat irritation from smoking.[21] Additionally, sugar combustion when combined with nicotine, increases nicotine's addictive effects.[22] Finally, the combustion of sugar in cigarettes forms many toxic and carcinogenic byproducts such as formaldehyde, acetaldehyde, acetone, and acrolein.[23] The elimination of sugar or other sweeteners as an additive could have a significant impact on public health. A prohibition on added sugar would also prevent one method for the industry to attempt to mitigate the effects of a prohibition on flavors.

The FDA should also consider prohibiting all chemicals or additives that could have a similar analgesic function as menthol or otherwise increases palatability of tobacco products. Such a prohibition should cover any pain relieving chemicals or additives that would not be otherwise be considered flavors. For example, levulinic acids, as well as other organic acid salts, cocoa, and ammonia are common additives to tobacco that promote smoking initiation and addiction by enhancing the delivery and addictiveness of nicotine and by reducing the harshness of tobacco smoke.[24] The presence of luvelinic acid in cigarettes increases the toxicity of the cigarette smoke.[25] These are only a few examples in a list of over 100 cigarette additives that researchers have documented that mask the unpleasant attributes of tobacco smoke and enhance the effects of nicotine.[26] The FDA should anticipate that the tobacco industry will attempt to circumvent a prohibition on flavor additives in any way possible. To prevent this, the FDA might consider establishing a product standard that establishes a "white list," or a list of ingredients that are permissible to use in commercial tobacco products that would not include harmful additives or constituents. From an enforcement standpoint, this would have two advantages.

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[20] SCIENTIFIC COMMITTEE ON EMERGING AND NEWLY IDENTIFIED HEALTH RISKS, EUR. COMM'N, *Addictiveness and Attractiveness of Tobacco Additives* (July 6, 2010), https://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_029.pdf.

[21] Reinskje Talhout et al., *Sugars as Tobacco Ingredient: Effects on Mainstream Smoke Composition,* 44 FOOD AND CHEM. TOXICOLOGY 1789 (2006); Shida Miao et al., *High-Intensity Sweeteners in Alternative Tobacco Products,* 18 NICOTINE & TOBACCO RES. 2169 (2016); Hillel R. Alpert et al., *A Study of Pyrazines in Cigarettes and How Additives Might Be Used to Enhance Tobacco Addiction,* 25 *Tobacco Control* 444 (2016).

[22] *Id.*

[23] *Id.*

[24] Michael Rabinoff et al., *Pharmacological and Chemical Effects of Cigarette Additives,* 97 AM. J. PUB. HEALTH 1981 (2007); Lois Keithly et al., *Industry Research on the Use and Effects of Levulinic Acid: A Case Study in Cigarette Additives,* 7 NICOTINE & TOBACCO RES. 761 (2005); Terrell Stevenson & Robert N. Proctor, *The Secret and Soul of Marlboro: Phillip Morris and the Origins, Spread, and Denial of Nicotine Freebasing,* 98 AM. J. PUB. HEALTH 1184 (2008); Natasha A. Sokol et al., *The Role of Cocoa as a Cigarette Additive: Opportunities for Product Regulation,* 16 NICOTINE & TOBACCO RES. 984 (2014).

[25] *Id.*

[26] *Id.*

First, assuming that the list of permissible ingredients is far shorter than a list of prohibited ingredients, the FDA would only need to test for the permissible ingredients, rather than tests for hundreds of additives and constituents. In addition, the FDA would not have to spend resources to continuously research and investigate new additives to combat industry efforts to get around the rule. No matter the form, the FDA must promulgate a comprehensive rule that addresses all of these additives and anticipates new formulations.

B. Comprehensive FDA Action Must Prohibit All Flavors in All Products.

The evidence is clear; youth are especially attracted to flavors in tobacco products and the tobacco industry intentionally uses flavor additives and imagery to attract youth and young adults. Rather than flavors attracting current combustible users to e-cigarettes, the evidence shows that the opposite is true: youth and adult non-users are attracted to products like e-cigarettes because of the alluring flavors. Recent research demonstrates that to maintain their nicotine addiction, these users are turning to the most harmful products, such as combustible tobacco products,[27] which have been engineered over decades to be the most effective nicotine delivery devices. This is even more troubling when youth transition from flavored non-combustible products to more harmful products where flavors are already prohibited. Leaving flavors in some products is only likely to establish nicotine addiction in youth and non-users that will likely lead to more harmful product use.

Allowing flavors to remain in combustible tobacco products other than cigarettes has already significantly damaged public health. As mentioned below, the industry has taken steps to deceitfully evade regulations and perpetuate health harms by color-coding cigarettes rather than use deceptive and illegal descriptors. To that same end, manufacturers have produced flavored little cigars that are

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[27] Benjamin W. Chaffee et al., *Electronic Cigarette Use and Progression From Experimentation to Established Smoking*, 141 Pediatrics 1 (2018), https://www.ncbi.nlm.nih.gov/pubmed/29507167; Katherine East et al., *The Association Between Smoking and Electronic Cigarette Use in a Cohort of Young People,* 62 J. Adolescent Health 539 (2018), https://www.ncbi.nlm.nih.gov/pubmed/29499983; Nancy A. Rigotti et al., *Association of E-Cigarette Use with Smoking Cessation Among Smokers Who Plan to Quit After a Hospitalization: A Prospective Study,* 168 ANNALS OF INTERNAL MED. 613 (2018), https://www.ncbi.nlm.nih.gov/pubmed/29582077; Kelly C. Young-Wolff et al., *Documentation of E-Cigarette Use and Associations With Smoking From 2012 to 2015 in an Integrated Healthcare Delivery System,* 109 PREVENTIVE MED. 113 (2018), https://www.ncbi.nlm.nih.gov/pubmed/29360481; Stanton A. Glantz and David W. Bareham, *E-Cigarettes: Use, Effects on Smoking, Risks, and Policy Implications*, 39 ANN. REV. OF PUB. HEALTH 215 (2018), https://www.annualreviews.org/doi/10.1146/annurev-publhealth-040617-013757; Richard Miech et al., *E-cigarette Use as a Predictor of Cigarette Smoking: Results From a 1-Year Follow-Up of a National Sample of 12th Grade Students,* 26 TOBACCO CONTROL e106 (2017), https://www.ncbi.nlm.nih.gov/pubmed/28167683; Krysten W. Bold et al., Trajectories of E-Cigarette and Conventional Cigarette Use Among Youth, 141 Pediatrics 1 (2017), https://www.ncbi.nlm.nih.gov/pubmed/29203523.

indistinguishable from cigarettes in the health harms they impose, yet are attractive to youth because of their flavorings.[28] Without a prohibition on flavors that applies to all combustible tobacco products, the health gains from the flavor restriction in the Tobacco Control Act are diminished.

The elimination of flavors in little cigars would also advance health equity. Research demonstrates that flavored little cigars and other flavored combustible products are more heavily marketed towards certain vulnerable populations, that use of flavored combustible products is highest among certain minority groups, and that these products are cheaper in low-income neighborhoods.[29] In fact, in one study, African American participants were 2.5 times more likely to recall prior exposure to little cigar or cigarillo advertising than non-Hispanic white participants, and a similar difference was observed between participants in the lowest SES group when compared to those in the highest SES group.[30] Ninety-five percent of the little cigars or cigarillos advertised in this study were flavored.[31] This research demonstrates that a flavor prohibition in all tobacco products, especially all combustible products would address health inequities and combat the industry's targeting of certain populations.

Finally, in conjunction with a nicotine product standard reducing nicotine in combustible products, there is no justifiable reason to continue to allow flavors in non-combustible products. In 2017, the FDA announced a bold plan to address the health harms of tobacco by reducing nicotine in tobacco products. This action has the potential to significantly decrease the morbidity and mortality inflicted by commercial tobacco products. The question of whether some flavors should be allowed to remain on the market to attract adult combustible tobacco users to less harmful products is rendered moot by a product standard that eliminates the addictiveness of nicotine in combustible products. If no combustible tobacco products have an addictive level of nicotine, that is all the incentive users would need to transition to non-combustible products that maintain addictive levels of nicotine. There is no longer an issue of attraction, combustible users will have to

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[28] U.S. GOV'T ACCOUNTABILITY OFF., GAO-12-475, TOBACCO TAXES: LARGE DISPARITIES IN RATES FOR SMOKING PRODUCTS TRIGGER SIGNIFICANT MARKET SHIFTS TO AVOID HIGHER TAXES (2012), https://www.gao.gov/assets/600/590192.pdf.

[29] Jennifer Cantrell et al., *Marketing Little Cigars and Cigarillos: Advertising, Price, and Associations with Neighborhood Demographics,* 103 AM. J. PUB. HEALTH 1902 (2013); Lisa Henriksen et al., *Neighborhood Variation in the Price of Cheap Tobacco Products in California: Results from Health Stores for a Healthy Community,* 19 NICOTINE & TOBACCO RES. 1330 (2017); Kurt M. Ribisl et al., *Disparities in Tobacco Marketing and Product Availability at the Point of Sale: Results of a National Study,* 105 PREVENTIVE MED. 381 (2017); Ganna Kostygina et al., *Tobacco Industry Use of Flavours to Recruit New Users of Little Cigars and Cigarillos,* 25 TOBACCO CONTROL 66 (2016).

[30] Meghan Bridgid Moran et al., "Ethnic and Socioeconomic Disparities in Recalled Exposure to and Self-Reported Impact of Tobacco Marketing and Promotions," 13 HEALTH COMMC'N 1 (2017).

[31] *Id.*

progress to other products to maintain their addiction or quit tobacco products entirely. In a world where there are no addictive combustible products, flavors in non-combustible products are unnecessary.

C. Comprehensive FDA Action Requires More Than Prohibiting the Advertising or Marketing of Flavors

A restriction on marketing or labeling rather than an actual prohibition on flavors is completely insufficient to protect public health. While deceptive advertising by the industry causes unique harms, any action that does not actually remove flavors from products will not address the bulk of the harm caused by flavors, the mitigation of the harsh flavor of tobacco and the increased attractiveness of the products.

In addition, existing restrictions on advertising and marketing have been met with immediate attempts at circumvention by a historically deceitful industry. For example, when the Tobacco Control Act prohibited the use of the descriptor "light" to address Big Tobacco's deceptive marketing of light cigarettes as less harmful, the industry responded by color-coding its packages and continuing to offer "light" cigarettes.[32] The FDA should not underestimate the industry's willingness to diminish the impact of any regulation that is less than a full prohibition of all flavors additives in all products.

III. Because Many Local Jurisdictions Have Already Prohibited Flavors in Tobacco Products, the Flavor Regulation Should Be Clear that Federal Action Does Not Preempt Existing Local Laws.

To ensure that state, local, and tribal governments can continue to serve as laboratories of democracy, the FDA must explicitly state that any product standard, sales restriction, or any other federal action related to flavors in tobacco products does not preempt any current or future state, local, or tribal policy. Many jurisdictions in the U.S. have begun to prohibit or restrict the sale of flavored tobacco products in the absence of comprehensive federal action.[33] Some of the first policies were challenged by the tobacco industry and its allies and upheld by two circuits of the U.S. Courts of Appeals.[34] Thus far, most challenges to local flavor restrictions have focused on the narrow preemption provision of the Tobacco

[32] Gregory N. Connolly & Hillel R. Alpert, *Has the Tobacco Industry Evaded the FDA's Ban on 'Light' Cigarette Descriptors?* 23 TOBACCO CONTROL 140 (2014), https://tobaccocontrol.bmj.com/content/23/2/140.
[33] TOBACCO CONTROL LEGAL CONSORTIUM, *U.S. Sales Restrictions on Flavored Tobacco Products* (2017), http://www.publichealthlawcenter.org/sites/default/files/resources/US-Sales-Restrictions-Flavored-Tobacco-Products-2017.pdf.
[34] U.S. Smokeless Tobacco Mfg. Co. v. City of New York, 708 F.3d 428 (2nd Cir. 2013); Nat'l Ass'n of Tobacco Outlets v. City of Providence, 731 F.3d 71 (1st Cir. 2013).

Control Act. Courts have correctly determined that state, local, and tribal authority to regulate the sales of tobacco products is not preempted by the Act and that restrictions on the sale of such products does not amount to a product standard that would require additional analysis. In any action undertaken by the FDA, the agency should make an affirmative statement that the federal action has no impact on state, local, and tribal authority. It is likely that the litigious tobacco industry will see FDA action on flavors as an opportunity to once again challenge existing policies. In making a statement related to preemption, the FDA could further reinforce what is already true: state, local, and tribal governments have full authority to restrict or prohibit the sale of flavored tobacco products within their jurisdiction.

IV. Conclusion

In promulgating a final regulation, we urge the FDA to create a comprehensive rule that maximizes public health benefits. The FDA should take swift action to address the role of flavors in attracting youth and adult never-users to initiate commercial tobacco use and in deepening the addictive effects of nicotine, making it harder for those that use commercial tobacco to quit. To accomplish this, the FDA should prohibit all flavors at all levels in all commercial tobacco products – including menthol at any level – and address the many additives that are added to tobacco that mimic the role of flavors in commercial tobacco products.

Respectfully,

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Staff Attorney

Menthol Cigarette Smoking among Lesbian, Gay, Bisexual, and Transgender Adults

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Background: Menthol can mask the harshness and taste of tobacco, making menthol cigarettes easier to use and increasing their appeal among vulnerable populations. The tobacco industry has targeted youth, women, and racial minorities with menthol cigarettes, and these groups smoke menthol cigarettes at higher rates. The tobacco industry has also targeted the lesbian, gay, bisexual, and transgender (LGBT) communities with tobacco product marketing.

Purpose: To assess current menthol cigarette smoking by sexual orientation among a nationally representative sample of U.S. adults.

Methods: Data were obtained from the 2009–2010 National Adult Tobacco Survey, a national landline and cellular telephone survey of non-institutionalized U.S. adults aged $\geq$18 years, to compare current menthol cigarette smoking between LGBT (n=2,431) and heterosexual/straight (n=110,841) adults. Data were analyzed during January–April 2014 using descriptive statistics and logistic regression adjusted for sex, age, race, and educational attainment.

Results: Among all current cigarette smokers, 29.6% reported usually smoking menthol cigarettes in the past 30 days. Menthol use was significantly higher among LGBT smokers, with 36.3% reporting that the cigarettes they usually smoked were menthol compared to 29.3% of heterosexual/straight smokers ($p<0.05$); this difference was particularly prominent among LGBT females (42.9%) compared to heterosexual/straight women (32.4%) ($p<0.05$). Following adjustment, LGBT smokers had greater odds of usually smoking menthol cigarettes than heterosexual/straight smokers (OR=1.31, 95% CI=1.09, 1.57).

Conclusions: These findings suggest that efforts to reduce menthol cigarette use may have the potential to reduce tobacco use and tobacco-related disease and death among LGBT adults.
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Introduction

In 2009, certain characterizing flavors in cigarettes were prohibited in the U.S.; however, menthol-flavored cigarettes can still be legally manufactured and sold.[1] Menthol is a mint-flavored additive with analgesic and cooling effects that can mask the harshness and taste of tobacco, making these products easier to use and increasing their appeal among youth and other vulnerable populations.[2–4] Additionally, menthol has a synergistic effect with nicotine.[5]

The tobacco industry has targeted youth, women, and minorities with menthol cigarettes,[2,6] and studies indicate that these groups smoke menthol cigarettes at higher rates.[2,7,8] Little is known about whether another vulnerable group, lesbian, gay, bisexual, and transgender (LGBT) individuals, smoke menthol at higher rates than their heterosexual/straight counterparts. The LGBT community is important to consider because LGBT individuals smoke at a higher rate than the general population,[9,10] and the tobacco industry has selectively targeted the LGBT community with tobacco product marketing.[11,12] The tobacco industry's strategy to target the LGBT community was first uncovered through the discovery of internal industry documents pertaining to "Project Subculture Urban Marketing (SCUM)."[12] The tobacco industry has continued to infiltrate LGBT communities by funding AIDS and LGBT organizations,

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and sponsoring LGBT pride parades, street fairs, and film festivals.[13]

During 2009–2010, current cigarette smoking was considerably higher among U.S. LGBT adults (32.8%) than the general adult population (19.5%).[9] Although one study of U.S. adults aged 18–34 years found comparable odds of menthol cigarette smoking between LGBT and heterosexual respondents,[14] the extent of menthol cigarette smoking among all U.S. LGBT adults is uncertain. To address this research gap, this study assessed current menthol cigarette smoking by sexual orientation among a nationally representative sample of adults using the 2009–2010 National Adult Tobacco Survey (NATS).

Methods

Sample

The 2009–2010 NATS is a stratified, national landline and cellular telephone survey of non-institutionalized adults aged ≥18 years residing in the 50 U.S. states and District of Columbia.[9] The sample was designed to yield nationally representative data. Respondent selection varied by phone type. For landline numbers, one adult was randomly selected from each eligible household. For cellular numbers, adults were selected if a cellular phone was the only method they could be reached by telephone at home. In total, 118,581 interviews were completed (n=110,634 landline, n=7,947 cellular) from October 2009 to February 2010, yielding a response rate of 37.6% (landline=40.4%, cellular=24.9%). Ethics approval was not required for this project because secondary data were used.

Measures

Current smokers were defined as respondents who reported smoking ≥100 cigarettes in their lifetime and reported smoking "every day" or "some days" at the time of interview. Among current smokers, menthol cigarette smoking was determined using the question *During the past 30 days, were the cigarettes that you usually smoked menthol?* Response options were *yes*, *no*, *don't know*, or *not sure*. Sexual orientation was determined using the question *Do you consider yourself to be…?* with the response options *heterosexual or straight*, *gay or lesbian*, *bisexual*, or *transgender*. Owing to sample size constraints, individual LGBT categories were combined for analysis.

Assessed respondent characteristics included sex (male or female); age group (18–24, 25–34, 35–50, or ≥51 years); race/ethnicity (non-Hispanic white, non-Hispanic black, non-Hispanic other race, or Hispanic); and education (less than high school, high school, some college, associate degree, college graduate, or graduate degree). "Other" races included Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander, multiple races, and "other" race.

Statistical Analysis

Data were analyzed during January–April 2014 using Stata, version 11. Data were weighted to adjust for the differential probability of selection and response. Final weights were also adjusted for undercoverage using post-stratification by sex, age, race/ethnicity, marital status, education, and telephone type. Data were analyzed using descriptive statistics (t-test, chi-square) and multivariate logistic regression, with menthol smoking as the dependent variable and sexual orientation as the independent variable; covariates included sex, age, race/ethnicity, and education.

Results

Among all respondents, current menthol cigarette smoking was higher among LGBT adults (9.7%) than heterosexual/straight adults (4.2%) (Table 1, $p<0.05$). Among current cigarette smokers, menthol cigarette smoking was higher among LGBT smokers (36.3%) than heterosexual/straight (29.3%) smokers. This difference was particularly notable among women (LGBT=42.9%, heterosexual/straight=32.4%, $p<0.05$); Hispanics (LGBT=57.6%, heterosexual/straight=36.0%, $p<0.05$); individuals of non-Hispanic other races (LGBT=41.8%, heterosexual/straight=29.2%, $p<0.05$); non-Hispanic whites (LGBT=28.9%, heterosexual/straight=23.2%, $p<0.05$); those with less than a high school education (LGBT=54.8%, heterosexual/straight=31.9%, $p<0.05$); and those aged 25–34 years (LGBT=47.7%, heterosexual/straight=32.6%).

Following adjustment, LGBT smokers had higher odds (AOR=1.31, 95% CI=1.09, 1.57) of smoking menthol cigarettes than heterosexual/straight smokers (Table 2). Higher odds of menthol smoking were also observed among current smokers who were female (AOR=1.63, 95% CI=1.51, 1.75); non-Hispanic black (AOR=13.79, 95% CI=11.99, 15.85); non-Hispanic other races (AOR=1.37, 95% CI=1.20, 1.56); Hispanic (AOR=1.73, 95% CI=1.46, 2.05); and aged 18–24 (AOR=2.05, 95% CI=1.78, 2.36) or 25–34 (AOR=1.31, 95% CI=1.18, 1.45) years.

Discussion

The findings from this study reveal that LGBT smokers have higher odds of using menthol cigarettes than heterosexual/straight smokers, which is consistent with previous evidence showing that the tobacco industry has selectively marketed tobacco products to LGBT individuals.[11,12] Younger people, women, and racial/ethnic minorities also have higher prevalence of menthol cigarette smoking, which is consistent with previous surveys.[15] For example, during 2004–2008, 44.8% of U.S. current cigarette smokers aged 12–17 years had smoked menthols, compared to 36.5% of those aged 18–25 years and 30.1% of those aged ≥26 years. Additionally, among current smokers, 36.4% of women and 82.6% of black individuals had smoked menthols compared to 28.3% and 23.8% among male and white individuals,

Table 1. Current menthol cigarette smoking among all adults and current cigarette smokers only, %

Characteristic	All adults (n=110,841)			Current cigarette smokers only (n=16,116)		
	Overall (n=110,841)	LGBT (n=2,431)	Heterosexual (n=108,431)	Overall (n=16,116)	LGBT (n=650)	Heterosexual (n=15,466)
Sexual orientation						
LGBT	9.7	—	—	36.3	—	—
Heterosexual/straight	4.2	—	—	29.3	—	—
Sex						
Female	4.4	11.1	**4.3**	32.8	42.9	**32.4**
Male	4.1	8.3	**4.0**	25.5	30.0	25.3
Race/ethnicity						
White, non-Hispanic	3.3	7.0	**3.1**	23.3	28.9	**23.2**
Black, non-Hispanic	14.8	25.6	**14.5**	77.9	81.8	77.7
Other race, non-Hispanic[a]	6.0	16.1	**5.7**	29.9	41.8	**29.2**
Hispanic	5.9	12.0	**5.6**	36.0	57.6	**36.0**
Education						
Less than high school	9.5	23.5	**9.2**	32.6	54.8	**31.9**
High school graduate	6.1	16.6	**5.9**	30.0	37.2	29.7
Some college	5.2	12.7	**5.1**	29.6	37.1	29.3
Associate's degree	5.3	12.9	**5.2**	31.5	40.2	31.2
College graduate	2.1	4.5	**2.1**	25.9	27.3	25.8
Graduate degree	1.3	3.5	**1.3**	24.2	26.3	24.0
Age (years)						
18–24	9.8	19.8	**9.2**	43.1	50.5	42.4
25–34	7.0	16.0	**6.8**	33.3	47.7	**32.6**
35–50	4.7	9.9	**4.5**	27.6	32.9	27.4
≥51	3.2	5.1	**3.2**	27.6	27.2	27.6
Total	4.3	9.7	**4.2**	29.6	36.3	**29.3**

Note: Boldface indicates value is significantly different from menthol use among corresponding LGBT subpopulation (χ^2; $p<0.05$). Current menthol cigarette smoking was determined using the question *During the past 30 days, were the cigarettes that you usually smoked menthol?*
[a]Other race included Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander, multiple race, and those of "other" race.
LGBT, lesbian, gay, bisexual, transgender.

respectively.[15] These findings suggest that efforts to reduce menthol cigarette use may have the potential to reduce tobacco use and tobacco-related disease and death among multiple vulnerable populations, including LGBT adults.

Targeted efforts to prevent smoking initiation among high-risk groups are warranted. In tailoring interventions, it is important to consider the complex interplay of multiple risk factors, including sexual orientation, race/ethnicity, and SES. Tobacco taxes and advertising restrictions have the potential to reduce smoking among vulnerable populations.[16] However, continued access to menthol cigarettes could diminish the public health impact these interventions would otherwise have on tobacco prevention and control in the U.S.

Strengths of this study include a large and representative sample, the inclusion of cell phone respondents, and the ability to assess differences across multiple sociodemographic subpopulations. However, at least four limitations should be noted. First, data were self-reported, which could lead to underrepresentation of LGBT individuals because of social stigma surrounding sexual orientation. Second, NATS did not

Table 2. Predictors of current menthol cigarette smoking among all adults and current cigarette smokers only

Characteristic	All adults		Current cigarette smokers only	
	n	AOR[a] (95% CI)	*n*	AOR[a] (95% CI)
Sexual orientation				
LGBT	2,431	**2.35 (2.03, 2.72)**	650	**1.31 (1.09, 1.57)**
Heterosexual/straight	108,410	ref	15,466	ref
Sex				
Female	66,967	**1.09 (1.03, 1.16)**	9,008	**1.63 (1.51, 1.75)**
Male	43,865	ref	7,106	ref
Race/ethnicity				
Other race, non-Hispanic[b]	5,876	**1.72 (1.53, 1.93)**	1,184	**1.37 (1.20, 1.56)**
White, non-Hispanic	92,040	ref	13,149	ref
Black, non-Hispanic	7,915	**4.28 (3.96, 4.61)**	1,507	**13.79 (11.99, 15.85)**
Hispanic	4,079	**1.23 (1.06, 1.41)**	667	**1.73 (1.46, 2.05)**
Education				
Education status	110,443	**0.72 (0.70, 0.73)**	16,116	0.99 (0.96, 1.02)
Age (years)				
18–24	4,932	**2.15 (1.93, 2.41)**	1,116	**2.05 (1.78, 2.36)**
25–34	11,529	**2.24 (2.05, 2.45)**	2,432	**1.31 (1.18, 1.45)**
35–50	29,205	**1.54 (1.43, 1.65)**	4,927	0.94 (0.87, 1.03)
≥51	63,354	ref	7,440	ref

Note: Boldface indicates statistical significance ($p < 0.05$)
[a]Adjusted for all covariates listed in table.
[b]Other race included Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander, multiple race, and those of "other" race.
LGBT, lesbian, gay, bisexual, transgender.

include institutionalized populations and the military; therefore, results might not be generalizable to these groups. Third, other differences between LGBT and heterosexual/straight populations may exist that were not included in the analysis. Finally, the response rate of 37.6% may have introduced bias; however, data were adjusted for non-response.

Conclusions

LGBT smokers, particularly those who are female, have less than a high school education, are non-Hispanic black or non-Hispanic other races, or are between the ages of 26 and 34 years, have higher odds of using menthol cigarettes than their heterosexual/straight counterparts. Efforts to reduce menthol cigarette smoking have the potential to reduce the health and economic burden of cigarette smoking among LGBT adults.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of CDC.

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RESEARCH ARTICLE

Flavored Tobacco Product Use in Youth and Adults: Findings From the First Wave of the PATH Study (2013–2014)

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Introduction: The 2009 Family Smoking Prevention and Tobacco Control Act banned characterizing flavors other than menthol in cigarettes but did not restrict their use in other forms of tobacco (e.g., smokeless, cigars, hookah, e-cigarettes).

Methods: A cross-sectional analysis of Wave 1 data from 45,971 U.S. adults and youth, aged ≥12 years in the Population Assessment of Tobacco and Health (PATH) Study collected in 2013–2014, was conducted in 2016. This study examined (1) the prevalence and reasons for use of flavored tobacco products; (2) the proportion of ever tobacco users reporting that their first product was flavored; and (3) correlates of current flavored tobacco product use.

Results: Current flavored (including menthol) tobacco product use was highest in youth (80%, aged 12–17 years); and young adult tobacco users (73%, aged 18–24 years); and lowest in older adult tobacco users aged ≥65 years (29%). Flavor was a primary reason for using a given tobacco product, particularly among youth. Eighty-one percent of youth and 86% of young adult ever tobacco users reported that their first product was flavored versus 54% of adults aged ≥25 years. In multivariable models, reporting that one's first tobacco product was flavored was associated with a 13% higher prevalence of current tobacco use among youth ever tobacco users and a 32% higher prevalence of current tobacco use among adult ever users.

Conclusions: These results add to the evidence base that flavored tobacco products may attract young users and serve as starter products to regular tobacco use.
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INTRODUCTION

Virtually all tobacco products include flavor additives. As of 2014, more than 1,300 flavoring ingredients had been identified in cigarettes, smokeless, and roll-your-own tobacco products.[1] Analyses of internal tobacco industry documents indicate that manufacturers have historically added flavoring ingredients to attract young customers.[2–11] The 2009 Family Smoking Prevention and Tobacco Control Act banned the inclusion of constituents or additives that impart characterizing flavors (e.g., candy, fruit) other than tobacco and menthol in cigarettes, but not other tobacco products.[12]

Data from the National Survey on Drug Use and Health collected in 2004–2008,[13,14] 2004–2010,[15] and 2004–2014[16] document the highest use of menthol cigarettes among youth and young adults compared with older adults in the U.S. This age gradient has also been observed in multiple national surveys of non–menthol flavored product use.[17–20] Evidence suggests that flavored tobacco, especially menthol cigarettes, may serve as starter products for young tobacco users.[21–23] Several studies in national samples have documented the appeal of flavored non-cigarette products in young people,[20,24–26] and one study has demonstrated a strong correlation between first use of a flavored tobacco product and current tobacco use among adult tobacco users.[27]

The Population Assessment of Tobacco and Health (PATH) Study represents the first national data source to ascertain use of tobacco products with characterizing flavors (flavored tobacco products) in both youth and adults. This paper reports on:

1. the prevalence and reasons for use of flavored tobacco products (including menthol);
2. the proportion of ever tobacco users who report that their first product was flavored; and
3. correlates of current flavored tobacco product use, comparing youth (aged 12–17 years), young adults (aged 18–24 years), and older adults (aged ≥25 years), in a large population-based U.S. sample.

METHODS

Data were from Wave 1 of the PATH Study conducted from September 12, 2013, to December 15, 2014. The PATH Study is a nationally representative longitudinal cohort study of 45,971 adults and youth in the U.S. aged ≥12 years. NIH, through the National Institute on Drug Abuse, is partnering with the U.S. Food and Drug Administration's Center for Tobacco Products to conduct the PATH Study under a contract with Westat. The PATH Study used audio computer-assisted self-interviews available in English and Spanish to collect information on tobacco use patterns and associated health behaviors. This analysis draws from the 32,320 adult interviews (age ≥18 years) and the 13,651 youth interviews (age 12–17 years). Parents and emancipated youth provided written consent, whereas youth assented to participate. Recruitment employed address-based, area-probability sampling, using an in-person household screener to select youths and adults. Adult tobacco users, young adults aged 18–24 years, and African Americans were oversampled relative to population proportions. The weighting procedures adjusted for oversampling and non-response; combined with the use of a probability sample, the weighted data allow the estimates produced by Wave 1 of the PATH Study to be representative of the non-institutionalized, civilian U.S. population. The weighted response rate for the household screener was 54.0%. Non-response analysis showed few differences with referent national surveys. Among households that were screened, the overall weighted response rate was 74.0% for the adult interview and 78.4% for the youth interview. Further details regarding the PATH Study design and methods appear elsewhere[28]; Wave 1 questionnaires and information on accessing the data are available at http://doi.org//10.3886/ICPSR36231. The study was conducted by Westat and approved by Westat's IRB.

Measures

Ever and current tobacco use were assessed among youth and adults for cigarettes, e-cigarettes, traditional cigars, cigarillos, filtered cigars, hookah tobacco, pipe tobacco, smokeless tobacco, snus pouches, and dissolvable tobacco. Youth were also queried about kreteks and bidis. For youth, current use was defined as past 30–day use (yes/no). For the purposes of this study, current established use (current use) in adults was defined as:

1. currently smoking/using some days or every day (or weekly or monthly for hookah) and
2. either smoking 100 lifetime cigarettes or using a non-cigarette tobacco product "ever fairly regularly."

A participant was classified as a current tobacco user if they were defined as currently using at least one tobacco product (yes/no).

Ever tobacco users were queried about:

1. age of first use and
2. whether the first product used was *flavored to taste like menthol, mint, clove, spice, candy, fruit, chocolate, alcohol (such as wine or cognac), or other sweets.*

These two items were used to create a derived variable for whether a respondent (youth or adult) first used a flavored tobacco product. For participants reporting ever use of multiple tobacco products, age of first use was determined by the youngest age a product was used (asked of each product ever used). If respondents reported first using multiple products at the same age category, any first product that was flavored was treated as the first product flavored. Response categories for age at first use in adults were grouped as <18, 18–24, 25–29, 30–34, 35–44, and ≥45 years.

Among adults, current smokers of manufactured and roll-your-own cigarettes were asked whether their regular brand was *flavored to taste like menthol or mint* (*yes*/*no*). Current users of all other tobacco products were asked whether their regular brand was *flavored to taste like menthol, mint, clove, spice, candy, fruit, chocolate, alcohol (such as wine or cognac), or other sweets* (*yes*/*no*).

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Youth current tobacco users were similarly asked about the use of menthol/mint-flavored cigarettes and flavored non-cigarette tobacco use, but in reference to the products they used in the past 30 days, rather than a regular brand. Participants were classified as current flavored tobacco users if they were defined as currently using at least one flavored tobacco product (yes/no).

Current tobacco users were asked to endorse reasons for use (e.g., *affordability*) separately for each product used except cigarettes (*yes*/*no*). One of these reasons was *comes in flavors I like*. Among youth, the ease of use of flavored products compared to unflavored products was also assessed. For each product, excluding cigarettes, participants aware of the product before the study were asked whether the flavored product is *easier*, *about the same*, or *harder* to use than the unflavored version of that product. All youth participants were asked whether cigarettes flavored like menthol or mint were *easier*, *about the same*, or *harder* to smoke than *regular cigarettes*. Participants that rated any flavored tobacco product *easier* to use than its unflavored counterpart were classified as perceiving flavored tobacco to be easier to use than unflavored (yes/no).

Sociodemographic variables used in these analyses included self-reported age, gender, race/ethnicity, educational attainment, and annual household income (adults only). Past 30–day alcohol and marijuana use were assessed. Respondents also completed the Global Appraisal of Individual Needs–Short Screener,[29] which measures severity of symptoms of internalizing problems, externalizing problems, and substance use problems in the past year (i.e., zero to one symptom [low]; two to three symptoms [moderate]; and four or more symptoms [high], depending on the scale).

Statistical Analysis

Analyses were conducted using SVY procedures in Stata/SE, version 12.1, to account for weighting. The main outcomes were ever and current product-specific use and flavored product use. Prevalence of each outcome was estimated in the youth and adult samples. Data with denominators <50 or relative SEs >30% were suppressed.[30] Next, multivariable modified Poisson regression models[31] were built separately for youth and adults to examine the relative association between the following domains and current tobacco use (Model A) or current flavored tobacco use (Model B): demographics; tobacco use (including whether the first tobacco product was flavored); and substance use and mental health severity. In the multivariable models of current flavored tobacco use (Model B), number of tobacco products currently used and age at first tobacco use were added at the second step in both the youth and adult samples. In youth, "ease of flavored use" was also added to the model at the second step.

RESULTS

The mean age of the youth sample was 14.5 years and 8.5% of youth reported use of a tobacco product in the past 30 days. Appendix Table 2 (available online) provides the following age breakdown of the adult sample: 13.0% aged 18–24 years, 8.7% aged 25–29 years, 9.0% aged 30–34 years, 16.5% aged 35–44 years, 34.5% aged 45–64 years, and 18.2% aged ≥65 years. Twenty-three percent of adults were current established tobacco users. Further detail about the sample appears elsewhere.[28]

Figure 1 presents the prevalence of tobacco products with characterizing flavors currently used by age in the full sample, and the prevalence of current exclusive menthol cigarette use; exclusive flavored non-cigarette tobacco product use (one or more products); and polyuse of flavored cigarette and non-cigarette products among current tobacco users. Among current tobacco users, flavored tobacco product use followed a clear age gradient, with the highest use among youth aged 12–17 years (79.8%) and lowest in those aged ≥65 years

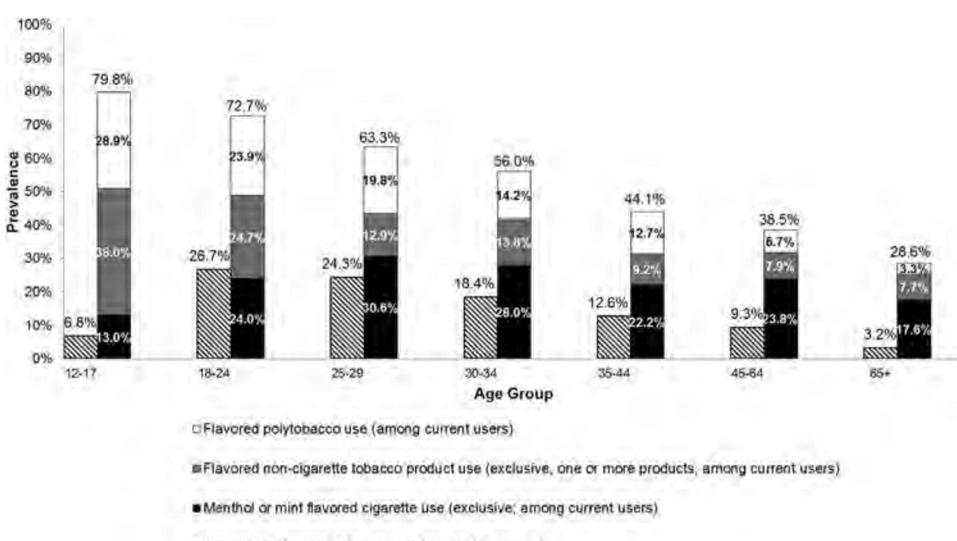

Figure 1. Prevalence of current flavored tobacco use in the full sample and among current tobacco users, by age; Population Assessment of Tobacco and Health, 2013–2014.[a]
[a]Percentages are weighted to represent the U.S. population.

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Table 1. Tobacco Product-Specific Ever Use, First Product Flavored, and Age at First Use by Age Group[a]

Variables	Youth (current age 12–17 years), age at first use (%)[b] (n=2,900)					Young adults (current age 18–24 years), age at first use (%)[b] (n=7,311)				Adults (current age 25+ years), age at first use (%)[b] (n=20,225)				
	Unweighted n	Total (%)	Age <12 (n=497)[c]	Age 12–14 (n=1,298)[c]	Age 15–17 (n=1,023)[c]	Unweighted n	Total (%)	Age <18 (n=4,971)[c]	Age 18–24 (n=2,334)[c]	Unweighted n	Total (%)	Age <18 (n=14,374)[c]	Age 18–24 (n=4,748)[c]	Age 25+ (n=1,057)[c]
Overall			16.9	45.4	37.7			65.1	34.9			68.7	25.7	5.6
Ever use of any tobacco product[d]	2,900	21.4	3.5	9.4	7.8	7,311	66.5	43.3	23.2	20,225	73.0	49.9	18.7	4.1
First product non-flavored	537	4.0	1.0	1.8	1.1	899	9.4	5.3	4.1	7,052	33.7	22.5	9.1	2.2
First product flavored	2,256	16.8	2.5	7.7	6.7	6,395	57.0	38.0	19.1	13,020	39.0	27.5	9.7	1.9
First product flavored/Ever use, %		81	72	81	86		86	88	82		54	55	52	46
Ever use of cigarettes[e]	1,838	13.4	2.6	6.1	4.4	5,964	53.2	35.2	17.9	19,218	69.0	47.1	18.4	3.4
% first cigarette non-menthol/non-flavored	883	6.5	1.5	3.1	1.9	2,945	27.0	18.0	9.0	12,188	46.8	33.0	11.7	2.1
% first cigarette menthol/ flavored	902	6.6	1.1	3.0	2.5	2,999	26.1	17.3	8.8	6,943	22.1	14.1	6.7	1.2
First product flavored/Ever use, %		50	41	49	56		49	49	49		32	30	36	40
% first cigarette menthol	777	5.8	0.9	2.6	2.1	2,751	23.9	15.9	8.0	6,476	20.6	13.3	6.1	1.0
First product mentholated/Ever use, %		43	34	43	48		45	45	45		30	28	33	36
Ever use of e-cigarettes	1,452	10.7	–	3.5	6.7	3,887	32.0	3.9	28.1	7,635	15.6	–	1.1	14.3
% first e-cigarette non-flavored	276	2.0	–	0.7	1.1	1,508	12.5	1.5	10.9	4,071	8.4	–	0.5	7.9
% first e-cigarette flavored	1,154	8.5	–	2.8	5.6	2,367	19.4	2.4	17.1	3,528	7.1	–	0.6	6.4
First product flavored/Ever use, %		81		80	84		61	61	61		46		52	46
Ever use of any cigar[f]	1,048	7.7	0.7	3.0	3.6	5,010	44.0	23.7	20.2	12,093	38.1	11.0	16.3	10.7
% first any cigar non-flavored	342	2.5	0.3	1.0	1.2	1,783	15.7	8.0	7.6	6,992	24.3	6.5	10.5	7.3
% first any cigar flavored	652	4.8	0.4	2.0	2.4	3,213	28.2	15.7	12.6	5,041	13.7	4.5	5.9	3.3
First product flavored/Ever use, %		65	58	67	66		64	66	62		36	41	36	33
Ever use of traditional cigars	297	2.3	–	1.0	1.0	2,046	18.5	9.1	9.3	8,176	27.3	7.2	11.8	8.3
% first traditional cigar non-flavored	154	1.2	–	0.5	0.6	1,200	11.0	5.0	6.0	6,235	21.8	5.4	9.5	6.9

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Table 1. Tobacco Product-Specific Ever Use, First Product Flavored, and Age at First Use by Age Group[a] *(continued)*

	Youth (current age 12–17 years), age at first use (%)[b] (*n*=2,900)					Young adults (current age 18–24 years), age at first use (%)[b] (*n*=7,311)				Adults (current age 25+ years), age at first use (%)[b] (*n*=20,225)				
Variables	Unweighted *n*	Total (%)	Age <12 (*n*=497)[c]	Age 12–14 (*n*=1,298)[c]	Age 15–17 (*n*=1,023)[c]	Unweighted *n*	Total (%)	Age <18 (*n*=4,971)[c]	Age 18–24 (*n*=2,334)[c]	Unweighted *n*	Total (%)	Age <18 (*n*=14,374)[c]	Age 18–24 (*n*=4,748)[c]	Age 25+ (*n*=1,057)[c]
% first traditional cigar flavored	142	1.1	—	0.5	0.5	841	7.4	4.2	3.3	1,913	5.5	1.7	2.3	1.4
First product flavored/Ever use, %		48		50	45		40	46	35		20	24	20	18
Ever use of cigarillos	863	6.3	0.5	2.5	3.2	4,500	39.0	20.7	18.3	9,052	26.0	7.3	11.5	7.2
% first cigarillo non-flavored	303	2.2	—	0.9	1.1	1,699	14.6	7.7	6.8	5,227	15.8	4.2	7.1	4.6
% first cigarillo flavored	551	4.0	—	1.7	2.1	2,794	24.4	13.0	11.4	3,798	10.1	3.1	4.4	2.5
First product flavored/Ever use, %		64		66	65		63	63	63		39	42	38	38
Ever use of filtered cigars	310	2.2	—	0.9	1.2	1,948	16.6	8.0	8.5	4,676	12.6	3.0	5.0	4.5
% first filtered cigar non-flavored	106	0.8	—	0.3	0.4	800	6.6	3.1	3.5	2,683	7.6	1.8	3.0	2.9
% first filtered cigar flavored	199	1.4	—	0.6	0.8	1,142	9.9	5.0	5.0	1,978	4.9	1.2	2.0	1.6
First product flavored/Ever use, %		65		63	65		60	62	59		39	40	40	39
Ever use of hookah	1,006	7.4	—	2.4	4.7	5,061	44.3	14.7	29.5	5,562	12.2	1.2	5.3	5.7
% first hookah non-flavored	115	0.8	—	0.3	0.5	603	5.0	1.6	3.4	1,386	3.2	0.5	1.3	1.5
% first hookah flavored	877	6.5	—	2.1	4.3	4,445	39.2	13.1	26.2	4,128	8.9	0.7	4.0	4.2
First product flavored/Ever use, %		89		87	90		89	89	89		74	58	76	75
Ever use of pipe	259	1.9	—	0.8	0.9	1,550	13.2	4.9	8.3	5,628	18.6	5.3	7.8	3.5
% first pipe non-flavored	175	1.3	—	0.6	0.6	1,127	9.7	3.5	6.1	3,935	13.1	3.9	5.4	2.5
% first pipe flavored	77	0.5	—	0.2	0.3	421	3.5	1.5	2.1	1,667	5.3	1.4	2.4	1.0
First product flavored/Ever use, %		30		26	33		27	30	26		29	26	31	30
Ever use of smokeless tobacco (SLT)[g]	574	4.4	0.6	1.9	1.7	1,633	14.2	8.4	5.8	4,979	15.5	7.7	5.1	2.7
% first SLT non-flavored	174	1.3	0.2	0.7	0.4	595	5.2	2.7	2.1	2,546	8.3	4.0	2.6	1.7
% first SLT flavored	391	3.0	0.4	1.3	1.3	1,033	9.0	5.7	3.7	2,420	7.1	3.7	2.5	0.9
First product flavored/Ever use, %		69	62	66	76		63	68	63		46	48	49	43
Ever use of snus[g]	227	1.7	—	0.8	0.8	1,296	11.1	5.0	6.1	2,575	6.7	1.4	2.3	3.0

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Table 1. Tobacco Product-Specific Ever Use, First Product Flavored, and Age at First Use by Age Group[a] *(continued)*

Variables	Youth (current age 12–17 years), age at first use (%)[b] (*n*=2,900)					Young adults (current age 18–24 years), age at first use (%)[b] (*n*=7,311)				Adults (current age 25+ years), age at first use (%)[b] (*n*=20,225)				
	Unweighted *n*	Total (%)	Age <12 (*n*=497)[c]	Age 12–14 (*n*=1,298)[c]	Age 15–17 (*n*=1,023)[c]	Unweighted *n*	Total (%)	Age <18 (*n*=4,971)[c]	Age 18–24 (*n*=2,334)[c]	Unweighted *n*	Total (%)	Age <18 (*n*=14,374)[c]	Age 18–24 (*n*=4,748)[c]	Age 25+ (*n*=1,057)[c]
% first snus non-flavored	41	0.3	–	0.2	0.1	381	3.3	1.1	1.3	1,362	3.8	0.3	0.5	0.7
% first snus flavored	184	1.4	–	0.6	0.6	914	7.8	4.0	4.8	1,206	2.9	0.6	1.0	1.2
First product flavored/Ever use, %		81		80	83		70	79	78		43	69	67	66
Ever use of dissolvable tobacco		–				103	0.9	–	0.5	244	0.5	–	0.1	0.3
% first dissolvable tobacco non-flavored		–				54	0.4	–	0.3	117	0.2	–	0.5	0.7
% first dissolvable tobacco flavored		–				47	0.4	–	0.3	124	0.2	–	1.0	1.2
First product flavored/Ever use, %							45		50		48		53	50
Ever use of bidis		–					N/A	N/A	N/A		N/A	N/A	N/A	N/A
% first bidis non-flavored		–					N/A	N/A	N/A		N/A	N/A	N/A	N/A
% first bidis flavored		–					N/A	N/A	N/A		N/A	N/A	N/A	N/A
First product flavored/Ever use, %							N/A	N/A	N/A		N/A	N/A	N/A	N/A
Ever use of kreteks	52	0.4	–	–	–		N/A	N/A	N/A		N/A	N/A	N/A	N/A
% first kreteks non-flavored	–	–	–	–	–		N/A	N/A	N/A		N/A	N/A	N/A	N/A
% first kreteks flavored	–	–	–	–	–		N/A	N/A	N/A		N/A	N/A	N/A	N/A
First product flavored/Ever use, %							N/A	N/A	N/A		N/A	N/A	N/A	N/A

Source: Population Assessment of Tobacco and Health, 2013–2014.
Note: Dashes represent values suppressed because of $n<50$ or coefficient of variation >30%.
[a]Percentages are weighted to represent the U.S. population and CIs are estimated using the balanced repeated replication (BRR) method.
[b]Youngest age at which tobacco product use was reported. Individuals who reported "don't know" or refused to answer were excluded from the denominator. Excluded from the denominator for youth *n*=82, young adults *n*=6, adults *n*=46.
[c]In addition to those who reported "don't know" or refused to answer whether their first product was flavored, those who reported "don't know" or refused to report the youngest age at tobacco use were also excluded from the denominator for each product. Excluded from the denominator for youth: any tobacco (*n*=32); cigarettes (*n*=3); e-cigarettes (*n*=15); cigars (*n*=10); traditional cigars (*n*=3); cigarillos (*n*=2); filtered cigars (*n*=2); hookah (*n*=3); pipe (*n*=9); smokeless tobacco (*n*=19); snus (*n*=3); and kreteks (*n*=4). Excluded from the denominator for young adults: any tobacco (*n*=4); cigarettes (*n*=14); e-cigarettes (*n*=22); cigars (*n*=18); traditional cigars (*n*=11); cigarillos (*n*=18); filtered cigars (*n*=14); hookah (*n*=19); pipe (*n*=28); smokeless tobacco (*n*=69); snus (*n*=129); and dissolvable tobacco (*n*=3). Excluded from the denominator for adults: any tobacco (*n*=41); cigarettes (*n*=59); e-cigarettes (*n*=117); cigars (*n*=118); traditional cigars (*n*=67); cigarillos (*n*=85); filtered cigars (*n*=76); hookah (*n*=37); pipe (*n*=100); smokeless (*n*=189); snus (*n*=790); and dissolvable tobacco (*n*=14).
[d]Ever use of any tobacco product is defined as reporting ever use of any tobacco product, "even one or two puffs" or "even one time." Individuals who reported "don't know" or refused to answer any part of the definition of ever use were excluded from the denominator. First flavored use is defined as reported the first product used was "flavored to taste like menthol, mint, clove, spice, candy, fruit, chocolate, alcohol (such as wine or cognac), or other sweets." Individuals who reported "don't know" or refused to answer whether their first product was flavored were excluded from the denominator. Excluded from the denominator for youth: any tobacco (*n*=107); cigarettes (*n*=53); e-cigarettes (*n*=22); cigars (*n*=54); traditional cigars (*n*=1); cigarillos (*n*=9); filtered cigars (*n*=5); hookah (*n*=14); pipe (*n*=7); smokeless tobacco (*n*=9); snus (*n*=2); and kreteks (*n*=1). Excluded from the denominator for young adults: any tobacco (*n*=17); cigarettes (*n*=20); e-cigarettes (*n*=12); cigars (*n*=14);

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(28.6%). Flavored non-cigarette tobacco product use and polytobacco use accounted for the majority of tobacco use among those aged <25 years. Among adults aged ≥25 years, menthol cigarettes were the dominant flavored tobacco product used. The prevalence of any current menthol cigarette use among current tobacco users by age group was 32.0% (95% CI=28.8, 35.4) in youth (aged 12–17 years); 33.2% (95% CI=31.1, 35.4) in young adults (aged 18–24 years); and 29.8% (95% CI=28.6, 31.1) in adults (aged ≥25 years). The prevalence of any current flavored cigar use among current tobacco users was higher in youth (20.6%, 95% CI=18.2, 23.3) and young adults (18.4%, 95% CI=16.9, 19.9) than adults (6.9%, 95% CI=6.4, 7.5). The prevalence of any current flavored e-cigarette use among current tobacco users followed an age gradient, with the highest use in youth (31.2%, 95% CI=27.8, 34.8) followed by young adults (13.6%, 95% CI=12.2, 15.2), and the lowest use in adults (7.0%, 95% CI: 6.4, 7.7). Data on youth and adults are presented in Appendix Table 1 (available online); more-detailed adult age categories are presented in Appendix Table 2 (available online).

Table 1 presents the percentage of ever tobacco users who reported that their first tobacco product was flavored, stratified by current age, age at first tobacco use, and type of tobacco product used. Eighty-one percent of youth ever tobacco users reported that their first product was flavored, with first flavored use highest for ever users of hookah (89%); e-cigarettes (81%); and snus (81%). Among youth ever users, the greatest trial of flavored tobacco before age 15 years occurred for hookah (87%); e-cigarettes (80%); and flavored snus (80%).

Adult ever tobacco users commonly reported their first hookah used was flavored (89% aged 18–24 years, 74% aged ≥25 years), with the proportion of ever users reporting first product flavored generally lower among adults compared with the youth and young adult ever hookah users. Among young adult ever users, the most prevalent trial of a flavored product before age 18 years occurred for hookah (89%) and snus (79%), whereas for older adults, flavored snus trial before age 18 years was higher (69%) than hookah (58%).

Overall, cigarettes were the top product ever used in all age groups. Fifty percent of youth who had ever used cigarettes reported use of flavored cigarettes at first use versus 49% of young adults and 32% of adults. E-cigarettes were the second most prevalent product tried in youth, with 81% of youth reporting using a flavored e-cigarette at first use, compared with 61% of young adults and 46% of adults; hookah was the second most prevalent product used among young adults (89% flavored at first use) and cigars (any) were the second most prevalent product used among adults (36% flavored at first use).

traditional cigars (n=5); cigarillos (n=7); filtered cigars (n=6); hookah (n=13); pipe (n=2); smokeless tobacco (n=5); snus (n=1); and dissolvable tobacco (n=2). Excluded from the denominator for adults: any tobacco (n=153); cigarettes (n=87); e-cigarettes (n=36); cigars (n=60); traditional cigars (n=28); cigarillos (n=27); filtered cigars (n=15); hookah (n=48); pipe (n=26); smokeless tobacco (n=13); snus (n=7); and dissolvable tobacco (n=3).

[e]Manufactured cigarette or roll-your-own.

[f]Respondents who indicated ever having used a cigar were asked about use of traditional cigars, cigarillos, and filtered cigars separately. Respondents indicating use of two or more types of cigars (traditional, cigarillo, or filtered cigars) were asked about the flavor status of each type of cigar separately. Any respondent who reported ever using two or more types of cigars had their responses aggregated, so that if any of the first traditional, cigarillo, or filtered cigars they used were flavored, they were included in the estimate of ever cigar users reporting that their first cigar was flavored.

[g]Ever use of snus and smokeless tobacco were based on a single item with the following response choices: (1) snus pouches, and (2) loose snus, moist snuff, dip, spit, or chewing tobacco. Participants were not reclassified from snus to smokeless tobacco use based on brand of product used (e.g., Skoal Bandits), nor were they excluded from the denominator if they did not identify a regular brand.

N, unweighted sample size; N/A, not applicable.

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Table 2. Correlates of Current Tobacco Use and Current Flavored Tobacco Use Among Youth[a]

	Model A. Adjusted prevalence ratios for current tobacco use among ever tobacco users in the youth sample (unweighted n=2,126)		Model B. Adjusted prevalence ratios for current flavored tobacco use among current tobacco users in the youth sample (unweighted n=886)	
Variables	%[b]	APR (95% CI)	%[b]	APR (95% CI)
Overall[c]	42		83	
Age, M (SD)[d]	15.88 (0.04)[e]	**1.17 (1.11, 1.24)**	15.90 (0.04)[e]	0.98 (0.95, 1.01)
Gender[d]				
Male	45	ref	85	ref
Female	40	**0.86 (0.79, 0.95)**	81	0.95 (0.89, 1.01)
Race[d]				
White	43	ref	83	ref
Black/African American	42	0.97 (0.84, 1.12)	83	1.01 (0.91, 1.11)
American Indian/Alaskan Native	51	1.22 (0.95, 1.57)	91	1.05 (0.91, 1.22)
Asian	37	0.76 (0.48, 1.20)	76	0.97 (0.70, 1.32)
Native Hawaiian/Pacific Islander	30	0.90 (0.59, 1.37)	68	0.84 (0.58, 1.21)
≥2 races	38	0.87 (0.74, 1.03)	86	1.03 (0.93, 1.14)
Hispanic[d]				
No	44	ref	83	ref
Yes	36	**0.80 (0.70, 0.90)**	82	1.01 (0.94, 1.10)
High school enrollment or completion[f]				
No	27	ref	75	ref
Yes	45	0.95 (0.74, 1.23)	84	1.15 (0.98, 1.35)
Number of tobacco products currently used, M (SD)			1.90 (0.04)[d]	**1.09 (1.06, 1.12)**
First tobacco use was flavored				
No	39	ref	71	ref
Yes	44	**1.13 (1.02, 1.26)**	88	**1.21 (1.11, 1.32)**
Age at first tobacco use, years				
<12	39	**1.22 (1.06, 1.40)**	86	1.00 (0.90, 1.10)
12–14	44	**1.26 (1.14, 1.40)**	82	0.96 (0.89, 1.03)
15–17	41	ref	84	ref
Perception that flavored tobacco is easier to use than non-flavored				
No	39	ref	78	ref
Yes	44	1.00 (0.89, 1.12)	85	0.95 (0.87, 1.03)
Past 30–day alcohol use				
No	34	ref	81	ref
Yes	64	**1.37 (1.22, 1.52)**	86	1.03 (0.96, 1.10)
Past 30–day marijuana use				
No	34	ref	81	ref
Yes	73	**1.64 (1.49, 1.80)**	86	1.01 (0.94, 1.09)
Substance use scale				
Low[g]	35	ref	81	ref
Moderate	59	**1.23 (1.09, 1.40)**	87	1.00 (0.93, 1.07)
High	67	**1.35 (1.16, 1.57)**	83	0.96 (0.87, 1.06)
Internalizing scale				
Low	40	ref	81	ref
Moderate	43	1.09 (0.96, 1.25)	82	1.01 (0.92, 1.10)
High	44	1.08 (0.93, 1.26)	85	**1.09 (1.00, 1.19)**

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Table 2. Correlates of Current Tobacco Use and Current Flavored Tobacco Use Among Youth[a] *(continued)*

Variables	Model A. Adjusted prevalence ratios for current tobacco use among ever tobacco users in the youth sample (unweighted *n*=2,126)		Model B. Adjusted prevalence ratios for current flavored tobacco use among current tobacco users in the youth sample (unweighted *n*=886)	
	%[b]	APR (95% CI)	%[b]	APR (95% CI)
Externalizing scale				
Low	46	ref	79	ref
Moderate	36	**0.70 (0.59, 0.82)**	87	1.08 (0.99, 1.18)
High	45	**0.79 (0.67, 0.92)**	83	1.01 (0.92, 1.11)

Source: Population Assessment of Tobacco and Health, 2013–2014.
Note: Boldface indicates statistical significance ($p < 0.05$). Respondents with missing outcome variables or missing covariates were excluded from the respective model's analytic sample. Missingness for Model A: gender (*n*=3; 0.1%); race (*n*=16; 0.4%); education (*n*=145; 4.9%); first tobacco use was flavored (*n*=79; 2.7%); age at tobacco trial (*n*=41; 1.4%); ease of use (*n*=34; 12.4%); alcohol (*n*=7; 0.2%); marijuana (*n*=18; 0.6%); substance use scale (*n*=97; 3.4%); internalizing scale (*n*=53; 1.8%); and externalizing scale (*n*=94; 3.1%). Missingness for Model B: race (*n*=8; 0.5%); education (*n*=82; 6.5%); first tobacco use was flavored (*n*=33; 2.7%); ease of use (*n*=101; 8.7%); age at tobacco trial (*n*=1; 0.1%); marijuana (*n*=11; 0.8%); alcohol (*n*=2; 0.2%); substance use scale (*n*=41; 3.4%); internalizing scale (*n*=27; 2.2%); and externalizing scale (*n*=38; 2.9%).
[a]Percentages are weighted to represent the U.S. youth population and CIs are estimated using the balanced repeated replication (BRR) method.
[b]Row percentages presented for prevalence of current tobacco use among ever tobacco users (Model A) and prevalence of flavored tobacco use among current tobacco users (Model B) across different correlates.
[c]Prevalence of the outcome among youth ever tobacco users included in the analytic sample in Model A and current (past 30 day) tobacco users included in the analytic sample in Model B.
[d]Missing data on age, gender, race, and Hispanic ethnicity were logically assigned from household screener data, as described in the PATH Restricted Use File User's Guide.[32]
[e]Mean and linearized standard error among ever tobacco users (Model A) and current tobacco users (Model B).
[f]Youth who are not enrolled in school, are home schooled, or are in ungraded schools were treated as missing. Individuals who had completed high school are treated as "yes".
[g]Never users of all of the following substances: alcohol, marijuana, painkillers, Ritalin, cocaine, stimulants, and "other drugs like heroin or ecstasy" are treated as "Low."
APR, adjusted prevalence ratio.

Appendix Table 3 (available online) shows the reasons for using a tobacco product among current tobacco users, stratified by type of product and age. Across all product types, one of the top reasons given for use of a tobacco product was *comes in flavors that I like*, with the exception of young adult and adult e-cigarette users who ranked *less harmful to me than cigarettes* highest. In youth, *comes in flavors that I like* was the most highly ranked reason among users of filtered cigars, cigarillos, and e-cigarettes; in both youth and adults, *comes in flavors that I like* ranked second below *I like socializing while using them* among cigar and hookah users. Within the full youth sample, the belief that the flavored product was easier to smoke/use than the unflavored counterpart ranged from 27.4% for cigarettes to 56.1% for hookah (Appendix Table 4, available online). Endorsing that a flavored tobacco product was easier to use than a non-flavored product, assessed only among youth, was significantly associated with current use of cigarettes (adjusted prevalence ratio [APR]=1.27); e-cigarettes (APR=1.13); any cigar type (APR=1.32); cigarillos (APR=1.31); and filtered cigars (APR=1.36) (Appendix Table 4, available online).

Controlling for all covariates in the model, reporting that one's first tobacco product was flavored was associated with a 13% higher prevalence of current tobacco use among youth ever users and a 32% higher prevalence of current established tobacco use among adult ever tobacco users (Model A; Tables 2 and 3). In Model B, the strongest correlate of current flavored tobacco use among both youth and adult current tobacco users was reporting a flavored tobacco product at first use (youth, APR=1.21; adult, APR=1.93) (Tables 2 and 3). When tobacco products were disaggregated, flavored tobacco at first use was strongly associated with current exclusive menthol cigarette use (APR=2.10); exclusive flavored non-cigarette product tobacco use (APR=1.84); and flavored polytobacco use (APR=1.44) (Appendix Table 5, available online).

DISCUSSION

The majority of youth and young adult tobacco users consume products with characterizing flavors. Considerable use of flavored tobacco products was observed in younger people, including menthol cigarettes and non-cigarette flavored products, especially hookah, cigars, and e-cigarettes, which are commonly marketed as flavored products. Menthol cigarette use remains the dominant form of flavored tobacco use in adults. Results from this

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Table 3. Correlates of Current Tobacco Use and Current Flavored Tobacco Use Among Adults[a]

	Model A. Adjusted prevalence ratios for current tobacco use among ever tobacco users in the adult sample (unweighted *n*=23,841)		Model B. Adjusted prevalence ratios for current flavored tobacco use among current tobacco users in the adult sample (unweighted *n*=12,568)	
Variables	%[b]	**APR (95% CI)**	%[b]	**APR (95% CI)**
Overall[c]	32		50	
Age, years[d]				
18–24	44	0.98 (0.95, 1.02)	73	**1.24 (1.19, 1.29)**
≥25	31	ref	46	ref
Gender[d]				
Male	37	ref	50	ref
Female	27	**0.77 (0.74, 0.80)**	51	**1.07 (1.03, 1.11)**
Race[d]				
White	31	ref	44	ref
Black/African American	39	**0.91 (0.86, 0.96)**	82	**1.63 (1.56, 1.70)**
American Indian/Alaskan Native	37	1.01 (0.86, 1.19)	60	**1.21 (1.06, 1.38)**
Asian	24	1.05 (0.90, 1.22)	50	1.11 (0.96, 1.29)
Native Hawaiian/Pacific Islander	30	0.95 (0.74, 1.21)	74	**1.30 (1.16, 1.45)**
≥2 races	42	**1.10 (1.00, 1.20)**	58	**1.12 (1.04, 1.21)**
Hispanic[d]				
No	33	ref	49	ref
Yes	28	**0.68 (0.64, 0.72)**	60	**1.17 (1.11, 1.24)**
Education				
<HS	45	**2.13 (1.97, 2.31)**	47	1.00 (0.93, 1.08)
GED	54	**2.40 (2.19, 2.63)**	49	1.02 (0.94, 1.12)
HS diploma	39	**2.00 (1.84, 2.17)**	51	**1.10 (1.01, 1.19)**
Some college	35	**1.82 (1.70, 1.94)**	54	**1.11 (1.04, 1.19)**
College or greater	15	ref	42	ref
Annual household income				
<$15,000	48	**1.31 (1.23, 1.39)**	56	1.00 (0.95, 1.05)
$15,000 up to $34,999	39	**1.19 (1.13, 1.26)**	51	1.01 (0.95, 1.06)
$35,000 up to $74,999	30	ref	47	ref
≥$75,000	19	**0.74 (0.69, 0.79)**	43	0.94 (0.89, 1.00)
Number of tobacco products currently used, M (SD)			1.29 (0.01)[e]	**1.22 (1.20, 1.24)**
First tobacco use was flavored				
No	27	ref	29	ref
Yes	39	**1.32 (1.27, 1.37)**	67	**1.93 (1.84, 2.03)**
Age at first tobacco use, years				
<18	37	**1.71 (1.50, 1.94)**	50	1.05 (0.94, 1.18)
18–24	22	**1.16 (1.02, 1.32)**	54	1.05 (0.93, 1.19)
≥25	19	ref	49	ref
Past 30–day alcohol use				
No	32	ref	47	ref
Yes	33	**1.10 (1.05, 1.16)**	53	1.03 (0.98, 1.07)
Past 30–day marijuana use				
No	29	ref	48	ref
Yes	62	**1.43 (1.37, 1.50)**	60	0.98 (0.94, 1.01)
Substance use scale				
Low[e]	29	ref	47	ref
Moderate	42	**1.15 (1.09, 1.21)**	57	**1.05 (1.00, 1.09)**

(continued on next page)

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Table 3. Correlates of Current Tobacco Use and Current Flavored Tobacco Use Among Adults[a] *(continued)*

	Model A. Adjusted prevalence ratios for current tobacco use among ever tobacco users in the adult sample (unweighted n=23,841)		Model B. Adjusted prevalence ratios for current flavored tobacco use among current tobacco users in the adult sample (unweighted n=12,568)	
Variables	%[b]	APR (95% CI)	%[b]	APR (95% CI)
High	62	**1.27 (1.19, 1.35)**	63	1.02 (0.96, 1.09)
Internalizing scale				
Low	28	ref	48	ref
Moderate	35	**1.09 (1.04, 1.15)**	52	1.01 (0.97, 1.05)
High	50	**1.32 (1.24, 1.41)**	56	1.01 (0.96, 1.07)
Externalizing scale				
Low	30	ref	47	ref
Moderate	33	**0.95 (0.90, 0.99)**	52	1.01 (0.97, 1.06)
High	47	0.99 (0.93, 1.05)	59	1.03 (0.97, 1.09)

Source: Population Assessment of Tobacco and Health, 2013–2014.
Note: Boldface indicates statistical signifiance ($p<0.05$). Respondents with missing outcome variables or missing covariates were excluded from the respective model's analytic sample. Missingness for Model A: age (n=5; 0.0%); race (n=79; 0.2%); education (n=153; 0.5%); annual household income (n=2;433; 9.8%); first tobacco use was flavored (n=25; 0.2%); age at tobacco trial (n=53; 0.4%); alcohol (n=36; 0.1%); marijuana (n=240; 0.8%); substance use scale (n=698; 2.5%); internalizing scale (n=327; 1.2%); and externalizing scale (n=595; 2.5%). Missingness for Model B: age (n=1; 0.0%); race (n=30; 0.2%); education (n=101; 0.8%); annual household income (n=1,220; 8.6%); age at first tobacco use (n=8; 0.1%); marijuana (n=146; 1.0%); alcohol (n=17; 0.1%); substance use scale (n=396; 2.8%); internalizing scale (n=183; 1.4%); and externalizing scale (n=315; 2.4%).
[a]Percentages are weighted to represent the U.S. adult population and CIs are estimated using the balanced repeated replication (BRR) method.
[b]Row percentages presented for the prevalence of current tobacco use among ever tobacco users (Model A) and prevalence of current flavored tobacco use among current tobacco users (Model B) across different correlates.
[c]Prevalence of the outcome among ever tobacco users included in the analytic sample in Model A and current (past 30 day) tobacco users included in the analytic sample in Model B.
[d]Missing data on age, gender, race, and Hispanic ethnicity were logically assigned from household screener data, as described in the PATH Restricted Use File User's Guide.[32]
[e]Never users of all of the following substances: alcohol, marijuana, painkillers, Ritalin, cocaine, stimulants, and "other drugs like heroin or ecstasy" are treated as "Low."
APR, adjusted prevalence ratio; GED, General Educational Development test; HS, high school.

study extend previous research on menthol cigarettes,[21–23] highlighting a significant association between first use of a flavored tobacco product and current tobacco use in a nationally representative study of youth and adults. The PATH survey presents tobacco-specific prevalence estimates comparable to other national tobacco surveys,[33,34] strengthening the generalizability of these findings.

The tobacco marketplace has become increasingly diversified in terms of product types and flavor offerings. Following the ban on characterizing flavors other than menthol in cigarettes, the market share of menthol cigarettes has increased[35] as has the sale of flavored cigarette-like small cigars.[36] In 2013, menthol/mint, fruit, and other flavored e-cigarettes accounted for 41% of e-cigarette market sales in traditional tobacco retail stores, up from 38% in 2012.[37] Increased sales of flavored cigarette and non-cigarette products are consistent with PATH Study data showing a high prevalence of flavored tobacco use, particularly in youth and young adults.

Limitations

The current study has several limitations. First, flavored tobacco product use in the study questionnaire is based on the respondent's perception of and ability to recall whether past or current products were flavored. The type of flavoring used (e.g., menthol, fruit, candy) was not captured in Wave 1. Second, as youth typically do not have established regular brands, the question about current flavored tobacco use referenced any of the particular products youth respondents used in the past 30 days, whereas adults were asked to identify whether their usual or regular brand was flavored. In cigarette users, 93% of adults reported a usual brand; of those, there was 97% agreement between self-reported menthol cigarette use and identified brand. By contrast, 69% of youth smokers had a usual brand, with 67% agreement of menthol status between identified brand and past 30–day menthol smoking. This discordance may arise either from recall error or multiple brand use in the past 30 days among youth. If in error, the observed age gradient in

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current flavored use could be inflated; however, an age gradient was observed among younger versus older adults who were asked the same item. This age gradient may reflect a potential cohort effect with differences in the reported use of flavored products between generations related to availability, visibility, and diversity of product choice in the retail environment at time of first use. Compared with adults, youth respondents therefore may be more likely to report first use of a flavored product owing to greater availability of flavored tobacco in their proximal environment.

Assessment of first tobacco product being flavored is subject to recall bias, with older participants potentially less likely to accurately recall the age at which they first used a tobacco product or whether that product was flavored. Those who currently use flavored products may also be more likely to report their first product was flavored, and those that tried multiple products have a greater chance of one of them being flavored. Sensitivity analyses conducted among youth using an additional variable on the first product used among multiple products to classify whether the first product was flavored had no impact on participant classification, nor study findings. Finally, modelwise deletion may result in biased estimates.

CONCLUSIONS

A central question in tobacco control is whether characterizing flavors in any or some tobacco products exert a significant effect on youth experimentation and progression to regular tobacco use. The results from this study illustrate the widespread use of flavored tobacco products especially in young tobacco users and the association between first use of flavored tobacco and current tobacco use. Findings from future waves of the PATH Study will allow for further elucidation of the role of flavors in tobacco use experimentation and progression to established use over time.

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ACV led this study, with substantial contributions to conception and design from all study authors. ACV and ALJ conducted the data analysis and all authors contributed to interpretation of the data. ACV drafted the manuscript and all authors provided critical revision of the manuscript for important intellectual content. All authors provided final approval of the version to be published and agree to be accountable for all aspects of the work.

ACV and ALJ had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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SUPPLEMENTAL MATERIAL

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Correlates and Prevalence of Menthol Cigarette Use Among Adults With Serious Mental Illness

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Abstract

Introduction: With a focus on protecting vulnerable groups from initiating and continuing tobacco use, the FDA has been considering the regulation of menthol in cigarettes. Using a large sample of adult smokers with serious mental illness (SMI) in the San Francisco Bay Area, we examined demographic and clinical correlates of menthol use, and we compared the prevalence of menthol use among our study participants to that of adult smokers in the general population in California.
Methods: Adult smokers with SMI (N = 1,042) were recruited from 7 acute inpatient psychiatric units in the San Francisco Bay Area. Demographic, tobacco, and clinical correlates of menthol use were examined with bivariate and multivariate logistic regression analyses, and prevalence of menthol use was compared within racial/ethnic groups to California population estimates from the 2008–2011 National Survey on Drug Use and Health.
Results: A sample majority (57%) reported smoking menthol cigarettes. Multivariate logistic regression analyses indicated that adult smokers with SMI who were younger, who had racial/ethnic minority status, who had fewer perceived interpersonal problems, and who had greater psychotic symptoms also had a significantly greater likelihood of menthol use. Smokers with SMI had a higher prevalence of menthol use relative to the general population in California overall (24%).
Conclusions: Individuals with SMI—particularly those who are younger, have racial/ethnic minority status, and have been diagnosed with a psychotic disorder—are vulnerable to menthol cigarette use. FDA regulation of menthol may prevent initiation and may encourage cessation among smokers with SMI.

Introduction

Tobacco use among persons with mental illness is a major public health concern. It is estimated that persons with psychiatric or addictive disorders consume nearly half the cigarettes sold in the United States, and are 2 to 4 times more likely than those in the general population to smoke.[1,2] In particular, those with serious mental illness (SMI) suffer disproportionately from tobacco-related diseases and are dying, on average, 25 years prematurely.[3] More targeted prevention and intervention strategies are critically needed to address the burden of tobacco-related consequences in this vulnerable group.[4]

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Of recent interest and attention is consideration of tobacco control regulation to address menthol as a flavoring in cigarettes. Approximately 27% of all cigarettes sold nationally are menthol[5] and adverse health effects of menthol cigarettes are documented.[5] Menthol cigarettes have been aggressively marketed to disproportionately impacted groups, including Black Americans, Native Hawaiians, adolescents, and low-income communities[6–8] and cost less than regular cigarettes within these communities.[9] Research has documented higher menthol smoking among certain groups, including women, racial/ethnic minorities, young adults, those with less education and income, unmarried individuals, and lighter smokers.[10–14]

A 2013 report issued by the U.S. Food and Drug Administration (FDA) indicated that menthol cigarette use is associated with a greater likelihood of smoking initiation among youth as well as greater addiction, and a lower likelihood of successful quitting.[15] With a focus on protecting at-risk groups from initiating and continuing tobacco use, the FDA has been considering whether regulation of menthol in cigarettes should be consistent with the ban on other flavorings, as mandated in the Family Smoking Prevention and Tobacco Control Act.[16] From a public health perspective, if smokers with SMI have elevated menthol smoking relative to the general population, this finding would have significant policy implications, signifying another vulnerable group that may be less likely to initiate smoking, and more likely to quit smoking, if the FDA adds menthol to its ban on characterizing flavorings.

Surprisingly, despite the public health relevance of menthol cigarettes and the elevated prevalence of smoking by people with mental health problems, limited investigation has examined their intersection. Two epidemiologic studies and one clinical investigation reported on associations between menthol use and mental distress. Data analyzed from Florida's Behavioral Risk Factor Surveillance System found menthol smokers had more days of poor mental health in the past month than nonmenthol smokers.[14] In a national sample, menthol use was more likely among smokers with severe psychological distress compared to smokers with none or mild distress.[17] In a study with 83 smokers diagnosed with schizophrenia and 53 control smokers,[18] menthol cigarette smoking was more common among non-Hispanic Caucasians diagnosed with schizophrenia relative to non-Hispanic Caucasians without mental illness. Studies have not examined the prevalence of menthol use in a large clinical sample of adult smokers representing a range of psychiatric disorders.

The current study, examining the prevalence and correlates of menthol use among adult smokers with SMI, aimed to: (a) Identify sociodemographic, tobacco, and mental health factors associated with menthol use and (b) Examine whether menthol smoking prevalence is higher among smokers with SMI overall and among different racial/ethnic groups relative to adult smokers in the general population in California. Given preliminary findings reported in the literature, we hypothesized that menthol use would be more common among racial/ethnic minorities, younger adults, and smokers with greater psychiatric severity and that the prevalence of menthol use among adult smokers with SMI would be higher relative to smokers in the general population.

Methods

Study Participants and Setting

We pooled secondary data from baseline interviews with 1,042 men and women, all current smokers with SMI, recruited as inpatients from psychiatric hospitals in the San Francisco Bay Area between 2008 and 2013, for two clinical tobacco treatment trials. The recruitment sites were all acute care, short-stay, psychiatric units with complete smoking bans. The units were located in two academic, one community, and one public hospital. The smoking cessation intervention components were of the same design across the three trials and included a transtheoretical model-tailored computer-assisted intervention, a stage-matched manual, motivational enhancement and cognitive behavioral counseling tailored to the smokers' stage of change, combined with nicotine replacement therapy (NRT).[19,20] Participants were not recruited as motivated to quit smoking and recruitment rates were high in all three trials (69%–79%).

Eligibility included smoking at least five cigarettes per day (CPD) prior to hospitalization and at least 100 cigarettes in their lifetime, given the studies' provision of NRT. Other inclusion criteria for all trials included plans to reside in the San Francisco Bay Area during the study period, fluency in written and spoken English, and demonstrated capacity to consent. Acutely psychotic, manic, or hostile patients with symptoms that did not resolve sufficiently during hospitalization and those with contraindication for NRT use, such as recent myocardial infarction, were excluded and provided alternative cessation treatment referrals. The Institutional Review Boards at the University of California, San Francisco; Stanford University; and the participating community hospitals approved of the study procedures, and participants provided informed consent.

Measures

Smoking Characteristics

In all three clinical trials, menthol smoking was assessed with the question, "Do you smoke menthol cigarettes?," coded as "menthol smoker," "nonmenthol smoker," or "smokes both." Consistent with prior population-level studies (including the NSDUH) and tobacco treatment trials, persons who responded menthol smoker or smokes both were categorized as "menthol smokers".[10,21] Cigarettes per day (CPD) were assessed by the question, "How many cigarettes do you usually smoke in a day?" Nicotine dependence was assessed using the 6-item Fagerström Test of Nicotine Dependence (FTND).[22] Readiness to stop smoking was categorized into one of three stages of change: Precontemplation (no intention to quit in the next six months), Contemplation (intending to quit in the next six months), or Preparation (intention to quit in the next 30 days and with a 24-hour quit attempt in the past year).[23]

Mental Health Functioning

Psychiatric diagnoses of unipolar depression, bipolar disorder, and non-affective psychotic disorder were obtained using the computerized version of the Mini-International Neuropsychiatric Interview (eMINI)[24] or by chart review. The eMINI is a brief structured psychiatric interview that screens mental disorders using criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).[25] The BASIS-24 assessed self-reported mental health functioning for the week prior to hospitalization; with subscale scores for depression/functioning, emotional lability, psychotic symptoms, and alcohol/drug use.[26] The Medical Outcomes Short Form (SF-12) assessed physical and mental health functioning.[27]

Sociodemographic Variables

Sociodemographic factors known to be associated with menthol cigarette use in the general population were examined in the current study and included gender (categorized as male, female); race/ethnicity (Hispanic, non-Hispanic Caucasian, Black, Native Hawaiian/

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Pacific Islander/Asian American, and multiracial/other), years of education (range: no formal education [0 years] to doctoral degree [21 years]); income (categorized as < $10,000, $10,000-$19,999, $20,000-$39,999, $40,000 or more); and marital status (categorized as never married; divorced, separated, or widowed; married). Transgender individuals were excluded due to the small sample size (11 individuals).

NSDUH Comparison Data

Population menthol smoking prevalence estimates among adults in the general population were obtained from the 2008 to 2011 administrations of the National Survey on Drug Use and Health (NSDUH), an annual in-person interview that assesses a cross-section of individuals aged 12 and older for tobacco, alcohol, and illicit drug use, and mental health status.[13,28,29] Data for the current comparative analyses were from adult smokers, 18 years and older, residing in California, who were assessed for menthol use (weighted N = 10,542). The NSDUH assessed menthol smoking among past month cigarette smokers in each administration using the question, "Were the cigarettes you smoked during the past 30 days menthol?"

Data Analysis

Descriptive analyses of sociodemographic, smoking-related, and mental health functioning measures were run to characterize our sample. Bivariate logistic regression analyses were conducted to examine how sociodemographic and smoking-related characteristics related to menthol smoking. Next, multivariate logistic regression analyses were conducted that simultaneously included sociodemographic characteristics, smoking-related variables, and mental health problems that were significantly associated with menthol smoking in bivariate analyses. The Asian American and Pacific Islander ethnic groups, and the American Indian and multiracial/other ethnic groups, were combined in the logistic regression models due to the small sample sizes of Pacific Islanders (n = 10) and American Indians (n = 20). Data were analyzed using SAS version 9.3.[30] Lastly, the prevalence of menthol smoking was calculated by race/ethnicity for our sample of smokers with SMI and compared to NSDUH population estimates among smokers aged 18 and older residing in California.[12,13,17,28]

Results

Table 1 presents descriptive statistics for demographic variables, tobacco characteristics, and clinical characteristics by menthol use, along with results from bivariate multiple regression analyses examining differences by menthol cigarette use. Participants with SMI had a mean age of 39 years (SD = 13); averaged 13.5 years of education (SD = 2.8); 57% were never married, 27% were divorced, widowed, or separated, and 16% were married; and 51% had an annual household income < $10,000. The racial/ethnic composition was 48% non-Hispanic Caucasian, 23% Black, 15% Hispanic Caucasian, 5% Asian/Pacific Islander, and 9% multiracial/other. Primary psychiatric disorders were psychotic disorder (28%), bipolar disorder (30%), major depression (28%), and other (13%). The sample reported 43% nonmenthol use only, 28% menthol use only, and 29% both menthol and nonmenthol use.

Results from bivariate logistic regression analyses predicting current menthol smoking from demographic, tobacco, and clinical characteristics are also presented in Table 1. Persons with SMI who were younger; with fewer years of education; lower income; and those who were Black, Hispanic, Asian/Pacific Islander, and multiracial/other versus Caucasian were significantly more likely to smoke menthol cigarettes. Smoking characteristics, including usual number of cigarettes per day, level of nicotine dependence, smoking within 30 minutes of waking, and stage of change were not significantly associated with menthol use. Those with a primary diagnosis of psychotic disorder or other disorder versus major depression were significantly more likely to smoke menthol cigarettes as were those reporting greater psychotic symptoms on the BASIS-24. In contrast, those with greater depression symptoms on the CES-D, greater problems with depression and interpersonal relationships on the BASIS-24, and poorer mental health functioning on the SF-12 were more likely to smoke only nonmenthol cigarettes.

Multivariate models that adjusted for age, race/ethnicity, years of education, income, psychiatric diagnosis, depression functioning, perceived interpersonal problems, and psychotic symptoms on the BASIS-24, and mental health functioning on the SF-12, indicated that those of younger age (adjusted odds ratio [AOR] = 0.98, 95% CI = 0.97, 0.99, p < .0001); Blacks (AOR = 5.52, 95% CI = 3.67, 8.32, p < .0001), Hispanics (AOR = 2.07, 95% CI = 1.39, 3.08, p = .0003), Asian Americans/Pacific Islanders (AOR = 2.00, 95% CI = 1.11, 3.62, p = .02), and identifying as multiracial/other (AOR = 2.17, 95% CI = 1.33, 3.56, p = .002) compared to Caucasians; those with fewer problems with interpersonal functioning (AOR = 0.85, 95% CI = 0.74, 0.98, p = .02); and those with greater psychotic symptoms (AOR = 1.15, 95% CI = 1.01, 1.31, p = .03) were significantly more likely to smoke menthol cigarettes.

Prevalence of menthol use among adult California smokers in the NSDUH 2008–2011 surveys was 27.5% and did not differ appreciably by survey year (range 25% to 30%). Compared to the general population of adult smokers in California, menthol smoking prevalence was higher among adult smokers with SMI (57%), and this was found within all examined racial/ethnic groups (Figure 1). The differences were smallest among Blacks, for whom menthol prevalence in both the general population and among those with SMI exceeded 70%.

Discussion

The current study characterized menthol smoking among Black, Hispanic, Asian American/Pacific Islander, Caucasian, and multiracial/other smokers with SMI relative to smokers in the general population and assessed the demographic and clinical correlates of menthol smoking in this disproportionately impacted group. Results indicated that relative to the average adult smoker in California, adult smokers with SMI reported a higher prevalence of menthol cigarette smoking across all racial/ethnic groups.

Within the sample and controlling for a number of demographic and clinical characteristics, younger age, minority race/ethnicity, fewer perceived interpersonal problems, and greater psychotic symptoms were associated with a significantly increased likelihood of menthol cigarette smoking among smokers with SMI. This finding complements and extends prior research indicating a higher prevalence of menthol smoking among Caucasians with schizophrenia relative to Caucasians without mental illness, and greater menthol cigarette use among those with poorer mental health.[14,17] With data analyzed from Florida, New Jersey, and now California, the associations between menthol use and mental illness/distress do not appear regionally-specific. Prior studies comparing to nonpsychiatric control groups have found greater depression and general distress among menthol versus nonmenthol users, while in the current sample, psychotic disorder and severity of psychotic symptoms showed stronger

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Table 1. Results From Bivariate Logistic Regression Predicting Current Menthol Smoking From Demographic, Tobacco, and Clinical Characteristics Among Smokers With Serious Mental Illness

	All *N* = 1,042	Menthol smokers (*n* = 595)	Non-menthol smokers (*n* = 447)		
	% or mean (*SD*)	% or mean (*SD*)	% or mean (*SD*)	OR[a] (95% CI)	*p*
Demographic characteristics					
Sex					
Male	52.4	50.5	55.0	0.83 (0.65, 1.06)	.14
Female	47.6	49.5	45.0	Reference	
Age	38.9 (13.4)	37.6 (13.3)	40.5 (13.2)	0.98 (0.98, 0.99)	.0005
Race/ethnicity					
Black	22.9	32.3	10.7	5.48 (3.81, 7.87)	<.0001
Hispanic	15.0	16.8	12.5	2.46 (1.69, 3.57)	<.0001
Asian/Pacific Islander	5.3	5.7	4.7	2.23 (1.26, 3.95)	.006
Multiracial/other	8.9	10.1	7.4	2.50 (1.58, 3.97)	<.0001
White	47.9	35.0	64.7	Reference	
Years of education	13.5 (2.8)	13.2 (2.9)	13.9 (2.6)	0.91 (0.87, 0.95)	<.0001
Income					
< $10,000	50.7	53.9	46.4	1.43 (1.05, 1.95)	.02
$10,000–$20,999	24.9	23.8	26.2	1.13 (0.79, 1.62)	.70
$21,000 or more	24.4	22.2	27.4	Reference	
Marital status					
Never married	56.9	58.7	54.6	1.11 (.78, 1.57)	.25
Divorced/separated/widowed	27.4	25.8	29.4	0.91 (.62, 1.34)	.33
Married/live with partner	15.7	15.5	16.0	Reference	
Smoking characteristics					
Usual cigarettes per day	17.0 (10.7)	17.0 (11.5)	17.0 (9.60)	1.00 (.99, 1.01)	.98
FTND total score	4.7 (2.2)	4.76 (2.2)	4.65 (2.24)	1.02 (0.97, 1.08)	.43
Smoke ≤ 30 min of waking	78.7	80.5	76.2	1.29 (0.96, 1.74)	.09
Stage of change					
Precontemplation	30.1	31.1	28.9	0.99 (0.71, 1.40)	.57
Contemplation	46.3	44.5	48.5	0.85 (0.62, 1.16)	.20
Preparation	23.6	24.4	22.6	Reference	
Clinical characteristics					
Primary psychiatric diagnosis					
Psychotic disorder	28.4	31.1	24.8	1.62 (1.17, 2.25)	.004
Bipolar disorder	29.9	29.4	30.7	1.24 (0.90, 1.71)	.18
Other	13.4	14.5	12.1	1.55 (1.03, 2.34)	.04
Major depression	28.2	25.0	32.4	Reference	
CES-D-10 score[b]	18.1 (7.7)	17.5 (7.8)	19.0 (7.5)	0.98 (0.96, 0.99)	.003
BASIS-24 scores[c]					
Depression functioning	2.5 (1.1)	2.4 (1.1)	2.6 (1.0)	0.84 (0.75, 0.95)	.005
Interpersonal relationships	1.7 (1.0)	1.7 (1.0)	1.8 (1.0)	0.87 (0.77, 0.98)	.03
Self-harm	1.5 (1.4)	1.5 (1.4)	1.5 (1.3)	0.97 (0.88, 1.06)	.46
Emotional lability	2.1 (1.2)	2.1 (1.2)	2.0 (1.1)	1.06 (0.95, 1.17)	.30
Psychotic symptoms	1.3 (1.2)	1.4 (1.3)	1.1 (1.2)	1.21 (1.09, 1.34)	.0003
Alcohol/drug abuse	1.2 (1.1)	1.2 (1.1)	1.2 (1.1)	0.99 (0.88, 1.10)	.82
Overall summary score	2.0 (0.8)	2.0 (0.8)	2.1 (0.7)	0.87 (0.74, 1.03)	.10
SF-12 scores[d]					
Physical component score	46.9 (12.6)	46.8 (12.3)	47.0 (13.0)	1.00 (0.99, 1.00)	.76
Mental component score	31.4 (14.2)	32.8 (14.1)	29.5 (14.1)	1.02 (1.01, 1.03)	.0003

BASIS-24 = Behavior and Symptom Identification Scale-24; CESD = Centre for Epidemiologic Studies Depression Scale; FTND = Fagerström Test of Nicotine Dependence; SF-12 = Short Form-12.

[a]Odds ratio (OR) = odds of being a menthol versus non-menthol smoker.

[b]Range = 0–30; ≥ 11 indicates significant depressive symptoms.

[c]Range = 0–4; higher scores indicate worse mental health.

[d]Range = 0–100, national normative value = 50, *SD* = 10; lower scores indicate worse functioning.

associations with menthol smoking than did depression. The lower depression scores among menthol users in the current study may reflect that the predominant disorder represented among menthol smokers was psychosis, which is not characterized by depression. When we examined the association between menthol smoking and psychiatric diagnosis separately for Caucasians and Blacks, psychotic disorder was only associated with a greater likelihood of menthol smoking (versus major depression) among Caucasian participants.

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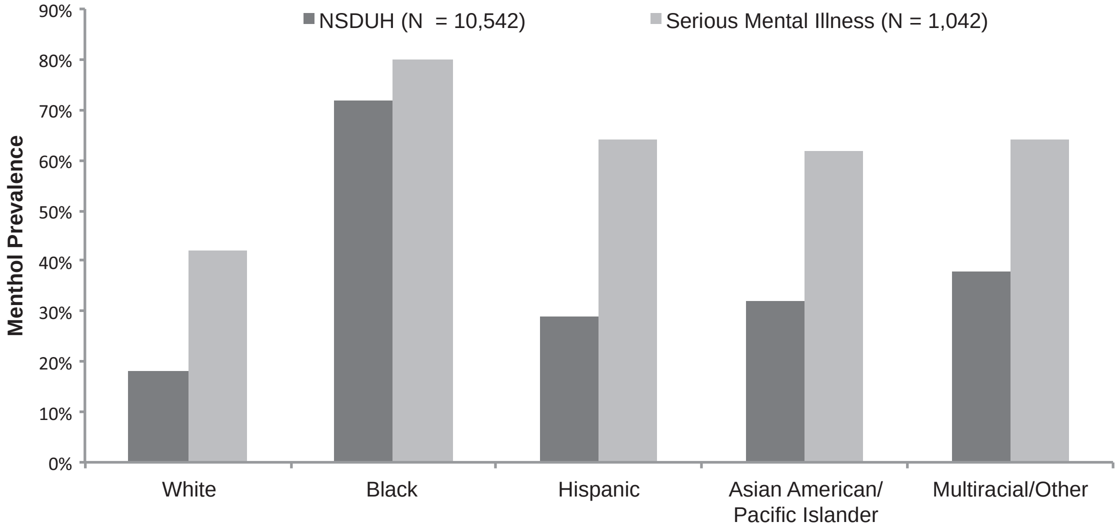

Figure 1. Menthol smoking prevalence according to race/ethnicity among adults with serious mental illness and a California representative sample of adult smokers. California representative estimates of menthol smoking come from the 2008–2011 National Survey on Drug Use and Health[17,28,29].

This suggests that the association between psychosis and menthol smoking was not simply driven by a higher prevalence of psychotic disorders and menthol smoking among Blacks. The lack of significant association among Blacks is likely attributable to a ceiling effect, as the large majority of Blacks in our sample smoked menthol (80%), challenging the ability of any variable to predict variance in menthol smoking in this group. The finding of greater interpersonal problems among solely nonmenthol smokers was statistically significant though the mean difference between groups was only 0.1 on a 4-point scale.

The high prevalence of menthol smoking among persons with SMI relative to the general population is striking and likely influenced by multiple factors. Tobacco industry research on marketing of menthol cigarettes and consumer perceptions indicates that menthol cigarettes are marketed, and perceived by consumers, as healthier than nonmenthol cigarettes.[31] Menthol may increase pleasure derived from inhaling cigarettes and reinforce smoking behaviors.[32] In the only other study of a clinical sample of menthol smokers, menthol use among patients with schizophrenia was associated with elevated serum nicotine and cotinine levels and greater exhaled carbon monoxide levels compared to nonmenthol smokers.[18] Although research is mixed with regard to elevated nicotine exposure levels from menthol,[5] nicotine levels are elevated among smokers with psychosis,[33] and menthol smoking may be a means to achieving higher nicotine levels in this population. Additional research is needed to investigate this possibility. Further, in the general population, menthol has been found to inhibit nicotine metabolism[34] and is associated with upregulation of beta-2 nicotinic acetycholine receptors in the brain relative to nonmenthol cigarettes.[35] Menthol's anesthetic and bronchodilatory effects numb the throat, reduce the perceived harshness of cigarette smoke, open airways, and facilitate deeper inhalation of cigarette smoke, increasing exposure to cigarette-related carcinogens and providing an oral sensation that appeals to smokers[36,37] and youth.[12]

Greater menthol use among persons with SMI overall, and among youth and racial/ethnic minorities in particular, could also be related to targeted marketing and advertising of menthol cigarettes. Persons with SMI have long been targeted by the tobacco industry,[38] and greater access to price promotions and advertisements for menthol cigarettes may contribute to, or exacerbate, menthol smoking among this vulnerable group. Smokers are price sensitive,[39] and the tobacco industry has targeted marketing of menthol cigarettes to poor neighborhoods across the United States.[40] In California, the greatest prevalence of menthol price promotions is found in low-income communities and convenience stores (22.1%), gas stations (28.6%), and liquor stores (14.5%), with virtually no price promotions among supermarkets (0%), which are more common in wealthier neighborhoods.[41] Further, tobacco companies also have aggressively marketed menthol cigarettes to urban Black communities[6,8] and have used savvy marketing strategies to link menthol smoking with Black culture. Correspondingly, research has shown that Black adolescents are exposed to a greater number of menthol price promotions and lower menthol prices in tobacco retailers near their high schools,[9] and are significantly more likely to recognize a menthol cigarette brand than nonmenthol brand.[42] Smokers with SMI in the current study tended to be poor, with unstable living conditions, and it is possible that greater exposure to targeted marketing and cheaper menthol prices could contribute to the higher prevalence of menthol use in this group overall, and among racial/ethnic minorities in particular, via earlier initiation, greater risk of addiction, and lower rates of successful quitting.

The high prevalence of menthol cigarette smoking among smokers with SMI has important implications for prevention, intervention, and social policy. Smokers with SMI are responsive to tobacco control policies, such as smoking bans,[43] and results from the current study suggest that a policy to include menthol in the FDA's ban on characterizing flavorings in cigarettes may afford substantial public health benefits for this vulnerable group. Although little is known about attitudes toward regulating menthol among persons with SMI, nationally representative studies indicate the majority of Americans, including 68%–76% of Blacks, support an FDA ban of menthol cigarettes.[44]

In the current sample of adults with SMI, approximately half of menthol smokers were dual users, while the other half smoked menthol cigarettes exclusively. If menthol cigarettes were banned, it is unknown though anticipated that most dual-users would continue

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smoking nonmenthol cigarettes, while those who only smoke menthol cigarettes would be more likely to quit or cut down on smoking. The majority of studies addressing the likelihood of menthol smokers switching to nonmenthol cigarettes indicate that only a small proportion of menthol smokers report plans to switch to nonmenthol cigarettes. For example, 39% of adult menthol smokers reported that they would quit smoking if menthol cigarettes were no longer available, and only 12.5% reported that they would switch to a nonmenthol brand.[45] Among young adult menthol smokers, 66% reported that they would quit smoking if menthol cigarettes were no longer available.[46] A study that modeled the impact of a menthol ban, estimated a 10% reduction in overall smoking prevalence in the United States (and 25% reduction among Blacks) by 2050, averting 323,107 smoking-attributable deaths.[47] Finally, although data from a large sample of adults suggested that smokers were less likely to support a ban on menthol than non-smokers (41% vs. 64%), there was a significant interaction with race such that, Black smokers were more likely to support banning menthol than non-Black smokers (71% vs. 38%).[48] Taken together, the current findings support recent recommendations to ban the sale of menthol cigarettes in California[41] and highlight the need for, and potential interest in, new tobacco control policies that reduce disparities in tobacco use among vulnerable populations.

Limitations

The current study and the NSDUH used different assessments of menthol use and the data from smokers with SMI were cross sectional; hence, inferences cannot be made about the risks and influences of menthol use over time. Further, smokers with SMI lived in the San Francisco Bay Area and may not be representative of smokers with SMI in the general California population. In our sample of smokers with SMI, 28% smoked menthol only, while 29% smoked both menthol and nonmenthol cigarettes. We are unable to tell from the current study what drives dual use (e.g., smoking anything that is available or price sensitivity), and additional research is needed to address this question.

Conclusions

The current study examined the prevalence and correlates of menthol cigarette use among a diverse sample of smokers with SMI. Findings indicate that menthol cigarette smoking is common and associated with greater psychotic symptoms, younger age, and racial/ethnic minority status. These cross-sectional data support the need for further investigation of menthol smoking as a potential vector contributing to tobacco-related disparities among individuals with SMI.

The FDA has the authority to regulate all tobacco products. Section 917(c) (4) of the Family Smoking Prevention and Tobacco Control Act included legislative language that prioritized an assessment of scientific findings regarding "…the impact of the use of menthol in cigarettes on the public health, including such use among children, African Americans, Hispanics, and other racial and ethnic minorities".[16] With a focus on protecting at risk groups, the FDA is currently considering regulation of menthol cigarettes,[15] but there is no required timeline or deadline for regulatory action, and the Secretary of Health and Human Services has yet to make a regulatory decision.[5] Results from the present study indicate that the FDA's regulation of menthol cigarettes may have cessation and prevention benefits for individuals with SMI in general, and those with greater psychotic symptoms, younger age, and minority ethnicity/race in particular. If menthol is no longer allowed as a characterizing flavoring, smokers who use menthol, and menthol only smokers in particular, may be more likely to quit smoking, and those vulnerable to initiating smoking with menthol cigarettes may be less likely to start. Longitudinal data or natural experiments are needed to test whether restricting targeted menthol marketing or banning menthol cigarettes would support smoking cessation efforts in this priority population.

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Declaration of Interests

None declared.

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Marketing of menthol cigarettes and consumer perceptions: a review of tobacco industry documents

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ABSTRACT

Objective To examine tobacco industry marketing of menthol cigarettes and to determine what the tobacco industry knew about consumer perceptions of menthol.

Methods A snowball sampling design was used to systematically search the Legacy Tobacco Documents Library (LTDL) (http://legacy.library.ucsf.edu) between 28 February and 27 April 2010. Of the approximately 11 million documents available in the LTDL, the iterative searches returned tens of thousands of results from the major US tobacco companies and affiliated organisations. A collection of 953 documents from the 1930s to the first decade of the 21st century relevant to 1 or more of the research questions were qualitatively analysed, as follows: (1) are/were menthol cigarettes marketed with health reassurance messages? (2) What other messages come from menthol cigarette advertising? (3) How do smokers view menthol cigarettes? (4) Were menthol cigarettes marketed to specific populations?

Results Menthol cigarettes were marketed as, and are perceived by consumers to be, healthier than non-menthol cigarettes. Menthol cigarettes are also marketed to specific social and demographic groups, including African—Americans, young people and women, and are perceived by consumers to signal social group belonging.

Conclusions The tobacco industry knew consumers perceived menthol as healthier than non-menthol cigarettes, and this was the intent behind marketing. Marketing emphasising menthol attracts consumers who may not otherwise progress to regular smoking, including young, inexperienced users and those who find 'regular' cigarettes undesirable. Such marketing may also appeal to health-concerned smokers who might otherwise quit.

INTRODUCTION

The concentration of menthol in tobacco products varies according to the product characteristics and the perceived flavour desired, but is present in 90% of all tobacco products, whether the products are marketed specifically as 'mentholated' or not.[1 2] The Family Smoking Prevention and Tobacco Control Act (FSPTCA) gave the US Food and Drug Administration (FDA) regulatory authority over tobacco products. On 22 September 2009, the FDA exercised this authority when it announced a rule banning cigarette flavourings specified in the Act. This ban did not include menthol, however, as it was excluded from the list of banned flavourings in the Act because of opposition by the tobacco industry. The fact that menthol was not included in the original list of banned flavours concerned many in the public health arena who argued that menthol is used by the tobacco industry to attract young, inexperienced smokers and/or African—Americans.[3] In addition to youth appeal, the addition of 'medicinal menthol' to cigarettes may also appeal to established health-concerned smokers who might otherwise quit.[4]

Others have investigated the internal tobacco industry documents for different but related questions on how tobacco companies manipulate menthol content in cigarettes to target young people[5] and consumer perceptions of the sensory characteristics of menthol.[6] This paper analyses internal tobacco industry documents to determine if tobacco companies marketed mentholated cigarettes as public health advocates allege, and how the tobacco industry managed consumer perceptions of menthol through marketing strategies. This knowledge can help inform the regulatory decisions by the US FDA and comparable agencies elsewhere in the world, and can augment public health's understanding of why the tobacco industry opposed menthol's inclusion in the list of banned flavouring additives.

Academics and government scientists independent of the tobacco industry have shown that the tobacco industry targets various population groups, including specific racial and ethnic populations, with marketing and advertising generally[7] and for mentholated products specifically.[8] A 2006 case study[9] of Kool, Brown & Williamson's best selling mentholated brand, described the company's use of music events to promote the brand to young, particularly African—American, people. Independent research has shown explicit and implicit health messages in advertisements for menthol cigarettes.[10 11] Some health messages are explicit, for example, in a 1942 advertisement asking 'Throat sore? Time to give it a rest!' and directing the reader to 'Change to Spuds. Enjoy their soothing coolness!' (the Spud brand was the first in the US to advertise that it was mentholated). It is nevertheless important to examine the intentions behind the creation of such marketing communications in the words of tobacco company insiders themselves, particularly if marketing shifted from communicating this type of explicit health message to messages that continue to communicate health benefits, but less explicitly.[10 11] The current study begins with historical examples and moves forward in time, but is not a strictly chronological treatment of the topic. The results are presented in three overall sections: marketing messages for menthol cigarettes, then consumer perceptions of those messages, and specific populations targeted by such messages.

A decline in per capita cigarette consumption in the US in 1953—1954 resulting from the 'health

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scare' marked the beginning of changes in health-related messages in cigarette marketing materials.[12] A decade later, after the 1964 US Surgeon General's Report 'Smoking and Health'[13] and the 1965 Cigarette Act,[14] US tobacco marketers continued to be faced with the challenge of marketing a product identified as harmful by health authorities while distracting consumers from those known harms. These challenges necessitated a move away from explicit health messages and towards other messages that would appeal to different groups of potential consumers of 'low-tar' or 'light' tobacco products. Research has elucidated many of these alternative marketing messages for 'low-tar' and 'light' cigarettes,[4 15] and has demonstrated that consumers tend to perceive 'low-tar' and 'light' cigarettes to be less harmful than 'regular' cigarettes.[16–20] less is understood about messages for menthol cigarettes or about how consumers perceive menthol. A 2010 scholarly commentary stated that the 'industry has used menthol's association with cold remedies to infer that smoking menthol cigarettes has some medicinal or health benefit for more than 70 years'.[21] Internal documents can shed light on whether consumers have accepted this inference of health benefits.

This paper addresses the following questions on marketing for and consumer perceptions of menthol cigarettes:

1. Are/were menthol cigarettes marketed with health reassurance messages?
2. What other messages come from menthol cigarette advertising?
3. How do smokers tend to view menthol cigarettes?
4. Were menthol cigarettes marketed to specific populations?

METHODS

A complete discussion of the general tobacco documents research methods employed in this study is found elsewhere in this issue.[22] Details specific to the current study are as follows: in this qualitative research study of the digitised repository of previously internal tobacco industry documents, a snowball sampling design[23] was used to search the Legacy Tobacco Documents Library (LTDL) (http://legacy.library.ucsf.edu). The LTDL was systematically searched between 28 February and 27 April 2010, using standard documents research techniques. These techniques combine traditional qualitative methods[24] with iterative search strategies tailored for the LTDL data set.[25]

Initial keyword searches combined terms related to: menthol, health/healthy/healthier, cool/cooling/cooler, market/markets/marketing, consumer perception, focus group, creative, advertisement copy, communication, market research, report, topline and target group. This initial set of keywords resulted in the development of further search terms and combinations of keywords (eg, menthol cigarette brand names, project names, individuals and companies named in correspondences and on research reports, and specific target groups). For each set of results, the first 50–300 documents were reviewed. If documents did not appear to be relevant to the research questions, or if there was a repetitive pattern of documents, the review moved on to the next search term. Among the reports, correspondence and studies conducted by product development and research departments of the major tobacco companies (American Tobacco (AT), British American Tobacco (BAT), Brown & Williamson (B&W), Lorillard, Philip Morris (PM) and RJ Reynolds (RJR)), relevant documents were found in the following subject areas: (1) marketing menthol using health assurance messages; (2) user-imagery focused marketing; (3) consumer perceptions of menthol products; and (4) targeting specific populations. A final collection of 953 documents, created between the 1930s to the first decade of the 21st century, relevant to 1 or more of the research questions were qualitatively analysed. Memos were written to summarise the relevant documents to further narrow down to the 60 representative documents that are cited in this paper.

RESULTS

Health reassurance messages in menthol advertising

Menthol cigarettes were marketed using health reassurance messages suggesting that menthol cigarettes were safer than 'full flavour' or non-menthol cigarettes. The first mentholated cigarette is credited to a young man, Lloyd 'Spud' Hughes, a chronic cold sufferer, when in the 1920s his mother prescribed a treatment of menthol crystals that he surreptitiously added to his smoking tobacco tin.[26 27] Bearing Hughes's nickname, Spud cigarettes became the first commercial menthol brand to be marketed in the US; B&W followed with Kool Menthol in 1933. Initially Kool Menthol, and menthol in general, was advertised as being 'for occasional use' in order to 'rest your throat'[28] rather than a regular, daily-use product.

Menthol cigarettes were first popularised as a remedy to the burn, dryness and throat irritation that accompany smoking (figure 1). B&W and Lorillard marketed menthols with health-reassuring slogans such as 'Breathe easy, smoke clean', 'When your throat tells you it's time for a change…'[29] and 'The beneficial head-clearing qualities of menthol'.[30] Similar claims made were that menthol brands act as a 'remedy or treatment for coughs' and counteract 'throat irritations due to heavy smoking'.[31]

Tobacco company executives sought to emphasise health messages in the marketing of menthol products relative to non-menthol products from the beginning. The advertising firm Cunningham & Walsh compiled a report for B&W in 1980 in which they observed that Kool's '(r)emedial specialty brand image' in the early 1950s 'benefits (the b)rand as smokers perceive menthol as less harmful'.[32] In a 1960s brand evaluation, B&W noted that '(e)mphasis on the throat, with its important

Figure 1 Spuds brand and Kool brand cigarettes, the earliest two brands to be marketed specifically as mentholated brands in the US, were presented in the 1920s and 1930s as brands that provide relief from the throat pain and irritation caused by smoking (images retrieved from http://lane.stanford.edu/tobacco/index.html).

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health implications, has… been an important part of Kool advertising since 1960’.[33] According to a 30 May 1973 Lorillard meeting agenda to discuss ‘Kent Menthol 100's’, the objective of a menthol line extension of Lorillard’s ‘low tar’ Kent brand was to ‘convince smokers of competitive menthols (as well as smokers contemplating entering the category) that Kent menthol is the menthol that offers refreshing menthol smoking satisfaction and health reassurance’.[34] B&W declared that ‘KOOL must move into the health reassurance segment so that 45% of KOOL business will be in the perceived product safety arena by 1982’.[35]

Other messages in menthol cigarette advertising

The 1950s marked the beginning of significant public awareness in the US of the health hazards of smoking.[36] With the introduction of RJR’s Salem brand in 1956, the ostensible ‘health’ benefit of menthol was overtaken by the ‘taste’ benefit of menthol, and menthol as a cigarette style moved from the occasional into the regular use arena.[37] The importance of this shift was neatly explained in a 1982 B&W market presentation:

> Salem created a whole new meaning for menthol. From the heritage of solves-the-negative-problem-of-smoking, menthol almost instantly became a positive smoking sensation. Menthol in the filter form in the Salem advertising was a ‘refreshing’ taste experience. **It can be viewed as very ‘reassuring’ in a personal concern climate.** Undoubtedly, **the medicinal menthol connotation carried forward in a therapeutic fashion**, but as a positive taste benefit.[37] (Emphasis added.)

The Newport brand’s entry into the market in 1957 with the advertising slogan ‘Rich taste—with a touch of refreshing mint’ made menthol ‘now a positive experience, not just a solver of smoking ‘problems’’.[37] Being aware that menthol also carried health connotations, tobacco companies were freed up to market menthol cigarettes as a thing of pleasure and personal preference while still providing health reassurances to menthol smokers.

Refreshing, fresh, cool and clean

Avoiding overt health messages by the late 1950s, Kool advanced new advertising copy such as, ‘What a wonderful difference when you switch to snow fresh KOOLs. Your mouth feels clean and cool, your throat feels soothed and fresh. Enjoy the most refreshing experience smoking’.[38] By the 1960s Kool advertising employed implicit health-related messages in print advertisements for college, military, and ‘Negro’ publications, such as ‘Only KOOL gives you real menthol magic’ or ‘Come all the way up to KOOL Filter Kings for the most refreshing coolness you can get in a cigarette’,[38] capitalising on the perception of cooling as healthier.

Smokers describe menthol’s ‘cooling’ or ‘refreshing’ effects variably as a taste or flavour on the one hand, or a sensation or impact on the other hand. A 1988 Philip Morris (PM) study of the menthol market noted that ‘menthol’s appeal primarily focused on the unique feeling or sensation it provides’, and that ‘menthol taste (is) more difficult to describe than menthol sensation’.[39] Menthol cigarette marketers were quick to exploit the perception of menthol as a sensation in addition to a taste. Major objectives for the Kool brand family from 1979 to 1985 included the necessity ‘to enhance the perception of the two major menthol buying motivations—satisfaction and refreshment’.[35] ADI Research, Inc. advised B&W similarly in a 1984 cigarette smokers study that ‘frequently mentioned positive characteristics of Kool Filter Kings were refreshingness, coolness, smell, sensation, and smoothness’[40] That year, Cunningham and Walsh advised B&W to forge Kool’s popularity worldwide by positioning the brand as ‘something enjoyable from US, most refreshing taste sensation’.[41] Figure 2 shows some examples of ‘refreshing’ and ‘cool’ messages.

Although there was shift away from overt health messages towards less tangible ‘refreshment’ and similar messages in menthol marketing triggered by the health scare of the 1950s, tobacco companies still wished to maintain health associations with menthol. According to a B&W brand planning document in 1978 (estimated date), a prime Kool objective for 1979–1985 was also to ‘(p)rovide product safety reassurance while enhanc(ing) the satisfaction and refreshment perception of the appropriate KOOL styles, through the successful, national launch in 1979 of either: 1. Low-‘tar’ parent (or) 2. Repositioned KOOL Milds’.[35]

Identity and in-group belonging

Menthol is commonly thought of as an African–American cigarette style in the US market, and to an extent, evidence from industry documents supports this perception. However, tobacco companies do not intend for menthol to be only or even mostly an African–American style, but rather a cigarette style associated with group identity for various subgroups in the market, including, but not exclusively, African–American identity.

Some industry analysts, such as Diane Burrows of the RJR Marketing Development Department (a competitor of B&W), observed a change in the cigarette market, particularly in the menthol market, in the 1960s. In her 1984 analysis of RJR’s Salem, Lorillard’s Newport and B&W’s Kool, Burrows stated:

> Younger adult Blacks of the 1930s to 1950s had basically gone with whatever brand was big among younger adult White smokers…. In the 1960s, they began to coalesce behind Kool, which only had a 2% share among younger adult Whites. It was time for Blacks to build their own brand in the 1960s, the heyday of Martin Luther King and ‘Black pride’.[42]

The strategy for exploiting this phenomenon was simple:

> Kool apparently capitalized on this aspect of the 1960s by simply advertising to Blacks before its competitors did. Kool ads were in

Figure 2 Triggered by the health scare of the 1950s and increasing after the 1964 US Surgeon General’s Report, advertisements for menthol brands emphasised general refreshment and coolness rather than the explicit health messages of earlier decades. Menthol nevertheless continued to carry the medicinal and health connotations of previous decades (images from the 1980s, retrieved from http://www.tobacco.org/ads).

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> Ebony consistently from at least 1962, when our records start…. Kool became 'cool' and, by the early 1970s, had a 56% share among younger adult Blacks—it was the Black Marlboro.[42]

Without referencing Dr King or 'black pride' specifically, B&W stated in a 1966 marketing analysis company presentation that the brands 'perform very well in ethnic markets because for some time we have been tailoring our advertising to fit local markets'.[43] Further, in a 1969 marketing report, B&W stated that Kool 'continues to direct advertising towards specific ethnic groups with special emphasis on the Negro market'.[44]

In 1979, B&W explicitly planned to '(e)nhance the social acceptance of the entire KOOL line through all creative efforts so that the product is equally acceptable to White smokers-as to Black smokers. This will be realized through smoker image creative management as well as specific media targeting'.[35] By 1983, M. A. Schreiber, Kool's Senior Brand Manager for B&W, wrote:

> In January, 1982, KOOL launched its current campaign. Pan-racial music imagery was established as KOOL's strategic property…. (A) n advertising exploratory was started to …specifically address how to communicate… (a)n attractive, contemporary image to young adult Whites.[45]

An urban image, which appealed to young people of many ethnicities, continued to be important to menthol marketing through the 1990s. Advertising agency Leo Burnett reported to PM in December 1995 that among 'urban dwellers, ages LA-24 (legal age to age 24), African—American and Caucasian, menthol loyalists… (u)rban terminology transcends beyond the African—American community'.[46] The agency tested marketing creatives (mock-up advertisements for participant feedback), including '(m)enthol approaches tied to identified urban smoker insights' with the theme 'Diversity/Community'.[46] One specific creative in the 'Diversity/Community' theme titled 'Huze Art' was observed by the agency to be '(b)y far the strongest of the approaches, its appeal was driven by the sense of urban multi-culturality expressed through art'.[46] The appeal of this execution was explained as follows:

- Urban lifestyle crosses ethnic boundaries.
- Urban lifestyle appeals outside of urban boundaries.[46]

To attach a menthol brand to in-group identity, Kapuler Marketing Research, Inc. conducted a study of a new campaign for Kool targeting ethnic Hawaiians in 1988 for B&W, titled 'Kool and Mild Today'. The agency concluded '(t)he use of ethnic models is seen as something new and respondents are generally positive about this concept. It could provide an opportunity for KOOL to capitalize on being the first to employ ethnic advertising in Hawaii'.[47] The agency noted the models should not look too Japanese but rather should appear to be ethnic Hawaiian Islanders. Preferred models were described as 'fun, happy-go-lucky young people in their 20 s. They have full social calendars and spend a lot of time outdoors at the beach… people who display what islanders call the aloha spirit'.[47]

Fun loving, sociable and youthful

RJR noted in 1981 that the 'Coolness Segment' (RJR's term for the menthol market, describing the cooling properties of menthol) is the youngest of all cigarette market segments.[48] RJR stated in 1981 that '(a)dvertising must convince younger adult smokers that SALEM is smoked by natural, unpretentious but interesting people who are social leaders/catalysts (make things happen) whose sense of humor and wit makes them fun and exciting to be with'.[49]

Youthfulness and sociability are not images restricted to menthol users. Social interaction is thought by tobacco marketers to be important to young adults and adolescents in general. RJR observed in 1981 that:

> (s)moking is frequently used in situations when people are trying to make friends, to look more mature, to look more attractive, to look 'cooler', and to feel more comfortable around others. These aspects of social interaction are especially prevalent among younger adult smokers…. The benefit of smoking which has most frequently and most successfully been exploited by brand families appears to be Social Interaction. For example, some brands, such as Newport, have focused on the younger adult 'peer group' aspect of social interaction.[50]

These user images carry particular weight within the menthol market. Speaking specifically about target users of a new Salem Lights 100 mm product, RJR asserted in 1982 that 'user imagery reflects aspirations of the Personal Experience segment identified by Yankelovich (Inc., a consumer research company)…. The lifestyle of the Personal Experience segment is defined as seeking direct experience and excitement… social interaction is a key element to personal fulfillment'.[51] The emphasis on sociability, fun and enjoyment is particularly evident in Lorillard's long-running Newport 'Alive with Pleasure' campaign.[52] These messages of sociability, fun and enjoyment proved so popular with young audiences that RJR created their 'Salem Spirit' campaign to communicate the values 'sociable' and 'have a good time',[53] though they noted problems with consumers confusing the campaign with Lorillard's similar Newport campaigns. PM observed in 1995 that Newport's '(c)onsistent theme ('Alive with Pleasure') and strategy ('Friends having fun') have given Newport a clear identity in smokers minds', that Newport was '(t)he only brand to capitalized on important 'sociability' aspect of category'.[54] Figure 3 shows a 'Newport Pleasure' campaign advertisement that communicates sociability and in-group belonging. It is perhaps menthol's younger profile relative to non-menthol that makes youthfulness and sociability particularly important to many menthol smokers.

Consumer perceptions of menthol marketing messages

Menthol smokers view menthol cigarettes as safer or less harmful than 'full flavour' or non-menthol cigarettes. Menthol smokers sometimes identified safety perceptions explicitly, but sometimes implicitly with terms such as 'mild', 'light', 'cooling', or 'soothing'; terms that suggest relative safety or health benefits. Terms that imply health messages, including 'light' and 'mild', have been determined to be deceptive in federal Judge Gladys Kessler's ruling that the US cigarette manufacturers violated the Racketeer-Influenced and Corrupt Organizations Act (RICO)[55] as well as by Congress in the FSPTCA.

A focus group study conducted for American Tobacco in 1969 tested, in part, perceptions of a new menthol product. It was observed that:

> Menthol smokers indicated that they smoked menthol cigarettes because they were 'mild', 'cooling', 'refreshing', and 'soothing to the throat'…. There were indications that the **menthol smokers subconsciously perceived menthol cigarettes as being healthier. There was somewhat of a 'health image' associated with menthol**, related to its masking of the tobacco taste, and its **association with medicine**, colds, and sore throats.[56] (Emphasis added.)

In 1976, B&W noted that 'evidence indicates that a pseudo-health image has accrued to mentholated cigarettes'.[57] Then, 2 years later, B&W explicitly acknowledged its Kool franchise '(r)ides on the

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Figure 3 This 2003 Newport advertisement communicates fun-loving youthfulness and sociability, as well as in-group belonging (African–Americans in an urban bar scene). The 'Alive with Pleasure' slogan of the 1990s is here replaced with simply 'Pleasure', further removing the campaign explicit health claims while continuing in the theme of the previous campaign that includes the health-suggestive word 'Alive' (image retrieved from http://www.trinketsandtrash.org).

connotation that menthol has health overtones',[58] and that the Kool Super Lights line extension's 'menthol and tar delivery has synergistic therapeutic implications'.[58] Such perceptions are exemplified in the statement of a respondent in a marketing study for B&W in 1980, 'that menthol cigarettes are better for you'.[59]

In 1975 (estimated date), Lorillard recognised the perception of protection against throat irritation as a boon to the company:

> Overall, menthol smokers appear to be a prime target for a low-irritation story because they seem to be very conscious of irritation. It is highly identifiable by them, and they already view menthol cigarettes as the best route to diminish irritation. Therefore, they would not have to be 'sold' on the idea that a menthol cigarette and diminished irritation are compatible.[60]

As RJR stated in a 1977 analysis of the potential for share growth with 'high filtration' menthol products, '(t)he health concern was perhaps the primary motive for switching to menthol in the first place. In the hierarchy of product benefits/attributes desired by menthol filter smokers, throat concerns rank just behind generic taste and satisfaction'.[61]

Smokers perceive 'mild' cigarettes as healthier than regular (non-'light') cigarettes.[62–65] Menthol's perception as a milder and therefore safer product as compared to 'regular' cigarettes has caused switching from non-menthol to menthol brands and styles. In a 1976 marketing plan for a 'low-tar' menthol cigarette, B&W asserted that 'Menthols and particularly Hi-Fi's (high filtration cigarettes) have a net gain from brand switching'.[57] The Sherman Group Inc. conducted a reconnaissance study of Newport for RJR in 1976 and found among young people:

> (i)n rejecting the 'regular' cigarette taste, the smokers are referring back to their own experiences. These young smokers began smoking the 'popular' brands, Winston, Marlboro, Tareyton and Kents, etc, and moved to menthols for a variety of reasons or circumstances; the rejection of tobacco taste, the search for a 'milder' cigarette, personal influence, or the circumstances of having a cold and wanting to continue smoking, but being unable to 'handle' the hot taste of cigarettes in an already irritated throat.[66]

Lorillard observed in 1972 that '(b)rand-switching has resulted in a 13% gain for Menthols which is larger than the 8% for Hi Fi brands, the only types gaining from claimed switching'.[67]

Beliefs about the health benefits of mentholated cigarettes prevent some potential quitters from quitting in favour of switching to a mentholated brand or style. A William Esty Co. study for RJR in 1973 stated:

> Generally when a respondent reported that he made a conscious decision to switch to a mentholated brand it was because of some problem, minor or major. For instance, **many switched to mentholated cigarettes because of throat irritation, colds, coughs or chronic bronchitis. Sometimes respondents saw smoking a mentholated brand as the only alternative to giving up smoking altogether.**[68] (Emphasis added.)

The Roper Organization prepared a study for PM in 1979 on the attitudes of menthol smokers and that '(m)enthol smokers express slightly less desire to quit smoking than do non-menthol smokers—39% would like to quit, versus 43% of non-menthol smokers'.[69] Burrows' analysis of key market trends of the 1960s concluded the tendency to switch from non-menthol to menthol rather than quit was important for Kool's rise in this decade:

> The key trend for Kool was the emerging importance of younger adult Black smokers in the market. In the health-concerned 1960s, younger adult Blacks didn't back off from smoking to the extent that Whites did. Because of this, their importance surged from 6% of 18-year-old smokers in the 1950s, to 10% in the 1960s.[42]

Marketing menthol cigarettes to specific populations

African–Americans

Advertisements for menthol cigarettes have been over-represented in popular African–American magazines relative to non-African–American magazines[11 70 71] and in predominantly African–American urban neighborhoods.[72] RJR stated in an in-house presentation on the 'US cigarette market in the 1990s (that) 95% of black younger adult smokers now choose menthol, and Newport has a 73 (percent) share-of-smoker among this group'.[73]

As an assessment of the menthol market from PM in 1986 recognised, '(r)elative to all smokers, menthol smokers tend to be: women, young (mainly 25–34), Black, light smokers (<20 cigarettes a day), lower-income earners, pack buyers, (and) 100 mm smokers'.[74] PM had earlier seen, in 1968, that menthol 'was a product which by some virtue was especially suited to the needs, desires and tastes of Negro consumers', speculating that the 'great enthusiasm for menthol cigarettes… was based both on dynamic sensory and on psychological gratifications'.[75]

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To exploit the 'potential opportunity sector' represented by black smokers, RJR produced a 'Black Opportunity Analysis' in 1985.[76] RJR noted, '(t)here are… gaps within Blacks. Several studies have suggested that Blacks are becoming polarized into an 'elite' and an 'underclass'…. It is the 'underclass' who are smokers'.[76] Acknowledging the disadvantages of underclass status, RJR concluded that, although health may be a concern, 'Blacks simply have more pressing concerns than smoking issues'.[76] The implication is that this market, with its myriad socioeconomic pressures, should remain reliable consumers even if they are aware of tobacco's health risks.

Heavy targeting of largely African–American urban populations is reflected in corresponding menthol brands and styles accounting for the bulk of African–American urban smoking. A 1983 'Cigarette Attitude Study (Among low-income Black smokers)' for Newport revealed '(t)he use of menthol cigarettes among the 18–34 lower-income Black segment is almost universal. Nearly 9 out of 10 smokers currently smoke a menthol brand'.[77] Noting changes from data in 1979, the study observed that '(o)verall, black smokers have better recall of advertising for specific menthol brands than in 1979' and 'showed a lower frequency of purchasing secondary brands, and more longevity with regard to the length of time current brand was smoked'.[77] B&W found in 1993 that 'Blacks are three times as likely to smoke menthol and four times as likely to smoke full revenue menthol compared to non-Blacks'.[78]

Other populations: young people, women and Asians

Although the preponderance of menthol usage among African–American smokers is widely known and important, most menthol cigarettes are smoked by non-black populations. B&W's 1993 study found that although 72.3% of black smokers used menthol compared to 25.3% of non-black smokers, the total menthol market was 73.5% non-black and only 26.4% black.[78]

A 1983 study in the Lorillard collection on its Newport market found that:

> (t)he three leading menthol brands exhibit distinct user profiles. Newport smokers tend to be younger (18–21), single and less educated. (B&W's) Kool is smoked more by men, those over 25 years of age and those with even slightly lower incomes. (RJR's) Salem users are more often female, over age 25, more likely to be married, and more often employed…. Younger smokers (18–24) were most concerned with brand(s) smoked by family members and/or friends, and women were more frequently interested in a mild tasting product.[77]

Menthol styles are often lumped together by tobacco marketers in marketing language such as RJR's 'Coolness Segment'. Consumers in this segment 'are the youngest, the most economically disadvantaged, and the most likely to be in minority and ethnic groups',[50] who 'tend, more than average, to desire their brand of cigarettes to symbolize personal qualities such as youth; modern womanhood; romance; career orientation; and success'.[50] Recognising the brand-specific image consciousness of the segment, RJR stated, 'brands in the Coolness Segment gain little or no imagery directly from the fact of their mentholation. Rather, they are able to develop a wide diversity of images'.[50]

The three largest standalone menthol brands, Kool, Newport and Salem, have different brand identities in the minds of the manufacturers and the consumers. RJR noted in 1977 that Salem was characterised by 'worried' smokers' and smokers who are 'passive, feminine'.[79] RJR appears to have embraced this image in 1981 particularly with its Salem Slim Lights line extension, positioning it for consumers 'who desire a refreshing, low-tar cigarette with (a) stylish, unpretentious, feminine image'.[48] Though the menthol segment 'skews female' (female consumers are overrepresented in the segment),[80–82] B&W's Kool has a more masculine image than the other standalone brands. Lorillard noted in 1994 that 'Kool is viewed as a strong tasting, 'tough guy' cigarette'.[83]

Of the major menthol brands, Lorillard's Newport was 'the brand with the youngest demographics in the industry' according to a 1992 Lorillard report.[84] Newport's marketing strategy through much of the 1990s was to 'continue to improve Newport's appeal as the 'peer' brand among younger adult smokers'.[85 86] Part of the strategy was to 'develop an 'attack plan' to establish an offensive posture in the general market to more aggressively compete with Marlboro Menthol in select markets'.[87] 'General market', a term denoting the overall cigarette market, is contrasted here with 'urban center',[87] the term for young inner city African–Americans. This attack plan included marketing initiatives to 'continue to define 'Newport Pleasure' in a variety of different ways: social interactions, 'zany' fun, smoking situations, intimate moments, and refreshment'.[87]

DISCUSSION

Menthol cigarettes were originally marketed on a health platform, and health messages convinced consumers that menthol cigarettes were healthier for them than non-menthol cigarettes. Descriptors and colouring of cigarette packs communicate health information to consumers with no actual mention of health.[88] Associations of menthol with health continue to this day, although health assurance marketing messages for menthol cigarettes have become more oblique.

There is not a single menthol user image across all mentholated products. The overrepresentation of African–Americans in the menthol cigarette market is widely discussed in the academic literature,[70 72 89–91] but in sheer numbers, more non-African–American smokers use menthol. It is important to examine if and how menthol products have been marketed to various other populations (eg, women, other ethnic/racial groups as well as African–Americans). Women and girls, as well as some ethnic/racial groups, are important potential consumers for the tobacco industry in the US and abroad in nations where smoking rates in these groups are currently low. Similar to Virginia Slims' targeting of women in the second wave of the feminist movement in the 1960s and 1970s with a product superficially designed for them and an aggressive marketing campaign,[92] menthol products, particularly Kool and Newport, aggressively targeted young black populations with socially relevant messages of in-group identity.

Menthol is also targeted to young people and women in the US. Consistent with the current findings, research in 2010 showed that in addition to a higher prevalence of menthol use among African–American men and women, female smokers of all races used mentholated cigarettes at higher than male smokers.[93–95] The 'young female skew' of menthol is evident not only within the borders of the US, however; menthol is strongly represented among young women in Asian countries. Although different menthol brands present their own brand personalities (such as Kool being perceived largely as an African–American man's cigarette in the US), menthol in general is perceived to be for women, younger people and lighter smokers. There is some international agreement on this latter point. That menthol skews female is particularly evident in studies of

Asians, Pacific Islanders and Asian–Americans. In 1991, PM analysed the four Asian countries most important to PM Asia's growth: Japan, Hong Kong, Korea and Singapore, and noted that:

> Salem King Size and Salem Lights are attracting a high proportion of young adult smokers under 25, traditionally the stronghold of the Marlboro franchise. The Salem franchise is also attracting a high proportion of young adult women, in markets where the incidence of young adult female smokers is growing as women become more emancipated.[96]

A 1985 study for B&W on menthol in Japan showed that 'menthol cigarettes tended to be considered as 'fashionable'' and that 'those who smoke menthol brands are somewhat 'different' people, if they were not young women'.[97] The report advised that these aspects 'should be seriously considered by a marketer of menthol cigarettes since the primary target segment is younger women, that is, female students and office girls'.[97] Marketing that emphasises coolness, refreshing sensations, mildness, soothing taste, and youthful, fun-loving imagery contributes to these perceptions.

Further evidence that these results replicate outside the US borders, the perception of health benefits of menthol over non-menthol has become global. A 1991 study by ASI Market Research Inc. in Japan for PM noted that men in particular '(t)ried (menthol cigarettes) when not in good physical condition/when throat was feeling sore, and found them enjoyable'.[98] This report also noted that '(m)enthol cigarettes were also felt to be somehow better for the health than non-menthol cigarettes (ie, gentler on the throat)'.[98] Marketing Decision Research (Pacific) Ltd. found similar results in a 1992 study of Hong Kong for PM:

The 'cooling' and 'refreshing' abilities of menthol have the following advantages:

- make smokers feel comfortable
- less easy to cause throat discomfort…

can also elate one's spirit but is much better than strong stimulation of nicotine in full-flavored cigarettes. **It is relatively healthier.**[99] (Emphasis added.)

A 1979 study by PACC Information Systems showed B&W that in Kuwait:

(M)enthol cigarettes are thought to present many good aspects; they are usually…

– relieving
– help to expell (sic) catharr (inflammation of the mucous membranes)
– help in the case of colds…

(M)enthol cigarettes are thought to be less harmful to health than ordinary cigarettes.[100]

These documents demonstrate that what the US tobacco companies do affects consumers around the globe. Transnational tobacco companies based in the US study consumers home and abroad, and it is not always clear which study or studies a certain bit of insight about effective marketing efforts originally came from. The consumer studies in Asia and in Kuwait echoing those that were conducted in the US reflect an interesting finding that US tobacco company activities are relevant beyond the borders of the US. Including menthol in the US FDA's list of banned cigarette flavouring additives as a policy measure help may lay a foundation for positive public health effects beyond the US borders in the future as well.

Menthol products have been marketed as, and are often perceived as, milder than 'regular' cigarettes and therefore less of a threat to health, similar to perceptions of 'low-tar' and 'light' products. Whereas menthol users appear less interested in 'tar' than traditional health-concerned smokers who seek 'light' and 'ultralight' styles, the perception of health-protective effects of menthol makes menthol products function similarly to 'light' products. The products attract consumers who may otherwise quit smoking and provide psychological health assurances to continuing smokers.

Based upon the findings of this study, it appears the importance of menthol to the tobacco industry (and likely a reason that the industry opposes menthol's inclusion in the FDA's list of banned additives) is that menthol makes cigarettes easier and more palatable to smoke for new initiators and for established health-concerned smokers. Making cigarettes more attractive to new smokers and less desirable to quit among established smokers contributes to the incidence of tobacco-related diseases; menthol should be included on the list of banned additives.

What this paper adds

- Marketing for menthol cigarettes targets specific populations in the US, such as African–Americans. Less is known about what specific messages are communicated in marketing for different populations or about how consumers perceive messages in menthol cigarette marketing.
- Menthol cigarettes were marketed as, and are perceived by consumers to be, healthier than non-menthol cigarettes. Additionally, menthol marketing targeting African–Americans, young people and women is perceived by these groups to signal social group belonging.
- Menthol consumers (new initiators and established health-concerned smokers) believe that menthol makes cigarettes easier and more palatable to smoke.

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Brief Report

Targeted Advertising, Promotion, and Price For Menthol Cigarettes in California High School Neighborhoods

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Abstract

Objectives: To describe advertising, promotions, and pack prices for the leading brands of menthol and nonmenthol cigarettes near California high schools and to examine their associations with school and neighborhood demographics.

Methods: In stores (n = 407) within walking distance (0.8 km [1/2 mile]) of California high schools (n = 91), trained observers counted ads for menthol and nonmenthol cigarettes and collected data about promotions and prices for Newport and Marlboro, the leading brand in each category. Multilevel modeling examined the proportion of all cigarette advertising for any menthol brand, the proportion of stores with sales promotions, and the lowest advertised pack price in relation to store types and school/neighborhood demographics.

Results: For each 10 percentage point increase in the proportion of Black students, the proportion of menthol advertising increased by 5.9 percentage points (e.g., from an average of 25.7%–31.6%), the odds of a Newport promotion were 50% higher (95% CI = 1.01, 2.22), and the cost of Newport was 12 cents lower (95% CI = −0.18, −0.06). By comparison, the odds of a promotion and the price for Marlboro, the leading brand of nonmenthol cigarettes, were unrelated to any school or neighborhood demographics.

Conclusions: In high school neighborhoods, targeted advertising exposes Blacks to more promotions and lower prices for the leading brand of menthol cigarettes. This evidence contradicts the manufacturer's claims that the availability of its promotions is not based on race/ethnicity. It also highlights the need for tobacco control policies that would limit disparities in exposure to retail marketing for cigarettes.

Introduction

Although more adolescents smoke nonmenthol than menthol cigarettes, preference for menthol cigarettes among teenage smokers in the United States increased from 43.4% in 2004 to 48.3% in 2008 (Caraballo & Asman, 2011). When annual surveys were combined over the five-year period, more Black smokers (ages 12–17) preferred menthols (71.9%) than Hispanic smokers (47.0%) and non-Hispanic Whites (41.0%). Newport (manufactured by Lorillard, Inc.) has been the most popular menthol brand since 1993, and its share of the total U.S. cigarette market was 9.8% in 2009 (Altria Client Services, 2010). The brand is distinctly more popular with younger smokers: In 2005, 23.2% of adolescent smokers (ages 12–17) and 17.8% of young adult smokers (ages 18–25) smoked Newport, but only 8.7% of older smokers preferred it (Office of Applied Studies, 2007). Newport is the most popular cigarette brand among Black smokers of all ages and second to Marlboro as the most popular brand among adolescent smokers (Tobacco Products Scientific Advisory Committee, 2011).

Tobacco industry documents provide ample evidence of efforts to target youth and Blacks with marketing for menthol cigarettes (Anderson, 2011; Hafez & Ling, 2006; Johnson et al., 2008; Yerger, Przewoznik, & Malone, 2007). For example, Brown & Williamson, a manufacturer of almost exclusively menthol cigarettes, placed a greater quantity of interior and exterior signs in so-called "focus" communities or stores—predominately low-income, Black areas that were identified as being critical to increasing market share (Cruz, Wright, & Crawford, 2010). Corroborating evidence is apparent in three studies that observed a disproportionate concentration of outdoor or storefront advertising for menthol cigarettes in predominantly Black neighborhoods of Boston, MA (Laws, Whitman, Bowser, & Krech, 2002; Pucci, Joseph, & Siegel, 1998; Seidenberg, Caughey, Rees, & Connolly, 2010). However, the extent to which selectively targeted advertising translates into a greater availability of promotions and lower prices for menthol cigarettes has received little attention.

Two previous studies examined promotions and prices for menthol and nonmenthol cigarettes by area demographics. The presence of promotion and the lowest advertised pack price for Newport and Marlboro were recorded annually in a representative sample of U.S. tobacco retailers (Ruel et al., 2004). Over time, a

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larger increase in the proportion of stores with promotion was observed for Newport (from 25% in 2000 to 44% in 2002) than for Marlboro (from 42% to 49%). Although an increase of Newport promotions in urban areas is consistent with an effort to target low-income and racial/ethnic minority residents, the demographic analysis was limited to type of locale (urban, suburban, and town, rural) and regions (West, Midwest, South, and Northeast). A different study purchased single packs of menthol and nonmenthol varieties of the same (unidentified) brand from a random sample of Minneapolis convenience stores (Toomey, Chen, Forster, Van Coevering, & Lenk, 2009). Menthol price was not correlated with the proportions of non-White residents and youth in the census tracts where the stores were located; nonmenthol price was positively correlated with the proportion of non-White residents and negatively correlated with the proportion of youth. The proportion of stores with a price promotion was not reported, and the use of single-pack purchases would miss any influence of multipack discounts on price. Moreover, neither study examined menthol promotions and price in relation to neighborhood demographics for Blacks, who are a primary target of menthol marketing (Gardiner, 2004; Unger, Allen, Leonard, Wenten, & Cruz, 2010) and who are more likely than other smokers to report using promotional offers (White, White, Freeman, Gilpin, & Pierce, 2006).

To remedy these concerns, we conducted a secondary analysis of retail cigarette marketing near a random sample of California high schools (Henriksen et al., 2008). This report extends the research about targeted marketing for menthol cigarettes in two ways. It examines the availability of promotions as well as the price for menthol and nonmenthol cigarettes as a function of neighborhood demographics for Blacks and youth. It also focuses on school neighborhoods where adolescents' exposure to retail cigarette marketing has been shown to promote smoking uptake (Henriksen, Schleicher, Feighery, & Fortmann, 2010; Slater, Chaloupka, Wakefield, Johnston, & O'Malley, 2007).

Methods

Of the 156 randomly selected schools that were invited to participate in the 2005–2006 California Student Tobacco Survey, 135 schools that agreed to be surveyed were eligible for an ancillary study about retail tobacco marketing in school neighborhoods. Using the state's tobacco retailer licensing records and ArcGIS (v9.3, ESRI, 2009), we identified 726 tobacco retailers within 0.8 km (1/2 mile; straight-line distance) of the surveyed schools. The 44 schools without any tobacco retailers within this distance were excluded from the analytic sample ($n = 91$).

In school neighborhoods with six or fewer tobacco retailers, we observed all of them; in 31 neighborhoods, we randomly selected 6 or 50%, whichever yielded the larger number. Trained coders completed observations in 407 stores ($M = 4.5$ per school neighborhood, $SD = 2.9$, completion rate = 94.9%) between September and October 2006. Because business classification data were not available with the retailer licensing records, the coders used standard definitions to categorize stores according to type: convenience with or without gas, gas station (only), liquor, small market, supermarket, pharmacy/drug store, and other. All cigarette advertisements were counted and categorized by flavor (menthol, nonmenthol, or both) and by brand (Marlboro, Newport, Camel, and other). Newport was an exclusively menthol brand at the time these data were collected. For the menthol and nonmenthol variety of each brand category (Marlboro, Newport, Camel, and other), coders noted the presence of any advertised promotion (multipack discount, other discount, or gift with purchase). Because collecting price data for the menthol and nonmenthol varieties of the three major brands was cost prohibitive, coders recorded the lowest pack price for Marlboro (nonmenthol), Newport (menthol), and Camel (nonmenthol). Coders indicated whether the price was discounted (e.g., a multipack discount or other sale price) and recorded the number of packs received for the advertised price. Prices for cartons were not recorded because the majority of smokers, particularly menthol smokers, purchase cigarettes by the pack (Fernander, Rayens, Zhang, & Adkins, 2010).

For analyses, we computed menthol share of voice for each store, defined as the proportion of all cigarette advertisements in a store that featured any menthol variety. Observed prices were converted to the price of a single pack before sales tax. For the current study, analyses of brand-specific data regarding advertised promotions and prices focused exclusively on Newport and Marlboro, the two most popular cigarette brands among U.S. youth.

To account for clustering of stores within school neighborhoods, multilevel models (HLM6.0) estimated each of the following outcomes as a function of neighborhood demographics: menthol share of voice, the presence of an advertised promotion for Newport and Marlboro (nonmenthol and menthol), as well as the lowest pack price for Newport and Marlboro (nonmenthol only). Enrollment data described the proportions of racial/ethnic groups and the proportion of students eligible to receive free or reduced-price lunches, a common measure of school socioeconomic status (Education Data Partnership, 2010). We used enrollment data for race/ethnicity because schools were the primary sampling unit. In addition, our previous research observed high correlations between those variables measured by school enrollment data and by census data for the ½-mile radius from the school (Henriksen et al., 2008). The total number of tobacco retailers in each school neighborhood was obtained from the geocoded licensing data. Neighborhood data for population density (residents per square mile) and proportion of residents ages 10–17 were obtained from Census 2000 and weighted in proportion to tract area. All multilevel models included a random intercept and adjusted for store type, treating convenience stores as the reference category because they were the most prevalent store type. All numeric predictors were centered at the mean. The predictors that represent percentages were scaled to equate a one-unit increase with an increase of 10 percentage points; population density was scaled to represent an increase of 1,000 residents per square mile. Linear outcome multilevel models were estimated using restricted maximum likelihood and robust *SE*s. For models of dichotomous outcomes, such as the presence of an advertised promotion for specific brands, hierarchical generalized linear population average models were estimated.

Results

Table 1 describes the characteristics of stores and schools/neighborhoods that comprised the study sample. The stores contained an average of 25.4 ($SD = 26.1$) cigarette advertisements, and the average share of voice for menthol was 25.7%

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Table 1. Sample Description and Associations of Cigarette Advertising With School/Neighborhood Demographics: California High School Neighborhoods, 2006

	Descriptive measures		Menthol advertising share of voice	Store advertised promotional offer	
			(% of ads for menthol)	Newport (menthol)	Marlboro (nonmenthol)
	% or *M*	*SD*	Coef (95% *CI*)	Odds (95% *CI*)	Odds (95% *CI*)
Level 1: stores (*n* = 407)					
Intercept			27.2** (24.4, 30.0)	0.7 (0.5, 1.0)	22.5** (10.1, 50.1)
Store type					
Convenience	31%		Ref	Ref	Ref
Gas only	4%		−2.1 (−11.5, 7.3)	0.9 (0.3, 2.8)	0.2* (0.0, 0.9)
Liquor	14%		3.5 (−2.1, 9.1)	0.6 (0.3, 1.3)	0.4 (0.1, 1.2)
Other	5%		−8.1** (−14.7, −1.5)	0.3 (0.1, 1.0)	0.1** (0.0, 0.3)
Small market	27%		−4.1 (−8.9, 0.7)	0.3** (0.1, 0.5)	0.1** (0.0, 0.2)
Supermarket/drug store	20%		−7.3** (−11.5, −3.1)	0.2** (0.1, 0.5)	0.1** (0.1, 0.3)
Level 2: schools (*n* = 91)					
School enrollment					
Non-Hispanic White, %	35%	25%			
Black, %	7%	7%	5.9* (0.9, 10.9)	1.5* (1.0, 2.2)	1.4 (0.9, 2.1)
Asian/PI, %	13%	14%	−1.5 (−3.5, 0.5)	1.0 (0.8, 1.3)	1.0 (0.7, 1.3)
Hispanic, %	39%	26%	0.0 (−1.6, 1.6)	1.0 (0.8, 1.2)	1.0 (0.8, 1.3)
Other, %	7%	6%	−5.7** (−8.9, −2.5)	0.8 (0.4, 1.3)	1.1 (0.6, 1.8)
Free/reduced price meals, %	34%	24%	−1.8** (−3.0, −0.6)	1.0 (0.8, 1.2)	1.0 (0.8, 1.2)
School neighborhood					
Residents ages 10–17, %	12%	3%	11.6* (1.7, 21.6)	5.3* (1.5, 18.7)	0.9 (0.2, 3.6)
Population density	7454	4609	0.8* (0.0, 1.6)	1.0 (0.9, 1.1)	1.0 (0.9, 1.1)
Number of tobacco retailers	8	7	0.0 (−0.4, 0.4)	1.0 (0.9, 1.1)	1.0 (0.9, 1.0)

Note. Estimates for promotional offers by brand were derived from hierarchical generalized linear models. *CI* = confidence interval.
*$p < .05$; **$p < .01$.

(*SD* = 20.1). For each 10 percentage point increase in the proportion of Black students at the nearby high school, the menthol share of voice increased by 5.9 percentage points (e.g., from an average of 25.7% to 31.6%; see Table 1). The menthol share of voice increased by 11.6 percentage points with each 10 percentage point increase in the proportion of neighborhood residents ages 10–17 years.

The proportion of observed stores that advertised a promotional offer was 27.0% for Newport, 75.2% for Marlboro (nonmenthol), and 51.4% for Marlboro Menthol. For each 10 percentage point increase in the proportion of Black students, the odds of a store advertising a Newport promotion were 1.5 times greater (see Table 2). For each 10 percentage point increase in the proportion of residents ages 10–17 years, the odds of a Newport promotion were 5.3 times greater. Unlike Newport, the odds of a store advertising a Marlboro (non-menthol) promotion were unrelated to any school/neighborhood demographic. Similarly, the odds of a Marlboro Menthol promotion were unrelated to any school neighborhood demographics (results for this subbrand are not shown).

The average pack price for Newport was $4.37 (*SD* = 0.51, *n* = 320 stores). The average estimated discount for Newport was $0.52 (95% *CI* = $0.42–$0.62; see Table 2). Adjusting for store type and other school neighborhood demographics, the price of Newport decreased 12 cents for each 10 percentage point increase in the proportion of Black students at the nearby high school. The average pack price for Marlboro was $3.99 (*SD* = 0.49, *n* = 388 stores). The average estimated discount was $0.39 (95% *CI* =$0.27–$0.51; see Table 2). Unlike Newport, the price of Marlboro was unrelated to any school or neighborhood demographics.

In an ancillary analysis, we examined whether the amount of a Newport discount varied across school neighborhoods. However, the variance estimate for this slope was not significantly different from zero. Although the availability of a promotion for Newport increased with the proportion of African-African students, the amount of the discount did not.

Discussion

This study is the first we know of to examine the availability of promotions as well as the price of menthol cigarettes by neighborhood demographics. The findings suggest that a disproportionate quantity of menthol advertising and a greater availability of promotions for menthol brands translate into lower prices for menthol cigarettes near California high schools with more Black students. The current study also provides further evidence that menthol marketing is concentrated in Black neighborhoods. Targeted advertising in school neighborhoods is particularly concerning because exposure to retail tobacco marketing is a risk factor for

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Table 2. Lowest Pack Price, by Brand in Relation to Store Type and Neighborhood Demographics: California High School Neighborhoods, 2006

	Newport (menthol)	Marlboro (nonmenthol)
	Coef (95% *CI*)	Coef (95% *CI*)
Level 1	($n = 318$)	($n = 387$)
Intercept	4.47** (4.37, 4.57)	4.21** (4.07, 4.35)
Store type		
Convenience	Ref	Ref
Gas only	−0.24* (−0.46, −0.02)	−0.08 (−0.34, 0.18)
Liquor	0.04 (−0.10, 0.18)	0.07 (−0.03, 0.17)
Other	−0.20 (−0.42, 0.02)	−0.16 (−0.40, 0.08)
Small market	−0.04 (−0.16, 0.08)	0.10 (−0.02, 0.22)
Supermarket/drug store	0.34** (0.20, 0.48)	0.24** (0.12, 0.36)
Price was discounted	−0.52** (−0.62, −0.42)	−0.39** (−0.51, −0.27)
Level 2	($n = 88$)	($n = 90$)
School enrollment		
Non-Hispanic White, %		
Black, %	−0.12** (−0.18, −0.06)	−0.01 (−0.09, 0.07)
Asian/PI, %	0.01 (−0.03, 0.05)	−0.01 (−0.05, 0.03)
Hispanic, %	−0.03 (−0.07, 0.01)	−0.03 (−0.07, 0.01)
Other, %	−0.01 (−0.07, 0.05)	0.04 (−0.04, 0.12)
Free/reduced price meals, %	0.00 (−0.04, 0.04)	0.00 (−0.04, 0.04)
School neighborhood		
Residents ages 10–17, %	−0.07 (−0.29, 0.15)	−0.08 (−0.34, 0.18)
Population density	0.00 (−0.02, 0.02)	0.02 (0.00, 0.04)
Number of tobacco retailers	0.01* (0.01, 0.01)	0.01 (−0.02, 0.02)

Note. Pack price before sales tax for single or multi-pack offer (excluded cartons); *CI* = confidence interval.
$^{*}p < .05$; $^{**}p < .01$.

smoking uptake and influences high school smokers' brand choice (Wakefield, Ruel, Chaloupka, Slater, & Kaufman, 2002).

The observation of higher prices for Newport than Marlboro is consistent with other studies that observed higher prices for menthol than for nonmenthol cigarettes (Tobacco Products Scientific Advisory Committee, 2011) and with Lorillard's statement that its Newport brand maintains the highest average retail price of major U.S. cigarette brands (Lorillard Tobacco Company, 2010; Ruel et al., 2004). One finding that is unique to this study is that Newport cigarettes cost less near high schools with more Black students, a pattern that was not observed for Marlboro.

According to Lorillard's submission to the Food and Drug Administration (Lorillard Tobacco Company, 2010), the company offers retail promotions for Newport in 27 states. Within a given state, approximately 34% of all retailers that sell cigarettes have a promotional agreement with Lorillard, and retailers with such promotions are typically located in areas where there is relatively strong Newport or menthol category sales. This study observed at least one Newport promotion in 27% of tobacco retailers near California high schools. However, the greater availability of Newport promotions and lower prices for the brand near schools with more Black students contradict the manufacturer's statement that "the availability and amount of Lorillard's retail price promotions are not, in any way, based on ethnicity" (Lorillard Tobacco Company, 2010, p. 39).

A limitation of studying prices for the leading brands of menthol and nonmenthol cigarettes is that these reflect promotional strategies that are determined by different manufacturers. Future research should examine prices for menthol and nonmenthol versions of multiple brands in order to determine whether more than one tobacco company charges less for menthol cigarettes in Black neighborhoods. This study was also limited to California high school neighborhoods, although we can think of no a priori reason why the observed associations would differ in other states. Research is needed to determine whether the observed patterns generalize to stores located further from schools or whether menthol marketing targets stores near high schools. In addition, these cross-sectional data cannot address how changes in retail marketing strategies contributed to recent increases in market share for some menthol brands (Tobacco Products Scientific Advisory Committee, 2011).

In California, the proportion of stores that advertised a promotion for cigarettes has increased over time and more so in neighborhoods with a larger proportion of Black residents (Feighery, Schleicher, Cruz, & Unger, 2008). Given that Black smokers and youth are among the most price-sensitive groups (Hyland et al., 2005) and that menthol smokers are more likely than others to take advantage of promotional offers (White et al., 2006), further investigation of the disparities in promotions and price for menthol and nonmenthol cigarettes is warranted. Evidence about the environmental (in)justice of menthol marketing should inform the Food and Drug Administration's regulation about the use of menthol as a characterizing flavor in cigarettes.

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Declaration of Interests

None declared.

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Smoking Control

Storefront Cigarette Advertising Differs by Community Demographic Profile

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Abstract

Purpose. *Tobacco manufacturers have targeted youth and ethnic/racial minorities with tailored advertising. Less is known about how characteristics of storefront tobacco advertisements, such as location, position, size, and content, are used to appeal to demographic subgroups.*

Design. *The occurrence and characteristics of storefront cigarette advertising were observed for all licensed tobacco retailers in two defined communities.*

Setting. *Measures were taken in two Boston, Massachusetts, area urban communities: a low-income, minority community and a high-income, nonminority community.*

Subjects. *No human subjects were involved in this study.*

Measures. *Advertisement position (attached or separated from storefront), size (small, medium, or large), mentholation, and price were recorded. Geographic coordinates of tobacco retailers and schools were mapped using ArcGIS 9.2.*

Analysis. *Differences between the communities in advertisement number and characteristics were assessed using bivariate analyses. Logistic regression was used to ascertain the odds of specific advertising features occurring in the low-income/minority community.*

Results. *The low-income/minority community had more tobacco retailers, and advertisements were more likely to be larger, promote menthol products, have a lower mean advertised price, and occur within 1000 feet of a school.*

Conclusion. *Storefront cigarette advertising characteristics that increase exposure and promote youth initiation were more prominent in a low-income/minority community. The findings emphasize the need for more effective regulation of storefront tobacco advertising. (Am J Health Promot 2010;24[6]:e26–e31.)*

Key Words: Tobacco, Health Disparities, Youth, Advertising, Prevention Research. Manuscript format: research; Research purpose: descriptive; Study design: quasi-experimental; Outcome measure: tobacco industry messaging; Setting: local community; Health focus: smoking control; Strategy: policy; Target population age: youth; Target population circumstances: education/income level, race/ethnicity

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PURPOSE

Everyday an estimated 3600 American youth commence smoking, 30% of whom become daily smokers.[1] Cigarette advertising influences youth perceptions of the pervasiveness and image of smoking[2] and has been found to be associated with smoking uptake among youth.[3,4] Moreover, research has shown that youth are highly exposed to cigarette advertising[5,6] and that youth prefer the most heavily advertised brands.[7,8]

As part of the 1998 Master Settlement Agreement (MSA) between the state Attorney Generals and the major cigarette companies, cigarette makers agreed to not directly or indirectly target youth in their advertising and marketing efforts. The MSA prohibits the depiction of cartoons in cigarette advertising, limits event sponsorship, and restricts the location and size of cigarette advertising. Specifically, the MSA bans cigarette billboard advertising, as well as promotions on or around public transit, stadiums, arenas, shopping malls, and video arcades. Thus, outdoor cigarette advertising is prohibited except on retailer property, on which individual advertising units are limited to 14 square feet.[9] Field surveys have documented increased numbers of exterior and interior retail tobacco advertising after implementation of the MSA.[10,11] Such changes suggest that tobacco companies have been adapting to MSA advertising constraints by increasing marketing efforts in retail outlets.

There has been substantial documentation of targeting of subgroups by the tobacco industry, particularly youth[12] and African-Americans.[13,14] Storefront cigarette advertising, which consists of externally visible advertisements placed on the retailer storefront and advertisements separated from storefronts and located on retailer property, may be one important strategy by which the industry promotes tobacco use in a manner designed to selectively reach specific populations. Since the MSA, increased retail tobac-

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co advertising has been found in African-American communities in both California[15] and Massachusetts.[16] Compared with white Americans (23.5%), a greater percentage of the African-American population is under 18 years (31.4%).[17] Therefore, youth populations may be greater in African-American communities. The enhanced presence of cigarette advertising in African-American communities raises concerns about youth exposure and menthol cigarette promotion. Historically, menthol cigarette advertising has been targeted toward African-Americans,[13,14] and menthol cigarettes have been implicated in facilitating smoking initiation among youth.[18] Moreover, tobacco advertising has been found to be more heavily displayed in areas of lower socioeconomic status,[16] where smoking prevalence is often higher.[19]

Although previous surveys have documented the quantity of storefront tobacco advertising,[10,11,15] relatively little is known about how specific characteristics of tobacco advertisements, such as their location, position, size, and content, are used to appeal to youth and minority populations. Earlier studies have reported that tobacco advertising located within 1000 feet of schools may provide an enhanced opportunity for exposure to youth.[16,20] Advertisements that are positioned at eye level for younger persons also may enhance opportunity for youth exposure.[11,16,] The size of an advertisement may affect the visibility of the messaging and the number of individuals exposed (e.g., a small sticker vs. a large poster). The significance of advertisement size has received limited attention. Glanz et al.[8] weighted outdoor cigarette advertising units by size to reveal Kool as the most advertised brand with and without adjusting for the size of all advertisements. Finally, advertisements may include content that enhances its impact on youth. The use of models who match the racial or ethnic profile of the neighborhood in which the advertisement is found may be one such strategy.[16] Although price has been demonstrated to be a significant factor related to youth smoking,[21] this potentially important content feature has not been well documented in storefront advertising and has been previously reported in only one known study.[22] Actual retail prices and indoor price promotions have been more commonly observed.[11,15,23]

The present study aimed to assess the features of storefront cigarette advertising that may be associated with youth exposure and smoking initiation a decade after the MSA. We hypothesized that advertisement features (location, position, size, and content) that may influence youth smoking would be more pervasive in a predominately low-income minority community compared with a predominantly high-income nonminority community.

METHODS

Study Design and Sample

A cross-sectional field survey of storefront cigarette advertising was conducted in two Massachusetts communities located within the greater Boston, Massachusetts, urban area: Dorchester and Brookline. The two communities were chosen because they share close proximity but have contrasting demographic composition and were each easily accessible by the research team. According to the 2000 U.S. Census,[24] Dorchester has a large African-American population (50.1%), with 21.7% of its residents living below the federal poverty line. By contrast, Brookline has a much smaller African-American population (2.7%) and 9.3% of its residents living below the federal poverty line (Table 1).

Tobacco retailer listings for Brookline and Dorchester were obtained from the Massachusetts Department of Public Health (MDPH) and City of Boston Public Health Commission (BPHC), respectively. Whereas MDPH provided a listing of all tobacco retailers within the town of Brookline, BPHC provided retailer listings for individual zip codes. Using the United States Postal Service Web site (http://www.usps.com), four zip codes were listed for Dorchester, Massachusetts, and retailer listings were obtained for each. A total of 43 registered tobacco retailers in Brookline and 196 in Dorchester were identified from these sources. According to the 2000 U.S. Census,[24] the populations of Brookline and Dorchester were 57,107 and 134,004, respectively (Table 1). Because of the discrepancy in the population of each community, Dorchester was limited to a single zip code, 02124, from the denominator of four zip codes. We selected the 02124 zip code of Dorchester for its similar population (50,781) to that of Brookline (57,107). (The three remaining zip codes in Dorchester [02122, 02121, and 02125] each had a population considerably smaller than Brookline's.) The 02124 zip code provided a good representation of the whole of Dorchester in terms of: racial/ethic characteristics, percent of population older than 18 years, median income, percent of population below the poverty line, and highest educational level reached (Table 1). The selection of one Dorchester zip code eliminated the large discrepancy in the number of tobacco retailers within the two communities—59 registered tobacco retailers were identified in Dorchester (02124) compared with 43 in Brookline—while continuing to emphasize the marked differences in minority and socioeconomic profile of the two communities.

Measures

Each identified tobacco retailer was visited by one of two members of the research team (A.B.S. and R.W.C.) from November 2007 to February 2008, and all outdoor retail cigarette advertising units were quantified and described using a standardized survey instrument. The survey was modeled after the Massachusetts Operation Storefront survey[20] but modified to meet additional aims of this study. Advertising for smokeless tobacco, cigars, and little cigars were excluded from this report because of low prevalence of advertising of these products. For every externally visible cigarette advertisement, position (attached to retailer or separated from storefront and located on retailer property), size (small: not exceeding an 8.5×11 inch [.06 m^2] area; large: 2×3 feet [.56 m^2] area or larger; and medium: sized between small and large), mentholation, and advertised price were recorded. Inter-rater reliability was validated using independent rater assessments of a mutual 10% (N = 10) sample of tobacco retailers. Advertisement number and individual feature characteristics were scored and compared. A high degree of inter-rater

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Table 1
Demographic Characteristics* of Brookline and Four Zip Codes of Dorchester

	Brookline	02124†	02122†‡	02121†‡	02125†‡
Population	57,107	50,781	24,548	25,057	33,618
White	81.1%	21.4%	41.8%	4.9%	35.1%
Black or African American	2.7%	59.9%	27.7%	77.3%	31.3%
Hispanic or Latino	3.5%	12.6%	10.3%	19.0%	16.3%
≥18 years	83.4%	69.4%	72.5%	65.1%	72.4%
Median family income	$92,993	$38,203	$40,874	$28,735	$36,195
Individuals below poverty level	9.3%	21.%	14.1%	24.1%	20.1%
Bachelor's degree or higher	76.9%	17.4%	17.7%	12.2%	19.1%
Tobacco licenses, no.	43	59	58	32	47

* Based on U.S. 2000 Census.
† Dorchester.
‡ Excluded from survey.

agreement was observed across all measures (Cohen's $\kappa \geq .886$).

Using ArcGIS 9.2, the geographic coordinates of all tobacco retailers were mapped. Primary and secondary school locations were plotted on the same map. Schools were identified using Geographic Names Information System and compiled by the makers of the mapping software (last updated January 2007). Geometric buffers of 1000 feet were created around each mapped school and tobacco retailers located within 1000 feet of any school were thus identified.

A two-part analytic approach was employed. Bivariate analyses were used initially to assess differences in advertisement number and characteristics between the two communities. Mean advertised cigarette pack price differences were examined using *t*-tests. Fisher's exact test and χ^2 tests were used to test for community-level differences between remaining advertisement features. These analyses were repeated using a weighting for size of advertisement, based on the assumption that larger tobacco advertisements may have a greater visual impact. Following the strategy developed by Glanz et al.,[8] small, medium, and large advertisements were assigned weighting factors of one, two, and three, respectively. Logistic regression analyses were then conducted to ascertain the odds of specific advertising features occurring in Dorchester, compared with Brookline, while simultaneously controlling for other advertising features.

RESULTS

The two communities observed differed in minority status, income, education, and age of the population (Table 1). Of the 102 registered tobacco retailers in Brookline and Dorchester, four were no longer in business or were not located at the listed addresses. Observations were completed for the remaining 98 retailers: 42 in Brookline and 56 in Dorchester. There was an overall significant difference in the proportion of store types found in each community ($\chi^2(5) = 13.3$; $p = .02$), with a greater number of convenience stores observed in Dorchester (Table 2). Ranging from 0 to 32 storefront cigarette advertisements per retailer, 403 individual cigarette advertisements were identified within the two communities. These included stickers, placards, posters, illuminated signs, and price listings.

Although tobacco retailers located in Dorchester represented 57% (56/98) of all retailers visited, they displayed 76% (308/403) of the storefront cigarette advertising units within the two communities. The percentage of retailers displaying storefront cigarette advertisements was also significantly higher in Dorchester (86%) than Brookline (43%) ($p < .001$). However, there was no statistical difference in the mean number of storefront cigarette advertisements per retailer between the two communities among retailers that displayed tobacco advertising (Dorchester and Brookline means, 6.6 and 5.3, respectively; $p = .444$) (Table 2).

Differences in size and other characteristics of storefront cigarette advertising were also found between the two communities. Compared with Brookline, Dorchester had a greater proportion of large ($p < .001$) and medium advertisements ($p = .010$), as well as an increased proportion of menthol brand advertising ($p < .001$). Moreover, a greater proportion of cigarette advertisements in Dorchester displayed a price ($p = .001$), and the mean advertised cigarette pack price was $0.39 less in Dorchester than in Brookline ($p < .001$). Although a greater proportion of detached advertisements and advertisements within 1000 feet of any school were found in Dorchester, these differences were not significant (Table 2).

Using the Glanz et al.[8] weighting factor, advertising characteristics were compared between the two communities weighting each advertisement by size. The weighted analysis found that the proportion of advertisements within 1000 feet of schools ($p = .006$) and detached advertisements ($p = .004$) were significantly greater in Dorchester. Dorchester retailers also showed a significantly greater proportion of menthol advertisements ($p < .001$) and advertisements featuring a price ($p < .001$), after weighting.

Factors associated with Dorchester cigarette advertising (compared with Brookline) were explored using logis-

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Table 2
Number and Characteristics of Storefront Cigarette Advertisements by Community

	Brookline	Dorchester*	p
Retailers, No.	42	56	
Retailer type, No.			0.02
Alcohol (wine/liquor)	9 (21.4%)	6 (10.7%)	
Convenience store	7 (16.7%)	27 (48.2%)	
Gas	8 (19.0%)	6 (10.7%)	
Grocery	7 (16.7%)	10 (17.9%)	
Pharmacy	7 (16.7%)	6 (10.7%)	
Other	4 (9.5%)	1 (1.8%)	
Total ads, No.	95	308	
Retailers with ads, No.	18 (42.9%)	48 (85.7%)	<0.001
Mean ads/retailer†	5.3	6.6	0.444
Location			
Ads within 1000-foot radius of schools, No.	26 (27.4%)	104 (33.8%)	0.244
Position			
Detached ads, No.	8 (8.4%)	50 (16.2%)	0.058
Size			
Small ads	54 (56.8%)	62 (20.1%)	<0.001
Medium ads	39 (41.1%)	173 (56.2%)	0.010
Large ads	2 (2.1%)	73 (23.7%)	<0.001
Content			
Menthol ads, no.	17 (17.9%)	166 (53.9%)	<0.001
Ads with price, no.	39 (41.1%)	185 (60.1%)	0.001
Mean advertised pack price‡	$4.94	$4.55	<0.001

* Limited to 02124 zip code.
† Means do not include retailers without advertisements.
‡ Limited to advertisements that displayed prices.

tic regression. Univariate analyses found that larger advertising units (medium and large), menthol brand advertisements, and advertisements displaying a price had, respectively, 4.42 (2.89–6.74), 5.36 (3.03–9.49), and 2.16 (1.35–3.45) greater odds of being found in Dorchester compared with Brookline (Table 3). After controlling for all other advertising characteristics, including the weighting of ad size described above, multivariate analyses revealed that advertisements located within 1000 feet of schools, larger advertisements, and menthol brand cigarette advertisements had 1.97 (1.09–3.56), 4.79 (2.83–8.11), and 4.99 (2.70–9.23) greater odds of being found in Dorchester compared with Brookline, respectively (Table 3).

Table 3
Odds of Tobacco Advertising Characteristic Being Found in Dorchester (02124) Compared With Brookline*

	Univariate Analysis OR (95% CI)	Multivariate Analysis OR (95% CI)
Within 1000 feet of schools	1.35 (0.81–2.25)	1.97 (1.09–3.56)
Detached from storefront	2.11 (0.96–4.62)	0.59 (0.22–1.57)
Size†	4.42 (2.89–6.74)	4.79 (2.83–8.11)
Menthol	5.36 (3.03–9.49)	4.99 (2.70–9.23)
Price presence	2.16 (1.35–3.45)	1.33 (0.76–2.33)

* CI indicates confidence intervals; and OR, odds ratio.
† Large- and medium-sized advertisements.

DISCUSSION

The characteristics of storefront cigarette advertising in the minority, low-income community of Dorchester (02124) were compared with the predominantly white, high-income community of Brookline. In Dorchester, a greater proportion of cigarette advertising was found and a significantly greater percentage of retailers displayed storefront cigarette advertising, compared with Brookline. Greater proportions of advertisements in Dorchester were larger, promoted menthol products, included a price, and featured a lower mean price, compared with Brookline. Such advertising features may appeal to youth. When advertisements were weighted by size, these differences in advertisement characteristics became more pronounced. Strikingly, after controlling for other advertisement characteristics, advertisements in Dorchester were almost twice as likely to be located within 1000 feet of a school, compared with Brookline. The data suggest that tobacco companies, with the implicit cooperation of retailers, may be using advertising features not explicitly banned under the MSA to promote tobacco use among youth and persons of minority race and low-income background.

The dissimilarities in storefront cigarette advertising raise serious concerns for public health protection and promotion. Current trends reveal that African-Americans are disproportionately affected more by tobacco-related morbidity and mortality compared with white Americans.[25] In addition, census data reveal that Dorchester has a larger proportion of residents under 18 years than Brookline (Table 1). This potential for greater exposure to youth, combined with use of advertisement features that are known to appeal to youth, may give rise to a disproportionately greater influence of tobacco advertising on youth in Dorchester, compared with Brookline.

The findings of more cigarette advertising and menthol cigarette advertising in Dorchester are consistent with previous advertising surveys conducted

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both before and after the MSA. Prior research has documented higher concentrations of tobacco billboards[26,27] and greater retail advertising[15,16] in minority and low-income communities. Pucci et al.[16] also identified a higher percentage of menthol brand advertising (Newport, Kool, and Salem) in predominantly Latino and African-American communities compared with predominantly nonminority communities. In addition, a survey conducted prior to the MSA in Massachusetts found menthol advertising to be two to three times more likely to be located in minority communities.[20]

Detached advertisements were commonly placed in prominent locations such as sidewalks, attached to telephone poles, and in parking lots. These placements may enhance visibility of the advertisements to customers and passersby. Unweighted analysis did not show a difference in the proportion of cigarette advertisements that were detached between the two communities. However, after weighting the advertisements by size, a significantly greater proportion of larger detached advertisements were found in Dorchester. Because of the larger size and detached placement of these advertisements, opportunities of exposure may be greater for youth in Dorchester.

To the authors' knowledge, this is the second study to document outdoor cigarette advertisement size and the first to compare other advertising characteristics based on size.[8] The study assumed that larger advertisements have a greater visual impact than smaller advertisements, and secondary analyses were performed after weighting each advertisement by size. Under the advertising regulations promulgated by the MSA, advertisement size was an important restriction implemented to help curtail advertising to youth. However, more research is needed to better understand how cigarette advertisement size affects visibility and perception of the advertisement's messaging. This is only the second study known to the authors to document advertised cigarette prices in storefront advertising. Jason et al.[22] found that the percentage of storefront tobacco advertisements with prices decreased between 1999 and 2001 in 11 towns in Northern Illinois. The authors cited increased cigarette prices following the MSA as a possible explanation for this trend. This study found a greater percentage of storefront cigarette advertisements featuring prices in Dorchester and a lower mean advertised price in Dorchester, compared with Brookline. Residents of lower-income communities may be more sensitive to price promotions, which may partly explain the lower advertised prices and greater occurrence of displayed prices in Dorchester compared with Brookline. However, mean advertised prices may reflect differences in the advertising frequency of premium and discount brands rather than price discounting. Moreover, adjustments were not made for other economic factors that can affect price. Despite these caveats, advertised prices are likely to be seen by consumers and may play an important role in shaping purchasing attitudes and decisions.

Although we documented no advertising violations of the MSA, this study reveals a major weakness in the advertising restrictions outlined under the settlement. The MSA limits individual cigarette advertising units to 14 square feet yet sets no restriction on the total amount of cigarette advertising that can be displayed by a retailer. One retailer displayed a total of 32 branded cigarette advertisements, many placed with no space between adjacent advertisements. The combined total amount of cigarette advertising at this and many other tobacco retailers far exceeded 14 square feet. In the absence of restrictions on the total amount of cigarette advertising on retailer property, manufacturers may be able to selectively reach subgroups, such as youth and minorities, through placement of cigarette advertising with tailored characteristics in selected areas.

We present this study as an analysis of a limited geographic area, and there are limitations that prevent generalization to other communities. Because of its cross-sectional design, this study was able to capture the status of advertising only at one point in time. It is not known whether or how frequently storefront cigarette advertising within the two communities might change. Only further surveying of the same retailers at a later time can establish whether the advertising characteristics observed are stable over time. The decision to include only one zip code in Dorchester allowed comparisons of similarly sized populations but prevents generalizability to all of Dorchester or to other communities across the United States. Factors not measured in the current study may influence the content of storefront advertising, including population density (less dense areas may use larger ads to attract persons traveling by car), and children's exposure may be influenced by availability of transportation and whether the school attended is in the same community as the child's residence. Finally, only outdoor cigarette advertising was assessed in this study. Considerable advertising and promotions have been identified inside the premises of tobacco retailers[11,15] as well, which may enhance youth cigarette advertising exposure.

The Commonwealth of Massachusetts attempted to prohibit storefront advertising near schools and playgrounds in 1998 through a consumer protection regulation, but it was prevented by a legal challenge. Had such a restriction been implemented, cigarette advertising within 1000 feet of schools would not have been observed in this study (combined total of 130 branded cigarette advertisements). The recently enacted Family Smoking Prevention and Tobacco Control Act[28] provides the U.S. Food and Drug Administration (FDA) with the authority to regulate tobacco products, including a provision that bans cigarette advertising within 1000 feet of schools and playgrounds. The FDA will also require additional advertising restrictions, including the requirement that all retail cigarette advertisements consist only of black text on white background. Moreover, the Family Smoking Prevention and Tobacco Control Act will now allow states and local communities to adopt further restrictions on cigarette advertising and promotions that were previously preempted under the Federal Cigarette Labeling and Advertising Act. Cities such as Boston (which includes Dorchester) and Brookline now have the capacity to ''ban or restrict the time, place, and manner, *but not the content*, of the advertising or promotion

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of any cigarettes''[28] (emphasis added). This is an important step toward providing protection from targeted advertising to youth in minority and lower-income communities. However, because the present data suggest that the content of cigarette advertising, such as price, is tailored toward lower-income communities, we would also recommend that advertisement content be considered for regulatory restriction. More work is required to complete a comprehensive, evidence-based regulatory strategy for outdoor cigarette advertising that will restrict tobacco promotion aimed at youth and further denormalize the acceptance of smoking in American communities.

SO WHAT? Implications for Health Promotion Practitioners and Researchers

What is already known on this topic?
The tobacco industry has used storefront advertising to target youth and minority ethnic/racial groups. Little is known about how specific characteristics of tobacco advertisements, such as their location, position, size and content, are used to appeal to youth and minority populations.

What does this article add?
This paper describes a study of the presence and features of storefront cigarette advertising in two demographically contrasting communities. We present evidence that features of tobacco advertising are manipulated to attract youth or racial minority sub-groups, and these features are disproportionately evident in low income, minority communities.

What are the implications for health promotion practice or research?
Despite the broad protections from targeted advertising for youth that the 1998 Tobacco Master Settlement Agreement provides, storefront advertising is not included in this agreement. However, recent congressional approval providing the US Food and Drug Administration with regulatory authority of tobacco products permits further restrictions on tobacco marketing and may help curtail youth exposure to this form of cigarette advertising.

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The relationship of neighborhood demographic characteristics to point-of-sale tobacco advertising and marketing

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Objectives. Exposure to tobacco marketing has been associated with an increased likelihood that youth start smoking and may interfere with tobacco cessation. We aimed to describe the prevalence, placement, and features of tobacco advertising at the point of sale by race, ethnicity, and other neighborhood demographics, as well as by store type.
Design. A cross-sectional assessment of the advertising environment in establishments that held tobacco licenses in our study region (a metropolitan area in the Midwest USA) was conducted in 2007. Stores were geocoded and linked with block group demographic data taken from the Year 2000 US census. We calculated associations between our hypothesized predictors, race, ethnicity, and other neighborhood demographics, and two types of outcomes (1) amount and (2) characteristics of the advertising.
Results. Tobacco advertising at the point of sale was most common in gas stations/convenience stores, liquor stores, and tobacco stores. A 10% difference in a block group's African-American/Black population was associated with 9% (95% confidence interval [CI] = 3%, 16%) more ads as well as a greater likelihood that ads would be close to the ground (prevalence ratio [PR] = 1.15 [95% CI = 1.04, 1.28]). Block groups with greater African-American/Black, Asian, people on public assistance or below 150% of the poverty threshold, or people under the age of 18 years had more ads for menthol brands. Block groups with greater proportions of Whites were more likely to have ads that used health words, such as 'light' or 'natural' (PR for 10% difference in White population = 1.41 [95% CI = 1.17–1.70]). Chain stores were more likely to have greater amounts of advertising, ads close to the ground, ads for price deals, or ads that use words that imply health.
Conclusion. Tobacco advertising targets communities with various racial and ethnic profiles in different ways. Now that US Food and Drug Administration has the authority to regulate the marketing and sale of tobacco products, there is new opportunity to reduce the harmful impact of tobacco advertising.

Keywords: tobacco marketing; point-of-sale-advertising; tobacco use disparities; tobacco regulation; tobacco advertising

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Introduction

Exposure to tobacco marketing at the point of sale is relevant to public health as it has been associated with an increased likelihood that youth initiate smoking (Schooler *et al.* 1996, MacFadyen *et al.* 2001, Lovato *et al.* 2003, Feighery *et al.* 2006, Wakefield *et al.* 2006, Henriksen *et al.* 2010) and may interfere with tobacco cessation (Germain *et al.* 2010, Hoek *et al.* 2010, Reitzel *et al.* 2011). Tobacco advertisements can communicate discounts available at the store and draw attention to the brand (Pollay 2007). The tobacco industry is directly involved in point-of-sale marketing of their products, working with merchants to advertise and promote their products by placing marketing materials both inside and outside of their stores (Feighery *et al.* 2003, 2004, Lavack and Toth 2006). One reason why tobacco market materials are ubiquitous at the point of sale is that tobacco companies engage tobacco vendors in marketing programs with lucrative incentives for the retailer (Feighery *et al.* 2004). Stores that sell tobacco are far more likely to receive incentives for displaying tobacco products or ads than for any other type of product (Feighery *et al.* 1999).

Point-of-sale tobacco marketing of tobacco varies greatly by area demographics. It has been shown to be more common in stores that are situated in lower income, high racial and ethnic minority areas (Barbeau *et al.* 2005, John *et al.* 2009, Seidenberg *et al.* 2010, Siahpush *et al.* 2010b, Henriksen *et al.* 2011). In addition, several authors have illustrated that communities that have more disadvantaged socioeconomic profiles tend to have more of the types of stores that sell cigarettes such as convenience stores (Laws *et al.* 2002, Peterson *et al.* 2005, Fakunle *et al.* 2010, Siahpush *et al.* 2010a, Yu *et al.* 2010). There is also evidence of more marketing of mentholated brands in lower income communities (Laws *et al.* 2002, Seidenberg *et al.* 2010). Thus, racial, ethnic, and low-income areas appear to be disproportionately targeted and at greater risk for the various consequences of tobacco marketing.

Point-of-sale tobacco promotion was largely unregulated by both the 1998 Master Settlement Agreement (MSA) and the 1998 Minnesota Tobacco Settlement (National Association of Attorneys General 1998) and became a key strategy used by the tobacco industry to recruit new consumers and market products as the MSA limited other marketing avenues (Celebucki and Diskin 2002, Jason *et al.* 2004, Ruel *et al.* 2004, Sloan *et al.* 2004, Loomis *et al.* 2006). From 1998 to 2008 the cigarette industry's US overall advertising and promotions budgets grew from \$6.7 billion to \$9.9 billion (Federal Trade Commission 2011). Approximately 72% of the industry's 2008 advertising and promotion budget was spent on discounts paid to retailers intended to reduce the price of cigarettes for consumers (Federal Trade Commission 2011). The measured amount of marketing at the point of sale increased in the decade after the MSA (Ruel *et al.* 2004, Feighery *et al.* 2008). There is evidence that the increase in point-of-sale advertising was more pronounced in communities that had a larger population of African-Americans (Feighery *et al.* 2008). Despite this decade-long trend, the regulatory environment for point-of-sale tobacco marketing is in flux. In the coming years, the Family Smoking Prevention and Tobacco Control Act of 2009 (Waxman 2009), which gave the US Food and Drug Administration (FDA) the power to regulate the marketing and sale of tobacco products, will be changing the point-of-sale landscape as it brings regulation to point-of-sale tobacco advertising. However, moving forward it is not yet clear exactly how this regulatory authority will be fully exercised, what policies will result, and where policy could be most beneficial to public health.

Beyond the amount of tobacco advertisement and marketing at the point of sale, its underlying strategy and placement are relevant to its effectiveness and may vary greatly by area demographics. Placement and content of ads can be used to target specific consumers (or potential future consumers) and stimulate them to make either a trial or repeat purchase. Price deals may be targeting disadvantaged communities as it is known that smokers of mentholated brands (typically racial/ethnic minorities) are more likely to take advantage of cigarette promotional offers than other groups (White *et al.* 2006). There is substantial evidence that consumers interpret health words such as 'light,' 'natural,' or 'mild,' used in cigarette advertising to mean that these products have reduced risk, which is not the case (Kozlowski *et al.* 1998, Borland *et al.* 2004, Kropp and Halpern-Felsher 2004, Borland *et al.* 2008, Peace *et al.* 2009, Wilson *et al.* 2009). These perceptions can reduce motivation to quit (Kozlowski *et al.* 1998, Wilson *et al.* 2009) or decrease the perception of cigarettes' danger and addictiveness (Kropp and Halpern-Felsher 2004). When an advertisement is positioned close to the ground, it is more likely that young children will see it.

In this current study, we aimed to describe tobacco advertising prevalence and placement at the point of sale by neighborhood and store characteristics in a mid-sized US Midwestern metropolitan area (St. Paul, MN). We conducted a census of all 654 licensed tobacco vendors in our region which includes urban and suburban communities. We hypothesized that stores in areas that have a greater proportion of racial/ethnic minority residents would have more advertising. We also hypothesized that certain features of advertising – ads being placed near the ground, ads that imply their products are more healthful, and ads for price deals would vary by a community's racial and ethnic composition.

Methods

Data collection

The data for this study came from two sources: (1) A cross-sectional assessment of the advertising environment in establishments that held tobacco licenses in our study region, conducted in 2007, and (2) Demographic data taken from the Year 2000 US census.

Store assessments

The store assessment process began with enumeration of all 654 establishments that held current tobacco licenses in the 18 cities within the study region (Ramsey County, MN which includes St. Paul, and a part of Dakota County, MN which is adjacent to Ramsey County). The area for the study is both ethnically and economically diverse. Ramsey County is the most densely populated and the most racially diverse county in Minnesota. St. Paul, the state capital, has large African-American, Latino, and Asian populations. In addition, St. Paul is home to a large population of immigrants and refugees, many of whom are from Southeast Asia. Of the 654 licensed vendors in the region, full interior and exterior assessments were completed on 484 establishments (74.0% of the list of licensed stores or 86.2% of the 561 licensed stores which were in business and selling tobacco at the time of assessment). The remaining 170 establishments that held licenses could not be observed because they had gone out of or had not yet opened their business, did not sell tobacco, could not be located by our assessors, or were not safe or accessible for the assessors. There were 14 additional stores that were excluded due to incomplete or contradictory information in their assessment forms. There was no association between store completion status and the store's US Census block group demographics.

The data collectors were trained to inspect each vendor and record their observations of tobacco advertising and promotion on a standard data collection form. The data collection forms were developed based on a review of the literature (Pucci *et al.* 1998, Laws *et al.* 2002, Henriksen *et al.* 2004, Barbeau *et al.* 2005, Wakefield *et al.* 2006) and consultation with other groups including Massachusetts Operation Storefront, Operation Storefront (TX), Operation Storefront (WA), Operation Storefront (WY), and California Strategic Tobacco Retail Effort (STORE) Campaign.

Assessors recorded their overall impression of a store's advertising in four categories, 'None,' 'Discreet,' 'Moderate,' or 'In your face' when an estimated 0%, $<10\%$, 10–25%, or $>25\%$, respectively, of the interior and exterior of the property was covered in tobacco (any type of product) advertising. While we did not formally test reliability by having establishments assessed by more than one assessor, when comparing the ratings of all establishments, there was no significant difference in ratings between the three assessors. We dichotomized these variables into a variable which we refer to as 'level of advertising' – 'None' or 'Discreet' was categorized as a low level vs. 'Moderate' or 'In your face,' a high level. Assessors also indicated whether there were indoor tobacco advertisements located less than three feet from the ground, advertisements for price deals (such as an advertisement for coupons, multi-pack discounts, a special price, or a statement that cigarettes were being sold at the state minimum price), and/or 'health words' such as 'low tar,' 'light,' 'natural,' or 'additive-free' used in tobacco advertising. In addition, a count of interior and exterior advertisements for all tobacco products and for menthol cigarettes (Camel Menthol, Kool, Marlboro Menthol, Newport brands) was recorded.

There were a wide variety of types of vendors in our region that held tobacco licenses. We assigned each establishment to one of eight categories: gas/convenience store (does not sell raw meat), supermarket, restaurant/bar and places with bars (which includes veteran clubs, billiard clubs, music venues, and bowling alleys), small grocery store (which must sell raw meat and milk), tobacco shop, liquor store, drug store (which primarily dispenses medications and personal care items), and miscellaneous (which includes discount stores, gift stores, hotel/motel/resort, automotive shops, car washes, adult entertainment venues, golf courses, amusement parks, assembly halls, and establishments that were notes by the assessors as 'unknown' or 'other'). We then reviewed this list and coded establishments as either 'chain' (retail outlets that share a brand and have central management) or 'independent.' Stores that were not located in the city limits of St. Paul were categorized at 'suburban.'

Demographic data

The addresses of 653 of 654 vendors labeled with the exact geographic coordinates (latitude and longitude). Using ESRI ArcGIS software (Redlands, California), these geocoded stores were spatially joined with year 2000 Census block groups. There were 232 block groups which included at least one store from the analytic sample.

We used the US Year 2000 Census data to characterize these block groups' demographic (% age,% African-American/Black,% Asian,% Hispanic,% White,% below 150% poverty level,% on public assistance).

Analysis

We first described the amount of tobacco advertising in stores in our study region by demographics and store type. Next, we calculated associations between US Census block group-level demographics and the amount of advertising in stores located in those block groups using zero-inflated negative binomial regression. While Poisson regression is often used when the dependent variable is a count, such as in our case, where we were aiming to predict number of advertisements, negative binomial regression is more appropriate when the data are over-dispersed (variance is higher than mean; Cameron and Trivedi 1998). In these data, the dispersion coefficient (alpha) was significantly different from zero which is indicative of over-dispersion. We chose to use a zero-inflated model due to concerns that there were excess zeros (or stores with no advertisements) in our data. Zero-inflated models are appropriate when there is reason to suspect that there might be different processes behind the zero and non-zero counts (Cameron and Trivedi 1998), for instance, various types of stores might have a tendency for different policies on whether advertisements are permitted. When we tested zero-inflated negative binomial regression models using store type to predict the zeros, the Vuong test (Vuong 1989) was significant implying that using a zero-inflated model would be a better fit compared to a non-zero-inflated model. We report prevalence ratios (PRs) with 95% confidence intervals (CI) representing the relative proportion of advertisements for various differences in our predictor variables of interest.

For the dichotomous dependent variables that we examined we used Poisson regression to calculate PRs with 95% CI for the demographic and store type relationships with features of the tobacco advertising environment. We chose to calculate PRs using Poisson rather than calculate odds ratios from logistic regression, because odds ratios derived from logistic regression can overestimate PRs when the outcome is not rare (when prevalence of the dependent variable is greater than approximately 10%; McNutt *et al.* 2003). Due to evidence of clustering of the outcomes, for instance, intraclass correlation coefficient (ICC) for number of smokeless advertisements within block groups was 0.025, our standard error and CI were calculated using robust sandwich estimators.

Due to Census block group demographics being highly correlated we did not run models that included multiple ethnicity/race variables. The magnitude of the Pearson coefficients ranged from 0.19 for the correlation between percent of block group Hispanic and African-American/Black to –0.82 for the correlation between percent White and on public assistance and ($p < 0.0001$ for every combination of two demographic characteristics). However, we did run models where race/ethnicity predictors were adjusted for our poverty proportion variable. We also ran several multivariable models where 'chain' was the predictor of interest due to concerns about confounding by demographics in these relationships. Due to evidence of interaction between 'chain' and store type, we also tested the associations between chain status within each store type. However, since there were small numbers of certain types of stores, not all stratified models converged. Our analyses were conducted in STATA/SE 10.1 (StataCorp, College Station, TX).

Results

The 232 block groups in which the 484 stores were situated exhibited substantial diversity in racial and ethnic composition (Table 1). For instance, the mean proportion African-American/Black was 7.7% (SD = 10.8%), however, the block groups ranged from 0% to just over 60% African-American/Black. Among the establishments that had any ads (70% of the sample), stores has a mean of 19.4 (standard deviation [SD] = 14.7) and median of 17 advertisements per store. Among the 60% of establishments that had menthol cigarette advertisements, the mean number was 6.1 (SD = 5.0) and the median was five. We observed that 28% of stores had advertisements three feet or less from the ground, 9.7% had 'health words' in their advertisements, and 47.5% had advertisements for price deals.

In Table 2, the mean number of total tobacco ads and menthol brand advertisements inside and outside the store is displayed by demographic characteristic, dichotomized at the median proportion of each demographic characteristic assigned to the 484 stores (unlike the medians reported in Table 1, which were for 232 block groups). We also report number of ads by store characteristics. The mean number of advertisements per store varies greatly by establishment type, for instance, restaurants/bars had an average of 0.2 ads per establishment, while the average for liquor stores was 30.0. Tobacco shops were more likely to be in block groups with higher proportions of Asians, Hispanics, those living in poverty, or those on public assistance and lower proportions of Whites (data not shown). Liquor stores were more likely to be in block groups with higher Hispanic populations.

The only demographic characteristic associated with a greater total number of advertisements was proportion African-American/Black (Table 3). For a 10% increase in block groups' proportion African-American/Black, the number of ads in stores would increase by 9% (PR = 1.09 [1.03, 1.16]). This remained significant after adjusting for proportion of the block group living below 150% of the poverty line (PR = 1.09 [1.02, 1.17]). For total number of menthol ads, the proportion African-American/Black, Asian, below 150% of the poverty line, on public

Table 1. Description of the 232 block groups in which the stores of the study were situated.

Race or ethnicity	Median (%)	IQR[a] (%)	Mean (%)	SD (%)	Minimum (%)	Maximum (%)
African-American/Black	3.6	0.9–9.5	7.7	10.8	0.0	60.5
Asian	4.6	1.5–11.2	9.0	11.7	0.0	61.3
Hispanic	3.8	1.3–7.4	5.7	7.0	0.0	48.3
White	86.3	64.6–93.0	76.3	22.5	6.3	100.0
Economic status and age						
Below 150% of poverty level	13.1	7.7–23.9	17.4	14.0	0.0	79.8
On public assistance	3.4	1.0–8.7	6.3	7.8	0.0	43.9
Under the age of 18	24.8	19.5–31.0	25.8	9.1	3.5	49.8

[a]Interquartile range.

Table 2. Mean number of point-of-sale tobacco advertisements per store by block group demographic and store characteristics.

Characteristics n = 484	Total ads		Total menthol ads	
	Mean	SD	Mean	SD
Demographics[a]				
African-American/Black				
< 4.2%	12.6	14.0	2.7	3.3
≥ 4.2%	14.5	16.2	4.6	5.9
Asian				
< 4.7%	12.4	13.9	2.8	3.7
≥ 4.7%	14.7	16.3	4.5	5.7
Hispanic				
< 4.1%	14.0	15.1	3.3	4.4
≥ 4.1%	13.2	15.3	3.9	5.3
White				
< 85.5%	14.4	16.1	4.6	5.9
≥ 85.5%	12.7	14.3	2.7	3.3
Below 150% poverty level				
< 14.4%	12.9	14.4	2.9	3.7
≥ 14.4%	14.2	15.9	4.4	5.7
On public assistance				
< 4.2%	12.7	14.4	2.8	3.7
≥ 4.2%	14.4	15.9	4.5	5.7
Under the age of 18				
< 23.4%	13.5	15.2	3.3	4.6
≥ 23.4%	13.6	15.2	3.9	5.1
Located in a suburb				
No ($n = 268$)	14.4	16.0	4.5	5.8
Yes ($n = 217$)	12.5	14.1	2.5	3.1
Chain				
No ($n = 270$)	8.4	13.4	2.7	4.8
Yes ($n = 215$)	20.0	14.9	4.8	4.7
Store type				
Gas/convenience ($n = 174$)	24.4	14.8	5.9	5.1
Supermarket ($n = 30$)	11.8	10.0	3.3	3.0
Restaurant + bar ($n = 87$)	0.2	0.7	0.0	0.0
Small grocery ($n = 56$)	5.2	8.4	1.3	2.4
Tobacco shop ($n = 8$)	17.1	14.9	6.6	6.6
Liquor store ($n = 76$)	30.0	23.6	6.1	4.7
Drug store ($n = 28$)	3.9	6.5	1.3	2.6
Misc ($n = 25$)	11.0	7.1	3.0	3.0

[a]Proportion of each demographic characteristic was dichotomized at each characteristic's median (weighted by number of stores in each block group).

Table 3. Block group demographic and store characteristic associations with total number of tobacco advertisements and total number of advertisements for menthol brands.

Characteristics $n = 484$	PR (total)	95% CI		PR (menthol)	95% CI	
Demographics[a]						
African-American/Black	**1.09**	1.03	1.16	**1.26**	1.17	1.36
Asian	1.01	0.94	1.09	**1.17**	1.08	1.27
Hispanic	0.92	0.77	1.10	1.07	0.91	1.26
White	0.97	0.93	1.01	**0.88**	0.85	0.91
Below 150% poverty level	1.04	0.98	1.11	**1.17**	1.10	1.24
On public assistance	1.11	0.97	1.27	**1.41**	1.23	1.62
Under the age of 18	1.00	0.91	1.11	**1.12**	1.00	1.25
Located in a suburb						
No (ref)	1.00					
Yes	0.95	0.80	1.13	0.58	0.48	0.71
Chain						
No (ref)	1.00					
Yes	**1.56**	1.27	1.90	0.98	0.77	1.24
Store type[b]						
Gas/convenience (ref)	1.00					
Supermarket	**0.57**	0.44	0.72	**0.56**	0.40	0.79
Restaurant + bar	**0.05**	0.03	0.09	**0.00**	0.00	0.00
Small grocery	**0.46**	0.29	0.71	**0.22**	0.10	0.45
Tobacco shop	**0.76**	0.60	0.95	1.11	0.81	1.50
Liquor store	1.17	0.72	1.91	1.03	0.63	1.69
Drug store	**0.25**	0.18	0.36	**0.21**	0.13	0.35
Miscellaneous	**0.43**	0.33	0.55	**0.50**	0.34	0.73

PR, prevalence ratio; values given in bold denote $p < 0.05$.
[a]PRs are for a 10% difference in proportions, for instance, a block group that is 70% White vs. 60% White.
[b]For store type, a zero-inflated model would not converge for the menthol outcome, so regular negative binomial regression was used. Zero-inflated negative binomial regression was used for store type associations with the total advertisement count.

assistance, and under the age of 18 years were associated with more ads; proportion White was associated with fewer. After adjusting for proportion of the block group living below 150% of the poverty line, only proportion Black (PR = 1.20 [1.12, 1.29]) and White (PR = 0.89 [0.84, 0.95]) remained significant. Store type predicted both total number of ads and number of menthol ads. Gas/convenience stores had more ads (and more menthol ads) than all other types of stores except for tobacco shops and liquor stores.

Table 4 indicates the PRs for a difference of 10% on the demographic predictors, for example, a block group that has a 10% larger proportion of Asian residents is predicted to be 15% more likely to have high levels ('In your face' or 'moderate') of exterior advertising. The proportion of a block group that was African-American/Black, Asian, on public assistance, and under the age of 18 years was positively associated with having high levels of exterior advertising; a larger White proportion was associated with less of a likelihood of having stores with high tobacco advertising levels (PR for 10% difference = 0.93 [0.87,0.99]). However, no demographic characteristics were associated with interior ad level classification. Stores in block

Table 4. Relationship of unadjusted block group demographics and store type with features of the tobacco advertising environment.

Characteristics	Exterior ad level[a]			Interior ad level[a]			<3 ft from ground			Price deals			Health words		
$n = 484$	PR	95% CI		PR	95% CI		PR	95% CI		PR	95% CI		PR	95% CI	
Demographics (proportions)[b]															
African-American/Black	**1.14**	1.02	1.29	0.94	0.83	1.07	**1.15**	**1.04**	**1.28**	1.05	0.96	1.15	**0.48**	0.31	0.76
Asian	**1.15**	1.02	1.29	0.98	0.88	1.09	0.88	0.77	1.02	1.01	0.93	1.10	**0.52**	0.30	0.88
Hispanic	0.92	0.72	1.18	0.86	0.69	1.06	0.88	0.66	1.18	1.05	0.93	1.19	**0.41**	0.20	0.83
White	**0.93**	0.87	0.99	1.03	0.97	1.10	0.98	0.91	1.05	0.97	0.93	1.02	**1.41**	1.17	1.70
Below 150% poverty level	1.08	0.96	1.22	0.95	0.86	1.05	0.98	0.87	1.11	1.03	0.97	1.10	**0.74**	0.58	0.94
On public assistance	**1.24**	1.02	1.50	0.91	0.75	1.11	0.96	0.78	1.20	1.07	0.94	1.22	**0.38**	0.21	0.69
Under the age of 18	**1.34**	1.15	1.56	1.02	0.91	1.15	0.89	0.76	1.03	1.05	0.94	1.17	**0.66**	0.47	0.94
Located in a suburb															
No (ref)	1.00			1.00			1.00			1.00			1.00		
Yes	0.77	0.53	1.14	1.22	0.94	1.59	0.91	0.66	1.24	0.93	0.74	1.16	**1.89**	1.00	3.57
Chain															
No (ref)	1.00			1.00			1.00			1.00			1.00		
Yes	**1.72**	1.21	2.45	**2.37**	1.79	3.14	**2.65**	1.95	3.62	**2.24**	1.83	2.73	**4.77**	2.57	8.85
Store type															
Gas/convenience (ref)	1.00														
Supermarket	**0.08**	0.01	0.56	**0.38**	0.20	0.73	1.01	0.64	1.58	0.76	0.55	1.05	1.01	0.64	1.57
Restaurant + bar	**0.03**	0.00	0.20	**0.00**	0.00	0.00	**0.05**	0.01	0.22	**0.00**	0.00	0.00	**0.05**	0.01	0.21
Small grocery	**0.29**	0.10	0.86	**0.13**	0.04	0.49	**0.37**	0.15	0.92	**0.37**	0.20	0.70	**0.37**	0.15	0.93
Tobacco shop	1.01	0.70	1.45	**0.73**	0.54	1.00	0.66	0.43	1.03	0.79	0.62	1.01	0.66	0.42	1.04
Liquor store	**1.91**	1.27	2.86	1.28	0.88	1.85	1.55	0.95	2.53	0.89	0.55	1.44	1.55	0.94	2.53
Drug store	**0.10**	0.03	0.30	**0.11**	0.05	0.25	**0.24**	0.13	0.47	**0.39**	0.26	0.57	**0.24**	0.12	0.48
Miscellaneous	**0.00**	0.00	0.00	**0.41**	0.21	0.80	1.08	0.71	1.64	0.76	0.54	1.09	1.08	0.70	1.66

PR, prevalence ratio; values given in bolb denote $p < 0.05$.
[a]'Level' refers to high ('In your face' or 'moderate') vs. low ('discrete' or 'none').
[b]PRs are for a 10% difference in proportions, for instance, a block group that is 70% White vs. 60% White.

groups that had higher proportions of African-American/Black residents were more likely to have interior tobacco advertisements less than three feet from the ground (PR for 10% difference = 1.15 [1.04, 1.28]). All of the demographic features we explored were associated with stores having advertisements that featured 'health words.' Specifically, a 10% difference in block groups' White proportion was associated with a 41% [17%, 70%] greater likelihood that stores would use these terms. All other racial/ethnic and economic categories were associated with a lesser likelihood of the use of health words.

Store type was often associated with features of the advertising environment. Gas station/convenience stores were, in almost all cases, more likely to have the five advertising features that we examined. Only liquor stores were more likely to have higher levels of exterior tobacco advertising (PR = 1.91 [1.27, 2.86]) compared to gas stations/convenience stores.

In our unadjusted models that are presented in Table 4, chain stores were more likely to have all of the advertising features that we examined. However, due to concerns about confounding by store type since whether or not a store was a chain was highly correlated with store type (for instance, gas stations and convenience stores were far more likely to be chains than restaurants and bars), we ran adjusted models. In all of these adjusted models, the associations were diminished compared to the unadjusted models, but the PRs remained significant or near significant. The PR for the association between being a chain and exterior ad levels was 1.55 [1.02, 2.34] when adjusted for store type and proportion of the block group population that was Asian, White, on public assistance, and under the age of 18 years. These demographic variables were added to the model as they were significant in their bivariable associations with exterior advertising level and could be associated with whether a block groups' stores are more likely to be chains. After adjustment for store type, the association between being a chain and the tobacco advertising features of interior advertising level and price deals was 1.65 [1.24, 2.19] and 1.59 [1.35, 2.89], respectively. After adjusting for store type and proportion of the block group's population that was African-American/Black, the PR for the association between chain and having ads less than three feet from the ground was 1.98 [1.26, 2.00]. The association between being a chain store and 'health words' after adjusting for all demographic proportion variables and store type was 3.45 [1.42, 8.36].

Finally, due to evidence of that being a chain might be associated with amount of advertising in different ways for the various store types, we ran models examining the relationship between being a chain-type store and advertising characteristics for each store type (data not shown). Many of these models would not converge due to small cells but we found that being a chain was associated with an increase in total number of ads, number of menthol ads, ads three feet from the ground, price deals, and use of health words for gas/convenience stores. Being a chain was associated with fewer menthol ads among tobacco shops.

Discussion

We found that an area's racial and/or ethnic composition is related to how tobacco is advertised in that community's retail establishments. The block group's African-American/Black proportion was associated with more total tobacco ads; higher minority proportion (and lower income) areas were more likely to have greater amounts of ads for menthol tobacco products. The proportion of a block group's population that was African-American/Black was also associated with a greater likelihood of having ads close to the ground. Block groups with greater proportions of Whites were more likely to have ads that used health words.

Tobacco advertising at the point of sale was most common in gas/convenience, tobacco, and liquor stores. Certain types of stores, such as liquor stores, tobacco shops, and gas stations/convenience stores were far more likely to have advertisements that were close to the ground, communicated price deals, and/or used health words. As Cohen and colleagues (2008) found in Canada, we found that chain stores, especially gas/convenience chains, tended to be more likely to have tobacco advertising. Since chain stores have some amount of central control, this could be due to chain-wide contracts with tobacco companies.

Stores in block groups that had greater proportions of African-Americans/Blacks, Asians, people living in poverty, and/or under the age of 18 years tended to have more menthol advertising. As previously mentioned, these demographic characteristics are highly correlated – in the St. Paul metro region, lower-income urban neighborhoods tend to have greater proportions of Asian, African-American/Black, and Hispanic residents. These also tend to be the groups that are most likely to use menthol cigarettes. Eighty-two percent of African-American, 32% of Hispanic, and 31% of Asian smokers report using menthol cigarettes in the past month, compared to 24% of Whites (SAMHSA 2009). Previous research has found, similarly, that stores in neighborhoods with similar racial and ethnic profiles tend to have greater amounts of visible marketing for menthol brands (Laws *et al.* 2002, Barbeau *et al.* 2005, John *et al.* 2009, Seidenberg *et al.* 2010). An important feature of this pattern was that a greater proportion of the population being under the age of 18 years was also associated with more menthol ads. While this may be more of a function of correlated neighborhood demographics – where minority neighborhoods have younger populations, rather than purposeful targeting it is important to note that youth are likely more vulnerable to being exposed to these ads.

Menthol cigarettes are of concern as they may be more attractive to young smokers who are just experimenting with tobacco since the menthol masks the harsh taste of tobacco (Hersey *et al*. 2006, Kreslake *et al*. 2008, Gundersen *et al*. 2009). Among past month smokers age 12–17 years, 45% used menthol cigarettes; however among past month smokers who are age 26 years and older, 30% smoked menthols (SAMHSA 2009). Though the evidence is not consistent, some studies have shown that smokers of mentholated cigarettes have more difficulty quitting (Okuyemi *et al*. 2007, Fu *et al*. 2008, Gandhi *et al*. 2009, Gundersen *et al*. 2009, Foulds *et al*. 2010, Stahre *et al*. 2010). As part of the act that gave the FDA power to regulate tobacco, congress mandated that the agency review menthol's impact on public health with a special focus on minorities and children. After synthesizing the evidence, the FDA panel concluded in March 2011 that, 'Removal of menthol cigarettes from the marketplace would benefit public health in the United States' (Tobacco Products Scientific Advisory Committee 2011).

Not only did stores in block groups with higher proportions of African-Americans/Blacks have more advertising, they were more likely to have advertising that, by virtue of its placement close to the ground, can be highly visible to children. It would be hard to argue that an advertisement that is placed less than three feet from the ground is intended for the eyes of a full-grown adult. While neither the MSA, nor the Minnesota Tobacco Settlement (Minnesota settled separately from the 46 states that joined the MSA) does much to regulate advertising at the point of sale, both settlements are unequivocal about the targeting minors. The MSA directs the participating tobacco companies not to:

> take any action, directly or indirectly, to target Youth within any Settling State in the advertising, promotion or marketing of Tobacco Products, or take any action the primary purpose of which is to initiate, maintain or increase the incidence of Youth smoking within any Settling State. (National Association of Attorneys General 1998)

Since tobacco companies are directly involved in creating the advertisement environment in stores, this could be a violation of the MSA or other settlement agreements.

Stores in block groups that were proportionally more Whites tended to have less advertising, with the exception being ads that used health words. Even though there is less overall tobacco advertising in these neighborhoods, we know that health words can be insidious in tobacco advertisements as the general public tends not realize that a 'natural' or 'mild' cigarette has just as much disease risk as regular cigarettes (Kozlowski *et al.* 1998, Borland *et al.* 2004, Kropp and Halpern-Felsher 2004, Borland *et al.* 2008, Peace *et al.* 2009, Wilson *et al.* 2009). While FDA regulation has prohibited the use of 'health words' such as light, mild, low or similar descriptors unless there is evidence for a product being healthier (Waxman 2009), we know that tobacco companies have remaining tools – using color, packaging, words such as 'natural' and product design intended to successfully communicate to consumers that their product is a healthier choice (Mutti *et al*. 2011).

There are new opportunities to regulate point-of-sale tobacco advertising and a worthy emphasis should be those appearing deceptive, or targeting disadvantaged groups or youth. Prior to the Family Smoking Prevention and Tobacco Control Act of 2009 (FDA regulation) the Federal Cigarette Labeling and Advertising Act (FCLAA) pre-empted states from restricting cigarette advertising at the point of sale. With the new FDA regulation this pre-emption has been overruled and states now have the power to regulate the time, place, and manner (but not content) of point-of-sale advertising. Also, the FDA legislation has strict standards for the use of language that implies a tobacco product presents reduced risk (Waxman 2009).

A strength of our study is the large number of stores we were able to observe which is a census of our study region. However, once we started to examine subgroups, such as advertising by store type, the number of observations was more limited which lead to some statistical models not converging and led to relatively imprecise estimates by store type. An additional limitation is that while the classification was done by staff familiar with the region and checked, sometimes establishment type or whether an establishment is a 'chain' is not straightforward and we may have mischaracterized some of the establishments on these variables. Finally, our data were collected in 2007, prior to FDA regulation and thus before banned the use of advertising tobacco with the specific words 'light,' 'mild,' and 'low' or similar words. Further research would be needed to determine the prevalence of the use of other types of words that might imply health but are allowed under current regulation.

A decade after the MSA and other state settlements with the tobacco companies were signed, advertisements continue to be placed in ways that are easy for children to view and this is more common in stores that are located in neighborhoods with larger African-American/Black populations. The FDA rule brings new opportunity to regulate point-of-sale advertising for a deadly product.

Key messages

(1) An area's proportion African-American/Black was associated with more total tobacco ads, ads close to the ground (at child-height), and ads for menthol products.
(2) Tobacco advertising at the point of sale was most common in gas/convenience, tobacco, and liquor stores.
(3) Block groups with greater proportions of Whites were more likely to have ads that used 'health words.'
(4) With the new law enabling the US FDA to regulate tobacco promotion in the US, and other similar policy changes around the world, there is greater opportunity to reduce the harmful impact of tobacco advertising.

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Racialized Geography, Corporate Activity, and Health Disparities: Tobacco Industry Targeting of Inner Cities

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ORIGINAL PAPER

Racialized Geography, Corporate Activity, and Health Disparities: Tobacco Industry Targeting of Inner Cities

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Abstract: Industry has played a complex role in the rise of tobacco-related diseases in the United States. The tobacco industry's activities, including targeted marketing, are arguably among the most powerful corporate influences on health and health policy. We analyzed over 400 internal tobacco industry documents to explore how, during the past several decades, the industry targeted inner cities populated predominantly by low-income African American residents with highly concentrated menthol cigarette marketing. We study how major tobacco companies competed against one another in *menthol wars* fought within these urban cores. Little previous work has analyzed the way in which the inner city's complex geography of race, class, and place shaped the avenues used by tobacco corporations to increase tobacco use in low-income, predominantly African American urban cores in the 1970s–1990s. Our analysis shows how the industry's activities contributed to the racialized geography of today's tobacco-related health disparities.

Key words: Smoking, tobacco industry, African Americans, racial disparities, inner city geography.

Despite significant reductions in overall smoking rates in the United States, smoking among poor, less educated, and underserved populations remains higher than among the general population.[1–5] For example, prevalence rates for low-income African Americans have been reported to range from 33% to 59%,[6–11] compared with 21% for the general population.[12] Tobacco company advertising and promotion are associated with increased cigarette consumption; their presence and pervasiveness serve as external cues to smoking.[13] Tobacco companies have strategically targeted marginalized communities,[14–25] who may have limited information about specific and relative health risks of smoking and few social supports and resources such as tailored cessation programs.[26–29] Tobacco-related diseases have hurt lower-income urban communities,

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where lack of educational opportunity is compounded by lack of access to health care, few employment opportunities, and environmental injustice.[7,30]

Tobacco use is a major contributor to health disparities in the United States.[5,31] Age-adjusted mortality rates for tobacco-related cancers,[32–37] cardiovascular disease and stroke are higher among African Americans than among White Americans.[38] Tobacco-related health disparities are defined as "differences in the patterns, prevention, and treatment of tobacco use; the risk, incidence, morbidity, mortality, and burden of tobacco-related illness that exist among specific population groups in the United States; and related differences in capacity and infrastructure, access to resources, and environmental tobacco smoke exposure."[30, p. 211] Individual level risk factors account for only part of persistent health disparities. In this paper, we suggest that it is not only tobacco use behavior that shapes disparities, but the disparate distribution of conditions that promote tobacco use. For example, African Americans who report experiencing racial discrimination as subjectively stressful are more likely to smoke.[39] Macro-level factors identified as fundamental causes of disease also influence multiple disease outcomes and affect both individual and social contexts.[40]

The expanding literature on social and environmental injustices recognizes the interplay between individual, social, and geographic factors, including racism and segregation, and their contribution to persistent racial disparities in health.[41–44] This interplay creates what have been called *riskscapes*,[45–46] within which poverty, racial discrimination, segregation, the environment, and other factors work together to shape health disparities. Work from critical geography, public health, and history has drawn attention to localized power relationships, emphasizing that space is neither neutral nor passive.[47–51] Rather, geographic location and social position intertwine and form a loop; places shape one's social station and the social station of a place's residents shapes societal views of that place.[52] *Racialized geography*, as described by Sundstrom, is a complex interplay between race, class, and place, occurring at the nexus of political, economic, and social systems.[52]

One factor shaping the riskscapes of inner cities is corporate activity, which has been identified as a fundamental structural cause of disease through producing and promoting products harmful to health.[53] The tobacco industry's disease-promoting activities[54] are among the most powerful corporate influences on inner city health. Such activities have included targeted marketing, thwarting and undermining tobacco control efforts, deceptive scientific practices, and influencing policymakers and community leadership groups.[55–59]

For this paper, we analyzed previously secret internal documents to explore how, during the past several decades, inner cities populated predominantly by poor African American residents were targeted with highly concentrated menthol cigarette marketing from the entire industry. Today, at least 70% of African American smokers consume menthol cigarettes, compared with 30% of White smokers.[5] Menthol cigarettes, which contain higher amounts of tar and nicotine than non-mentholated brands,[60–64] are associated with nicotine dependence and lower cessation rates,[65–69] and may play a role in increasing systemic exposure to tobacco toxins and carcinogens;[70–76] thus, it is reasonable to consider how activities that promoted tobacco use and mentholated cigarette use specifically have contributed to today's tobacco-related health disparities disfavoring African Americans.

This study shows how the major tobacco companies between the late 1970s–1990s aggressively competed against one another in the *menthol wars* fought within inner city urban cores. The most popular menthol brands were Kool (manufactured by Brown & Williamson, which merged with RJ Reynolds in 2003 to become Reynolds American Tobacco Company), Salem (Reynolds American), Newport (Lorillard), and Philip Morris's Benson & Hedges Menthol. During the time of this marketing blitz, smoking among African Americans increased,[77] the use of menthol cigarettes among African Americans increased,[78] and the overall menthol share of the tobacco market exploded. During the same time period, smoking prevalence among African Americans exceeded that among Whites, and African Americans (especially the poor and less educated) were among those least likely to quit smoking.[79–80] While previous research has described disproportionate levels of menthol cigarette advertising in poor inner city neighborhoods compared with predominantly White neighborhoods,[16,31,81] little work has demonstrated the specific ways in which the inner city's complex geography of race, class, and place shaped the avenues used by tobacco corporations to increase tobacco use in low-income, predominantly African American urban cores during the 1970s–1990s.

Methods

We used archival approaches[82] to conduct this study, using data from previously undisclosed tobacco industry documents made public under *State of Minnesota versus Philip Morris, Inc.*[83] and electronically available following the 1998 Master Settlement Agreement between 46 state attorneys general and 7 tobacco industry defendants.[84] Between May 2005–August 2006, we collected and analyzed more than 400 documents related to tobacco industry targeting of low-income, inner-city communities. Documents were retrieved in paper form from the Minnesota Depository and electronically from the University of California, San Francisco Legacy Tobacco Documents Library (http://legacy.library.ucsf.edu) and from industry document websites.[85]

We searched using an iterative snowball approach,[86] beginning with combinations of search terms such as *African American*, *Black*, *ethnic*, *ghetto*, *inner city*, *menthol*, *Negro*, and *urban*. Retrieved documents were used to identify additional search terms. We focused primarily on Brown & Williamson, Lorillard, Philip Morris, and RJ Reynolds, as their menthol brands were the most heavily marketed in African American communities.

To begin interpreting the data, the first and second authors reviewed all documents and selected key documents for review by the third author. Drawing on findings from the retrieved tobacco documents and other relevant textual data sources, we developed an account of tobacco industry marketing activities focused on inner cities. Table 1 shows a geographic account, and Figure 1 shows temporal concentration of selected major tobacco marketing initiatives. We organized material by company and by strategy. The results are presented as follows: we first review background information about menthol cigarettes and industry interest in inner city areas, derived predominantly from

Table 1.

TOBACCO ACTIVITIES AND CENSUS DATA, 1980, IN SELECT CITIES[a]

		Race				Tobacco company inner city activities			
		White		Black					
City (census year)	Total population	Number	Percent	Number	Percent	Brown & Williamson	Lorillard	Philip Morris, USA	RJ Reynolds
Atlanta, GA	425,022	137,879	32.4	282,911	66.6		X	X	X
Baltimore, MD	786,775	345,113	43.9	431,151	54.8	X	X	X	X
Boston, MA	562,994	393,937	70.0	126,229	22.4		X	X	
Chicago, IL	3,005,072	1,490,216	49.6	1,197,000	39.8	X	X	X	X
Cincinnati, OH	385,457	251,144	65.2	130,467	33.8	X	X		
Cleveland, OH	573,822	307,264	53.5	251,347	43.8		X	X	X
Columbus, OH	564,871	430,678	76.2	124,880	22.1		X	X	
Dallas, TX	904,078	555,270	61.4	265,594	29.4		X	X	
Detroit, MI	1,203,339	413,730	34.4	758,939	63.1	X	X	X	X
Durham, NC	100,831	52,317	51.9	47,474	47.1			X	
Ft. Lauderdale, FL	153,279	118,983	77.6	32,225	21.0		X		
Hartford, CT	136,392	68,603	50.3	46,186	33.9		X		
Houston, TX	1,595,138	978,353	61.3	440,346	27.6	X	X	X	
Indianapolis, IN	700,807	540,294	77.1	152,626	21.8			X	
Jackson, MS	202,895	106,285	52.4	95,357	47.0			X	
Jacksonville, FL	540,920	394,756	73.0	137,324	25.4		X	X	
Los Angeles, CA	2,966,850	1,816,761	61.2	505,210	17.0	X	X	X	X
Louisville, KY	298,451	212,102	71.1	84,080	28.2		X		
Memphis, TN	646,356	333,789	51.6	307,702	47.6	X	X	X	X

(Continued on p. 14)

Table 1 *(continued)*.

City (census year)	Total population	Race: White Number	Race: White Percent	Race: Black Number	Race: Black Percent	Tobacco company inner city activities: Brown & Williamson	Lorillard	Philip Morris, USA	RJ Reynolds
Miami, FL	346,865	231,008	66.6	87,110	25.1		X	X	
Milwaukee, WI	636,212	466,620	73.3	146,940	23.1		X		
New Haven, CT	126,109	78,326	62.1	40,235	31.9		X		
New Orleans, LA	557,515	236,987	42.5	308,149	55.3	X	X	X	
New York, NY	7,071,639	4,294,075	60.7	1,784,337	25.2	X	X	X	X
Norfolk, VA	266,979	162,300	60.8	93,987	35.2				X
Oakland, CA	339,337	129,692	38.2	159,281	46.9		X		
Paterson, NJ	137,970	70,203	50.9	47,091	34.1		X		
Philadelphia, PA	1,688,210	983,084	58.2	638,878	37.8		X	X	
Pittsburgh, PA	423,938	316,694	74.7	101,813	24.0		X		X
Richmond, VA	219,214	104,743	47.8	112,357	51.3		X	X	
St. Louis, MO	453,085	242,576	53.5	206,386	45.6		X	X	
San Francisco, CA	678,974	395,081	58.2	86,414	12.7		X	X	
Washington, D.C.	638,333	171,768	26.9	448,906	70.3	X	X	X	X

[a]U.S. Census Bureau selected historical census data, 1980.

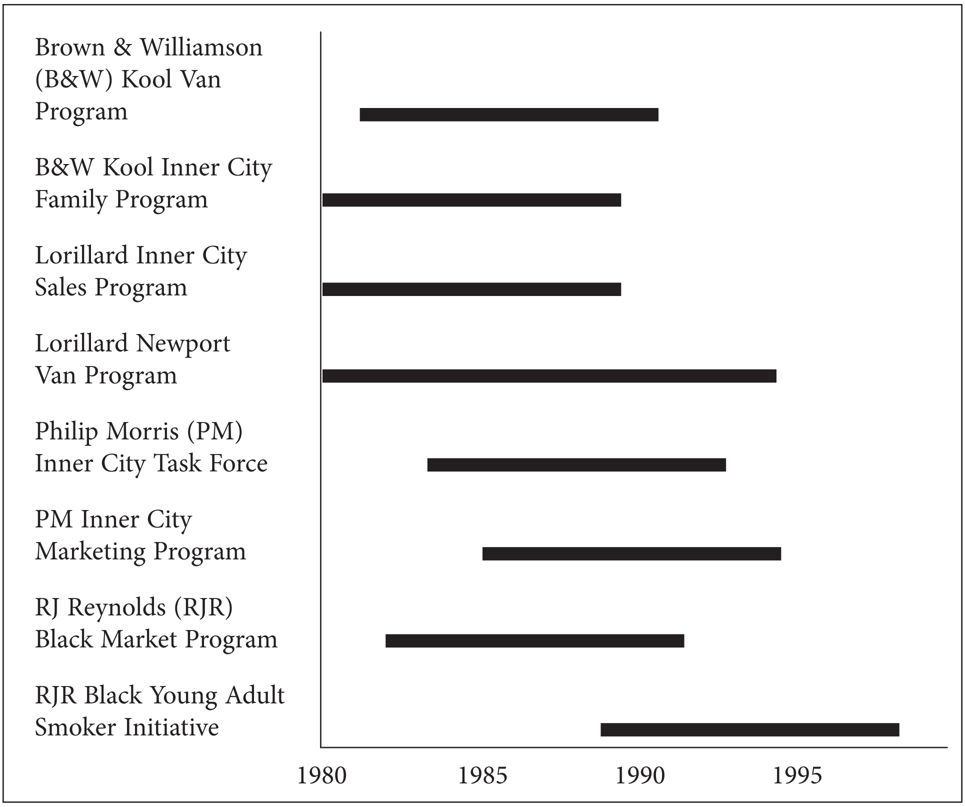

Figure 1. Temporal concentration of selected major tobacco marketing initiatives in U.S. inner cities.

industry documents and secondary sources. We then discuss specific tobacco industry strategies, including studying African American consumers using psychographic and other data; giving out free samples of cigarettes and the use of mobile vans to drive into neighborhoods; specialized inner city retailer programs; and community engagement. We conclude by discussing how today's tobacco-related health disparities were shaped by geographically-specific, intentional and aggressive corporate activity.

Results

Background: The tobacco industry and the African American inner city consumer. Menthol cigarettes have been marketed since the 1920s.[87] Between 1957 and 1963, the menthol share of the total cigarette market grew from 5% to 16%.[88–89] (See Table 2.) By 1964, there were 9 menthol brands, and 23 by 1971.[90] During the 15-year period 1956–1971, the menthol market grew by 48%.[90] By 1982, menthol sales had grown 6 times as fast as sales in the general cigarette market.[91] Salem had dominated the menthol market from its inception in 1956 to 1972, but Kool now led menthol sales. Kool's rise was due in part to its embrace by the African American community.[92]

Table 2.

MENTHOL U.S. MARKET SHARE, 1920–2001

Year	Market share (%)
1920–1955	2
1955–1957	5
1963	16
1978	28
1990–2001	27–29

Source: Gardiner PS. The African Americanization of menthol cigarette use in the United States. *Nicotine Tob Res* 2004;6 Suppl 1:S55–65. (Used with written permission from Nicotine and Tobacco Research.)

As competitive tobacco companies began noticing Kool's increased popularity, especially among African Americans, they began aggressively marketing their menthol products in inner city African American communities.[78,93–97] (Tobacco companies used the term *inner city* to refer to "the usually older and more densely populated central section of a city with large ethnic populations."[98, p. 5851]) Data collected by or on behalf of tobacco companies revealed that "smoking characteristics of blacks differ significantly from those of whites," requiring "a different marketing strategy . . . for black consumers."[99, p. 9184] For decades, tobacco industry research suggested that African Americans were heavy menthol smokers who presented an opportunity for tobacco companies to increase their menthol market share.[100–101] The tobacco companies used multiple avenues designed specifically for the "difficult to reach"[102, p. 5434] group of inner city Black smokers, including analysis of residents' psychographic profiles, mobile van programs through which free cigarettes were distributed, specialized marketing programs, and tailored retail programs. (See Table 3.) According to a 1982 Philip Morris marketing plan, two segments in the African American market were "becoming increasing polarized—half more affluent than ever, and the other significantly lagging the general market in Education and Income."[103, p. 5627] Tobacco companies were interested in the latter African American consumers, the "younger, less educated, lower in income, urban, [and smoking full-flavor and menthol cigarettes]."[103, p. 5628] Tobacco companies often relied on ethnic marketing firms to provide them with psychographic profiles of African American consumers.[104–110] At least one ethnic marketing firm had multiple tobacco companies as clients.[111–115]

Ethnic marketing firms did more than provide insights into the personalities, behaviors, attitudes, and lifestyles of urban African American consumers. For example, in 1982, SMSi (Special Market Services, Inc.), a Chicago firm that specialized in sampling (giving out for free) cigarettes in minority communities, produced for Philip Morris a report focused on strategies for promoting Benson & Hedges among African American and Hispanic consumers, suggesting specific cities where cigarettes could be sampled.[108] The firm recommended that Philip Morris maintain a "first-class approach" to target

Table 3.

SAMPLING OF TOBACCO INDUSTRY ACTIVITIES IN U.S. INNER CITY NEIGHBORHOODS DURING THE 1970s TO 1990s

Marketing activity	Dates	Locations
Brown & Williamson		
Marketing Plans Sales Force	01/73–12/73	
Kool Inner City Music Program	1982	Baltimore, MD; Chicago, IL; Cincinnati, OH; Detroit, MI; Houston, TX; Los Angeles, CA; Memphis, TN; New Orleans, LA; New York City, NY; Washington, DC
Kool Music on Tour Program	03/83	
Kool Van Sampling Program	01/84–12/91	All regions across the U.S.
Lorillard		
Media Mix	09/71–12/71	
Criterion (3 Sheet) Program	08/74–07/75	Chicago; New York City
Newport's 3 and 8 Sheet Showings	09/74–06/75	New Jersey; New York City
Lorillard Marketing Research Study		
Pre-test	09/13/78–09/14/78	Chicago; Detroit
Pilot Study	09/28/78–09/29/78	Atlanta, GA; Boston, MA; Chicago; Detroit
Main Study	01/02/79–01/06/79	Atlanta; Boston; Chicago; Detroit; Jacksonville, FL; Los Angeles; Memphis; New York City
Vantastic Newport Sampler Van	09/01/83–09/30/83	Bronx and Queens, New York City; Dallas, Houston, and San Antonio, TX; Hartford, CT; Los Angeles, Oakland, Sacramento, and San Francisco, CA; Paterson, NJ; Philadelphia, PA; Providence, RI
Play Ball with Newport	01/85–12/85	New York
Krush Groove Concert Van Sampling	12/27/85	Madison Square Garden, New York

(Continued on p. 18)

Table 3 *(continued)*.

Marketing activity	Dates	Locations
Newport Van Program (10 Vans)	1988–1991	All regions across the U.S. (including Alabama; Baltimore/Washington, DC; Cincinnati, Cleveland and Columbus, OH; Chicago; Connecticut; Detroit and Flint, MI; Florida; Knoxville and Louisville, KY; Massachusetts; Memphis; Milwaukee, WI; Mississippi; New Orleans; Philadelphia and Pittsburgh, PA; Rhode Island; St. Louis, MO; Texas)
Newport Inner City Lighter Promotion	01/89–03/89	Baltimore; Boston; Chicago; Detroit; Milwaukee; New York City; Providence; Richmond, VA; Springfield, MA
Pleasure on Wheels (P.O.W.)	11/93–3/31/94	Detroit; Ft. Lauderdale and Miami, FL; Philadelphia
Newport Promotion Plan	01/94–12/94	Baltimore/Washington, DC; Albany, Bronx, Brooklyn, Buffalo, Rochester and Syracuse New York; Bridgeport, Hartford, New Haven and Stamford, CT; Chicago; Cleveland; Detroit; Ft. Lauderdale; Philadelphia; Pittsburgh; Miami; New Jersey
Newport Special Events Program	01/94–12/94	Daytona Beach and Panama City, FL; Jersey Shore, NJ; Virginia Beach, VA
Philip Morris, USA		
Benson & Hedges (B&H) Inner City Sampling Program	06/03/85–08/23/85	
B & H Inner City Program	06/87–08/87	Baltimore; Cleveland/Akron and Columbus/Augusta; Chicago; Dallas/Ft. Worth; Houston; Jackson, MS; Jacksonville; Los Angeles; Memphis; Miami; New Orleans and Shreveport, LA; Philadelphia; Raleigh/Durham, NC; Richmond, VA; St. Louis; San Francisco
Marlboro Inner City Bar Nights	07/88	
Soul Food Picnic	06/18/88–06/19/88	Indianapolis, IN
Indiana Black Expo Celebration	07/07/88–07/10/88	Indianapolis

(Continued on p. 19)

Table 3 *(continued)*.

Marketing activity	Dates	Locations
Jazz under the Stars	07/10/88	Indiana
Golden Memories under the Stars	07/88–12/88	
Region 4 Urban Task Force	06/94–07/94	Chicago; Cleveland; Detroit
Cleveland, Chicago, Detroit		
Menthol Urban Program	06/95–08/95	Atlanta; Baltimore/Washington, DC; Chicago; Detroit; Houston; Los Angeles; Miami; New York City; Philadelphia
Marlboro/B & H Urban Visibility Program	12/96–01/97	
Wave 1		Baltimore/Washington, DC; Boston; Chicago; Detroit; Miami; New York City; Philadelphia
Wave 2		Atlanta; Houston; Los Angeles; New Orleans
Club B & H Club/Bar Program	07/96–11/96	Atlanta; Chicago; Dallas/Fort Worth; Houston; Los Angeles; New Orleans
RJ Reynolds		
Bright/Salem Free Pack Coupon In		
Ebony/Essence Magazines	04/81–08/82	
Bright Black Smoker Trail Sampling	03/83–07/83	
Sterling Sampling Plan	12/83	Chicago
Salem Black Market Promotion Plan	01/84–11/84	Atlanta; Baltimore/Washington, DC; Chicago; Detroit; Harlem, New York City; Los Angeles; Memphis; Norfolk, VA; Pittsburgh; Other regions in the North and South Atlantic, North and Mid-Central
Black Initiative Program	04/89–12/89	Chicago; Cleveland; Memphis
Innovative Sales/Marketing Program	04/89–06/89	
Black YAS Initiative Van Program	04/89–04/90	Chicago; Cleveland; Memphis
Black Initiative Program Expansion	07/90	

upscale women in beauty salons and boutiques, suggesting that the company present customers in these establishments with the product sample and a single live long stem flower.[108] Philip Morris chose not to implement SMSi's recommendation, perhaps because it had begun to recognize that Benson & Hedges was gaining "acceptance among the important younger Black smoker group,"[91, p. 8889] ages 18–24, a segment of the population that positioned "the brand very well for the future."[91, p. 8889]

Sampling and mobile vans. However it could be accomplished, tobacco companies sought to distribute cigarettes for free. They engaged in street sampling, where sales staff on foot handed out free cigarettes. Sampling included both street corner distribution and *quality sampling*.[116] (Quality sampling indicated an interaction wherein the sampler would spend more time with an individual consumer, as opposed to passing out mass quantities within a small window of time.) At times, samplers were expected to pass out as many as 90 packs per hour, approximately 1.5 packs every minute.[116]

A 1985 sampling manual emphasized, "It is important that sampling be confined to the inner city area to maximize the benefits of Benson & Hedges sampling on the target market,"[116, p. 8013] suggesting that the National Urban League would be a "good recruiting source." Sampling programs sometimes lasted only a few weeks, as tobacco companies implemented intensified, short term targeted menthol marketing programs confined to inner cities to generate interest, trial, and brand-switching among residents.[116] For example, during an 8-week promotional period in 1986, Philip Morris carried out sampling in the top 20 African American markets, passing out free 6-cigarette packs and an attached "Buy 1 Get 1 Free" (B1G1F) coupon.[117] The African American population in each of the markets was used to determine the number of samplers allocated to the market. During a 2-month period in 1991, Philip Morris launched a nationwide Benson & Hedges Menthol B1G1F offer in urban markets that hit some 17,000 outlets, expecting to reach almost 350,000 smokers.[118]

However, street sampling in inner city communities presented challenges. Lorillard, for example, was not only concerned about the lack of high traffic locations in these neighborhoods, but also considered these "minority areas" as "high risk" with the threat of product theft and equipment loss or damage.[102] Therefore, after a dalliance with street sampling, Lorillard introduced an innovation, the Newport Pleasure Van, in 1979.[102] Lorillard's van program started with a single van in the New York metropolitan area and then expanded to 10 vans circulating across the U.S.[119–125]

Vans allowed sample distributors to be protected from "unruly crowds"[122,126] while handing out free cigarettes. Vans not only offered a sense of safety to tobacco company workers as they penetrated what they perceived to be dangerous territory, but provided a way to distribute cigarettes "with a unique attention getting sampling device specifically targeted to difficult to reach minority groups."[102, p. 5434] Vans were reported to have stopped at street corners, perhaps for only 10 minutes, while playing loud music and distributing free cigarettes.[127–128]

Newport van drivers were provided with a daily schedule, detailing a list of cross-street starting points and street corners of interest in the neighborhoods, where free packs of 10 cigarettes were distributed. Vans were parked near selected stores based on their geographic locations and "to reinforce Newport's image as the 'peer brand' among young adult smokers."[129, p. 2731] In a 1981 memo to all division managers in the

Cincinnati, Dayton, and Columbus, Ohio regions, an assistant Newport brand manager wrote that "The Newport Van is proving to be a uniquely effective vehicle for reaching this target market in their own enviroment [*sic*]," as "Newport's target group of young adults/blacks is difficult to reach via coupons and standard street corner crew sampling."[120, p. 6117] The van program catch phrase, shown as a signature on Lorillard van-related documents, was: "When your target group is hard to reach / With a standard marketing plan, / Get out and sample them on their streets / With the 'Vantastic' Newport Sampler Van."[120, p. 6117]

In March 1983, Brown & Williamson instituted its Kool van program for inner cities, determining that vans had "proven to be an intrusive non-traditional media venue as well as an effective, cost-efficient sampling device."[130, p. 0535] The Kool van program, also known as Kool Music on Tour,[131] was created to access "Kool's hard-to-reach, low readership starter market and target audience,"[130,132] specifically targeting "inner city, young adult competitive smokers."[133, p. 1291] (The phrase *starter market* is usually interpreted as referring to youth, since the great majority of smokers take up tobacco before the age of 18.[134]) Kool vans were staffed with a professional DJ and a tobacco company employee who handed out free cigarettes.

By 1985, vans were the primary sampling medium for distributing Kool cigarettes, entering neighborhoods in more than 50 cities where Newport, Salem, and Benson & Hedges Menthol sales were strong.[133] Brown & Williamson evaluated demographic information from the Chambers of Commerce, regional festival directors and groups, state fairs, trade shows and exhibitions to identify sampling opportunities.[130] The Kool Music on Tour program continued until at least 1991 with 3 vans, concentrated in the Northeast and Midwest.[135]

RJ Reynolds had determined that Lorillard's van program was instrumental to Newport's growth among African American young adult smokers.[127] Inspired by Lorillard, Reynolds also established a van sampling program, aimed to increase Salem's visibility in Chicago. Brightly-painted video vans were fitted with state-of-the-art electronic equipment and displayed music videos.[136] Sent to Chicago nightclubs, the vans caught potential Salem customers entering and leaving the clubs. The vans also displayed live video coverage of the inside club action, thereby entertaining the younger crowd hanging around outside the club.[136]

During the day, the three video vans called on retailers and Salem sales teams in the Chicago area.[136] The vans also traveled to parks, construction sites, bingo halls, street corners, parking lots, and local sports events.[128,137] They made appearances at urban street malls, public aid offices, currency exchanges, housing projects, public transit stops, and other venues.[138] Vans were also used to increase Salem's visibility at street festivals and other neighborhood events. A Reynolds marketing representative proposed that the video vans display community service messages focusing on drug awareness, staying in school, and African American History.[139] Each van took part in as many as 60 events per week. A field marketing manager reported that the vans "work the streets and stores all day and the clubs at night. It can be 20 hours a day, seven days a week."[136, p. 8941]

Although other companies used vans to distribute cigarettes in inner cities, Lorillard's van program was the most far-reaching. In 1993, Lorillard decided to change "the strategic thrust of the Newport Van Program from a sampling vehicle to a more aggressive approach,"[140, p. 4259] whereby retail store sales were tracked and smokers were offered inducements to generate impulsive purchases of Newports.[140–141] Participant "name capture" cards were used to collect contact information from Newport and competitive brand smokers in exchange for a promotional item.[142–143] Lorillard ran this POW (Pleasure On Wheels) van program from February through November 1994. The program drew business away from competitors (especially Kool)[144] in the inner city neighborhoods of New York, Miami/Fort Lauderdale, Philadelphia, St. Louis, and Detroit.[145–147] After Newport came to dominate the urban menthol market, Lorillard reduced the number of vans it operated and then shifted its van program to the general market, though the company continued to focus on lower socioeconomic groups.[148] According to a March 1992 memo to regional sales managers, Lorillard's plan was to "move out of the inner City Core to the general market . . . van sampling will be targeted to blue collar smokers."[149, p. 7856]

In some cities, such as Atlanta, public restrictions prevented van sampling. There, sampling specialists were used to gain access to privately owned areas including bars, small events, and other allowable venues.[125] Philip Morris relied on local samplers to use their area-specific knowledge to identify the best locations. Samplers were to work at inner city high traffic locations or events, such as sporting events, concerts, factory shift changes, bowling alleys, and outside movie theaters, and "where a relaxed, personalized message can be delivered."[116, p. 8014] Other locations included nightclubs, beauty salons, barbershops, fashion boutiques, and restaurants. Samplers were instructed not to get involved in conversations about smoking and health. Rather, they were urged to respond to such inquiries with, "I respect your opinion, and I'm sorry that you feel that way. Thank you" or "I'm afraid I am not sufficiently qualified to comment on that question. Thank you."[116, p. 8025]

Specialized marketing programs. All the companies developed special inner city sales programs for menthol brands. For example, during the early to mid-1970s, Kool did well in the inner city market; in 1976, 38% of African American smokers used Kools,[92] a jump of 24 percentage points in 8 years. Among African American male smokers under age 35, nearly 60% smoked Kool. Increased competition for these African American menthol smokers led to a marketing blitz.[150] A summary provided by Brown & Williamson's advertising and brand management team noted, "Competitors have been increasing their efforts to counter Kool's success, and means to combat this activity will be a continuing effort."[151, p. 9109] For the next 10 years, Brown & Williamson focused on maintaining Kool's visibility in inner cities.

To compete with Kool, Lorillard increased Newport's marketing efforts in geographical areas with large concentrations of African Americans.[96] Lorillard aggressively targeted Kool smokers, developing inner city sales programs to support markets where Newport sales were already strong and seeking to narrow the sales ratio in those markets where Newport was trailing Kool.[152] Lorillard initially decided to target both African American and Hispanic young adults with a high school education or less who resided "in tough inner city neighborhoods;"[153–154] however, the company soon found that "Newport, along with other menthol brands, have [sic] been unable to crack this [Hispanic] market."[96, p. 7635] Field sales reps reported that Newport was succeeding "predominantly among males, in the Black inner city."[155, p. 4936] Therefore, the company reallocated funds to the African American inner city market's "more promising opportunities."[96] By 1988, Lorillard had implemented inner city sales programs in the urban markets of Detroit and Flint, Michigan.[152] Within 2 years, these efforts reached over 30 "ethnic niches" in the Northeast and Midwest, including Chicago, Baltimore, Detroit, Boston, and Cleveland; and nightclubs in New Orleans, Atlanta, St. Louis, Los Angeles, San Francisco, and Indianapolis.[156–157]

Lorillard's strategies included maintaining a highly visible Newport brand presence, focusing on trial and conversion from smokers of competitive brands, distribution drives, increased numbers of point-of-sales materials, sampling, special event coverage, increased levels of advertising support, and rewarding retailers for promoting Newport.[158] Promotional items such as key chains, sports bags, sunglasses, lighters, and B1G1F offers were used as tools to encourage smokers of other menthol brands, but particularly Kool smokers, to switch to Newport.[96,153,159]

Recognizing minority markets as "virgin territories,"[103] Philip Morris implemented African American ethnic and urban programs beginning in 1982 and continuing through the early 1990s. In its 1982 minority marketing plan, Philip Morris proposed to improve the performance of Benson & Hedges among African American smokers.[103] The plan contains pages of demographic profiling of African Americans and Hispanics and charts showing advertising expenditures of competitive brands in African American print media. Philip Morris's action plan recommended company sponsorship of community and national events and included a list of African American organizations.

In 1984, Philip Morris's Black Marketing Task Force met in Washington D.C. to discuss "the very important Black smoker segment."[160, p. 0074] The task force concluded that Benson & Hedges Menthol and Virginia Slims were the only Philip Morris brands "that can be really 'worked' [in the] inner city."[161, p. 1444] Strategies presented by the task force included promotional plans, incentives, advertising, sampling programs, materials, communication, and the assignment of African Americans samplers to the inner city. As with Lorillard, a heavy emphasis was placed on B1G1F deals, incentives for inner city retailers, and promotional items that would appeal to African American consumers, such as playing cards, blank cassette tapes, cigarette cases, and lighters.[162]

With its share of the menthol market declining from 22.4% in 1981 to 15.8% in 1987, Reynolds began to focus heavily on Black young adult smokers (BYAS), who were considered critical to the success of all menthol styles.[127] Inner city African American young adults were also important because they were seen as trendsetters. As a marketing research report presented to RJ Reynolds suggested, "The daring, flamboyant aspect of YA [young adult] Black smokers' personalities are evident in **the many trends they start.** And the fact that these trends often spread to the general population speaks to the **unrecognized power and influence** this subgroup yields on society. . . . Trends are often started by lower income Black males who are looking for a way to be important or interesting, to create their own identity . . . [emphases in original]."[163, p. 7657]

Reynolds concluded that Newport was doing so well in the menthol market because Lorillard concentrated its efforts with one brand targeted to one population. Deciding to do the same, Reynolds focused all "BYAS [black young adult smoker] marketing resources" on Salem "since it is an acceptable choice among BYAS and accounts for two-thirds of RJR's BYAS share."[127, p. 0163] From April 1989 to April 1990, Reynolds implemented its BYAS Initiative, targeting high density lower-income African American neighborhoods of Chicago, Cleveland, and Memphis.[127–128] To determine specific boundaries of target neighborhoods within these markets, Reynolds conducted interviews in ZIP code areas pre-defined as inner city, at least 50% African American, and with yearly household incomes under $20,000.[164]

The BYAS Initiative sought to reverse Salem's declining trend among younger adult African American smokers and increase sales by getting African Americans to try Salem. Special advertising, promotions, and "a variety of other carefully coordinated sales and marketing programs"[136, p. 8939] began appearing in these markets. When radio stations featured known performers, Salem would be there, too.[136] Reynolds marketers emphasized that "Salem should be seen as a friend."[163] "The best way to reach minority consumers," they argued, was "through their local communities, . . . [which] tend to support brands that they see are doing something for them. [But these efforts] must be seen as authentic and as being backed by other Blacks—not as a big White company's tactic to sell to Blacks."[163, p. 7655]

Inner city retailer programs. Retail outlets located in inner cities presented challenges, including limitations on product availability and visibility, space constraints, retail clutter, high crime rates, and cash flow restrictions.[126,155,160] Additionally, inner city retail outlets were often secured with bullet-proof shields, which not only limited the space available for advertisements and merchandise but also eliminated self-service product selection. Tobacco companies' field representatives and/or ethnic marketing firms developed special efforts aimed at smaller, crowded neighborhood retail outlets in inner cities.[115,136]

Philip Morris acquired "Black accounts," primarily smaller liquor, grocery, and convenience stores in inner cities. These accounts were intended to replace others lost due to the larger supermarkets moving out of inner cities.[162] Philip Morris sought to remove impediments that prevented these small retailers from maintaining and selling cigarettes at acceptable levels. To save space, suction cups were used to hang signs from bullet-proof shielding; pricing signs incorporated personalized messages concerning such matters as the availability of check cashing services.[162] Product displays, existing versions of which were too large and required a major retailer investment, were specially re-designed for inner city retail outlets.[161] To ensure that cigarette displays were visible and well-stocked, inner city retailers were also offered incentives to display promotional items.[156] For example, Philip Morris paid retailers $20 to $40 to expand inventories and maintain visually prominent displays.[165] Additionally, Philip Morris increased the number of promotions offered monthly. This program, described as "the living laboratory," was initially tested in Detroit.[165] The program then expanded nationwide, including only menthol brand extensions of Benson & Hedges, Marlboro, Virginia Slims, and Alpine.[166]

Using ZIP codes to identify inner city neighborhood boundaries, Brown & Williamson implemented its Kool Inner City Point of Purchase (POP) Program in 1978 "to reach the core of Kool's franchise (young, black, relatively low income and education)"[98, p. 5852] and tackle the issues of poor product display and out-of-stock conditions. Later named the Kool Inner City Family Program, it targeted the top 20 African

American markets in the U.S., concentrating in the Northeast, Central, Southeast, and Southwest. Promotions included free gifts for retailers with monthly payments, a free carton of cigarettes for every 10 cartons purchased by distributors, and a multitude of consumer offers.[167]

Ethnic POP materials were employed, including marketing items with African American models that were poised to be "down to earth and not resemble the Harvard Black . . . ."[167, p. 0342] Special community events were also an important part of inner city targeting. In 1974, for example, Reynolds sponsored the Winston/Salem Cadillac sweepstakes in Chicago, in which Cadillacs were the prizes for both smokers and the local retailers of cigarettes. This promotion was intended to "generate excitement" and "strengthen Winston and Salem position [*sic*] in the young urban adult Black community."[168, p. 0004]

In the 1980s, because event sponsorship was a key element of its "Special Market" activities, Reynolds developed Salem Summer Street Scenes.[169,170] These 2-day festivals were held in the early 1980s "inside neighborhoods that [were] predominantly Black" to position Salem as a member of the community while distributing cigarettes. Reynolds reported that Salem Street Scenes reached at least 50% of the African American population in Memphis, Detroit, Chicago, New York, and Washington D.C.[170] The company also sponsored neighborhood events to "create an association between the brand and culturally relevant activities for the inner city Black smoker."[171, p. 7889]

Brown & Williamson also determined that involvement in community events was "critical to the success of its inner city program."[172, p. 3353] It operated the Kool Jazz festivals[173] and Summer Fest inner city music program[174] for years; it also considered funding inner city music festivals that were free to the public as a direct extension of Kool advertising.[175]

Philip Morris, similarly, was urged to "become more intimately involved in community affairs" to increase visibility in inner cities.[160] Philip Morris began sponsoring Black Expos around the country, beginning with the 1988 Indiana Black Expo.[176] Sponsoring national expos gave Philip Morris the opportunity both to advertise its product and to distribute free Benson & Hedges cigarettes to crowds of over 325,000. At the Indiana Black Expo, for example, Philip Morris's promotion included stage signage, a $25,000 check presentation, and remarks made on stage during the concert, and distribution of 10,000 samples, primarily Benson & Hedges cigarettes.[177]

Between 1995 and 1998, Philip Morris activities included "Club Benson & Hedges" promotional bar nights, which targeted 21–45 year-old "urban/ethnic markets."[178] "The brightest up and coming stars in urban music" were showcased in front of an estimated 100,000 consumers, who were "rewarded" with VIP treatment and preferential purchase opportunities. "Passport to 100 Urban Night Clubs," a promotional item billed as "America's only national entertainment guide which features establishments located within the inner city, frequented by African-Americans," was distributed to those attending any Club Benson & Hedges event.[179] It provided information about nightclubs, restaurants, attractions, annual events, and other social happenings in African American communities. After 13 years of using music to promote its Benson & Hedges brand while seeking a "diverse consumer base," Philip Morris suspended the brand's promotional activities in 1999.[180]

The "menthol wars": Summary. For 3 decades, the major tobacco companies competed aggressively to attract inner city African American smokers. In 1976, Kool had a 32.1% share of the African American market, and Salem followed with 13.5%. Benson & Hedges and Newport trailed behind with 3.1% and 2% shares, respectively. By 1978, Kool was still in the lead, but with only a 4% increase from 1976, compared with Benson & Hedges's 39% increase.[181] As other brands increased market share, Brown & Williamson grew concerned. Kool's share of the market was leveling off, possibly due to competitive advertising leading to brand switching.[182] Newport, which had consistently received the largest budget of all Lorillard brands, doubled its share of the menthol market from 22.4% in 1981 to 47.8% in 1987, while its competitors all lost half their market share.[127] As a result, Salem, Kool, and Benson & Hedges Menthol sales faltered during the 1980s.

Discussion

Our study has limitations. The Legacy Tobacco Documents Library contains more than 7 million internal tobacco industry documents (over 40 million pages). Because our search terms retrieved only those documents where our particular search terms were associated with indexed fields (e.g., title, author, date), we were not able to search the full text within the document pages; thus, we may not have retrieved every document relevant to our research topic, and this may have caused us to understate the true extent of tobacco industry activities in inner city neighborhoods during the late 1970s–1990s. Since we completed data collection for this study, a full-text site containing the documents has been developed (http://ltdlftd.library.ucsf.edu/queryform.jsp) which might be used to identify additional documents; however, the sheer quantity of material available forces researchers to make decisions about which search terms retrieve the most relevant material. In any historical or archival study, the possibility always exists that material that later becomes available will shed additional light on the phenomena of interest. However, we believe that the documentary evidence abundantly supports our primary findings, highlighting the consistency of geographical patterns of activities across companies.

Though the targeting of African Americans and poor people has been previously documented,[16,17,78,81] this study shows specifically how temporal intersections between race, class, geography, and corporate marketing shaped and perpetuated "inner cities" as marginalized places and, in turn, how the racialized geography of those places spurred development of innovative technologies for the industrial promotion of menthol cigarettes. Race and class fundamentally shaped the inner city menthol wars described here. While African Americans were not the largest group of menthol smokers, African American smokers overwhelmingly chose menthol, and African Americans were quitting at lower rates than Whites. Thus, geographic areas such as inner cities, with their large concentrations of African American residents, represented efficient sites for promotion and growth opportunities for every menthol brand.

As "White flight" left inner city cores of poverty and racial segregation during the late 20th century,[41–42,183–186] it left behind neighborhoods that were challenging for marketers. Lack of employment opportunities contributed to rising poverty and crime.

These sociogeographic circumstances led tobacco companies to develop the innovation of the mobile van for distributing free samples of cigarettes throughout neighborhoods in which employees felt unsafe on foot. The insulated mobility of vans, accompanied by music and other attractions, enabled tobacco companies to safely counter the threat of crime while covering larger territories.

Other technological innovations were also developed specifically to deal with the geographic particularities of the inner city. As major retailers moved out of urban cores, the multiple small retail outlets that spread throughout these neighborhoods became the only places through which companies could sell goods. As this study shows, the smaller scale of these stores prompted tobacco companies to develop scaled down, specialized display units that served other purposes for retailers, kept products always attractive, visible, and easily accessible, and ensured that retailers did not run out of stock.

The menthol wars were also aided by the refinement during this period of demographic and psychographic profiling that allowed marketers to appeal more effectively to different groups. Even with these tools, however, companies made many missteps in trying to connect with inner city African Americans.[187–189] Companies addressed these missteps by engaging African American marketers who specialized in reaching poor, less educated, and predominantly African American populations.

It would be wrong to suggest that inner city residents were simply passive victims of tobacco marketers. Many within these communities built their capacity and infrastructure to actively resist the targeting of their communities via marketing for deadly products, and in some cases did so with remarkable effectiveness.[16,190–192] One cannot ignore, however, the enormous power differentials that exist between corporations and inner city neighborhood groups, and the ways in which the innovations of tobacco companies allowed them to overcome the disadvantages that inner cities posed for their marketing activities. Those activities, which contributed to increased cigarette smoking, had negative health and economic consequences for inner city residents, reinforcing their marginalized social position and increasing the likelihood that they would be unable to extricate themselves from poverty.[193]

Lung cancer is perhaps the disease most associated with cigarette smoking. Prior to the early 1960s, the mortality rate for lung cancer for White men was higher than for African American men.[194] During the 1960s, African American men and White men were dying of lung cancer at similar rates. However, beginning in the 1970s, the overall age-adjusted death rate for lung cancer for African American men surpassed that of White men. Similarly, beginning in the 1970s, the overall age-adjusted death rate for oral cancer among African American men surpassed that of White men and by the 1980s the death rate was twice as high for African American men than for White men.[194] The overall age-adjusted death rate for cancer of the larynx remained stable for Whites; however, between the 1950s and 1990s the rates had increased by 260% for African American men and approximately 233% for African American women.[194]

This study suggests that the tobacco-related health disparities that disfavor residents of many lower-income urban cores today were not solely determined by factors such as unhealthy habits and unequal access to health services. Tobacco-related health disparities were shaped as well by geographically specific and (when compared with White neighborhoods) intentionally disproportionate levels and *types* of aggressive cigarette marketing and promotion,[16,31,81] carried out over multiple decades. They were in a fundamental way *industrially created*. Ending health disparities, therefore, cannot focus merely on identifying individual health behaviors or risk factors: it also means naming, resisting, and politically organizing resourceful defenses against corporate vectors of disease and attending to the social injustices that shape inner cities as targets. Recent efforts to emphasize community participatory research[195–198] could represent opportunities to organize efforts to counter industry influence and re-shape the racialized geography of health in inner cities.

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Has the tobacco industry evaded the FDA's ban on 'Light' cigarette descriptors?

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ABSTRACT

Background Under the Family Smoking Prevention and Tobacco Control Act (FSPTCA), the Food and Drug Administration (FDA) banned the use of "Lights" descriptors or similar terms on tobacco products that convey messages of reduced risk. Manufacturers eliminated terms explicitly stated and substituted colour name descriptors corresponding to the banned terms. This paper examines whether the tobacco industry complied with or circumvented the law and potential FDA regulatory actions.

Methods Philip Morris retailer manuals, manufacturers' annual reports filed with the Massachusetts Department of Public Health, a national public opinion survey, and market-wide cigarette sales data were examined.

Results Manufacturers substituted "Gold" for "Light" and "Silver" for "Ultra-light" in the names of Marlboro sub-brands, and "Blue", "Gold", and "Silver" for banned descriptors in sub-brand names. Percent filter ventilation levels, used to generate the smoke yield ranges associated with "Lights" categories, appear to have been reassigned to the new colour brand name descriptors. Following the ban, 92% of smokers reported they could easily identify their usual brands, and 68% correctly named the package colour associated with their usual brand, while sales for "Lights" cigarettes remained unchanged.

Conclusions Tobacco manufacturers appear to have evaded a critical element of the FSPTCA, the ban on misleading descriptors that convey reduced health risk messages. The FPSTCA provides regulatory mechanisms, including banning these products as adulterated (Section 902). Manufacturers could then apply for pre-market approval as new products and produce evidence for FDA evaluation and determination whether or not sales of these products are in the public health interest.

INTRODUCTION

The Food and Drug Administration (FDA) regulates industries accounting for nearly 25% of consumer spending in the USA for protection of the nation's public health and safety.[1] On 23 June 2009, the US President signed into law the Family Smoking Prevention and Tobacco Control Act (FSPTCA, the Act) extending the FDA authority to tobacco products, which take the lives of over 400 000 Americans each year.[2] The FSPTCA vests the FDA with the authority to set standards for tobacco products and the power as gatekeeper to control the entry of new products into the market, while products that were on the market prior to the Act's passage were allowed to remain. The significance of the FDA's new role is comparable with its authority over pharmaceuticals, which according to Professor Daniel Carpenter, member of the Institute of Medicine advisory panel to the FDA, allows it 'to check and constrain a very large and politically dominant industrial sector'.[3] Premarket approval is required for any tobacco product introduced after 15 February 2007 that is not deemed by the FDA to have substantial equivalence to a predicate product on the market as of that date. Importantly, Section 900 of the Act defines a brand as 'a variety of tobacco product distinguished by the tobacco used, tar content, nicotine content, flavoring used, size, filtration, packaging, logo, registered trademark, brand name, identifiable pattern of colors, or any combination of such attributes,', which allows the FDA to regulate the label and brand name as part of the tobacco product.[2]

This article examines the industry response to Section 911(b)(2)(ii) of the law, which came into effect on 22 June 2010, banning the use of explicit or implicit descriptors that convey messages of reduced risk including 'light', 'mild' and 'low', or similar descriptions in a tobacco product, label, labelling or advertising unless the manufacturer demonstrates to the FDA that the product significantly reduces harm and the risk of tobacco-related disease to individual tobacco users and benefits the health of the population as a whole.[3] This action was based on findings, including a 2006 US federal court decision that the major US cigarette manufacturers were guilty under the Racketeer-Influenced and Corrupt Organization Act (RICO), citing 'longstanding and continuing fraudulent efforts to deceive the American public about 'light' and 'low tar' cigarettes', marketing them as less harmful when manufacturers knew they were not.'[4] Judge Gladys Kessler ruled, 'Consumers' false belief [of Lights] is so pervasive and longstanding and has been exploited and promoted by Defendants [tobacco manufacturers] for so long, that preventing and restraining Defendants' future fraud requires a ban on any future use of descriptors which convey a health message.'[4]

Marketing of 'Light' cigarettes, a term used in this paper to include 'light' 'mild', 'medium', 'low', '1owest' and 'ultralight' cigarettes, surged after the first U.S. Surgeon General's 1964 report which found that cigarette smoking causes disease.[5] During that time, tobacco manufacturers introduced filter ventilation, small holes placed before the machine attachment to lower tar and nicotine yields of cigarettes, using a standardised method developed by the Federal Trade Commission. Manufacturers used these measures to describe brands as light based on low yields and to convey messages of reduced risk despite the fact that the Federal Trade Commission method was neither intended nor able to predict actual human exposure

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to toxins. According to Philip Morris (PM), filter ventilation allows the mixing of air with smoke at controlled ratios and was used to classify cigarettes with 'Lights' and full-flavour categories: 0%–10% ventilation 'full flavour', 20%–30% ventilation 'light', 45%–70% ventilation 'ultra-light' and 60%–75% ventilation 'lowest'.[6]

The 2001 National Cancer Institute (NCI) Monograph (Number 13) found that smokers compensate for the lower yield of Lights cigarettes by smoking more intensely, more often, or by fully or partially covering the ventilation holes to obtain a desired level of nicotine, thus negating any predictive value of Lights categories regarding disease risk.[6] NCI also found that the manufacturers intentionally used Lights descriptors to market cigarettes as safer, and many smokers believed this message and switched in lieu of quitting.[7] In the FSPTCA preamble, Congress stressed the public health significance of the Lights deception noting, "mistaken beliefs about the health consequences of smoking 'low tar' and 'light' cigarettes can reduce the motivation to quit smoking entirely and thereby lead to disease and death."[2]

Tobacco manufacturers responded to the ban by removing the terms explicitly listed in the law and substituting colour brand name descriptors that exactly corresponded to the banned Light descriptors. At the same time, they were appealing to the federal court, arguing that passage of the FSPTCA eliminated any reasonable likelihood that they would commit future RICO violations.[8] However, following actions similar to the FSPTCA in other nations, manufacturers responded by using colour substitutes on packages as well as alternative terms.[9–13] Subsequent studies found that consumers perceive colour descriptors on packaging as they do Lights descriptors, as less harmful to smoke than regular brands,[14–18] and thus the colour descriptors are apt to perpetuate the Lights deception. The purpose of the present study is not to further examine consumer perceptions of risk associated with package colours and descriptors, but to address the urgent question for the FDA: Did Section 911 end the Lights deception as Congress intended, or has the provision been circumvented by the manufacturers' systematic colour-name coding of Lights brands?

To address this question, this study examined three complementary lines of evidence: manufacturer intent reflected by brand name changes and marketing materials sent by PM to its retailers prior to the ban[19] and by manufacturers' annual reports required by Massachusetts Department of Public Health (MDPH) listing filter ventilation by full brand and sub-brand name;[20] consumer response to the package changes based on a nationally representative survey of smokers conducted 1 year following the date of implementation; and market response based on national sales of Lights versus regular cigarettes before and after the ban. The combined evidence of this paper assesses tobacco industry compliance with the ban on Lights descriptors and regulatory actions available if the FSPTCA has been violated.

METHODS

Materials sent by PM to retailers in spring, 2010 were identified in the Legacy Tobacco Documents Library,[19] and reviewed to determine company intent and manner of modifying Lights brand names in response to the ban. Manufacturers' annual reports of nicotine yield and related features of all products filed with MDPH were analysed for the years 2009–2011 focusing on the brand family with the largest market share by each of the major manufacturers: Marlboro by PM, Camel by Reynolds American, and Newport by Lorillard Tobacco, inclusive of 83 sub-brands for a total market share near 60%.[21]

A sub-brand in MDPH reports is specified as a unique combination of physical design and labelling characteristics. The numbers of sub-brands with a Lights descriptor and the numbers of sub-brands with one of the new typically used colour descriptors in the brand name, identified as described above, were tabulated for the years 2009 and 2011. Changes in these numbers were examined for the year just prior to and following the ban. The mean per cent filter ventilation among sub-brands was computed and compared across Lights descriptor categories prior to the ban and across colour descriptor categories following the ban. A paired t test was used to test for a difference between per cent ventilation of PM sub-brands with Lights descriptors in 2009 prior to the ban and corresponding sub-brands in 2010 following the ban, using the PM retailer brochure which directly links new colour descriptors with the substituted Lights descriptors.[19]

A public opinion survey representative of the US adult population ages 18 years and older excluding Hawaii and Alaska was conducted via telephone from 18 May to 5 June 2011 by Social Science Research Solutions an independent research company, under contract with Harvard School of Public Health. The sample was obtained by bilingual random digit-dialling of landline telephones in households and of cell phone numbers, and with random selection of a single respondent within each household. This survey oversampled smokers and a minimum of 30 interviews was conducted in Spanish for representation of the Hispanic population. The response rate was 51%. A total of 1021 completed the smoking component of the survey until reaching quotas of current smokers (n=510) for the present study and non-smokers (n=511) for other unrelated research. All data were weighted in a multi-phase design to adjust for the probability of selection and systematic non-response bias. The final weighting stage involved poststratification adjustment by raking so that the weighted sample reflects the US adult population along the lines of age-by-gender, race/ethnicity, education and census region. The survey was exempt from Institutional Review Board (IRB) approval. All respondents were asked about current and prior year smoking status in addition to demographics. Current smoking status was determined in the survey on the basis of responses to the questions, 'Have you smoked at least 100 cigarettes in your entire life?', and 'Do you now smoke cigarettes every day, some days or not at all?' Prior smoking status was determined on the basis of responses to the question, 'Six months ago, were you smoking cigarettes every day, some days, or not at all?' Smokers were first asked to name their usual cigarette brand based on the Lights descriptors banned a year before, and then asked three additional questions: 'In the past six months, how difficult has it been for you to identify your usual brand of cigarettes?'; 'Has it been very easy, somewhat easy, somewhat difficult, or very difficult?'; and 'What is the main color on the cigarette package of [your usual brand] that you smoked most often during the past 30 days?' Descriptive statistics incorporating the sampling weights were computed, and percentages and 95% CIs are reported. The proportions of correctly identified package colours were compared across respondent usual brand descriptor categories using contingency table analysis and the Pearson χ^2 statistic. All statistical analyses incorporated survey weights.

Cigarette sales and market share were derived from annual and quarterly ScanTrack scanner data licensed from ACNielsen[22] for the years 2009 and 2010. Data for 2011 were not available at the time of the study. ScanTrack sampling is projected to represent approximately 95% of food and drug stores, 100% of convenience stores and 40% of mass merchandisers in the USA.

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PM sub-brands marketed with a colour in the brand name in 2009 prior to the ban were identified in the MDPH data. Sub-brands introduced with one of the new colour descriptors in the fourth quarter of 2010 following the ban were identified by the retailer brochure that directly links the new colour descriptors to the substituted Lights descriptors. The total 2009 and fourth quarter 2010 market shares of these colour named sub-brands were compared.

The total market shares of Marlboro, Camel and Newport sub-brands with Lights terms in the brand names in the first half of 2010 were compared with the total market shares of the corresponding brands linked by Universal Product Code (UPC) used for tracking trade items in stores in each of the last two quarters of 2010 following the ban.

RESULTS

Brand name changes

Examination of PM's retailer manual and analysis of the reports to MDPH confirmed that in response to the ban, the major cigarette manufacturers removed the terms explicitly stated in the law and substituted new colour terms for Lights brand name descriptors. The PM retailer manual states, 'current pack descriptors such as light, ultra-light and mild will be removed from all packaging' and new names were provided for each brand specified. 'Marlboro Light' sub-brands were renamed 'Marlboro Gold'. 'Marlboro Mild' sub-brands were renamed 'Marlboro Blue'. 'Marlboro Ultra-light' sub-brands were renamed 'Marlboro Silver'.[19] The same colour substitutions occurred for Parliament, Virginia Slims, L&M and Basic sub-brands; while R.J. Reynolds (RJR) used 'Blue' for 'Camel Lights' sub-brands and 'Silver' for Ultra-light sub-brands; and Lorillard used 'Blue' and 'Gold' for 'Lights' sub-brands.

The numbers of Marlboro, Camel and Newport sub-brands with one of the colour descriptors Blue, Gold or Silver in the name increased over 10-fold from three in 2009 to 33 in 2010 as well as 2011, while the number of sub-brands with Lights descriptors dropped from 35 to zero in 2011 following the ban (figure 1). These Lights sub-brands, which were subsequently renamed with colour descriptors, represented 31.8% of the US cigarette market in 2009.[22]

Filter ventilation

The mean per cent filter ventilation for Lights categories of the major brands in year 2009, prior to the ban, were graduated with levels that corresponded to the ventilation ranges of Lights categories described in PM internal industry documents, listing 20%–30% filter ventilation for light and 45%–70% filter ventilation for 'ultra-light' cigarettes (table 1).[6] Prior to the ban, per cent filter ventilation levels did not correspond with colour-named descriptor categories. Filter ventilation was 13.0% for Marlboro Blue, 31.0% for Camel Gold and 32.4% for Camel Silver. In contrast, per cent filter ventilation did correspond with the Blue, Gold, and Silver colour brand name descriptors following the ban. Further, the same categories of per cent ventilation levels that were previously associated with Lights descriptors were associated with the postban colour brand name descriptor categories (table 1).

A comparison of the per cent filter ventilation levels among 30 discrete PM sub-brands with Lights descriptors in 2009 that were renamed with colour descriptors following the ban found no statistical significance (mean difference, 3.4 percentage points; $p=0.701$) (table 2), indicating that per cent ventilation of these Lights sub-brands did not change when renamed with the new colour descriptors.

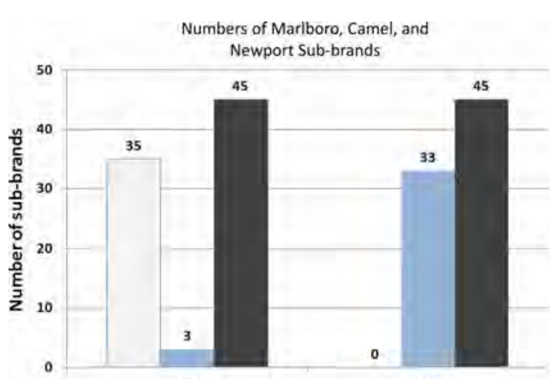

Figure 1 Numbers of sub-brands named by Lights and colour descriptors.

Consumer response to package changes

Current smoker respondents in the public opinion survey were mean age 43.2 years; 46.4% female; 66.4% White, 14.5% Black, Non-Hispanic and 10.7% Hispanic; 51.1% married or living with a partner; 57.8% with high school or less education; and 56.3% had ≤ $30 000 household income. Smokers identified their usual brand smoked as 51% 'full flavour', 5% 'medium', 31% light, 7% 'ultralight' and 4% 'none of the above'.

One year after the ban, 88%–91% of smokers found it either 'somewhat easy' or 'very easy' to identify their usual brand of cigarettes by the banned descriptor names, Lights, Mediums or Ultra-lights. No statistically significant differences in the percentages were found across Lights and full-flavour categories, ranging from 88% to 92% (figure 2). In all, 68% of smokers correctly associated the substituted colour on their packages with the banned terms, ranging from 52.4% among smokers of ultra-lights to 79.9% among smokers of full flavour/regular cigarettes ($p<0.001$) (figure 3).

Market response to package changes

A total market share of 0.36% was found for the two PM sub-brands that used colour brand name descriptors in 2009 and 30.3% market share for PM sub-brands that used one of the brand name colour descriptors in 2010, for a nearly a 100-fold increase. The total market share of the sub-brands with Light descriptors among Marlboro, Camel and Newport brands in the first two

Table 1 Mean per cent filter ventilation corresponding to 'Lights' and colour-named descriptor categories among major brands

	Mean per cent filter ventilation		
Category	Marlboro	Camel	Newport
Year: 2009			
Light	29%	32%	23%
Ultra-light	46%	56%	–
Year: 2010			
Blue	–	29%	28%
Gold	29%	38%	34%
Silver	50%	40%	–
Year: 2011			
Blue	–	34%	32%
Gold	28%	40%	36%
Silver	47%	42%	–

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Table 2 Comparison of ventilation in Philip Morris cigarette brands with colour names and the Lights brands replaced

Sub-brand	Colour name substitute	Per cent ventilation 2009	Per cent ventilation 2010	Δ Per cent ventilation
Basic lights 100s box	Gold	23	16	7
Basic lights 100s soft pack	Gold	23	16	7
Basic lights box	Gold	17	15	2
Basic lights soft pack	Gold	16	15	1
Basic menthol lights 100s box	Gold	20	23	3
Basic menthol lights 100s soft pack	Gold	19	25	6
Basic menthol lights box	Gold	16	17	1
Basic menthol lights soft pack	Gold	12	14	2
Basic menthol ultra-lights 100s box	Blue	49	45	4
Basic menthol ultra-lights box	Blue	42	39	3
Basic ultra-lights 100s box	Blue	47	52	5
Basic ultra-lights 100s soft pack	Blue	50	48	2
Basic ultra-lights box	Blue	41	42	1
Basic ultra-lights soft pack	Blue	43	46	3
Marlboro lights 100s box	Gold	30	24	6
Marlboro lights 100s soft pack	Gold	30	24	6
Marlboro lights 25s box	Gold	18	25	7
Marlboro lights box	Gold	25	23	2
Marlboro lights soft pack	Gold	24	23	1
Marlboro medium 100s box	Red label	20	23	3
Marlboro medium 100s soft pack	Red label	25	21	4
Marlboro medium box	Red label	18	17	1
Marlboro medium soft pack	Red label	22	23	1
Marlboro ultra-lights 100s box	Silver	49	52	3
Marlboro ultra-lights box	Silver	43	53	10
Merit lights 100s soft pack	Gold	33	32	1
Parliament lights 100s soft pack	White	30	34	4
Parliament lights box	White	30	35	5
Parliament menthol lights box	White	22	23	1
Virginia slims luxury lights 120s box	Gold	27	28	1
Mean absolute difference in per cent ventilation				3.4

Sources: Philip Morris, USA[7] and Annual Reports to Massachusetts Department of Public Health.[18]

quarters of 2010 (34% and 33%) was similar to that of sub-brands matched by UPCs in each of the second two quarters of 2010 (31% and 30%), showing no marked decline in annual sales.

DISCUSSION

Tobacco manufacturers appear to have circumvented the ban on Lights descriptors by intentionally substituting colour brand name descriptors, while maintaining the same gradient of ventilation used for Lights designations in the new colour-coding scheme. The present findings appear to support the FDA's position in a letter to PM regarding the use of a Marlboro Lights package onsert prior to the ban.[23] The onsert advised consumers regarding the pack changes and substitution of colour name descriptors as listed in the retailer manual. The FDA stated that the onsert suggests that Marlboro in the gold pack will have the same characteristics as Marlboro Lights, including any mistaken attributes associated with light cigarettes and may perpetuate the mistaken beliefs associated with these cigarettes.[24]

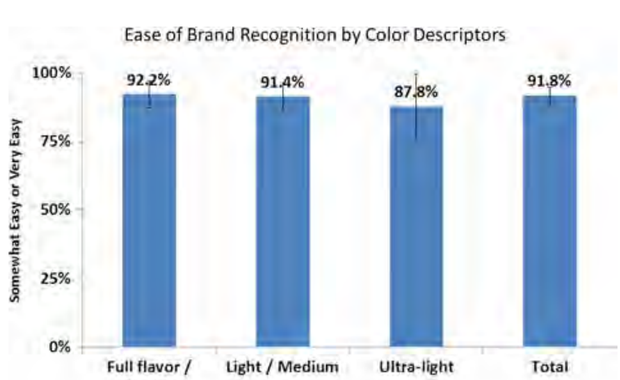

Figure 2 Percent of smokers reporting "somewhat easy" or "very easy" to identify their usual cigarettes by the banned descriptor names.

The population survey found that 1 year following the ban smokers still perceived their usual brands as Lights or full flavour. While smokers of full flavour cigarettes were more often correct than smokers of Lights category brands in identifying their usual brand's pack colour, the majority of smokers of brands in all categories correctly identified their brands' pack colour. The NCI Monograph findings suggest that when smokers no longer perceive certain brands as Lights, fewer youth will initiate to low yield cigarettes and less switching from 'full flavour' to light cigarettes will occur.[7] Consequently, a relative decrease in the sales of low yield cigarettes should be expected. However, national cigarette sales for Lights cigarettes did not change after the ban, suggesting the perpetuation of mistaken beliefs associated with these brands.

A review of industry practices following similar bans in other countries concluded that nations should ban Lights descriptors

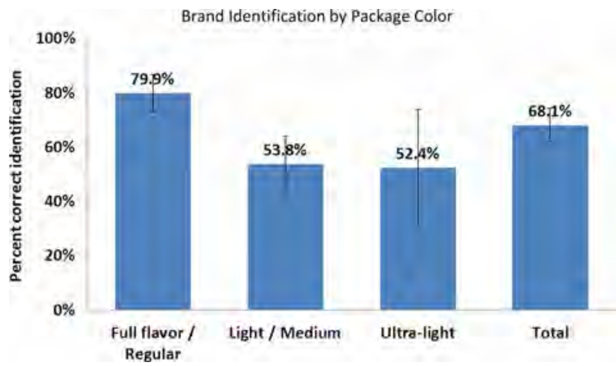

Figure 3 Percent of smokers correctly associating substituted colours with banned terms.

and 'misleading numbers, the use of colours, imagery, brand extensions, and other devices that contribute to deception'.[24] The FDA appears to have the authority to do this based on the FSPTCA in order to end the deception of reduced risk associated with cigarette descriptor terms. The FDA's Draft Guidance in September 2011 states if 'the name of the cigarette brand was modified or changed, the cigarette is a new tobacco product and… the manufacturer must follow an appropriate regulatory pathway to market (i.e., a substantial equivalence report under 905(j), or a premarket [new] tobacco application under 910(b)).'[25] Substantial equivalence pertains to products marketed after 15 February 2007 and requires that the product has the same characteristics as a predicate product on the market as of that date or that the manufacturer demonstrate to the FDA that it does not raise different questions of public health. Similar to the language of substantial equivalence guidance for the FDA regulated medical devices, 'different questions' may be raised by changes in the product only and not necessarily by the product's negative effects.[26] Different questions of public health are strongly suggested by: (a) manufacturers' substitution of new colour brand name descriptors for Lights, while maintaining the gradient of per cent ventilation levels associated with the brand name descriptors and (b) consumers' continued identification and smoking of these brands on the basis of the colour name descriptors.

Section 902 ('Adulterated Tobacco Products') allows the FDA to require removal of the modified brands and varieties from the market.[2] Without a finding of substantial equivalence, the law requires manufacturers to submit premarket new tobacco product applications for the FDA approval prior to marketing modified brands.[25] Manufacturers could remove all packaging changes not required by Section 911 and conduct testing to demonstrate to the FDA that the new products are appropriate for the protection of the public health and that the proposed packaging, labelling and design do not create false or misleading perceptions of safety.[2]

Other tobacco product characteristics in addition to labelling may contribute to false perceptions regarding risk, including concentrations of smoke constituents attributable to filter ventilation, and chemosensory effects. Colour-coded brand name descriptors associated with the ventilation of Lights appear to perpetuate the deception. Whether these descriptors maintain the false perception that such brands are 'safer' than others is not addressed in this study. Previous findings suggest that consumers do perceive brands with colours used as descriptors on packaging as being less harmful to smoke than regular brands.[14–18] The present study is exploratory but does highlight the need for manufacturers to apply for premarket approval of these brands as new products in which they produce evidence that the FDA can evaluate and determine whether sales of these products are in the public health interest.

This study has limitations. Marketing materials of only one of the three major manufacturers were available for examination, the company with the largest market share. Annual reports of all manufacturers were available for examination, and coverage included all cigarette sub-brands whose brand families accounted for at least 3% of market in respective years as required by the Massachusetts regulation. The public opinion survey did not ascertain whether respondents had their cigarette pack in hand when querying about its colour, which might have led to overestimation of their ability to identify pack colour. Smoking status of respondents was not verified with biomarkers, and their reported usual brand was not verified independently. ACNielsen ScanTrack data are comprehensive with respect to the food, drug and convenience store channels, but less so for mass merchandisers, although we are unaware of significant differences in market share in mass merchandisers that would account for the present findings. Finally, the postban market data in the last quarter of 2010 had not yet incorporated the new colour-named brand descriptors; nevertheless, comparisons made on the basis of UPC codes are believed to be reliable.

The findings of the present research strongly suggest that tobacco manufacturers have evaded one of the most important provisions of the FSPTCA for protecting the public health from the leading cause of preventable death and disease. The federal court has ordered tobacco companies to publicly admit that they have lied about the dangers of smoking in the past.[27–29] Yet, far more important to the public health would be to ensure that the industry does not misuse Section 905(j) regarding substantial equivalence or other key provisions of the law or the FDA regulatory process to perpetuate public deception into the future.

What this paper adds

- By substituting colour brand name descriptors for banned Lights descriptors, tobacco manufacturers appear to have circumvented the FDA ban on misleading descriptors that convey messages of reduced health risk, a critical provision of the FSPTCA for protecting the public health from the leading cause of preventable death and disease.
- Ninety percent of smokers are still able to recognize their usual brand as "light" one year after the ban.
- The FPSTCA provides appropriate regulatory mechanisms to address the tobacco industry's perpetuation of the public deception concerning Lights cigarettes, including banning products that have evaded the law as adulterated (Section 902) and ensuring that the industry does not misuse Section 905(j) regarding substantial equivalence or other key provisions or FDA regulatory processes.

Contributors All authors contributed significantly to the conception, design and interpretation of data; drafting the article and revising it critically for important intellectual content; and final approval of the version to be published.

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Patient consent Patient consent was not applicable.

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Epidemiology of menthol cigarette use

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Approximately one-fourth of all cigarettes sold in the United States are mentholated. An understanding of the consequences, patterns, and correlates of menthol cigarette use can guide the development and implementation of strategies to reduce smoking prevalence and smoking-attributable morbidity and mortality. This paper summarizes the literature on the health effects of mentholated cigarettes and describes various patterns of use as indicated by consumption and survey data from the United States and other nations. The epidemiological literature on menthol cigarettes and cancer risk is inconclusive regarding whether these cigarettes confer a risk for cancer above that of nonmentholated varieties. Available data indicate that mentholated cigarettes are at least as dangerous as their nonmentholated counterparts. In addition, because mentholation improves the taste of cigarettes for a substantial segment of the smoking population and appears to mask disease symptoms, this additive may facilitate initiation or inhibit quitting. Menthol market share is high in the Philippines (60%), Cameroon (35%–40%), Hong Kong (26%), the United States (26%), and Singapore (22%). Newport has become the leading menthol brand in the United States. Surveys from four nations indicate that menthol use among adult smokers is more common among females than males. Among U.S. smokers, 68.9% of Blacks, 29.2% of Hispanics, and 22.4% of Whites reported smoking a mentholated variety. Research is needed to better explain factors that may influence menthol preference, such as marketing, risk perceptions, brand formulation, and taste preferences. Such research would guide the development of potentially more effective programs and policies.

Introduction

Menthol, a monocyclic terpene alcohol, is a stimulant of cold receptors (Eccles, 1994; Gelal, Jacob, Yu, & Benowitz, 1999). Frequently derived from the oils of the peppermint and cornmint plants, menthol is added to about 90% of commercial cigarettes sold in the United States ("The situation on the world menthol market," 1984; Eccles, 1994). Brands marketed as menthol cigarettes contain from 0.1% to 1.0% of their tobacco weight in menthol ("The situation on the world menthol market," 1984; Reid, 1994). In most other brands, however, the amount of menthol is so low (approximately 0.03% of the tobacco weight) that the mint flavor and cooling sensations are not perceptible. Concern has been raised that mentholated cigarettes may pose a relatively greater health risk because the menthol makes them more addictive or because of direct adverse affects of this additive in cigarette smoke (Henningfield et al., 2003). Menthol may facilitate initiation or prevent quitting by making the smoke taste less harsh (Hymowitz, Mouton, & Edkholdt, 1995; Stratton, Shetty, Wallace, & Bondurant, 2001). It also may mask symptoms of respiratory disease, potentially leading to delays in seeking medical attention and suppressing motivation to quit (Garten & Falkner, 2003).

Epidemiological data on menthol cigarette use can help researchers and policy makers to understand the consequences of using menthol cigarettes, identify high-risk groups and correlates of risk, justify and evaluate policies and programs meant to curtail use,

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and justify research initiatives. To facilitate these objectives, we first briefly review the literature on the health consequences of smoking mentholated cigarettes, describe the menthol composition of 140 U.S. cigarette brands, and review the results of previous surveys on brand preference. Then we provide a brief overview of market share data in 55 countries and Hong Kong, followed by population estimates from analyses of four national surveys on brand preference.

Health consequences of menthol cigarettes

The three leading causes of mortality in the United States are diseases of the heart (predominantly coronary heart disease), accounting for 30% of all deaths in 2000; cancer (23%), and cerebrovascular diseases (7%) (Anderson, 2002). Epidemiological studies on menthol cigarettes have examined their influence on tobacco-attributable cancers. A prospective study in the Kaiser Permanente Medical Care Program found that mentholation was associated with an increased risk of lung cancer in men but not in women among current smokers who had smoked at least 20 years (relative risk = 1.45 for men, 95% $CI = 1.03$–2.02; and 0.75 for women, 95% $CI = 0.51$–1.11). The data were adjusted for age, race, education, number of cigarettes smoked per day, and duration of smoking (Sidney, Tekawa, Friedman, Sadler, & Tashkin, 1995). Two case-control studies in the United States, however, found similar risks for lung cancer in current smokers regardless of preference for menthol cigarettes (Carpenter, Jarvik, Morgenstern, McCarthy, & London, 1999; Kabat & Hebert 1991). Stellman and colleagues (2003) recently updated the 1991 American Health Foundation study of Kabat and Hebert (1991), using more than three times as many cases. Although Stellman and colleagues used a different analytical approach, they also found similar lung cancer risks for smokers of menthol and nonmenthol cigarettes.

Another Kaiser Permanente study showed similar risks for nonlung smoking-related cancers (upper aerodigestive, pancreas, renal adenocarcinoma, other urinary tract, and uterine cervix) across menthol use categories (Friedman, Sadler, Tekawa, & Sidney, 1998). Other case-control studies have shown similar risks, among menthol and nonmenthol smokers, for esophageal cancer (Hebert & Kabat, 1989) and oropharyngeal cancer (Kabat & Hebert, 1994), although the earlier study showed a marginally significant increased risk of esophageal cancer associated with longer menthol use in women.

What is it about menthol that might alter the adverse health effects of cigarette smoking? One theory suggests that menthol smokers may get greater exposure to the toxins in tobacco smoke, because menthol masks the harshness of the smoke, thereby facilitating greater inhalation. For example, menthol may desensitize the tongue to nicotine, which can produce a burning, painful sensation (Dessirier, O'Mahoney, & Carstens, 2001). Several studies have examined differences in puffing behavior between menthol and nonmenthol smokers. In one study of 95 women, menthol smokers had significantly larger puff volumes and higher plasma cotinine levels than nonmenthol smokers (Ahijevych & Parsley, 1999). In other studies, mentholated cigarette smoking was associated with lower individual puff volumes and cigarette smoke exposure (cumulative puff volumes) than nonmentholated cigarette smoking (Ahijevych, Gillespie, Demirci, & Jagadeesh, 1996; Jarvik, Tashkin, Caskey, McCarthy, & Rosenblatt, 1994; McCarthy et al., 1995). In those and other studies, smoking mentholated cigarettes resulted in comparable (McCarthy et al., 1995) or higher (Ahijevych et al., 1996; Clark, Gautam, & Gerson, 1996; Jarvik et al., 1994) levels of carbon monoxide (CO) exposure, as measured by expired CO or carboxyhemoglobin. The higher CO content of mainstream smoke from mentholated cigarettes may contribute to this result (Jarvik et al., 1994). Other speculative mechanisms included increase in diffusivity of the alveolar capillary membrane for CO transfer or in the affinity of hemoglobin for carbon monoxide (Jarvik et al., 1994), as well as increased breath holding (Clark et al., 1994; Henningfield et al., 2003) and increased oral absorption (Clark et al., 1995). Further research is needed to resolve apparent discrepancies in findings to date and to clarify mechanisms.

D,L-Menthol was not carcinogenic when administered in food to rats and mice (National Cancer Institute, 1979). However, two recent studies suggest that menthol may enhance the uptake and metabolism of polycyclic aromatic hydrocarbons from mainstream smoke (Melikian et al., 2002; Zhang et al., 2003). Zhang et al. found an effect only in males. These studies, however, cannot rule out racial differences in carcinogen metabolism. In contrast, one experiment indicated that menthol does not increase tobacco-specific nitrosamine-induced DNA adduct formation in rats that were administered menthol via drinking water (Richie et al., 1997). Tobacco-specific nitrosamines produced adenocarcinoma of the lung in mice, rats, and hamsters when administered orally, topically, or by injection (Hecht & Hoffman, 1988).

Cotinine is the primary metabolite of nicotine. Mentholated cigarette smoking may result in higher cotinine concentrations than smoking nonmentholated cigarettes (Ahijevych & Parsley, 1999; Clark et al., 1994), and duration of mentholated cigarette smoking is associated with a nonsignificant trend toward increased cotinine values (Wagenknecht, Haley, & Jacobs, 1992). Both CO and nicotine may be causally related to the development or triggering of cardiovascular events (U.S. Department of Health and Human Services [USDHHS], 1983).

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The observation of higher cotinine values in menthol smokers has led to speculation that these smokers may have more difficulty quitting. The observation that quit ratios are higher in Whites, who smoke predominately nonmenthol brands, than in Blacks, who smoke predominately mentholated brands (USDHHS, 1998), supports the hypothesis that menthol may increase level of nicotine addiction and hinder smoking cessation. Furthermore, a national retrospective cohort study suggested that Black smokers were more likely than White smokers to try to quit in a given year but were less likely to remain abstinent (Centers for Disease Control and Prevention [CDC], 1993). However, a prospective study of 13,000 smokers over a 5-year period failed to detect a difference in cessation rates between smokers of mentholated and nonmentholated cigarettes (Hyland, Garten, Giovino, & Cummings, 2002), a finding also reported by Muscat, Richie, & Stellman (2002). Neither study, however, measured actual menthol delivery by brand, slight variations in which may influence the likelihood of quitting.

We are unaware of any studies regarding mentholation and cardiovascular disease or any other noncancer disease endpoints, and only a few small studies have examined the cardiovascular effects of menthol or mentholated cigarettes. In a study of 22 young adult volunteers, the pre- to postsmoking heart rate increase was greater in smokers of mentholated cigarettes than in other cigarette smokers (Pritchard, Houlihan, Guy, & Robinson, 1999). In an earlier study of 29 adult volunteers, baseline heart rate was higher in those who preferred mentholated cigarettes than in those preferring nonmentholated brands; no difference in blood pressure was found (McCarthy et al., 1995). The blood pressure response to rapid smoking did not differ by the two types of cigarettes. Finally, in a study of 12 healthy adult volunteers, oral administration of menthol and of placebo capsules produced a decrease in heart rate that was less in those who received menthol than in those given the placebo (Gelal et al., 1999). No significant difference in blood pressure response was seen between the two preparations.

In summary, although physiological reasons exist that could explain why mentholation of cigarettes might increase risk for disease, available data are inconclusive. Still, the data are consistent with the notion that mentholated cigarettes are at least as dangerous as their nonmentholated counterparts and these data indicate a need for further studies, including some to determine if mentholated cigarettes increase the risk for cardiovascular disease. Ideally, future studies of cancer risk would include analyses stratified by sex, race, and tumor histology and include a sufficient number of observations to adequately assess the effects of long-term menthol exposure. Research is needed to determine whether menthol alters the toxicity and carcinogenicity of smoke constituents, how smokers smoke the cigarettes, the acceptability of the cigarettes, and long-term and short-term health outcomes. Additionally, research is needed to understand how different brands and brand varieties differ in their menthol content and how these differences might relate to health outcomes.

Consumption and brand data

Federal Trade Commission (FTC) data indicate that menthol market share increased from 1963 (16%) to 1979 (29%) and declined slightly from 1982 (29%) to 1994 (25%); menthol share was 26% from 1998 to 2001 (FTC, 2003). The FTC requires manufacturers of domestically sold cigarettes to report tar, nicotine, and CO values using a standardized protocol. A total of 1,294 varieties of cigarettes were listed for 1998, the commission's most recent report at the time of this writing (FTC, 2000). (Varieties are determined by characteristics such as brand name, filter status, length, menthol status, package style, and FTC tar yield.) A total of 140 separate brands (e.g., Marlboro, Newport) were listed for 1998. Thus, each brand had, on average, 9.24 (range = 1–44) varieties (also known as subbrands or line extensions). Of the 129 brands available in more than one variety, 4 were exclusively mentholated (the number of varieties follows each brand name): Alpine (6), Belair (2), Kool (18), and Salem (14). Another 18 brands were available only in nonmentholated varieties: American (6), Barclay (3), Bee (2), Bucks (2), Canadian Players (8), Chesterfield (5), Gridlock (5), House Blend (2), Jumbos (2), Lark (8), Lucky Strike (4), Magna (4), Pall Mall (7), Rothmans (5), State (4), Tareyton (4), Viceroy (11), and Winston (19). Of the 1,294 total varieties, 418 (32.3%) were mentholated.

FTC reports on tar, nicotine, and CO in cigarette brands sold in the United States indicate that 11 (of 44) varieties of Marlboro cigarettes were mentholated in 1998 (FTC, 2000), more than twice the number in 1997 (5 out of 23) (FTC, 1999b). At least as far back as 1981, Marlboro had offered no more than five mentholated varieties in any one year (FTC, 1983, 1985, 1988, 1990, 1991, 1993, 1995, 1997, 1999a, 1999b). Newport, on the other hand, which previously had sold only one or two nonmenthol varieties, sold five (of a total of 21) in 1998 (FTC, 1983, 1985, 1988, 1990, 1991, 1993, 1995, 1997, 1999a, 1999b, 2000). These developments suggest that competition has occurred based on menthol status. Unfortunately, the FTC report on 1998 brands is the latest one available, and the commission's reports do not indicate how relevant brands were marketed.

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Market share and survey data

As of 2001, Marlboro dominated the overall U.S. cigarette market, with 38.8% market share (Maxwell, 2002). Newport was second (7.8%), followed by Doral (5.8%), Winston (5.6%), Basic (5.0%), Camel (4.8%), GPC (3.2%), Kool (2.8%), and Salem (2.6%). In 1999, National Household Survey on Drug Abuse data indicated that three brands dominated the adolescent (ages 12–17 years) and young adult (ages 18–25 years) markets: Marlboro (54.5% of adolescent smokers and 56.6% of young adult smokers), Newport (21.6% and 15.6%, respectively), and Camel (9.8% and 11.3%, respectively) (Kopstein, 2001). Among persons aged 26 years or older, the top seven brands were preferred by two-thirds of smokers: Marlboro (35.3%), Newport (6.5%), Basic (6.1%), Doral (5.7%), Winston (5.0%), GPC (4.6%), and Camel (4.3%).

Among adolescent smokers in 1999, the figures for Marlboro and Newport, respectively, were as follows by race or ethnicity: Whites, 58.4%, 16.5%; Blacks, 8.1%, 73.9%; Hispanics, 59.7%, 18.6% (Kopstein, 2001). Thus, Marlboro and Newport were the top two brands smoked by White, Black, and Hispanic adolescent smokers. Camel was third for both White (11.2%) and Hispanic (7.1%) adolescents. Kool (5.4%) was third among Blacks.

According to the 1989 Teenage Attitudes and Practices Survey, 5.6% of White smokers and 61.3% of Black smokers used Newport, 71.4% of White smokers and 8.7% of Black smokers used Marlboro, 1.0% of White smokers and 9.7% of Black smokers used Salem, and 0.6% of White smokers and 10.9% of Black smokers used Kool (CDC, 1992).

The 1986 Adult Use of Tobacco Survey found that 76% of adult Black smokers and 23% of White smokers smoked mentholated brands (USDHHS, 1989), with Salem, Kool, and Newport most commonly used (CDC, 1990). Other studies have consistently shown Black smokers to be significantly more likely than smokers in other racial or ethnic groups to use menthol cigarettes (Carpenter et al., 1999; Cummings, Giovino, & Mendicino, 1987; Kabat & Hebert 1991; Kopstein, 2001; Sidney et al., 1995; USDHHS, 1998). In 1986, 34.0% of male and 24.9% of female adult smokers selected mentholated brands, according to the Adult Use of Tobacco Survey (USDHHS, 1989), a pattern reported elsewhere (Kabat & Hebert, 1991; Sidney et al.).

We expand upon and update this literature in the remainder of this paper.

Method

International market share data

Market share data of menthol brands in 55 countries and Hong Kong were drawn from *World Cigarettes 1 and 2: The 2001 Survey* (ERC Group, 2001). Profiles were developed for key world cigarette markets, including menthol market share in most of these nations. When necessary, data from *World Cigarette Market—The 1999 Survey* (ERC Group, 1999) were incorporated, as were data from *The World Tobacco File* (4th edition) (DMG World Media, 2001).

Survey data

The survey data for this report come from four national surveys: the National Household Survey on Drug Abuse, the Monitoring the Future surveys, and the National Youth Tobacco Survey (all U.S. surveys), as well as the International Tobacco Control Policy Evaluation Survey (conducted in the United States, Canada, the United Kingdom, and Australia).

National Household Survey on Drug Abuse. The Substance Abuse and Mental Health Services Administration (SAMHSA) sponsored the 2000 National Household Survey on Drug Abuse. Details are provided elsewhere (SAMHSA, 2001). Briefly, the survey collects information on alcohol, tobacco, and other substance use (the major focus of the survey) as well as on correlates of use from residents of households, noninstitutional group quarters, and civilians living on military bases. Since 1999, the survey has used independent, multistage area probability sampling for each state and the District of Columbia. Data in 2000 were collected via computer-assisted interviewing, primarily in the form of audio computer-assisted self-interviews. There were 71,764 respondents in 2000: 25,717 aged 12–17 years, 22,613 aged 18–25 years, and 23,434 aged 26 years or older. Current smokers (18,359 respondents) were those who had smoked during the previous 30 days. These respondents were asked, "During the past 30 days, what brand of cigarettes did you smoke most often?" and "During the past 30 days, did you smoke (name of brand) menthol or regular cigarettes most often?" Data were weighted to provide nationally representative estimates, and standard errors for 95% confidence intervals were calculated in a way that reflected the complex survey design. As with the other two surveys in this study, differences between prevalence estimates were considered significant if the 95% confidence intervals did not overlap.

To test the accuracy of responses to the menthol question, we assessed responses for smokers of brands that were available in 1998 only as mentholated varieties (i.e., Alpine, Belair, Kool, and Salem) or nonmentholated varieties (i.e., Barclay, Lark, Lucky Strike, Magna, Pall Mall, Tareyton, Viceroy, and Winston; these were the only nonmentholated brands from the 18 listed above that were used by 2000 survey

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respondents). Overall, 7.9% of respondents who reported smoking brands that were available only in mentholated varieties reported smoking "regular" cigarettes. Among smokers who reported smoking brands that were available only in nonmentholated varieties, 4.2% reported smoking mentholated brands. Discrepancies were higher among adolescents (aged 12–17 years) and young adults (aged 18–25 years) than among persons aged 26 years or older. Because of these discrepancies, we do not report data on brand-specific menthol status (e.g., mentholated Marlboro, nonmentholated Newport). However, we do present data on menthol status by sociodemographic status, because the estimated effects of response bias were relatively small. For example, when we assumed that the true overall prevalence of menthol use was 28% (as in Table 2) and applied misclassification rates that were observed for the brands listed above, we found that the adjusted prevalence of menthol use was 29%. The age-specific differences in observed and adjusted prevalences also were relatively small: 32% vs. 31% for persons aged 12–17 years, 26% vs. 24% for persons aged 18–25 years, and 29% vs. 30% for persons aged 26 years or older.

Monitoring the Future surveys. Funded by grants from the National Institute on Drug Abuse, Monitoring the Future (Johnston, O'Malley, & Bachman, 2002) is conducted by the Survey Research Center in the University of Michigan's Institute for Social Research. Annual school-based surveys of 12th-grade students have been conducted since 1975 and of 8th and 10th graders since 1991. Focusing primarily on illicit drug use, the surveys also collect information on tobacco and alcohol use as well as correlates of the use of all substances. Data are collected via self-administered questionnaire in about 420 public and private schools, using a multistage random sampling procedure. A question on cigarette brand preference ("What brand of cigarettes do you usually smoke?") was added in 1998 and asked of persons who had smoked during the previous 30 days (current smokers). The 23 top brands by overall market share were listed along with "other" and "no usual brand." Data reported here are from the 1998, 1999, and 2000 surveys, which in total had approximately 136,000 participants. The cigarette brand questions were asked only of cigarette smokers on selected modules for each grade, however, and the data presented here are for 16,313 students. All data were weighted to provide national estimates and calculation of 95% confidence intervals took into account the complex survey design.

National Youth Tobacco Survey. The National Youth Tobacco Survey (CDC, 2001; Farrelly, Vilsaint, Lindsey, Thomas, & Messeri, 2001) focuses on the tobacco-related beliefs, attitudes, and behaviors of youth. It is sponsored by the American Legacy Foundation and conducted by the CDC Foundation (Atlanta, Georgia) and MACRO International, Inc., with technical support from the CDC's Office on Smoking and Health. The 2000 survey used a three-stage cluster sample involving 324 public and private middle and high schools. Data were collected via self-administered questionnaire (35,828 participants in 2000). Current smokers (had smoked during the previous 30 days) were asked, "During the past 30 days, what brand of cigarette did you usually smoke?" and "Is the brand of cigarettes that you usually smoked during the past 30 days mentholated?" Data were weighted to adjust for nonresponse and probability of selection. The 95% confidence intervals were calculated using sample weights and controlling for the complex survey design. Because 11.2% of smokers of Kool cigarettes reported that they didn't smoke a mentholated brand, we do not report brand-specific data on menthol status.

International Tobacco Control Policy Evaluation Survey. The International Tobacco Control Policy Evaluation Survey is a cohort survey of adult smokers (aged 18 years or older who report having smoked at least 100 cigarettes in their lifetime and who have smoked at least once in the past 30 days) in each of four countries: Canada, the United States, the United Kingdom, and Australia. Respondents participate every 6 months in the two-part telephone survey (10-minute recruitment survey, followed by a 40-minute main survey usually conducted 1 week after the recruitment survey). The cohort was constructed from probability sampling methods (random-digit dialing methods from list-assisted phone numbers) with numbers selected at random from the population of each country within strata defined by geographic region and community size. The research team obtained samples of phone numbers for three of the countries (United States, Canada, and United Kingdom) from Survey Sampling International, which uses a random-digit dialing methodology in which each exchange and working block of numbers has a probability of selection equal to its share of listed telephone households (RDD B methodology). Because no comparable source was available for number banks generated from such methods in Australia, the research team developed its own comparable probability sampling methods to generate number banks in that country. The next birthday method (Binson, Canchola, & Catania, 2000) was used to select the respondent in households with multiple smokers. Cooperation rates were high for a survey of this

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kind: United States, 77.0%; Canada, 78.5%; United Kingdom, 78.7%; and Australia, 78.8%. The data reported in this article are from the baseline recruitment survey, which was conducted during October–December 2002, with sample sizes as follows: Canada ($N=2{,}507$), United States ($N=2{,}500$), United Kingdom ($N=2{,}728$), and Australia ($N=2{,}562$).

In the United States, the relevant questions were "What is the brand of cigarettes that you smoke more than any other?" and "Are they menthol, plain, or some other flavor?" In Canada, respondents were asked, "What brand of [cigarettes/roll-your-own cigarettes] do you smoke more than any other?" Respondents from the United Kingdom and Australia were asked, "What brand do you smoke most?" Researchers from Canada, the United Kingdom, and Australia identified menthol brands based on the detailed brand names provided by respondents.

Results

International market share patterns

As shown in Table 1, mentholated brands accounted for fewer than 5% of market share in half the countries with data. Relatively high shares were observed in the Philippines (60%), Cameroon (35%–40%), Hong Kong (26%), the United States (26%), and Singapore (22%). Varieties of mentholated Marlboro brands are listed for 12 countries; varieties of Salem are listed for 9. In the United States (data not shown in a table), Newport brands accounted for 29.7% of all menthol sales, with Kool (10.8%), Marlboro menthol (10.5%), and Salem (10.3%) about equally distributed (ERC Group, 2001).

Patterns of brand preference in the United States

Data from the 2000 National Household Survey on Drug Abuse indicated that Newport was by far the most popular brand among Blacks and that Marlboro was most popular among Hispanics and Whites (Table 2). Among Black smokers, more than three-fourths of adolescents (aged 12–17 years) and young adults (aged 18–25 years) used Newport; less than one-third of those aged 26 years or older did so. Kool and Salem were more common among Black smokers aged 26 years or older than among those of other ages. Among White smokers, about three of every five adolescents and young adults used Marlboro; less than two of every five of those aged 26 years or older did so. Nearly one of every five White adolescent smokers used Newport. Among Hispanic smokers, young adults were most likely to use Marlboro. About one of three adolescents and one of every six young adults used Newport.

Data from the 2000 National Youth Tobacco Survey confirmed that Newport was by far the leading brand among Black adolescents and that Marlboro dominated among Asians, Hispanics, and Whites (Table 3). Newport was the second most popular brand among Asian, Hispanic, and White adolescents, although among Whites, Camel was statistically similar to Newport. Marlboro was the second most popular brand among Black adolescents.

Patterns of menthol cigarette use

According to National Household Survey on Drug Abuse data, Black smokers were generally more likely to report smoking mentholated cigarettes than Hispanic or White smokers, when stratified by age, age and sex, region, and educational status (Table 4). Among Whites, adolescents were more likely to report using mentholated brands than adults; the opposite pattern was observed among Black smokers.

Baseline data gathered in 2002 for the International Tobacco Control Policy Evaluation Survey indicated that, among adult smokers from the United States, Blacks (78.4%) were more likely to smoke mentholated brands, compared with Hispanics (38.8%) or Whites (19.6%) ($p<.001$). Menthol preference among Black smokers surveyed in Canada and the United Kingdom was not as strong. In Canada, 4 (9.8%) of 41 Black smokers and 72 (3.2%) of 2,236 White smokers used mentholated brands ($p<.05$). In the United Kingdom, 117 (4.6%) of 2,567 White smokers and 1 (3.0%) of 33 Black smokers used a mentholated brand (not significant).

Although reported menthol use was generally more prevalent for females than males across race and age strata, differences were significant only for persons aged 26 years or older, particularly for Whites (see Table 4). Baseline data from the International Tobacco Control Policy Evaluation Survey indicated that among adult smokers, females were more likely than males to use mentholated brands in the United States (31.8% vs. 22.1%), Canada (4.7% vs. 1.5%), the United Kingdom (3.7% vs. 2.0%), and Australia (5.4% vs. 1.8%). All differences were statistically significant.

Table 1. *footnote*

Notes. [a]In 1998 or a more recent year, depending on data availability. Estimates are for all cigarettes, including both mentholated and nonmentholated varieties. [b]Inferred from market share of leading menthol brand. (-) = marginal or negligible sales or market share; N/A = not available.

Sources. For menthol market share and menthol brand data: ERC Group, 1999, 2001 (with permission); for per capita consumption data: Mackay & Eriksen, 2002. [c]From ERC Group, 2001 (with permission).

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Table 1. Menthol cigarette market share, leading menthol brands, and per capita cigarette consumption in 55 countries and Hong Kong.

Region or country	Menthol market share (percent)	Leading menthol brands	Per capita cigarette consumption (sticks)[a]
Africa			
Cameroon	35–40	Aspen Menthol, Delta Menthol	652
Democratic Republic of Congo	(-)	Ambassade Filter King Size Mentholée	135
Ghana	5	London Menthol, Bond Menthol	161
Ivory Coast	(-)	Fine, St. Moritz	580
Kenya	9	Sweet Menthol	200
Nigeria	13+[b]	Sweet Menthol	189
Senegal	<5	St. Moritz, Excellence Menthol	340
South Africa	4.1		1,516
Tanzania	10+[b]	Sweet Menthol	177
Zimbabwe	14	Everest	399
Americas			
Argentina	(-)	L&M Menthol	1,495
Canada	4	Craven 'A' Menthol	1,976
Costa Rica	19	Marlboro Light Menthol, Belmont Extra Light Menthol, Delta Menthol, Derby Menthol	690
Dominican Republic	9.4	Nacional Menthol, Marlboro Menthol, Marlboro Lights Menthol, Constanza	754
Guatemala	15	Rubios Menthol, Casino Menthol	609
Honduras	N/A	Belmont Menthol, Pinares	595
United States	26	Newport, Salem, Kool, Marlboro Menthol	2,255
Venezuela	(-)	Kool, Salem	1,079
Australia/Asia			
Australia	9–10	Alpine	1,907
China	N/A	Salem, More, Yves St. Laurent	1,791
Hong Kong	26	Marlboro Menthol, Salem	N/A
India	<1	N/A	129
Japan	6–7	Marlboro Lights Menthol, Salem Pianissimo	3,033
Korea, Republic of	5–6	N/A	2,918
Malaysia	9	Salem, A-Mild Menthol	910
New Zealand	10–14	N/A	1,213
Pakistan	(-)	N/A	564
Philippines	60	Hope, Salem	1,849
Singapore	22[c]	Salem	1,230
Taiwan	2–3	N/A	N/A
Thailand	18+[b]	Falling Rain 90, Wonder Menthol	1,067
Vietnam	1[c]	Bastos Menthol	1,025
Eastern Mediterranean			
Cyprus	(-)	N/A	>2,500
Egypt	1	Marlboro Menthol, Kool, Vogue, Karelia Slims	1,275
Israel	2–3	Montana Menthol, Vogue Menthol, Cartier Vendôme Menthol, Yves St. Laurent	2,162
Lebanon	1–2	Kim, More	N/A
Tunisia	5	Mentha, 20 Mars Inter Mentholated, Royale Mentholated	1,341
Europe			
Bulgaria	1.9	Gorna Djurnaya Menthol, Vector, Salem	2,574
Czech Republic	4.9	N/A	2,306
Denmark	5+[b]	Look Menthol, Prince Light Menthol	1,919
Estonia	15–20	Ekstra Royal Menthol, Barclay Menthol, Prince Menthol, Quattro Menthol, Marlboro Menthol, L&M Menthol	1,983
Finland	18.2	L&M Lights Menthol, Marlboro Lights Menthol, Marlboro Menthol, Barclay Menthol, Belmont 2002 Menthol, Pall Mall Lights Menthol	1,351
France	<3[c]	N/A	2,058
Germany	1.3	Marlboro Menthol	1,702
Hungary	1	N/A	3,265
Italy	<1	Pack	1,901
Latvia	<2	Barclay, Prince, Quattro	N/A
Lithuania	5–10	Marlboro Menthol, Barclay Menthol, Elita, Quattro, Prince	N/A
Norway	3.1	N/A	725
Poland	11.7	Marlboro Menthol Light, Cristal Lights Menthol, Cristal Menthol Super Lights, Caro Lights Menthol	2,061
Romania	15.4	N/A	1,676
Slovakia	(-)	Petra, Trussardi	2,282
Sweden	12	Blend Menthol, Blend Ultra Menthol, Right Menthol	1,202
Switzerland	1.8	N/A	2,720
Turkey	(-)	Marlboro Menthol	2,394
United Kingdom	3.9	Berkeley Superkings Menthol, John Player Superkings Menthol, Lambert & Butler Menthol, Consulate Menthol, Mayfair Menthol, Dickens & Grant Superkings Menthol	1,748

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Table 2. Cigarette brands used most often among current smokers by race or ethnicity and age: National Household Survey on Drug Abuse—United States, 2000.

Race or ethnicity and cigarette brand	Age group (years)							
	Total		12–17		18–25		26 or Older	
	Percent	95% *CI*	Percent	95% *CI*	Percent	95% *CI*	Percent	95% *CI*
Black								
Newport	40.9	(36.6–45.4)	79.2	(72.2–84.7)	76.7	(72.3–80.5)	31.5	(26.7–36.7)
Kool	12.1	(8.9–16.1)	2.1	(0.8–5.1)	4.6	(2.7–7.5)	14.1	(10.2–19.2)
Marlboro	6.7	(4.7–9.5)	5.3	(2.9–9.7)	7.3	(5.1–10.4)	6.6	(4.2–10.1)
Salem	5.8	(4.2–7.9)	1.6	(0.5–5.1)	1.6	(0.8–3.2)	6.9	(4.9–9.5)
Basic	4.8	(2.8–8.4)	1.9	(0.5–6.5)	1.9	(0.9–3.8)	5.6	(3.1–10.0)
Benson & Hedges	4.5	(2.5–7.9)	0.7	(0.2–3.2)	0.6	(0.2–1.6)	5.5	(3.0–9.8)
Virginia Slims	3.9	(1.9–7.7)	–	–	0.4	(0.1–1.4)	4.8	(2.3–9.6)
Doral	3.6	(2.1–6.2)	–	–	0.5	(0.2–1.3)	4.4	(2.5–7.6)
Winston	3	(1.6–5.4)	–	–	–	–	3.7	(2.0–6.7)
GPC	2.6	(1.5–4.6)	–	–	0.5	(0.2–1.6)	3.2	(1.8–5.7)
Camel	1.5	(0.7–3.4)	2.9	(1.1–7.7)	1.9	(0.9–3.8)	1.4	(0.5–4.1)
Unknown	1.3	(0.7–2.4)	3.1	(1.2–7.8)	2.3	(1.1–4.8)	1	(0.4–2.4)
Hispanic								
Marlboro	57.1	(52.4–61.7)	52.5	(45.3–59.6)	67.7	(63.8–71.4)	54	(47.5–60.4)
Newport	11.0	(8.9–13.5)	31.4	(24.9–38.7)	16.7	(13.6–20.3)	7.1	(4.8–10.3)
Camel	4	(2.3–7.0)	5.3	(3.1–8.8)	4.7	(3.2–6.9)	3.7	(1.6–8.3)
GPC	3.7	(2.3–5.9)	0.7	(0.3–1.4)	1	(0.6–1.8)	4.9	(3.0–8.0)
Basic	2.9	(1.9–5.6)	0.3	(0.1–1.3)	1.5	(0.8–2.7)	3.7	(1.7–7.7)
Winston	2.9	(1.7–5.0)	0.7	(0.2–3.1)	0.3	(0.1–1.0)	4	(2.3–6.9)
Benson & Hedges	2.8	(1.6–4.9)	1	(0.4–2.7)	1.8	(0.9–3.3)	3.4	(1.7–6.4)
Kool	2.8	(1.3–5.9)	0.3	(0.1–1.2)	0.9	(0.3–2.3)	3.6	(1.6–8.2)
Salem	2.5	(1.1–5.5)	–	–	0.2	(0.0–0.7)	3.4	(1.5–7.7)
Doral	2.2	(1.1–4.4)	0.2	(0.0–1.7)	0.5	(0.1–1.5)	3	(1.4–6.2)
Virginia Slims	1.4	(0.7–2.9)	0.3	(0.1–1.4)	0.6	(0.2–1.6)	1.8	(0.8–4.0)
Unknown	1	(0.5–2.2)	3.4	(1.9–6.1)	0.7	(0.3–2.0)	0.9	(0.3–2.9)
White								
Marlboro	43.8	(42.4–45.3)	58.8	(56.4–61.2)	61.4	(59.8–63.0)	37.9	(35.9–39.8)
Camel	7.1	(6.5–7.8)	11.6	(10.1–13.2)	14.3	(13.2–15.6)	4.8	(4.1–5.6)
Basic	5.3	(4.7–6.1)	1.8	(1.3–2.5)	2.1	(1.7–2.5)	6.5	(5.6–7.5)
Doral	5.3	(4.4–6.2)	0.7	(0.4–1.3)	0.8	(0.6–1.1)	6.8	(5.7–8.1)
Newport	5.0	(4.5–5.6)	18	(16.2–20.0)	9.3	(8.4–10.3)	2.9	(2.3–3.6)
Winston	4.8	(4.1–5.7)	1	(0.7–1.6)	1.8	(1.4–2.3)	5.9	(4.9–7.1)
Virginia Slims	2.9	(2.4–3.6)	0.4	(0.2–0.7)	0.4	(0.3–0.6)	3.8	(3.1–4.7)
GPC	2.8	(2.4–3.4)	0.4	(0.2–0.8)	0.6	(0.5–0.9)	3.6	(3.0–4.4)
Salem	2.3	(1.9–2.9)	0.3	(0.1–0.7)	0.4	(0.3–0.6)	3	(2.4–3.7)
Merit	1.6	(1.2–2.1)	0.3	(0.1–0.6)	0.1	(0.1–0.3)	2.1	(1.6–2.8)
Kool	1.6	(1.2–2.0)	0.7	(0.4–1.1)	0.8	(0.6–1.2)	1.8	(1.4–2.4)
Unknown	1	(0.7–1.4)	1.9	(1.4–2.6)	0.5	(0.4–0.8)	1	(0.7–1.5)

Notes. Current smokers had smoked during the previous 30 days. Beacuse of low precision, estimates for American Indians and Alaska Natives and for Asians, Native Hawaiians, and Other Pacific Islanders are not presented. Differences between column totals and 100% represent the percentage of smokers who smoked some brand other than one listed. Dashes indicate low precision, no estimate reported.
Source. Substance Abuse and Mental Health Services Administration, Rockville, MD.

Table 3. Cigarette brands use most often among current smokers by race or ethnicity: National Youth Tobacco Survey, middle and high school students, combined—United States, 2000.

Usual brand	Black		Asian[a]		Hispanic		White	
	Percent	95% *CI*	Percent	95% *CI*	Percent	95% *CI*	Percent	95% *CI*
Marlboro	10.4	7.4–14.4)	52.1	(44.1–59.9)	51.5	(46.2–56.8)	58.5	(55.2–61.7)
Newport	68.5	(62.1–74.2)	28.3	(21.2–36.7)	21.3	(15.8–28.1)	13.7	(11.1–16.7)
Camel	2.5	(1.5–4.1)	5.4	(2.7–10.8)	5.5	(3.9–7.8)	11.7	(9.4–14.3)
No usual brand	5.5	(3.8–8.0)	4.2	(2.0–8.6)	9.6	(7.5–12.2)	7.6	(6.8–8.5)
Some other brand	6.7	(5.0–8.9)	5.4	(2.7–10.5)	7.2	(5.2–9.9)	4.9	(3.9–6.2)
Kool	2.6	(1.6–4.0)	3.1	(.9–10.2)	1.2	(.6–2.4)	0.9	(.6–1.4)
Major discount brand[b]	2.1	(1.0–4.0)	0.6	(.2–2.2)	1.1	(.6–2.2)	1.5	(1.0–2.3)
Virginia Slims	1.4	(.6–3.0)	0.4	(.1–1.7)	1.8	(1.0–3.5)	0.8	(.6–1.1)
Lucky Strike	0.5	(.2–1.7)	0.5	(.0–3.7)	0.7	(.3–1.7)	0.4	(.3–.7)

Notes. Current smokers are those who smoked during the previous 30 days. Because of low precision, estimates for American Indians and Alaska Natives are not presented. [a]Asian, Native Hawaiian and Other Pacific Islanders. [b]GPC, Basic, or Doral.
Source. American Legacy Foundation, Washington, DC.

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Table 4. Percentages of current smokers who most often smoked menthol cigarettes by age, age and sex, region, education, and race or ethnicity: National Household Survey on Drug Abuse, ages 12 years or older—United States, 2000.

Demographic characteristic	Black		Hispanic		White		Overall[a]	
	Percent	95% *CI*	Percent	95% *CI*	Percent	95% *CI*	Percent	95% *CI*
Age (years) and sex								
12–17	55.7	(48.1–63.1)	35.7	(29.1–42.8)	28.4	(26.3–30.7)	31.6	(29.6–33.7)
Male	59.7	(49.7–68.9)	32.9	(23.8–43.5)	26.5	(23.4–29.9)	30.3	(27.4–33.4)
Female	49.5	(38.5–60.6)	38.9	(30.2–48.4)	30.2	(27.3–33.2)	32.9	(30.3–35.7)
18–25	68.6	(64.1–72.7)	25.9	(22.1–30.1)	20.1	(18.8–21.5)	25.8	(24.5–27.1)
Male	70.7	(65.1–75.8)	22.8	(18.5–27.9)	18.4	(16.8–20.2)	24.9	(23.2–26.6)
Female	65.7	(58.9–71.8)	31.6	(25.2–38.7)	21.9	(20.1–23.8)	26.8	(25.1–28.6)
26+	69.5	(64.3–74.3)	29.7	(24.1–35.9)	22.5	(20.8–24.3)	28.6	(27.0–30.2)
Male	65.8	(58.4–72.6)	25.3	(18.9–33.1)	17.7	(15.6–20.0)	24	(21.8–26.4)
Female	73.3	(65.6–79.8)	36.3	(26.8–47.1)	27.4	(24.9–30.1)	33.4	(31.0–35.9)
Region								
Northeast	64.0	(54.4–72.6)	50.5	(39.5–61.4)	28.1	(25.3–31.1)	33.4	(30.6–36.3)
South	74.4	(65.7–81.5)	33.8	(25.5–43.2)	22.9	(20.8–25.1)	28.6	(26.6–30.6)
North Central	67.0	(61.0–72.5)	29.5	(22.3–37.9)	22.3	(20.0–24.8)	29.2	(27.1–31.4)
West	73.9	(57.9–85.3)	19.1	(13.6–26.3)	15.6	(12.6–19.0)	21.2	(18.3–24.5)
Education[b]								
<High school	64.2	(52.2–74.6)	29.5	(21.6–38.9)	18.8	(15.0–23.2)	26.7	(23.3–30.4)
High school	69.8	(62.2–76.4)	22.4	(14.6–32.8)	22.4	(20.0–25.1)	28.0	(25.7–30.5)
Some college	74.4	(63.9–82.7)	39.6	(26.7–54.0)	25.9	(22.4–29.7)	33.6	(30.0–37.4)
College graduate	69.3	(53.2–81.8)	30.0	(13.4–54.2)	21.7	(18.1–25.8)	24.2	(20.4–28.5)
Total	68.9	(64.6–72.9)	29.2	(25.0–33.7)	22.4	(21.1–23.7)	28.2	(27.0–29.4)

Notes. Current smokers had smoked during the previous 30 days. Because of low precision, estimates for American Indians and Alaska Natives and for Asians, Native Hawaiians, and Other Pacific Islanders are not presented. Estimates are based on respondents answers to the question of whether their usual brand was menthol or regular. See text for discussion of misclassification bias on this item. [a]Includes American Indians and Alaska Natives; Asians, Native Hawaiians, and Other Pacific Islanders; other; multiple; and unknown races. [b]For those aged > 25 years.
Source. Substance Abuse and Mental Health Services Administration, Rockville, MD.

Among White U.S. smokers, those residing in the Northeast were more likely to report smoking mentholated brands than were those in any other region (see Table 4). Overall, reports of menthol smoking were least common among smokers residing in the West, and smokers with some college were more likely to report smoking mentholated brands than were smokers who had graduated from college.

Although low precision did not permit presentation of estimates for Asians, Native Hawaiians, and Other Pacific Islanders and for American Indians or Alaska Natives for all categories in Table 4, we report estimates overall and by age. Among Asian, Native Hawaiian, and Other Pacific Islander smokers, 31.1% (95% CI = 19.3%–46.1%) of those aged 12 years or older, including 48.7% (95% CI = 31.2%–66.5%) of 12–17 year olds, 37.7% (95% CI = 29.1%–47.0%) of 18–25 year olds, and 28.5% (95% CI = 14.5%–48.3%) of those aged 26 years or older reported using mentholated brands. Among American Indian or Alaska Native smokers, 14.3% (95% CI = 8.6%–22.9%) of those aged 12 years or older, including

Table 5. Percentages of current smokers who smoked Newport, Kool, or Salem, by grade and race or ethnicity: Monitoring the Future surveys, grades 8, 10, and 12—United States, 1998–2000.

Race or ethnicity and grade	1998		1999		2000	
	Percent	95% *CI*	Percent	95% *CI*	Percent	95% *CI*
Black						
8th	72.5	(63.4–81.6)	79.4	(71.0–87.8)	74.5	(64.0–85.0)
10th	76.4	(68.0–84.8)	80.1	(70.4–89.8)	82.1	(71.5–92.7)
12th	83.9	(74.5–93.3)	77.8	(66.6–89.0)	70.4	(57.8–83.0)
Hispanic						
8th	22.4	(14.8–30.0)	24.5	(16.6–32.4)	24.5	(13.5–35.5)
10th	20.1	(12.6–27.6)	17.9	(10.3–25.5)	31.6	(21.2–42.0)
12th	24.6	(14.6–34.6)	19.3	(9.4–29.2)	23.9	(12.5–35.3)
White						
8th	15.6	(12.3–18.9)	20.1	(16.1–24.1)	18.0	(13.9–22.1)
10th	13.7	(11.2–16.2)	15.4	(12.5–18.3)	13.1	(10.3–15.9)
12th	8.1	(6.0–10.2)	9.9	(7.5–12.3)	9.3	(6.7–11.9)

Notes. Current smokers had smoked during the previous 30 days. Because of low precision, estimates for Native Americans and for Asians and Pacific Islanders are not presented.
Source. Institute for Social Research, University of Michigan, Ann Arbor.

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32.4% (95% $CI=17.2\%–52.4\%$) of 12–17 year olds, 16.7% (95% $CI=8.0\%–31.7\%$) of 18–25 year olds, and 11.5% (95% $CI=5.3\%–22.9\%$) of those aged 26 years or older reported using mentholated brands.

Although Monitoring the Future questions do not assess menthol use in particular, we decided to examine it by using the three leading brands of primarily mentholated varieties (i.e., Newport, Kool, and Salem). Monitoring the Future data confirmed that Black adolescent smokers were more likely to smoke one of these three brands than were White or Hispanic smokers (Table 5). The survey data allowed comparison of Newport, Kool, and Salem use among grade cohorts over a 3-year period. For example, among Whites in 1998, 15.6% of 8th-grade smokers smoked one of these brands; in 2000, 13.1% of 10th-grade smokers did so. Similarly, in 1998, 13.7% of 10th-grade smokers chose one of these brands; in 2000, 9.3% of 12th-grade smokers did so. These point estimates were not significantly different and must be interpreted carefully, given that some 8th grade students will drop out of school before they reach 12th grade.

Daily cigarette consumption

Because of the high preference for mentholated brands among Blacks and because White smokers smoke more cigarettes each day than do Blacks (USDHHS, 1998), differences in daily cigarette consumption were investigated separately for each racial group. In 2002, as indicated by data from the U.S. component of the International Tobacco Control Policy Evaluation Survey, White smokers of mentholated brands smoked slightly fewer cigarettes each day than did White smokers of nonmentholated brands (18.1 vs. 19.8; $p<.01$). Among Black smokers, the difference was not significant (12.1 cigarettes per day for menthol smokers vs. 13.2 cigarettes per day for smokers of nonmentholated brands).

Menthol cigarette preference and use of blunts and Ecstasy

Further analysis of the 2000 National Household Survey on Drug Abuse indicated a relationship between menthol use and the use of blunts (cigars with some of the tobacco replaced by marijuana) for adolescent Black and White smokers. Specifically, among Whites, 34.2% (95% $CI=30.9\%–37.7\%$) who had ever used blunts reported smoking mentholated cigarettes, vs. 23.8% (95% $CI=21.5\%–26.4\%$) of those who had never used blunts. Among Black adolescent smokers, reports of menthol cigarette use were more common among those who had ever used blunts (66.3%; 95% $CI=57.0\%–74.5\%$) than among those who had never used them (41.1%; 95% $CI=29.2\%–54.1\%$).

Finally, to check a potential relationship between menthol cigarette preference and the use of Ecstasy (the "club drug" methylenedioxymethamphetamine [MDMA]), Monitoring the Future data were analyzed for 12th-grade cigarette smokers in 2000 and 2001. Of 1,001 smokers, 14.9% of those who smoked mostly mentholated brands (i.e., Newport, Kool, or Salem) and 20.8% of those who smoked other brands had used Ecstasy during the previous year. The difference was not significant.

Discussion

Blacks

For the past three decades, menthol cigarettes have accounted for about one-fourth (ranging from 23% to 29%) of cigarette sales in the United States (FTC, 2003). The ongoing predominance of menthol cigarette use among Blacks suggests that interventions to reduce smoking in this group should address the reasons for menthol use and attempt to counter any misperceptions about menthol cigarettes. Evidence indicates that smokers of mentholated cigarettes, including Blacks, perceive them to be less hazardous than nonmenthol cigarettes. In Project Y, conducted in 1977 for the R. J. Reynolds Tobacco Company, menthol smokers were classified as more "concerned"[1] than smokers of nonmentholated varieties (R. J. Reynolds, 1977). According to a 1968 report for Philip Morris on focus group work done to assess the attitudes of Black smokers about mentholated cigarettes,

> There are indications that menthols tend to be considered generally "better for one's health." That impression refers not only to the health of the respiratory tract, but the whole organism. The majority view is that menthols are "less strong" than regular cigarettes, and that a cigarette which is "less strong" is better for a person's health. (Tibor Koeves, 1968)

This report also noted that individual sampling of menthol cigarettes often occurred because of a cold or sore throat (Tibor Koeves, 1968), a finding consistent with a 1973 report that menthol use was more common during the winter months (R. J. Reynolds, 1973). It also is consistent with earlier marketing of Kool cigarettes (Stratton et al., 2001). The back of a 1946 pack of Kool cigarettes, for example, read, "Head stuffed up? Got the sneezes? Switch to Kools… The flavor pleases!" (Brown & Williamson, 1946).

[1]According to industry documents, "concerned" smokers are concerned about the effects of smoking on their health. Smokers of low-tar cigarettes are often referred to in industry documents as "concerned smokers" (Pollay, 2000).

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An R. J. Reynolds document on the Black consumer market reported that Blacks were more likely than Whites to believe that menthol cigarettes were "better if you smoke a lot," "lower in tar and nicotine," "less likely to make you cough," "better when you have a cold," and "less irritating to the throat" (R. J. Reynolds, 1979). In a more recent survey of 213 smokers of menthol cigarettes attending a smoking cessation clinic, 83% of 174 Blacks and 74% of 39 Whites reported that they smoked menthol cigarettes because they preferred the taste (Hymowitz et al., 1995). Additional reasons were that they were soothing to the throat (51% of Whites, 52% of Blacks), easier to inhale (21% of Whites, 48% of Blacks), and could be inhaled more deeply (10% of Whites, 33% of Blacks). Only 2 (5%) Whites and 13 (7%) Blacks reported they smoked menthol cigarettes because they were "better for you than regular non-menthol cigarettes." Not surprisingly, few respondents openly asserted that menthol cigarettes provide any health advantage over nonmenthol varieties. As Kozlowski (2000) pointed out, however, concepts like "smooth" and "mild" also serve as indicators of the perception of a less hazardous cigarette. Thus, reports that mentholated varieties were more soothing and easier to inhale could indicate a perception of a lower health risk.

Further research is needed to determine exactly how current smokers of mentholated brands cognitively process the soothing sensations provided by menthol cigarettes and how these sensations relate to perceived taste. More research also is needed to understand how consumers perceive the health risks of mentholated cigarettes and marketing terminology (e.g., cool, refreshing, mild, and smooth) used to promote these brands. We also suggest research on different approaches to measuring perceived risk. For example, cognitive work should be done comparing various ways to assess relative health effects (e.g., "they are better for you" vs. "they are not as bad for you"). Such research could inform media messages to counter misperceptions about smoking mentholated cigarettes and perhaps guide future regulatory efforts. In the interim, messages that portray the suffering caused by cigarette smoking may counter the "Alive With Pleasure" Newport theme. Informing consumers that menthol cigarettes are just as dangerous as other varieties, even though they taste better and are easier to smoke, could motivate quitting (Kozlowski & Pillitteri, 2001; Shiffman, Burton, et al., 2001; Shiffman, Pillitteri, Burton, Rohay, & Gitchell, 2001).

Patterns among youth

Industry documents indicate that the brand that dominates the youth market eventually makes significant inroads into overall market share as adolescents age and become adults (Cummings, Morley, Horan, Steger, & Leavell, 2002; U.S. Food and Drug Administration, 1996; Wayne & Connolly, 2002). In the menthol market, Kool displaced Salem as the dominant brand in the 1960s and early 1970s, in part by capturing the youth market. Newport did the same to Kool in the mid- to late 1970s (R. J. Reynolds, 1985). A 1984 industry document made clear the concern that Philip Morris had about the threat posed to Marlboro by Newport (Johnston, 1984) and recommended competing with that cigarette by strengthening Marlboro's presence in the menthol arena. In recent years, Marlboro has increased its mentholated varieties (FTC, 1999b, 2000), and in 2000 it introduced Marlboro Milds to further compete for the menthol market (Teinowitz, 2000). However, 1989–2000 trend data on adolescent brand preference from national surveys indicate that Marlboro has lost share among Whites and remained constant among Blacks, whereas Newport has gained substantially among Whites and maintained its substantial share among Blacks (CDC, 1992, 1994; Kopstein, 2001; see Table 4).

Other sociodemographic comparisons

We found that menthol cigarettes are used among adult women more commonly than among men in the United States; the same pattern was found in Canada, Australia, and the United Kingdom, countries with substantially smaller menthol market shares. This finding has been observed in the United States since the mid-1980s (Kabat & Hebert 1991; Sidney et al., 1995; USDHHS, 1989). By improving taste and facilitating inhalation, mentholated cigarettes may have promoted initiation among girls, a mechanism similar to one postulated for low-tar cigarettes (Silverstein, Feld, & Kozlowski, 1980).

Our finding that, among Whites, menthol use was more common in the northeastern United States reflects a pattern previously seen for Newport in the Teenage Attitudes and Practices Survey data (CDC, 1994). In that study, Newport was least popular in the West. A 1984 industry document described the West as a low menthol area and recounted the rapid growth of menthol smoking (particularly of Newport) among young people in New York, New Jersey, and southern New England (Johnston, 1984). Tobacco industry marketing practices may account for these differences.

Daily cigarette consumption

The finding that White smokers of mentholated cigarettes smoke slightly fewer cigarettes each day seems consistent with the notion that smoke constituents are more readily absorbed from mentholated brands, an interpretation suggested by the work of

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several authors (Ahijevych et al., 1996; Ahijevych & Parsley, 1999; Clark et al., 1996; Jarvik et al., 1994). Further work is needed to determine if the patterns we found are observed consistently.

Menthol preference and use of blunts and Ecstasy

Using data from the National Household Survey on Drug Abuse, we found that adolescent smokers who reported using a mentholated brand were more likely to smoke blunts, compared with adolescents who reported using a regular brand. One 1974 industry document indicated that Black smokers of Kool cigarettes reported that Kools tasted like a "joint" and that Kools were the best cigarette to "keep a high going" (R. J. Reynolds, 1974). A similar focus group conducted in 2003 would have to assess the relationship, if any, between Newport smoking and blunt use.

We inquired about a possible association of menthol cigarettes and the use of Ecstasy because of the observation that mentholated products such as Vicks VapoRub are frequently used at raves (huge, all-night dance parties, characterized by fast, high-energy dance music and at which Ecstasy use is common) ("Raves, Ecstasy, and menthol," n.d.). Menthol smoking was not, however, associated with Ecstasy use in the 2001 and 2002 Monitoring the Future data. The relationship between menthol cigarette use and use of Ecstasy should be assessed in the National Household Survey on Drug Abuse data.

International market share data

Internationally, menthol cigarettes account for a minimal amount of sales in about half of countries with data. Still, some patterns are intriguing and potentially illustrative. Why, for example, do the majority of smokers in the Philippines smoke mentholated brands? Smoking prevalence is high among Filipino adults: 75% among males and 18% among females (CDC, 2003). The experimental growth of a plant from which menthol used in cigarettes is extracted has been cited as one factor contributing to the "remarkable recovery" in 1981 of the Philippine cigarette industry (Palacpac, 1982). We do not know, however, whether this development contributed to the substantial menthol market share in the Philippines.

Also, menthol market share in all the African countries was substantially less than we observed among Blacks in the United States, as was menthol preference among Black smokers surveyed in Canada and the United Kingdom, suggesting that social or marketing influences play an important role. We speculate that the various cigarette companies might make and market different products in different countries. Taste preferences may vary, perhaps due to genetic reasons or sociocultural conditioning. International cigarette menthol share may be related to nation-specific preferences for mentholated candies. Also, menthol use may vary with tar level: As manufacturers lower the average tar yields of their products (FTC, 2000), they may perceive a need to compensate for low flavor by adding extra menthol. These hypotheses should be investigated.

Misclassification bias

This study is limited by misclassification of self-reported menthol status. We estimated the extent of misclassification in the National Household Survey on Drug Abuse based on the findings with purely mentholated and purely nonmentholated brands and determined that the effects were relatively small for the overall population. However, we are not at all certain that the findings for the overall population apply to various subgroups. An extreme example appears to exist for Black adolescent smokers, 55.7% of whom reported smoking mentholated brands in 2000 (see Table 4). But 79.2% used Newport, and another 3.7% used Kool or Salem (see Table 2). Kool and Salem are exclusively mentholated. A. C. Nielsen data on sales of Newport in stores with scanners that detect the Universal Product Code (UPC) indicate that more than 99% of packs of Newport sold in 2000 were mentholated (John Tauras, personal communication).

Smokers in the National Household Survey on Drug Abuse were asked if they smoked "menthol or regular" cigarettes. Some smokers of menthol cigarettes may have confused *regular* with *full flavor* or some other factor and indicated that they smoked regular cigarettes. More than 11% of all survey respondents who smoked Newport reported that they smoked regular varieties of the brand (data not shown). Similarly, some middle and high school students may have misunderstood the word *mentholated*, which was used in the 2000 National Youth Tobacco Survey question on menthol status. Alternative approaches to collecting this information include incorporation of the UPC classification system, which provides information at the subbrand level, as well as simply changing the question to ask if the brand smoked most often is a menthol or nonmenthol (i.e., plain) variety. The results of this work would likely inform future epidemiological studies on the health effects of mentholated products.

Conclusion

Adding menthol to cigarettes appears to "sweeten the poison." We question whether it makes sense to permit tobacco manufacturers to continue to add

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menthol flavoring to an admittedly toxic product to make it more palatable. Public health researchers and practitioners would have a far greater understanding of the many components of the risks posed by mentholated cigarettes if a comprehensive surveillance system, as recommended by the Institute of Medicine (Stratton et al., 2001) and elsewhere (Giovino, 2000, 2002) were established. An optimal system would assess far more than simple prevalence of use. It also would assess whether products have changed over time in ways that make them more appealing, addictive, or toxic. It also would facilitate our understanding of how various marketing strategies (e.g., "Alive With Pleasure") might influence health beliefs and motivation to quit. We lack information on the reach and styles of marketing strategies used to promote various menthol and nonmenthol cigarettes. Such information would provide important contextual information for program planners and policy makers.

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Flavored e-cigarette use: Characterizing youth, young adult, and adult users

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ABSTRACT

The purpose of this study is to investigate how the use of flavored e-cigarettes varies between youth (12–17 years old), young adults (18–29 years old), and older adults (30+ years old). Cross-sectional surveys of school-going youth ($n = 3907$) and young adult college students ($n = 5482$) in Texas, and young adults and older adults ($n = 6051$) nationwide were administered in 2014–2015. Proportions and 95% confidence intervals were used to describe the percentage of e-cigarette use at initiation and in the past 30 days that was flavored, among current e-cigarette users. Chi-square tests were applied to examine differences by combustible tobacco product use and demographic factors. Most e-cigarette users said their first and "usual" e-cigarettes were flavored. At initiation, the majority of Texas school-going youth (98%), Texas young adult college students (95%), and young adults (71.2%) nationwide said their first e-cigarettes were flavored to taste like something other than tobacco, compared to 44.1% of older adults nationwide. Fruit and candy flavors predominated for all groups; and, for youth, flavors were an especially salient reason to use e-cigarettes. Among adults, the use of tobacco flavor at initiation was common among dual users (e-cigarettes + combustible tobacco), while other flavors were more common among former cigarette smokers (P = 0.03). Restricting the range of e-cigarette flavors (e.g., eliminating sweet flavors, like fruit and candy) may benefit youth and young adult prevention efforts. However, it is unclear what impact this change would have on adult smoking cessation.

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1. Introduction

An astonishing number of "characterizing flavors" are now widely available for those who use e-cigarettes – by one estimate, over 7500 (Zhu et al., 2014). In addition to tobacco and menthol, e-cigarettes come in sweet flavors, like fruit, candy, and dessert. Enticing flavors like these were banned from conventional cigarettes in 2009 to reduce youth smoking, as they were often used as a starter product (FDA. Family Smoking Prevention and Tobacco Control Act, 2015; US Department of Health Human Services, 2012). Flavors alone are harmful to health (Barrington-Trimis et al., 2014; Hutzler et al., 2014; Grana et al., 2014; Kosmider et al., 2016; Tierney et al., 2015; Behar et al., 2014). Toxic compounds like diacetyl, which has been linked to severe respiratory disease, have been found in 75% of flavored e-cigarettes (Allen et al., 2015; Farsalinos et al., 2014).

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Data on the occurrence of flavored e-cigarette use across different age groups are sparse. The prevalence of flavored e-cigarette use among youth current (i.e., past 30 day) e-cigarette users is estimated between 63.3% (Corey et al., 2015) and 85.3%, (Ambrose et al., 2015) according to the 2014 National Youth Tobacco Survey (NYTS) and the 2013–2014 Population Assessment of Tobacco and Health Study (PATH), respectively. Preliminary, unpublished results from 2013 to 2014 PATH suggest the proportion of flavored e-cigarette use among 18–24 year old young adult current users is similar to youth, at 83.0%, while that among adults 25+ years old is lower, at 63.0% (Hyland et al., 2016). Only one published study of young adults' flavored tobacco products use is available, which showed only 17% of 18–34 year old young adult current e-cigarette users used a flavored e-cigarette in 2012, before the sharp increase in e-cigarette use nationwide (Villanti et al., 2013). There are no published studies on adults' flavored e-cigarette use. Until more data on this topic are available, it remains unclear whether preferences for flavored e-cigarettes vary by age group. This evidence will be important to determine whether regulation, like the ban on cigarette flavors, is also needed for e-cigarettes.

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Though some adults begin using e-cigarettes as a device to stop smoking conventional cigarettes (Grana & Ling, 2014; McRobbie et al., 2014), other reasons, like curiosity (Schmidt et al., 2014; Biener et al., 2015; Kong et al., 2014; McDonald & Ling, 2015; Surís et al., 2015; Sutfin et al., 2015; Biener & Hargraves, 2014), are more relevant to youth and young adult e-cigarette users. Among these reasons, flavors play a particularly prominent role. In the 2013–2014 PATH survey, 81.5% of youth e-cigarette users said that they used e-cigarettes "because they come in flavors I like" (Ambrose et al., 2015). Data from smaller, qualitative studies of young adults suggest flavors are an attractive aspect of using e-cigarettes, contributing to the novelty of these devices, which are "fun toys" (McDonald & Ling, 2015; Choi et al., 2012). Among adults use e-cigarettes to quit conventional cigarette smoking, tobacco flavor is often preferred at the start, though sweet flavors become more relevant as e-cigarette use continues (Farsalinos et al., 2014; Dawkins et al., 2013).

The impact of flavors on the uptake of e-cigarettes among youth compared to adults is not without controversy. The most influential study to date that drives this debate is that by Shiffman and colleagues (Shiffman et al., 2015). Nonsmoking youth ($n = 216$, 13–17 years old) and adult cigarette smokers with varied histories of e-cigarette use ($n = 432$, 19–80 years old) were asked to rate their preferences for flavors being offered in 2014 by NJOY e-cigarettes. Across all flavors, adult smokers' interest surpassed that of nonsmoking youth. The authors concluded their data do *not* support the hypothesis that flavors in e-cigarettes will entice nonsmoking youth to use them. Concerns about the reliability and validity of this study, funded by NJOY, have been raised (Glantz, 2015). Additional research is needed to elucidate if flavors are disproportionately preferred by young people or adults.

The purpose of this paper is to investigate whether the use of flavored e-cigarettes varies between youth (12–17 years old), young adults (18–29 years old), and adults (30+ years old). We examine the use of flavored e-cigarettes at initiation and whether "usual" e-cigarettes, for current users, are flavored. Differences in flavored e-cigarette use by combustible tobacco product use are considered, as are differences by sex and race/ethnicity. We investigate a variety of flavors: tobacco; menthol or mint; fruit (e.g., cherry, strawberry); candy (e.g., gummy bear) or dessert (e.g., chocolate, vanilla); coffee or alcohol; and spice (e.g., cinnamon); as well as unflavored e-cigarettes, among adults. Finally, we consider the relevance of flavors as a reason to use e-cigarettes.

2. Methods

2.1. Data sources

Data are derived from three separate studies to represent e-cigarette use profiles across three age groups and include studies of youth (12–17 years old), young adults (18–29 years old), and adults (30+ years old). The studies are the (a) Texas Adolescent Tobacco and Marketing Surveillance System (TATAMS); (b) Marketing and Promotions Across Colleges in Texas Project (M-PACT); and (c) the Tobacco Products and Risk Perceptions Survey (TPRPS). The first two studies are characteristic of the 4 largest metropolitan areas in Texas (i.e., Houston, Dallas/Fort Worth, San Antonio, and Austin), while the last study is representative of non-institutionalized adults in the United States. This study was a collaboration across two different Tobacco Centers of Regulatory Science (TCORS) recently established by the Food and Drug Administration and, as such, represents value in cross-institutional collaboration.

2.1.1. TATAMS

The Texas Adolescent Tobacco and Marketing Surveillance System (TATAMS) is a multiple component, rapid response surveillance system administered by the Texas Tobacco Center of Regulatory Science on Youth & Young Adults (Texas TCORS). Data from the Texas Education Agency, Texas Private School Accreditation Commission, and the National Center for Education Statistics were used to generate a sampling frame of all public, private and charter schools with 6th, 8th and 10th graders in 2014–15 in the 5 counties surrounding the 4 largest cities in Texas (Houston, Dallas/Ft. Worth, Austin, San Antonio). A complex multistage probability sample of public schools was drawn using probability proportional to the grades' enrollment, and all private and charter schools were invited to participate. Details about this procedure are provided in Pérez et al. (Pérez et al., 2015). Data for this manuscript are taken from the baseline survey, which was administered October 2014–June 2015, on an electronic form on computerized tablets (Delk et al., n.d.). Seventy nine schools and 3907 middle and high school students participated, representing a population of 461,069 6th, 8th, and 10th graders in these major metropolitan areas (Pérez et al., 2015). The Institutional Review Board at University of Texas' Health Science Center, Houston approved all protocols (HSC-SPH-13-0377).

2.1.2. M-PACT

The Marketing and Promotions Across Colleges in Texas Project (M-PACT) is also affiliated with the Texas TCORS and is a rapid-response surveillance system that runs parallel to TATAMS in 2- and 4-year colleges across the same cities. Three colleges of each type were selected from each city, for a total of 24. Participants were full- or part-time degree- or certificate-seeking 18–29 year old undergraduate students attending the 4-year college or a vocational/technical program at the 2-year college. Recruitment at 2-year colleges was limited to students enrolled in vocational/technical programs as they have an elevated prevalence of cigarette use (Loukas et al., 2008). Over 13,000 college students ($n = 13,714$) were eligible to participate and recruited via an e-mail invitation. Of these, 5482 (40%) completed the baseline survey in November 2014–February 2015, from which the data here are drawn. More details regarding the sampling for this study can be found elsewhere (Loukas, 2015). The University of Texas at Austin's Institutional Review Board approved all protocols (2013-06-0034).

2.1.3. TPRPS

The Tobacco Products and Risk Perceptions Survey (TPRPS) is administered by the Georgia State University Tobacco Center of Regulatory Science (GSU TCORS). The survey presented here was conducted August to September 2015 and was administered to a cross-sectional, probability sample drawn from GfK's KnowledgePanel, a probability-based web panel representative of non-institutionalized US adults. Of these KnowledgePanel members, 8135 were invited to participate in the online survey and 6091 qualified as completers. Forty cases were excluded due to refusing to answer more than one-half of the survey questions, for a final sample of 6051 adults, representing 238,226,996 nationwide. The average panel recruitment rate (RECR) for this study, reported by GfK, was 13.8% (rate at which those from the target population accept the invitation to join KnowledgePanel), the average profile rate (PROR) was 64.6% (rate at which those of the target population who accept the invitation to join KnowledgePanel complete the required GfK profile surveys to become members of KnowledgePanel), and the study completion rate (COMR) was 76.0% (the percentage invited to participate in the survey that completed the survey) for a cumulative response rate of 6.8% (RECR*PROR*COMR). More details about this design and the computation of these response rates are found here (Callegaro & DiSogra, 2008; Weaver et al., n.d.). The Institutional Review Board at Georgia State approved all study protocols (H14028).

2.2. Experimental

2.2.1. Measures

Survey questions for all three studies were developed from a catalogue of valid and reliable measures used in state and national tobacco

Table 1
Constructs, questions, and operationalization of e-cigarette measures (2014–2015).

	Questions and responses			
Constructs	TATAMS[a]	M-PACT[b]	TPRPS[c]	Operationalization
Behaviors				
Ever use	Have you EVER used an electronic cigarette, vape pen, or e-hookah, even one or two puffs? No/Yes	Have you ever used an ENDS[d] product, (i.e. e-cigarette, vape pen, or e-hookah) as intended (i.e. with nicotine cartridges and/or e-liquid/e-juice), even one or two puffs? No/Yes	Have you ever used electronic vapor products, even one or two times? No/yes	0 = No; 1 = Yes
Current use	During the past 30 days, on how many days did you use an electronic cigarette, vape pen, or e-hookah? Please enter the number of days (from 0 to 30 days) 0–30	During the past 30 days, have you used any ENDS product, (i.e. an e-cigarette, vape pen, or e-hookah), even one or two puffs, as intended (i.e. with nicotine cartridges and/or e-liquid/ejuice)? No/yes	In the past 30 days, have you used electronic vapor products, even one or two times? No/yes	TATAMS: 0 = no; 1 = yes, ≥1 day Others: 0 = no; 1 = yes
Flavors				
Flavor use at initiation	Think back to the FIRST electronic cigarette, vape pen, or e-hookah you tried. What flavor was it? Tobacco; menthol or mint; Candy, such as gummy bear Fruit, such as grape; Coffee or an alcoholic drink, such as wine; Spice, such as cinnamon; other flavor; I don't remember	When you first started using any ENDS products (i.e. e-cigarettes, vape pens, or e-hookah), were they flavored to taste like… Check all that apply Tobacco; Not flavored; Menthol or Mint; Candy (e.g. chocolate, vanilla); Fruit (e.g. strawberry, banana); Coffee or an alcoholic drink (e.g. pina colada); Other I don't remember, but I know it was flavored	When you first started using electronic vapor products, were they flavored? No-unflavored; yes-tobacco flavored; yes-flavored but not tobacco flavor; don't remember	Unflavored; Tobacco flavored; Flavored, not tobacco
Current flavor use	When you use an electronic cigarette, vape pen, or e-hookah, do you usually use any of the following flavors? (yes or no response for each flavor) Tobacco; menthol or mint. Candy, such as gummy bear; Fruit, such as grape; Coffee or an alcoholic drink, such as wine; Spice, such as cinnamon; other flavor	Is your usual brand of disposable e-cigarette or e-cigarette with disposable nicotine cartridges flavored to taste like… AND When you use a vape pen/personal vaporizer, do you usually use e-liquid/e-juice flavored to taste like… (yes or no response for each flavor) Tobacco; Not flavored; Menthol or Mint; Candy (e.g. chocolate, vanilla) Fruit (e.g. strawberry, banana); Coffee or an alcoholic drink (e.g. pina colada); Other	In the past 30 days, have you used electronic vapor products that are flavored (including tobacco flavor)? Yes/no If NO, they are coded as unflavored product users. If YES, they are asked the question stated here. Which flavors have you used in electronic vapor products in the past 30 days? (yes or no response for each flavor) Mint, wintergreen, menthol; fruit (e.g. cherry, blueberry, strawberry, watermelon, coconut, etc.); coffee (coffee or any related flavor–e.g. espresso, latte, cappuccino, etc.); candy or dessert flavors (e.g. caramel, vanilla, chocolate, ice cream, mud pie); Spice (e.g. clove, cinnamon, nutmeg); Alcohol or cocktail (e.g. wine, bourbon, rum, brandy, tequila, whiskey beer, mai-tai, daiquiri); Tobacco flavor; Some other flavor	Unflavored; Tobacco flavored; Flavored, not tobacco Tobacco flavored; mint/menthol; fruit Coffee/alcohol; candy/dessert; spice; other
Reasons to use: flavors	How much do you agree or disagree with the following statements? I tried using electronic cigarette, vape pen, or e-hookah because electronic cigarettes come in flavors I like. Strongly disagree; disagree; agree; strongly agree	I tried ENDS products (i.e. e-cigarettes, vape pens, or e-hookah) as intended because… they came in flavors I liked.	Please indicate how important it is to you in your use of electronic vapor products. They come in flavors I like was measured using 6 point Likert scale where, 0 (not at all important) and 6 (very important)	TATAMS: 0 = strongly disagree/disagree; 1 = agree/ strongly agree M-PACT: 0 = no; 1 = yes TPRPS: 0–3 = no; 4–6 = yes

[a] TATAMS-The Texas Adolescent Tobacco and Marketing Surveillance System.
[b] M-PACT- Marketing and Promotions Across Colleges in Texas Project.
[c] TPRPS- The Tobacco Products and Risk Perceptions Survey.
[d] ENDS- Electronic Nicotine Delivery Systems.

surveillance, including the PATH study (United States Department of Health and Human Services. National Institutes of Health. National Institute on Drug Abuse, a.U.S.D.o.H.a.H.S.F.a.D.A. Population Assessment of Tobacco and Health (PATH) Study, 2013-2016). Measures specific to e-cigarettes in the three studies are summarized in Table 1. The constructs are included ever and current use; use of flavors at initiation and "regularly"; and flavors as a reason to use e-cigarettes. The differences across studies in these measures include the following. For *flavor use at initiation*, TATAMS did not ask about unflavored e-cigarette use, and M-PACT participants were asked to check all flavor categories that applied. If any flavor was chosen, respondents were categorized as "flavored, not tobacco" in Table 2. This same rule was applied to all studies for *current use of flavors* in Table 2. In Fig. 1, the raw "check all that apply" form of current use item was retained instead to illustrate the maximum variability in flavors across the studies. M-PACT applied the *flavor use at initiation* question to only current users, while the other studies also applied it to ever users. For *flavors as a reason to use*, responses were dichotomized across all studies. The TPRPS survey only asked this question of adult current e-cigarette users (Table 3).

The measure of combustible tobacco product use included cigarettes, hookah, and all types of cigar products (large cigars, cigarillos, and little filtered cigars). *Former combustible* use was defined as participants who reported ever use of any combustible product, but not current use. TPRPS defined ever use of cigarettes as reporting smoking 100 or more cigarettes in their lifetime; ever use of all other products was defined as having used the product even one or two times in their lifetime. TATAMS and M-PACT defined ever use of each product the same: reporting using the product (even one or two times) in their lifetime. *Current combustible* product use was defined as participants who reported use of any combustible product at least 1 day in the past 30 (for TATAMS or M-PACT participants) or "every day" or "some days" (for TPRPS participants). In addition, we also focused in analyses on the subset of current combustible users that were currently smoking cigarettes, regardless of their other combustible product use; these are noted as *current cigarette* (Tables 2 and 3). *Never combustible* use was defined as those who reported "no" to ever use of all of these products. Questions that define ever use and current use of these products are identical to the questions in Table 1 for e-cigarette use, except e-cigarettes are replaced by these other tobacco products, each with a separate question.

2.2.2. Data analysis

Proportions and 95% confidence intervals were used to describe the percentage of e-cigarette use at initiation and in the past 30 days that can be attributed to the use of flavored e-cigarettes (Table 2). Statistics were calculated overall and then stratified by combustible tobacco product use. Sample sizes for never combustible users were only large enough to be examined in TATAMS and M-PACT, as most adult e-cigarette users had already used combustible tobacco products. Chi-square tests were used to study differences between current and former combustible users (Table 2) and to investigate differences by sex and race/ethnicity across e-cigarette flavor categories among current e-cigarette users (results presented in text). Proportions of e-cigarette use in the past 30 days that could be attributed to all types of flavors, including tobacco, mint/menthol, fruit, coffee/alcohol, candy/dessert, spice, or other flavor were calculated (Fig. 1). To determine the salience of flavors as a reason to use e-cigarettes, proportions and 95% confidence intervals were calculated (Table 3). Analyses of TPRPS data were stratified by age group (18–29 years old vs. 30 + years old) to provide estimates for young adults nationwide that could be compared with those from Texas (M-PACT). Sampling weights were applied to the TATAMS and TPRPS data, but not to M-PACT, as M-PACT employed a convenience sample, while TATAMS and TPRPS used random sampling protocols that allow the results to generalize back to the population from which the sample was drawn, when weights are applied. Detailed information about the calculation and application of sampling weights is provided elsewhere (Pérez et al., 2015; Callegaro & DiSogra, 2008; Weaver et al., n.d.). Estimates that relied on denominators ≤50 were suppressed as the results would be statistically unreliable.

3. Results

E-cigarette use was most common among young adult college students in Texas. The prevalence of ever e-cigarette use among Texas youth and young adult college students (18–29 years old) was 19.5% (95% CI: 15.9%, 24.0%) and 44.6% (95% CI: 43.3%, 46.0%), respectively, while it was 29.5% (95% CI: 26.0%, 33.3%) and 13.8% (95% CI: 12.6%, 15.0%) among young adults (18–29 years old) and adults (30 + years old) nationwide. Current e-cigarette use was 7.4% (95% CI: 5.9%, 9.0%), 15.3% (95% CI: 14.3%, 16.3%), 9.3% (95% CI: 7.2%, 12.0%) and 4.5% (95% CI: 3.8%, 5.2%) across these different samples, respectively.

3.1. Use of flavored e-cigarettes at initiation

Most youth, young adult, and adult e-cigarette users said their first e-cigarette was flavored, with the majority reporting their first e-cigarette was flavored to taste like something other than tobacco (Table 2). The proportion of current users who started with an e-cigarette flavored with something other than tobacco was considerably higher in Texas youth (98.6%) and young adults in Texas (95.2%) and nationwide (71.2%) compared to older adults nationwide (44.1%). Tobacco flavor was significantly more common among older adults nationwide (47.5%), compared to young adults nationwide (21.0%) and young adult college students (4.8%), and youth (1.4%) in Texas.

No significant differences were noted by combustible tobacco product use for youth in Texas, but significant differences emerged for young adult college students in Texas and adults nationwide. At initiation, the use of tobacco-flavored e-cigarettes was more common among current dual users (e-cigarette and combustible tobacco product users) than exclusive e-cigarette users (i.e., former combustible tobacco product users), for both age groups ($p < 0.05$, both). Among adults nationwide, 43.5% of current combustible users said their first e-cigarette was flavored to taste like tobacco, compared to 27.8% of former combustible product users.

3.2. Current use of flavored e-cigarettes

Similar trends in flavored e-cigarette use in the past 30 days were noted (Table 2). Overall, most youth, young adult, and adult e-cigarette users reported the "usual" e-cigarette they used in the past 30 days was flavored, with the majority reporting that it was flavored to taste like something other than tobacco. The proportion of current users whose "usual" e-cigarette was flavored but not with tobacco was appreciably higher for Texas youth (97.9%) and young adults (96.7%) in Texas and nationwide (82.2%) compared to older adults nationwide (69.3%). In older adults, current use of an e-cigarette flavored with something other than tobacco (69.3%) was also significantly higher than the same at initiation (44.1%). No differences by combustible product use were observed for any age group.

3.3. Preference for and salience of flavors

Among current e-cigarette users, there were no significant differences in use of flavored e-cigarettes at initiation or "usually" by sex or racial/ethnic group for any age group (all $p > 0.05$, data not shown in Table). Fig. 1 illustrates preferences for specific flavors among current e-cigarette users, for the "usual" e-cigarette. Across all studies, fruit flavors predominated, endorsed by 76% of Texas youth, 83% of Texas young adult college students, 74% of young adults nationwide, and 47% of older adults nationwide. The next most popular flavor was candy or dessert, reported by 57% of Texas youth, 52% of Texas young adult college students, 50% of young adults nationwide, and 27% of older adults nationwide. Tobacco flavor was the least commonly reported as a usual flavor among all groups, at 13% of Texas youth, 23% of Texas young adult college students, 1% of young adults nationwide, and 13% of older adults nationwide.

Table 2
Use of flavored e-cigarettes among youth, young adult, and adult current e-cigarette users (2014–2015).

		n	N	Unflavored		Tobacco flavored		Flavored, not tobacco		P-value
				%	95% CI	%	95% CI	%	95% CI	
Use of flavored e-cigarettes at initiation										
TATAMS [a]	**Youth (overall)**	218	28,301			1.4%	0.5%, 3.9%	98.6%	96.1%, 99.5%	
	Never combustible[d]	78	9853			0.2%	0.0%, 1.4%	99.8%	98.6%, 100.0%	
	Current combustible[e]	88	12,317			1.8%	0.4%, 7.2%	98.2%	92.8%, 99.6%	
	Current cigarette[f]	42	5477			2.5%	0.4%, 15.0%	97.5%	85.0%, 99.6%	
	Former combustible[g]	52	6132			2.5%	0.4%, 13.4%	97.5%	86.6%, 99.6%	0.33
M-PACT [b]	**Young adults (overall)**	944	NA			4.8%	3.6%, 6.3%	95.2%	93.7%, 96.4%	
	Never combustible[d]	21	NA			***	***	***	***	
	Current combustible[e]	740	NA			5.5%	4.1%, 7.4%	94.5%	92.6%, 95.9%	
	Current cigarette[f]	498	NA			7.4%	5.4%, 10.1%	92.6%	89.9%, 94.6%	
	Former combustible[g]	183	NA			1.6%	0.6%, 4.7%	98.4%	95.3%, 99.4%	0.05
TPRPS [c]	**Adults (overall)**	355	11,020,944	8.2%	5.1%, 12.9%	37.7%	31.3%, 44.6%	54.1%	47.0%, 61.1%	
	Never combustible[d]	6	375,247	***	***	***	***	***	***	
	Current combustible[e]	279	7,650,505	9.2%	5.3%, 15.5%	43.5%	35.4%, 51.9%	47.3%	38.8%, 56.0%	
	Current cigarette[f]	256	6,483,643	9.0%	4.8%, 16.2%	47.4%	38.6%, 56.3%	43.6%	34.9%, 52.8%	
	Former combustible[g]	70	29,95,192	6.5%	2.7%, 14.9%	27.8%	17.9%, 40.3%	65.7%	52.7%, 76.7%	0.03
	Young adults (18–29 y)	86	4,074,947	7.8%	2.9%, 19.6%	21.0%	12.9%, 32.4%	71.2%	58.2%, 81.4%	
	Never combustible[d]	4	288,503	***	***	***	***	***	***	
	Current combustible[e]	58	2,416,473	11.6%	3.9%, 30.0%	25.2%	14.1%, 41.0%	63.2%	45.5%, 77.9%	
	Current cigarette[f]	49	1,747,919	***	***	***	***	***	***	
	Former combustible[g]	24	1,369,971	***	***	***	***	***	***	
	Older adults (30+ y)	269	6,945,996	8.3%	5.1%, 13.4%	47.5%	39.8%, 55.4%	44.1%	36.5%, 52.1%	
	Never combustible[d]	2	86,744	***	***	***	***	***	***	
	Current combustible[e]	221	5,234,031	8.1%	4.5%, 14.0%	51.9%	42.7%, 61.0%	40.0%	31.3%, 49.4%	
	Current cigarette[f]	207	4,735,724	7.3%	3.9%, 13.4%	53.5%	43.8%, 63.0%	39.2%	30.1%, 49.1%	
	Former combustible[g]	46	1,625,221	***	***	***	***	***	***	
Current or "usual" use of flavored e-cigarettes										
TATAMS [a]	**Youth (overall)**	235	30,756			2.1%	0.5%, 8.7%	97.9%	91.3%, 99.5%	
	Never combustible[d]	87	11,340			0.2%	0.0%, 1.2%	99.8%	98.8%, 100.0%	
	Current combustible[e]	93	13,604			3.5%	0.5%, 20.8%	96.5%	79.2%, 99.5%	
	Current cigarette[f]	46	6543			7.2%	1.0%, 36.3%	92.8%	63.7%, 99.0%	
	Former combustible[g]	55	5813			2.6%	0.4%, 13.8%	97.4%	86.2%, 99.6%	0.26
M-PACT [b]	**Young adults (overall)**	798	NA			3.3%	2.2%, 4.7%	96.7%	95.3%, 97.8%	
	Never combustible[d]	21	NA			***	***	***	***	
	Current combustible[e]	626	NA			3.8%	2.6%, 5.6%	96.2%	94.4%, 97.4%	
	Current cigarette[f]	444	NA			4.7%	3.1%, 7.1%	95.3%	92.9%, 96.9%	
	Former combustible[g]	152	NA			0.7%	0.1%, 3.6%	99.3%	96.4%, 99.9%	0.07
TPRPS [c]	**Adults (overall)**	378	11,802,533	17.3%	12.6%, 23.1%	8.7%	6.0%, 12.2%	74.1%	67.9%, 79.5%	
	Never combustible[d]	7	410,639	***	***	***	***	***	***	
	Current combustible[e]	298	8,126,307	16.9%	11.8%, 23.6%	9.1%	6.1%, 13.3%	74.0%	66.9%, 80.1%	
	Current cigarette[f]	271	6,832,639	16.8%	11.4%, 24.1%	10.3%	6.9%, 15.2%	72.9%	65.1%, 79.5%	
	Former combustible[g]	73	3,265,586	18.9%	9.8%, 33.1%	8.7%	4.0%, 17.8%	72.5%	58.5%, 83.1%	0.89
	Young adults (18–29 y)	92	4,352,335	16.7%	9.2%, 28.4%	1.1%	0.3%, 4.8%	82.2%	70.5%, 89.9%	
	Never combustible[d]	4	288,503	***	***	***	***	***	***	
	Current combustible[e]	62	2,452,927	10.2%	5.0%, 19.7%	0.6%	0.1%, 4.3%	89.2%	79.6%, 94.6%	
	Current cigarette[f]	52	1,734,218	9.0%	4.2%, 18.2%	0.9%	0.1%, 6.0%	90.1%	80.7%, 95.2%	
	Former combustible[g]	26	1,610,905	***	***	***	***	***	***	
	Older adults (30+ y)	286	7,450,198	17.6%	12.3%, 24.6%	13.1%	9.1%, 18.4%	69.3%	61.9%, 75.9%	
	Never combustible[d]	3	122,136	***	***	***	***	***	***	
	Current combustible[e]	236	5,673,380	19.8%	13.3%, 28.4%	12.8%	8.6%, 18.6%	67.4%	58.7%, 75.1%	
	Current cigarette[f]	219	5,098,420	19.5%	12.7%, 28.7%	13.5%	9.0%, 19.8%	67.0%	57.7%, 75.2%	
	Former combustible[g]	47	1,654,682	***	***	***	***	***	***	

*** Estimates suppressed as denominators <50 and are therefore statistically unreliable. Note. P-values obtained from a chi-square test of differences in flavored e-cigarette use by combustible product use status.

[a] TATAMS-The Texas Adolescent Tobacco and Marketing Surveillance System.

[b] M-PACT- The Marketing and Promotions Across Colleges in Texas Project.

[c] TPRPS- The Tobacco Products and Risk Perceptions Survey

[d] Never combustible: reported never using cigarettes, hookah, and cigar products.

[e] Current combustible: reported past 30-use (TATAMS and M-PACT) or "every day"/"someday" use (TPRPS) of cigarettes, cigar products, or hookah.

[f] Current cigarette: subset of current combustible; reported current use of cigarettes.

[g] Former combustible: reported ever use of cigarettes, cigar products or hookah, but not current use of these products; n = survey sample size; N = weighted sample size or the population size to which estimates generalize back to cells are grayed out because unflavored e-cigarette use was not assessed in TATAMS and only three participants reported exclusive unflavored e-cigarette use in the M-PACT study, so tobacco and unflavored were combined.

Table 3 presents the proportion of participants who said they used e-cigarettes because they "come in flavors I like". Among current e-cigarette users, more Texas youth (72.9%) than young adult college students in Texas (57.4%) and young adults (64.8%) and adults (54.0%) nationwide endorsed this item. The same trend was noted for ever users, overall, comparing youth (64.9%) to young adult college students (49.5%) in Texas. Among youth and young adult ever e-cigarette users in Texas, this was lowest among those who had never used a combustible tobacco product (53.5% and 34.0% respectively) and higher among those who had some experience with combustible tobacco product use (79.8% and 50.9% respectively).

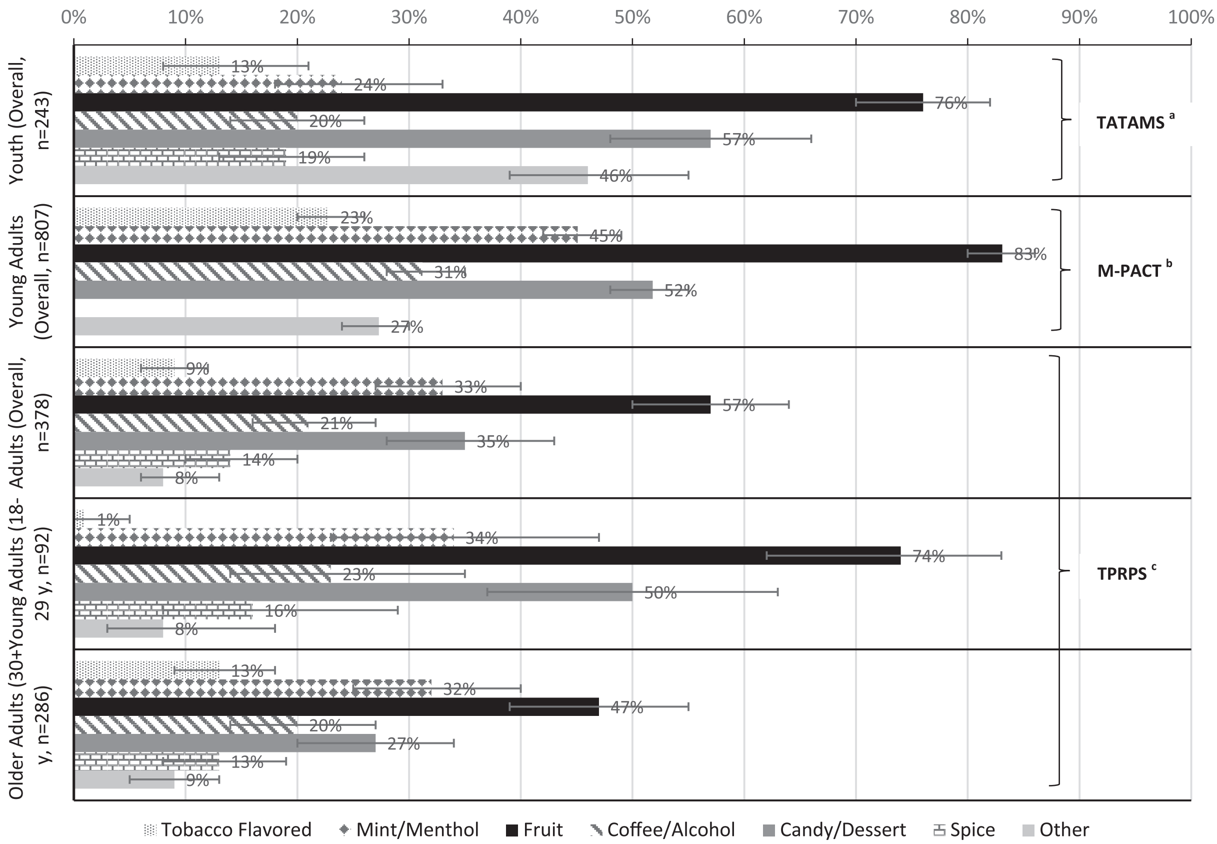

Fig. 1. Variability in flavored e-cigarette use among youth, young adult and adult current e-cigarette users.

4. Discussion

Although the use of flavored e-cigarettes was not uncommon among older adults, our study underscores the relevance and importance of this issue for both youth and young adults. For school-going youth and young adult college students in Texas, almost all first (>95%) and "usual" (>96%) e-cigarette use was with a product flavored to taste like something other than tobacco. The large majority of young adults nationwide also preferred flavored e-cigarettes (71.2% and 82.2%, at first and "usual" use respectively). By comparison, fewer adults nationwide reported the same at initiation (44.1%), and at "usual" use (69.3%). The latter finding suggests flavors other than tobacco become increasingly relevant to older adults as they continue using e-cigarettes.

This study is the first one to date that explicitly compares patterns of flavored e-cigarette use across age groups. Our findings are troubling and suggest that, like conventional cigarettes (US Department of Health Human Services, 2012), characterizing flavors could be especially enticing to young people, at onset and with continued use. Eliminating or restricting e-cigarette flavors in future could be an essential element of comprehensive tobacco control policies designed to reduce the appeal of tobacco products for young people. Already, Chicago and New York City have begun to restrict the sale of flavored tobacco products and e-cigarettes (Emanuel, 2013). As e-cigarettes are now under the authority of FDA to regulate (FDA/USDA, 2014), other regulations like the ban placed on flavored cigarettes (FDA. Family Smoking Prevention and Tobacco Control Act, 2015) could be considered, also. No rules specific to flavorings in e-cigarettes were set forth in the recent deeming action taken by the FDA.

Given our findings and that of others', regulatory actions would not only impact youth and young adults, but also older adults. Preferences for certain flavors differ slightly by age group in studies to date, including this one, and also by cigarette smoking status (Krishnan-Sarin et al., 2015; Berg, 2015). Sweet flavors, like fruit and candy, are most commonly preferred by youth, young adults, and adults alike and exceed >75% of flavored e-cigarette use in most studies (Farsalinos et al., 2014; Dawkins et al., 2013; Krishnan-Sarin et al., 2015; Berg, 2015). In one study from the UK, sweet flavors reduced perceptions of harm from e-cigarettes among youth (Ford et al., 2015). In our study, preference for sweet flavors was appreciably lower among older adults, at <50%. Across studies of youth, young adults, and adults, mint or menthol and tobacco flavors are preferred more often among e-cigarette users who also smoke cigarettes (dual users), compared to exclusive e-cigarette users, and those who have never smoked a cigarette, especially at initiation (Farsalinos et al., 2014; Dawkins et al., 2013; Krishnan-Sarin et al., 2015; Berg, 2015). Still, use of these flavors is at considerably lower rates than sweeter flavors, varying between 25% and 50% of youth and adult cigarette smokers, respectively (Farsalinos et al., 2014; Dawkins et al., 2013; Krishnan-Sarin et al., 2015; Berg, 2015). These data suggest that tobacco and mint/menthol flavored e-cigarettes could be most relevant to and helpful for adult cigarette smokers who may use e-cigarettes to try to quit smoking. Thus, restricting the range of flavors by eliminating sweet ones may offer the most benefit to youth and young adult prevention efforts, without doing harm to adults. Though e-cigarettes are not a proven tool for adult cigarette smoking cessation, it is unclear what impact this action may have on these efforts, instead (Grana et al., 2014; Grana & Ling, 2014; McRobbie et al., 2014). Remarkably, trends in flavored e-cigarette use reported here did not vary by sex or race/ethnicity for any of the age groups, suggesting the impact of any actions specific to this issue might only differ across different life stages and/or by combustible product use.

Limitations include the study's reliance on self-report and cross-sectional analyses that do not allow for the direct estimation of the role that flavors have in initiation or cessation among youth, young adults, or

Table 3
Salience of flavors as a reason to use e-cigarettes among youth, young adults, and adults (2014–2015).

		Ever e-cigarette users					Current e-cigarette users				
		n	N	%	95% CI	P-value	n	N	%	95% CI	P-value
TATAMS [a]	**Youth (overall)**	681	88,953	64.9%	61.0%, 68.8%		259	34,005	72.9%	65.4%, 80.3%	
	Never combustible[d]	315	38,511	53.5%	45.6%, 60.9%		99	12,793	58.2%	42.5%, 73.9%	
	Current combustible[e]	136	22,551	79.8%	70.1%, 89.5%		103	14.727	83.7%	76.0%, 91.3%	
	Current cigarette[f]	68	12,496	76.9%	60.5%, 93.3%		50	7086	88.4%	79.8%, 97.1%	
	Former combustible[g]	230	27,892	68.8%	61.4%, 76.2%	< 0.01	57	6492	77.2%	57.1%, 97.3%	0.03
M-PACT [b]	**Young adults (overall)**	2636	NA	49.5%	47.6%, 51.4%		944	NA	52.2%	49.0%, 55.4%	
	Never combustible[d]	144	NA	34.0%	26.8%, 42.1%		21	NA	***	***	
	Current combustible[e]	1493	NA	50.9%	48.4%, 53.4%		740	NA	53.0%	49.4%, 56.5%	
	Current cigarette[f]	1003	NA	48.0%	44.9%, 51.0%		498	NA	51.2%	46.8%, 55.6%	
	Former combustible[g]	997	NA	49.6%	46.6%, 52.8%	< 0.01	183	NA	50.3%	43.1%, 57.4%	0.55
TPRPS[c]	**Adults (overall)**						355	1,1370,853	57.9%	50.2%, 65.1%	
	Never combustible[d]						7	410,639	***	***	
	Current combustible[e]						279	7,627,740	52.6%	44.0%, 61.0%	
	Current cigarette[f]						259	6,536,123	48.9%	40.0%, 57.8%	
	Former combustible[g]						69	3,332,474	69.8%	52.0%, 83.1%	0.22
	Young adults (18–29 y)						86	4,092,588	64.8%	49.6%, 77.4%	
	Never combustible[d]						4	288,503	***	***	
	Current combustible[e]						63	2,570,723	60.9%	43.6%, 75.9%	
	Current cigarette[f]						54	1,894,898	51.8%	33.4%, 69.8%	
	Former combustible[g]						19	1,233,361	***	***	
	Older adults (30 + y)						269	7,278,265	54.0%	45.4%, 62.3%	
	Never combustible[d]						3	122,136	***	***	
	Current combustible[e]						216	5,057,017	48.4%	39.1%, 57.8%	
	Current cigarette[f]						205	4,641,225	47.7%	37.9%, 57.5%	
	Former combustible[g]						50	2,099,112	***	***	

Notes. P-values obtained from a chi-square test of differences in salience of flavored e-cigarette use by combustible product use status.
***Estimates suppressed as denominators <50 and are therefore statistically unreliable.
[a] TATAMS-The Texas Adolescent Tobacco and Marketing Surveillance System.
[b] M-PACT- The Marketing and Promotions Across Colleges in Texas Project.
[c] TPRPS- The Tobacco Products and Risk Perceptions Survey.
[d] Never combustible: reported never using cigarettes, hookah, and cigar products.
[e] Current combustible: reported past 30-use (TATAMS and M-PACT) or "every day"/"someday" use (TPRPS) of cigarettes, cigar products, or hookah.
[f] Current cigarette: subset of current combustible; reported current use of cigarettes.
[g] Former combustible: reported ever use of cigarettes, cigar products or hookah, but not current use of these products; n = survey sample size; N = weighted sample size or the population size to which estimates generalize back to; salience of flavors as a reason to use e-cigarettes was not assessed among ever e-cigarette users in TPRPS, so these cells are grayed out in the table.

older adults. TATAMS and M-PACT are specific to school-going participants, who may not generalize to out-of-school youth. Also, these studies from Texas may not be representative of similarly-aged students living elsewhere, though e-cigarette use rates are comparable to those from national studies (Ford et al., 2015; Singh, 2016). Studies have not yet evaluated whether e-cigarette use rates are similar between young people who do and do not attend school, though data indicate that youth and young adults who do not attend school are more likely to smoke combustible cigarettes (United States Department of Health and Human Services, 2012). Finally, minor differences in the wording of items and procedures used across all three studies to assess flavored e-cigarette use may be a potential limitation of the study, too. Though these three studies were not designed to be directly comparable, every effort was made post-hoc to align measures and analyses.

5. Conclusion

Characterizing flavors, especially sweet ones (e.g., fruit, candy, dessert), appear to be particularly relevant to e-cigarette use among young people, the rates of which have risen substantially in recent years (Singh, 2016; United States Department of Health and Human Services, 2012; Neff et al., 2015; Arrazola et al., 2015). Nationwide, past 30 day e-cigarette use was highest in 2014 among youth (13.4%) (Neff et al., 2015) and young adults (14.2%, 18–24 year olds) (Arrazola et al., 2015) compared to adults (2.4%, 25–44 year olds). (Agaku et al., 2014) Given new longitudinal research that shows that e-cigarette use also predicts the onset of combustible tobacco product use among both youth and young adults (Leventhal et al., 2015; Primack et al., 2015; Wills et al., 2016), acting like a "gateway" drug, it is imperative to identify feasible and effective intervention strategies that could potentially decrease the onset of and continued e-cigarette use. Eliminating or restricting characterizing flavors for e-cigarettes, especially sweet ones (e.g., fruit, candy, dessert) may offer the most benefit to youth and young adult prevention efforts. However, it is unclear what impact this strategy might have on adult cigarette smoking cessation.

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Marketing Little Cigars and Cigarillos: Advertising, Price, and Associations With Neighborhood Demographics

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Objectives. We have documented little cigar and cigarillo (LCC) availability, advertising, and price in the point-of-sale environment and examined associations with neighborhood demographics.

Methods. We used a multimodal real-time surveillance system to survey LCCs in 750 licensed tobacco retail outlets that sold tobacco products in Washington, DC. Using multivariate models, we examined the odds of LCC availability, the number of storefront exterior advertisements, and the price per cigarillo for Black & Mild packs in relation to neighborhood demographics.

Results. The odds of LCC availability and price per cigarillo decreased significantly in nearly a dose-response manner with each quartile increase in proportion of African Americans. Prices were also lower in some young adult neighborhoods. Having a higher proportion of African American and young adult residents was associated with more exterior LCC advertising.

Conclusions. Higher availability of LCCs in African American communities and lower prices and greater outdoor advertising in minority and young adult neighborhoods may establish environmental triggers to smoke among groups susceptible to initiation, addiction, and long-term negative health consequences. (*Am J Public Health.* 2013;103:1902–1909. doi:10.2105/AJPH.2013.301362)

During the past decade, the popularity of little cigars and cigarillos (LCCs) has risen dramatically. From 2000 to 2011, cigar sales increased by 221%,[1] whereas cigarette sales continued a decades-long decline.[2,3] As other venues for tobacco advertising have become increasingly limited, the point-of-sale environment is a critical battleground for companies to market their products.[4] Although there is no recent data on tobacco industry advertising budgets for LCCs specifically, the latest reports indicate that companies spent more than 90% of their $8.4 billion marketing budget in 2011 for retail advertising and promotions.[2] Evidence suggests this strategy is highly effective: exposure to point-of-sale displays is a risk factor for youth initiation[5,6] and higher levels of smoking among adults.[7]

LCCs are popular among populations of interest to tobacco control, including young adults and African Americans. National surveys show that the average age at first cigar use was 20.5 years in 2010.[8] Young adults aged 18 to 25 years have the highest rates of past month cigar use (11.2%) compared with youths and older adults.[8] However, these estimates may underestimate prevalence. Because most state and national surveillance surveys do not ask questions specific to LCCs, it is difficult to validly estimate patterns of use of these products among different populations.[9–12] One exception is a recent nationally representative study of young adults aged 18 to 34 years, which reported that 26.0% of respondents had ever smoked little cigars, cigarillos, or bidis and that 16.0% of everyday or occasional smokers currently smoked these products.[13]

Recent regional surveys that include brand-specific items for LCCs document higher estimates of use, particularly for minority populations. Tercheck et al.[12] found a near doubling of reported cigar use among adolescents when use of the brand Black & Mild, a popular cigarillo product, was measured by a question added to a regional Youth Risk Behavior Survey. This increase was most distinctive among African Americans, among whom reported prevalence rose from 11.7% to 22.0%. LCC product use and dual use of cigars and cigarettes[14] have been found to be more common among males, African Americans, and low-income adults.[9,15,16]

Ample evidence demonstrates greater point-of-sale cigarette advertising in neighborhoods with minority and younger populations, including more storefront cigarette advertising,[17] a greater number of cigarette advertisements and promotions,[18,19] and a trend toward higher levels of cigar self-service in low-income communities.[20] Furthermore, studies suggest selective marketing to young people and minorities with specific product types, such as smokeless tobacco in neighborhoods with younger populations[21] and menthol cigarettes in minority communities.[17,22–29] Although self-reported data from inner-city youths and young adults point to community-level factors as determinants of LCC use,[30,31] to our knowledge no previous research has systematically documented how LCCs are advertised and priced in the retail environment and how marketing may differ by community demographics.

Unlike cigarettes, LCCs are not currently regulated by the Food and Drug Administration under the 2009 Family Smoking Prevention and Tobacco Control Act (FSPTCA).[32] Thus, LCCs are not subject to the same regulations as cigarettes regarding characterizing flavors, sales, and marketing. For example, the FSPTCA bans on flavored cigarettes and sales of packages containing fewer than 20 cigarettes do not apply to LCCs. LCCs are often sold individually or in packs of fewer than 20. Furthermore, these products often come in flavors appealing to youth and young adult populations, including candy and alcohol flavors. Moreover, differences in federal and state taxing of cigarettes, cigars, and LCCs often make these products less expensive than cigarettes.[33]

Surveillance of LCC advertising in the point-of-sale environment is critical for monitoring tobacco industry marketing strategies and informing Food and Drug Administration policy. Because of the current lack of data on LCC marketing and a history of differential marketing of tobacco products in vulnerable communities, we have documented LCC availability, advertising, and price in the retail environment and examined differences by neighborhood demographics. We examined availability and store exterior advertising of LCCs overall and across communities as a function of neighborhood proportion of African Americans and young adults. We also examined prices for Black & Mild LCC packs, a top-selling cigarillo brand.[1,9,12,15] Specifically, we examined Black & Mild price per cigarillo as a function of neighborhood and other characteristics.

METHODS

From September 2011 to March 2012, trained fieldworkers visited retail outlets designated as licensed to sell tobacco in 2011 ($n = 1060$) by the Department of Health of Washington, DC. Washington, DC, the capital city of the United States, is a midsized urban city with a large African American population and is among the top 25 largest cities in the country.[34] We obtained data on store type, exterior and interior advertising, prices, and placement for every tobacco retail outlet using a multimodal surveillance system. The system utilized phone-based interactive voice recording, photo, and Web capabilities to unobtrusively collect information in the point-of-sale environment. We used ArcGIS 10.1[35] to create routes and guide fieldworkers through the city. Fieldworkers visually inspected retail outlets, emailed interior and exterior store photos, and recorded observations via interactive voice recording. All data flowed directly into a real-time surveillance database that the study coordinator monitored.[36] Although all outlets on the license list were surveyed, for this analysis we excluded outlets that were no longer in business or not open to the public (i.e., in a secured building; $n = 212$) or did not sell tobacco despite having a license ($n = 98$). The final sample totaled 750 outlets.

As business classification data on licensed outlets were unavailable, we categorized stores as convenience store, gas station, pharmacy, grocery store, liquor store, tobacco store, mass retailer, newsstand or kiosk, and other store types. Convenience stores were the most common store type, constituting nearly 30% of the sample, followed by liquor stores (21%), other store types (20%), gas stations (12%), grocery stores (11%), and pharmacies (7%). Other store types included small percentages of a variety of store types, including mass retailers, newsstands or kiosks, gift and discount stores, restaurants, and bars and hookah lounges.

We developed the survey on the basis of a literature review, including surveys of retail environments that surveyor groups used,[37–39] cigar brand sales,[40] price and purchasing behavior,[25,41] and corporate guidelines on point-of-sale marketing.[42] A 3-month pilot phase included development of the data collection system, testing questions for the survey, development of the protocol for conducting interactive voice recording surveys and collecting photos, and staff training. We conducted reliability assessments in 9 stores in a single block group. We chose 3 of each of the most common store types (convenience, grocery, and liquor) and 6 fieldworkers independently visited each store. We calculated interrater reliability using ICC.[43,44] ICCs ranged from 0.62 to 1.00 for LCC items, with the exception of tax items, which were closer to 0.30. Fieldworkers were retrained on items that fell below 0.75.

We enumerated all tobacco advertisements and LCC-specific advertisements on the exterior. Fieldworkers recorded LCC product availability and noted whether products came in singles or packs of more than 1 cigarillo and whether packs of Black & Mild cigarillos were sold. We noted the type of LCCs and categorized them as regular, menthol, or flavored. We recorded the lowest price without tax for a pack of Black & Mild (excluding single cigarillos), the number of cigarillos in the lowest priced pack, and whether this price was advertised. We also recorded promotions for Black & Mild with response options of buy 1 and get 1 free, other multipack discount, and other bonuses, rebates, or coupons. We defined the 3 study outcomes as whether LCCs were available in the store, the number of LCC advertisements on the store exterior, and the price per cigarillo for the lowest priced pack of Black & Mild. We converted prices to the price of an individual cigarillo because lowest priced Black & Mild packs ranged in size.

We geocoded the addresses of all stores and spatially joined them with census block groups using ArcGIS software.[35] We used data from the 2010 US Census, Short Form 1, to determine the demographic characteristics at the block group level. The final analytic sample of 750 stores were located in 265 census block groups, with the number of outlets ranging from 1 to 25 per block group (mean = 5.5; SD = 5.4). Block groups in Washington, DC, range from less than 0.5 miles to 2.5 miles, which represents a walking area range similar to accessibility studies found in the literature.[45–48] Census variables included percentage of African Americans aged 18 to 34 years and population per square mile, which we categorized into quartiles on the basis of the sample distribution (cutpoints: % African American at 11.4%, 56.1%, 89.1%; % aged 18–34 years at 23.2%, 31.1%, 44.0%; population per square mile: 8872, 15 991, 23 778). The use of categories derived from the distribution is a common approach, as it makes no assumptions regarding linearity and is easy to interpret. Other independent variables included store type and the number of registers (a proxy for store size), dichotomized as less than 3 versus 3 or more. For the price model, additional variables included whether the Black & Mild price was advertised and whether the cigarillos came in 2-packs or 5-packs.

We examined the study outcomes of LCC availability, exterior advertising, and price per cigarillo as a function of census block group demographics, number of outlets, store type, and number of registers. For the number of LCC advertisements on the store exterior, we used zero-inflated negative binomial regression rather than Poisson regression, similar to the methodology Widome et al. used.[21] We utilized zero-inflated negative binomial models, which are appropriate when the data include excess zeros (i.e., stores with no LCC advertisements) and there are concerns that processes, such as store policies around exterior tobacco advertising, might drive the zero and count values. We used a variable to reflect the total amount of non-LCC advertising to predict the zeros and used the other predictors for the LCC advertisement count. We used robust sandwich estimates to address clustering. The dispersion coefficient (α) was significantly different from zero, indicating that the data were overdispersed and the negative binomial was more appropriate than a Poisson model.[49] The Vuong test[50] was significant, indicating that the zero-inflated negative binomial was superior to a standard negative binomial. The predictor of excess zeros was statistically significant as well. We have reported prevalence ratios with 95% confidence intervals (CIs).

We used Stata version 11.2 (StataCorp, LP, College Station, TX) to calculate outcomes for availability of LCC products and the price per cigarillo using binary and linear multilevel models, respectively, which included a random intercept and adjusted for predictors at the store and block group level. We have provided a visual analysis of findings from the price model, utilizing ArcGIS 10.1. We mapped the geographic distribution of the African American population in Washington, DC, with a quartile distribution map of the African American population by 2010 US Census block groups.

Next, we utilized the Geostatistical Analysts extension toolbar to produce a prediction map of LCC price using kriging methodology. Kriging produces an estimate of the underlying surface by a weighted average of the data, with weights declining with distance between the point at which the surface is being estimated and the locations of the data points. We assumed data points and the associated surface at nearby locations to be more similar to each other than points at locations distant from each other. For our prediction map, data points are the spatial locations of tobacco retail outlets in Washington, DC, that have an associated Black & Mild price. We then chose ordinary kriging using a K-Bessel model to produce our kriged surface. This model tends to produce surfaces that are more smooth locally than those of other models.

RESULTS

Nearly 40% of stores had exterior tobacco advertising of any kind, whereas 12% of stores had exterior LCC advertisements, as shown in Table 1. Among stores with any exterior tobacco advertising, the number of tobacco advertisements per store ranged from 1 to 20, with a mean of 3.3 (SD = 2.7), and among stores with any LCC advertising, the number of LCC advertisements ranged from 1 to 8, with a mean of 1.9 (SD = 1.3). LCCs were available for sale at more than 80% of stores selling tobacco in Washington, DC. Nearly 60% of these stores sold single LCCs, 74% sold LCC packs, and 70% offered Black & Mild packs. Of the stores that sold LCCs, a full 95% sold LCCs in flavors, such as fruit, candy, and wine, and 13% sold menthol LCCs. Black & Mild pack types for the lowest priced pack were most commonly available as 2-packs and 5-packs. Promotions on packs of Black & Mild were available in approximately 6% of stores. The average price per cigarillo for the lowest priced Black & Mild pack was $0.91 (SD = 0.21). Price varied across Washington, DC, with the maximum per cigarillo price 6 to 7 times higher ($1.65) than was the lowest per cigarillo price ($0.25). Prices for Black & Mild cigarillos were advertised in 37% of stores. A *t* test indicated that price per cigarillo was significantly lower for 2-packs versus 5-packs ($P \leq .001$) and for advertised prices versus nonadvertised prices ($P \leq .001$).

Block groups in the higher quartiles for proportion of African American residents were significantly more likely to have LCCs available than were block groups in the lowest quartile (Table 2). There were no differences in LCC availability by quartiles of the population aged 18 to 34 years. For LCC exterior advertisements, the estimated prevalence of exterior LCC advertisements also increased significantly with each quartile increase in proportion of African Americans in a dose-response manner, with the highest quartile reaching a prevalence ratio of 10.16. Block groups in the third and fourth quartiles for proportion of young adults aged 18 to 34 years also had a significantly higher prevalence of exterior LCC advertisements than did those in the first quartile.

Price per cigarillo decreased significantly in a dose-response manner, with increasing quartiles for African American population (Table 3). Price per cigarillo in areas in the third quartile for proportion of young adults was significantly lower by $0.09 than was the first quartile. Price per cigarillo for cigarillos sold in 2-packs was significantly lower than were those sold in 5-packs; advertised prices were significantly lower than were nonadvertised prices. Figure 1a shows the quartile distribution of the African American population for Washington, DC, with darker colors representing the higher quartiles. Figure 1b

TABLE 1—Descriptive Statistics of Little Cigar and Cigarillo Availability, Advertising, and Price Across Tobacco Retail Outlets: Washington, DC, 2011–2012

Variable	% or Mean (SD)	Minimum	Maximum
Among all stores (n = 750)			
Stores with exterior LCC advertising	12.00	0.00	1.00
Store sells any LCCs	80.00	0.00	1.00
Store sells single LCCs	60.00	0.00	1.00
Store sells packs of LCCs	74.00	0.00	1.00
Store sells Black & Mild LCCs	70.00	0.00	1.00
Among stores selling LCCs (n = 588)			
Store sells regular LCCs	98.00	0.00	1.00
Store sells menthol LCCs	13.00	0.00	1.00
Store sells flavored LCCs	95.00	0.00	1.00
Among stores selling Black & Mild (n = 513)			
Price had a promotion	6.00 (24.00)	0.00	1.00
Price was advertised	37.00 (48.00)	0.00	1.00
Price/cigarillo, $			
Advertised	0.84 (0.24)	0.49	1.65
Nonadvertised	0.95 (0.18)	0.25	1.60
Overall	0.91 (0.21)	0.25	1.65

Note. LCC = little cigar and cigarillo.

TABLE 2—Associations for Little Cigar and Cigarillo Availability and for Exterior Advertising Regressed on Store Characteristics and Neighborhood Demographics: Washington, DC, 2011–2012

Variable	% or Mean (SD)	LCCs available (n = 725), OR (95% CI)	Exterior Advertising (n = 731), PR (95% CI)
Intercept		1.80 (0.65, 5.00)	0.12*** (0.04, 0.36)
Store			
Convenience store	29	1.00 (Ref)	1.00 (Ref)
Gas station	12	1.81 (0.67, 4.85)	1.19 (0.70, 2.01)
Pharmacy	7	3.14 (0.90, 10.92)	0.00*** (0.00, 0.00)
Grocery	11	0.56 (0.28, 1.24)	0.79 (0.38, 1.64)
Liquor	21	0.51* (0.28, 0.93)	0.81 (0.43, 1.53)
Other	20	0.29*** (0.16, 0.52)	0.36 (0.12, 1.04)
Store's registers, no.			
< 3	87	1.00 (Ref)	1.00 (Ref)
≥ 3	13	1.02 (0.46, 2.28)	0.22 (0.02, 2.41)
African American,%			
First quartile		1.00 (Ref)	1.00 (Ref)
Second quartile		2.82*** (1.67, 4.77)	2.50* (1.10, 5.70)
Third quartile		13.5*** (5.56, 32.82)	5.30*** (2.21, 12.71)
Fourth quartile		11.8*** (4.51, 30.67)	10.16*** (4.21, 24.56)
Residents 18–34 y, %			
First quartile		1.00 (Ref)	1.00 (Ref)
Second quartile		0.99 (0.42, 2.32)	1.27 (0.61, 2.65)
Third quartile		1.36 (0.46, 4.00)	2.92* (1.13, 7.50)
Fourth quartile		0.96 (0.34, 2.70)	3.23** (1.52, 6.8)
Population/square mile			
First quartile		1.00 (Ref)	1.00 (Ref)
Second quartile		0.75 (0.39, 1.45)	1.05 (0.59, 1.89)
Third quartile		1.25 (0.59, 2.66)	0.72 (0.33, 1.58)
Fourth quartile		1.50 (0.68, 3.30)	1.20 (0.52, 2.73)
Outlets, no.	4.6 (2.9)	0.98 (0.93, 1.02)	0.92* (0.86, 0.99)

Note. CI = confidence interval; OR = odds ratio; PR = prevalence ratio. We did not include newsstands and kiosks in this analysis, as these establishments did not have exterior walls.
*$P < .05$; **$P < .01$; ***$P < .001$.

TABLE 3—Regression Coefficients for Price per Little Cigar and Cigarillo Regressed on Store and Product Characteristics and Neighborhood Demographics: Washington, DC, 2011–2012

Variable	Price Model 1 (n = 449), b (95% CI)
Intercept	1.05*** (0.97, 1.14)
Store	
Convenience store (Ref)	1.00
Gas station	0.02 (−0.04, 0.07)
Pharmacy	0.17*** (0.08, 0.27)
Grocery	0.04 (−0.03, 0.10)
Liquor	0.03 (−0.02, 0.08)
Other	0.04 (−0.01, 0.10)
Store registers, no.	
< 3 (Ref)	1.00
≥3	0.02 (−0.05, 0.10)
Packs, no.	
5 (Ref)	1.00
2	−0.07* (−0.12, −0.02)
Price	
Nonadvertised (Ref)	1.00
Advertised	−0.15*** (−0.19, −0.10)
African American, %	
First quartile (Ref)	1.00
Second quartile	−0.08** (−0.14, −0.02)
Third quartile	−0.12** (−0.19, −0.05)
Fourth quartile	−0.14*** (−0.22, −0.07)
Residents 18–34 y, %	
First quartile (Ref)	1.00
Second quartile	−0.00 (−0.06, 0.05)
Third quartile	−0.09* (−0.16, −0.01)
Fourth quartile	−0.02 (−0.09, 0.06)
Population/square mile	
First quartile (Ref)	1.00
Second quartile	−0.01 (−0.05, 0.04)
Third quartile	0.02 (−0.03, 0.07)
Fourth quartile	0.00 (−0.06, 0.06)
Outlets, no.	0.00 (−0.00, 0.01)

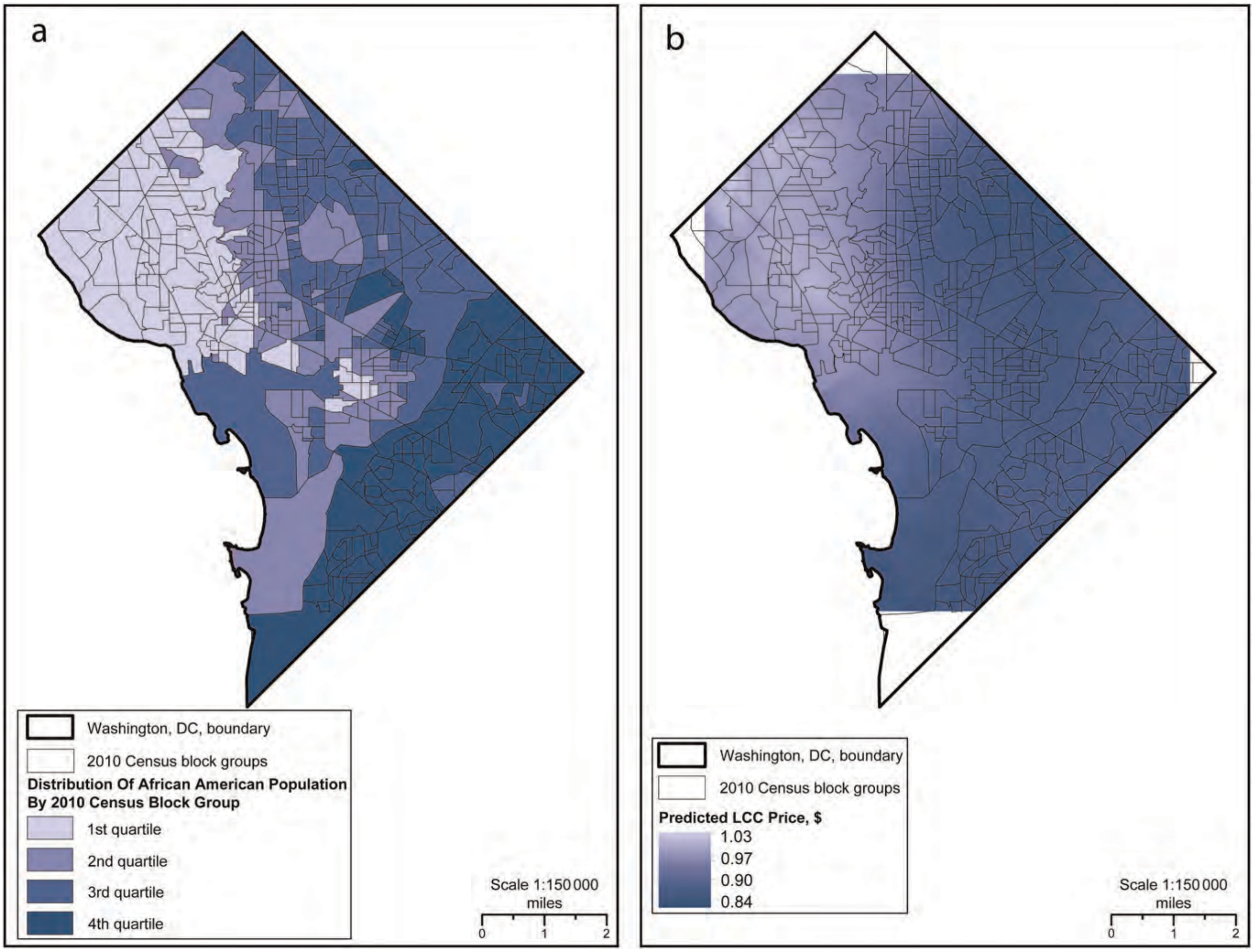
Note. CI = confidence interval.
*$P < .05$; **$P < .01$; ***$P < .001$.

shows the prediction map of price per cigarillo across block groups using kriging methodology, with the darker color representing lower prices. Side-by-side, these maps illustrate the inverse relationship between proportion of African Americans in the block group and lower predicted price.

DISCUSSION

To our knowledge, this study is the first to examine LCC marketing and price in the retail environment in relation to neighborhood demographics. Data indicated that LCCs are more available in predominantly African American neighborhoods, and cheaper in African American and some young adult neighborhoods. The use of exterior advertising is significantly more prevalent in neighborhoods with African Americans and young adults. As previous studies have shown, initiation of LCC use typically occurs early in young adulthood.[8] Without ever entering a store or approaching an LCC retail display, young adults and individuals in African American communities are disproportionately exposed to storefront LCC advertisements in their neighborhoods. Furthermore, individuals in African American neighborhoods and in certain young adult neighborhoods can purchase LCCs at lower prices, a proven technique for increasing demand among price-sensitive populations.[51,52]

Similar to menthol cigarettes that have been marketed to minority communities,[17,22–29] LCCs were more likely to be available in



Note. LCC = little cigar and cigarillo. Figure 1a shows the quartile distribution of the African American population for Washington, DC, with darker colors representing the higher quartiles. Figure 1b shows the prediction map of price per cigarillo across block groups of Washington, DC, using kriging methodology, with the darker color representing lower prices.

FIGURE 1—Inverse relationship between proportion of (a) African Americans in the block group and (b) lower predicted price per cigarillo: Washington, DC, 2011–2012.

neighborhoods with more African American residents. Widespread availability of tobacco products can contribute to a normative environment that reinforces smoking and undermines cessation.[41,53–55] Such norms may be further compounded by the misperception of LCC products as less harmful than cigarettes,[56–59] despite being as, or more, toxic and carcinogenic than are cigarettes. Prosmoking norms, perceptions of reduced harm, and easy access are likely to increase use of LCCs and magnify disparities among a population that already suffers from a disproportionate burden of tobacco-related morbidity and mortality.[60–62]

Beyond the concentration of LCCs in stores in African American communities, exterior advertising of these products was greater in communities with more minority and young adult members. The findings echo previous studies demonstrating greater storefront advertising of menthol cigarettes in minority communities.[17,27,29] The higher level of exterior advertising in communities with young adults has not been previously reported. This age group continues to experiment with tobacco products, particularly novel or emerging products and occasional use.[63–66] After the 1998 Master Settlement Agreement, advertising shifted from billboard to storefront exterior cigarette advertising in minority communities[17,18,29,67] and has increasingly focused on young adults.[68] We might expect similar shifts in marketing after the passage of the FSPTCA. Although exterior advertising of LCCs was not widespread overall, storefront advertising remains a potentially salient venue to further market LCCs in anticipation of greater restrictions on cigarette advertising and decreasing cigarette sales. These trends, if left unchecked, can serve to increase initiation and progression to established smoking and delay cessation.

Findings also indicated lower prices for LCCs in neighborhoods with more African Americans. Similarly, Henriksen et al. found lower prices for Newport cigarettes in communities with a higher percentage of African American students.[25] The average price per cigarillo for the lowest priced packs of Black & Mild was relatively high at $0.91 without sales tax compared with an approximate per cigarette price of $0.24 without sales tax for a 20-pack of cigarettes at current estimated DC prices.[69] However, the overall price range for LCC packs is lower considering that the products generally come in smaller pack sizes, ranging from 2 to 5 cigarillos. This provides an affordable way for price-sensitive customers to purchase the product, even though the unit cost is considerably high. Smaller pack products are reminiscent of "loosies," cigarettes that were highly popular in certain inner-city African American communities before the FSPTCA was passed.[55,70] LCC prices were lower in some young adult neighborhoods as well, but prices did not consistently decrease in a dose-response fashion for increasing quartiles of young adults, as did prices across African American block groups. Considering previous research pointing to youths as a price-sensitive population,[52,71] the industry may focus promotional allowances that reduce price while enticing potential young adult smokers in venues other than retail outlets, such as bars, cafes, and nightclubs.[66,72,73]

Our data suggest that retail marketing of LCCs is widespread, with 80% of tobacco-selling outlets providing LCCs. Furthermore, 2 key provisions of the FSPTCA—the ban on single sales and flavored cigarettes—are undermined by the widespread presence of single-pack LCCs (60% of tobacco-selling outlets) and flavored versions (95%). It will be critical for researchers and policymakers to continue to monitor the LCC market, particularly considering its rapid growth and increasing industry interest in these products.[74,75]

Limitations

In this survey, we focused on the presence of product, price, and exterior advertising but did not include the characteristics of advertising inside the store. Our efforts were limited in obtaining reliable tax data on the basis of posted prices and discussions with store clerks. Interviews with fieldworkers indicated that price data collected did not include taxes, but error may have been introduced to the extent that price data with or without taxes differed between neighborhoods.

Because this study was conducted in a single city, findings may not be generalizable to all areas, including smaller cities or areas with fewer minorities. However, results likely reflect other medium to large urban areas with large populations of minorities living in concentrated neighborhoods. In addition, results may have differed if neighborhoods were measured at larger or smaller area ranges. However, these results are consistent with findings from retail surveys of Newport, menthol, and related cigarette products that have been identified as more prevalent in areas with a greater number of minorities and youths.[17,19,25,27,29]

Conclusions

Multiple approaches are needed to counteract the marketing and promotion of LCCs. First, LCCs should be subject to the same federal regulations as cigarettes, specifically bans on flavors, taxation, and advertising restrictions. Second, state and local governments can take action to counter advertising of LCCs in their communities, including restrictions on pack sizes[76] and bans on exterior storefront advertising of tobacco.[4] Furthermore, legislative mandates to report yearly advertising and promotion expenditures for cigar products, similar to those mandated for cigarettes and smokeless products,[77,78] can be enacted for systematic monitoring of LCC marketing and advertising practices. Lastly, ongoing consumer behavior and product surveillance [79,80] can inform our understanding of the potential public health impact of these new products and improve the ability to respond through regulatory channels such as the FSPTCA.

Research among young adults and African Americans demonstrating the increasing popularity of LCCs has been accumulating for the past decade, yet strategies used to market to these populations at retail have not been widely documented. To our knowledge this study is the first to examine LCC marketing in the retail environment and differences in marketing by neighborhood demographics. Findings of broad LCC availability, including single sales and flavored versions, likely reflect differential regulation of cigarettes as compared with cigar products. Higher availability of these products, lower prices in African American and some young adult communities, and greater outdoor advertising in minority and young adult neighborhoods may establish environmental triggers to smoke among groups susceptible to initiation, addiction, and long-term negative health consequences.[60–62,64] Real-time surveillance of the retail environment can allow rapid policy responses to emerging tobacco products to prevent industry targeting of vulnerable populations. ■

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Contributors

J. Cantrell conceptualized the study, conducted the analysis, and wrote the article. J. M. Kreslake contributed to the writing. O. Ganz contributed to writing and coordinated the study. J. L. Pearson, D. Vallone, and T. R. Kirchner contributed to writing and revisions. A. Anesetti-Rothermel, J. M. Kreslake, and H. Xiao contributed to the analyses. A. Anesetti-Rothermel conducted the ArcGIS analyses. T. R. Kirchner was the principal investigator of the broader study.

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Human Participant Protection

No protocol approval was necessary because this study involved no human participants, as determined by the Independent Institutional Review Board, Inc.

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Original investigation

Neighborhood Variation in the Price of Cheap Tobacco Products in California: Results From Healthy Stores for a Healthy Community

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Abstract

Background: Retail marketing surveillance research highlights concerns about lower priced cigarettes in neighborhoods with a higher proportion of racial/ethnic minorities but focuses almost exclusively on premium brands. To remedy this gap in the literature, the current study examines neighborhood variation in prices for the cheapest cigarettes and a popular brand of cigarillos in a large statewide sample of licensed tobacco retailers in a low-tax state.

Methods: All 61 local health departments in California trained data collectors to conduct observations in a census of eligible licensed tobacco retailers in randomly selected zip codes (n = 7393 stores, completion rate=91%). Data were collected in 2013, when California had a low and stagnant tobacco tax. Two prices were requested: the cheapest cigarette pack regardless of brand and a single, flavored Swisher Sweets cigarillo. Multilevel models (stores clustered in tracts) examined prices (before sales tax) as a function of neighborhood race/ethnicity and proportion of school-age youth (aged 5–17). Models adjusted for store type and median household income.

Results: Approximately 84% of stores sold cigarettes for less than $5 and a Swisher Sweets cigarillo was available for less than $1 in 74% of stores that sold the brand. The cheapest cigarettes cost even less in neighborhoods with a higher proportion of school-age residents and Asian/Pacific Islanders.

Conclusions: Neighborhood disparities in the price of the cheapest combustible tobacco products are a public health threat. Policy changes that make all tobacco products, especially combustible products, less available and more costly may reduce disparities in their use and protect public health.

Implications: Much of what is known about neighborhood variation in the price of combustible tobacco products focuses on premium brand cigarettes. The current study extends this literature in two ways, by studying prices for the cheapest cigarette pack regardless of brand and a popular brand of flavored cigarillos and by reporting data from the largest statewide sample of licensed tobacco retailers. Significantly lower prices in neighborhoods with a higher proportion of youth and of racial/ethnic groups with higher smoking prevalence are a cause of concern. The study results underscore the need for policies that reduce availability and increase price of combustible tobacco products, particularly in states with low, stagnant tobacco taxes.

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Introduction

Higher prices for tobacco products discourage initiation, reduce consumption, promote quitting, and prevent relapse.[1] Therefore, widespread availability of cheap, combustible tobacco constitutes a significant public health concern, both in the United States and in other countries.[2] In California, where this study was conducted, the $0.87 per pack cigarette tax ranked 37th among the 50 states and had not increased for almost two decades. Before voters approved a tobacco tax increase in 2016, the average cigarette pack price was $5.47.[3] In addition, California young adults, women, African Americans, and heavy smokers were significantly more likely than others to take advantage of cigarette price promotions practically every time they see one.[4]

Data sources for monitoring tobacco prices in the United States are typically aggregated to states or designated market areas.[5] Unfortunately, these large geographies make it impossible to answer important research questions about how tobacco companies or retailers manipulate prices to target specific groups by age or race/ethnicity. To remedy this concern, a growing number of studies examine neighborhood variation in cigarette prices by comparing advertised prices from randomly sampled stores.[6,7] The majority of such studies typically monitor cigarette prices for popular premium brands. For example, Marlboro cost less in neighborhoods with a lower median household income and in neighborhoods with a higher proportion of Hispanic residents, even after adjusting for store type.[8–10] Newport, the leading brand of menthol cigarettes, cost less in neighborhoods with a higher proportion of African American residents[8–10] and in neighborhoods with a higher proportion of residents who are school-age youth.[11,12]

Fewer studies monitor cigarette prices for discount brands. In one city in Great Britain, a study documented that pack prices clustered at three modes and that the minimum advertised price was 61% of the maximum advertised price.[13] In Minneapolis convenience stores, the average price for a discount brand was 16% less than that of a premium brand from the same manufacturer and 25% less than the menthol variety from the same unidentified premium brand.[14] The menthol price was not correlated with the proportion of nonwhite residents or youth; however, the discount variety cost less in neighborhoods with a higher proportion of nonwhite residents. In our previous research, the most popular discount brands were not as widely available as the most popular premium brands[9]; therefore, this study assessed the price of the cheapest cigarette pack regardless of brand.

Too little is known about neighborhood variation in price of other combustible tobacco products. This study also focuses on cigarillos, a product category that raises several public health concerns: fruit, sweet, and alcohol flavors that appeal to youth, misperceptions that cigarillos are less harmful than cigarettes, and marketing that promotes concurrent use of tobacco and marijuana.[15–19] In Washington, DC, the average price per cigarillo was less than $1 for the brand Black & Mild.[20] In addition, the unit price was significantly lower in neighborhoods with a higher proportion of African Americans. However, determining whether this association is independent of neighborhood income was impossible because race and income were so highly correlated. The current study extends this literature by examining neighborhood variation for the price of a different popular brand in a representative sample of licensed tobacco retailers in California. The analyses examine percentage of youth and young adults and adjusted for neighborhood income.

An alternative explanation to target marketing by race and/or income for the observed disparities in cigarette and cigarillo prices is that neighborhoods characterized by socioeconomic disadvantage contain a disproportionately higher concentration of tobacco retailers.[21,22] The theory that prices fall as the number of retailers in a market rises[23] predicts that tobacco products would cost less at stores with more competitors nearby. However, our previous research found that the number of tobacco retailers in a neighborhood was associated with slightly higher prices for Newport and was unrelated to the price of Marlboro.[11] The current study extends this literature by examining variation in price of cheap combustibles as a function of neighborhood demography. To our knowledge, the current study is unique in examining the number and proximity of nearby competitors and the prices in those stores.

Methods

This study reports a subset of data from the baseline evaluation for a statewide campaign in California, *Healthy Stores for a Healthy Community*, which is, a collaboration between tobacco use prevention, nutrition, alcohol abuse prevention, and other public health partners.[24] The campaign goals are to improve the health of Californians through changes in community stores and to educate people about how point-of-sale marketing influences consumption of unhealthy products. In a statewide sample of licensed tobacco retailers, all 61 county and municipal local health departments assessed retail availability and marketing for tobacco, alcohol, and food and beverage items. The current study uses data for all tobacco prices from the core survey.[24]

Sample

Beginning with a state licensing list of 36 777 tobacco retailers, the sampling frame excluded stores that prohibited minors (e.g., bars or nightclubs that sell alcohol), required paid memberships (e.g., Costco), or restricted entry (e.g., military bases, state or national parks). For each of the 61 local health departments, a target sample size was based on the number of tobacco retailers within the jurisdiction and their funding level. Sample sizes were designed to yield minimum margin of errors for a percentage: 0.05 for the largest local health department, 0.075 for mid-size departments, and 0.10 for the smallest departments. Within each jurisdiction, zip codes were randomly selected until the target sample size was reached: 8128 eligible tobacco retailers in 616 randomly selected zip codes.

Data Collection

Programmed using the iSurvey application, a 30-question core survey assessed the availability and marketing for tobacco products, including product availability, presence of interior and exterior marketing materials, and price. Following a train-the-trainers model, approximately 200 local health department leaders participated in several hours of in-person instruction, field practice, and an online quiz. These leaders then recruited and trained more than 700 data collectors, including health department staff, environmental health inspectors, and nearly 300 youth volunteers. Every jurisdiction used a standardized training protocol and manual, the same slide set with pictures and speaker notes, and online quizzes. In the field, data collectors referred to a pocket guide for key instructions and could access telephone support for questions. Between June and September 2013, data collectors completed marketing assessments in 7393 stores (completion rate = 91%).

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The core survey averaged 8 min per store. Data collectors classified stores into 1 of 11 categories using standard definitions.[9] These were collapsed into the following: convenience, drug/pharmacy, liquor store, small market/deli/produce market, supermarket, discount store (including dollar stores and Wal-Mart), gas station kiosks, hookah cafe/tobacco shops, and other.

Tobacco Prices

The two price outcomes in the core survey were price of cheapest cigarette pack regardless of brand, and price of a single, flavored Swisher Sweets cigarillo, one of the top-selling brands in the United States.[25] Prices could be requested or observed, and the priority differed by product. Based on our pilot studies, data collectors were trained to first ask for cigarette price and to first look for advertised cigarillo price. Data collectors were trained to use either method to obtain price and to record whether sales tax was included. Cigarette brand was not recorded because our pilot studies revealed that the same lowest price may be available for multiple brands. Interrater reliability was not assessed. However, previous studies that used similar methods (albeit fewer observers) obtained good agreement about price of cigarettes[6,9] and cigarillos.[20]

Neighborhood Demographics

Previous studies examined tobacco prices as a function of neighborhood demography defined by census tracts,[26] census block groups,[20,27] and store-centered buffers.[14] Although zip code was the sampling unit, the current study modeled stores clustered in census tracts because there was insufficient clustering within block groups, and zip codes are larger than a typical "neighborhood" in previous research. Tracts were characterized using intercensal estimates (GeoLytics, Inc.) for median household income, race (% African American, Asian/Pacific Islander, and other nonwhite residents), ethnicity (% Hispanic), percentage of school-age youth (aged 5–17), percentage of young adults (aged 18–24), and population density.

Localized Competition

Using ArcGIS v10.1, all stores were geocoded to latitude/longitude (mapping rate = 99.8%), and distance between all stores was computed in roadway miles. Tobacco retailer density for each tract was calculated as retailers per 1000 residents. Proximity measured distance to the nearest tobacco retailer.

Analyses

Cigarettes were sold in 98.0% of stores, and valid data for price (with sales tax information) was obtained in 94.0% of those stores. For analysis, we excluded cigarette prices that were less than the sum of federal and state taxes ($1.88 in 2013, n = 94) and greater than $15.00 (n = 6). All cigarette prices were computed to exclude sales tax. San Francisco prices included the city's 20-cent litter mitigation fee.

Single Swisher Sweets cigarillos were sold in 57.2% of stores, and valid price data were obtained in 93.4% of those stores. For analysis, we excluded prices greater than $2.00 (n = 22) because there was a large break in the distribution at that price. We were concerned that higher prices indicated that data collectors inadvertently recorded price for larger pack sizes. All cigarillo prices were computed to exclude sales tax. Weighting variables were not applied because analyses focus on subsamples with valid price.

The current study reports two approaches to the analysis. Using HLM 7.0 software, multilevel modeling (stores nested within census tracts) examined price as a function of store type and distance to nearest competitor as well as neighborhood demographics (including tobacco retailer density). The number of stores per tract ranged from 1 to 21 (mean = 3.9, SD = 2.9). Two-level multilevel models with random intercepts and robust standard errors were used to test the relationship between neighborhood characteristics and local competition (proximity—level 1 and tobacco retailer density—level 2) while controlling for store type. Models without predictors were fit for each price, and intraclass correlation coefficients (ICCs) were computed. Unadjusted models were fit for level 1 predictors: (a) store type with convenience store as the reference group and (b) distance to nearest tobacco retailer (grand mean centered). While controlling for store type (level 1), the next set of models examined unadjusted relationships between price and level 2 predictors: (a) race/ethnicity (% African American, % Asian/Pacific Islander, % other/multiple races, % Hispanic), (b) age (% school age youth and % young adults), (c) median household income, (d) population density, and (e) tobacco retailer density. The census variables were standardized based on statewide data. The measures were treated as continuous because a preliminary examination of quartiles suggested that associations with price were linear.

The second approach utilized spatial regression techniques because a covariance analysis revealed that prices between nearby stores were positively correlated even after accounting for neighborhood characteristics and the other variables in the multilevel model. The spatial regression modeling allowed us to adjust for these unknown factors to ensure that inferences about the primary factors are still valid. Separate spatial regression models examined price of cheapest pack and cigarillo as a function of store type and neighborhood (census tract) demography. The reason for conducting spatial regression analyses was to take into account that the influence of neighborhood characteristics diminishes, as the distance increases from the tract in which each store is located (i.e., correlated errors). Analyses were performed using Python 3.5.

Results

Table 1 summarizes the distribution of store type and tract-level demographics for the total sample, the subset with price for cheapest pack regardless of brand, and the subset with price for a flavored Swisher Sweets cigarillo. Convenience stores were the most prevalent store type in all three samples, and neighborhood demographics were comparable. The average tract in the total sample contained 0.9 tobacco retailers per 1000 residents. The average distance to the nearest competitor was 1.3 miles (SD = 3.8), and 16.5% of observed stores were located within 500 feet of another tobacco retailer.

As shown in Table 2, the average price for the cheapest cigarette pack regardless of brand was $4.33 (SD = 0.97). More than three in four (83.5%) stores sold cigarettes for less than $5. The average price for a flavored Swisher Sweets cigarillo was $0.93 (SD = 0.30). Of the stores that sold this brand, 73.0% charged less than $1. Even after removing outliers, the maximum price for the cheapest cigarette pack was 6.6 times greater than the lowest price. The maximum cigarillo price was 10.5 times the lowest price.

Initial multilevel models indicated significant variation in price across census tracts (variance estimate between stores=0.236, p values < .001; model not shown). For the cheapest cigarettes, 25.1% of the total variance (ICC = 0.251) was between tracts as opposed to

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between stores. As shown in Table 3, store type explains some variation in the cheapest pack, with lower prices found in tobacco shops and higher prices in small market, supermarkets, discount stores, and gas kiosks compared to convenience stores. In bivariate models, the cheapest pack price was significantly lower in tracts with higher proportions of African American and Hispanic residents, in neighborhoods with higher proportions of school-age youth and young adults, and in neighborhoods with lower median household income. In a multivariate model that adjusted for store type, neighborhood demographics, the cheapest cigarette pack cost $0.17 less for each SD increase in the proportion of school-age youth (equivalent to a 5.7 percentage point increase; $p < .001$). The price was $0.04 less for each SD increase in the proportion of Asian/Pacific Island residents ($p < .05$). In addition, the cheapest pack cost less in lower income neighborhoods (an estimated $0.22 for each *SD* decrease in median household income, $p < .001$). The proportion of young adults did

Table 1. Descriptive Statistics for Store Type and Neighborhood Demographics for Analysis Samples and Total Sample: Healthy Stores for a Healthy Community, California (2013)[a]

	Store with cheapest pack price		Stores with single Swisher sweets Price		All HSHC stores unweighted	
	N = 6687		*N* = 3928		*N* = 7392	
Store characteristics	*n*	%	*n*	%	*n*	%
Store type						
Convenience	2084	31.1	1537	39.0	2171	29.4
Pharmacy	427	6.4	233	5.9	470	6.4
Liquor	1020	15.2	699	17.7	1154	15.6
Small market	1578	23.5	799	20.3	1775	24.0
Supermarket	594	8.9	98	2.5	636	8.6
Discount store	117	1.7	41	1.0	126	1.7
Gas kiosk	407	6.1	276	7.0	446	6.0
Tobacco shop/hookah bar	316	4.7	234	5.9	381	5.2
Other	168	2.5	27	0.7	233	3.2
Distance to nearest competitor (miles)	1.4	3.6	1.2	3.2	1.3	3.8
	N = 1823		*N* = 1524		*N* = 1874	
Neighborhood traits (Census tracts)	Mean	SD	Mean	SD	Mean	SD
Race/ethnicity						
% African American	5.3	8.0	5.3	7.8	5.3	8.0
% Asian/Pacific Islander	10.0	12.8	9.9	12.6	10.0	12.8
% Other/multiple race	16.0	11.0	16.6	11.2	16.0	11.0
% Hispanic	34.4	25.5	35.8	25.9	34.3	25.5
Age						
% School-age youth (ages 5–17)	17.3	5.7	17.6	5.7	17.3	5.7
% Young adults (ages 18–24)	10.3	6.4	10.4	6.4	10.4	6.5
Household median income	59,925	26,928	58,477	58,477	59,999	26,955
Population density	6065	8303	9169	8382	6095	8305
Tobacco retailers (per 1000 residents)	0.9	0.8	1.0	0.9	0.9	0.7

[a]Prices were cheapest pack of cigarettes regardless of brand and single Swisher Sweets.

Table 2. Price of Cheapest Pack of Cigarettes and Single Swisher Sweets Cigarillo, by Store Type: California, 2013

	Cheapest pack of cigarettes			Single Swisher sweets		
Store type	*n*	Mean	SD	*n*	Mean	SD
Convenience	2084	4.12	0.67	1537	0.93	0.26
Pharmacy	427	4.19	0.45	233	1.41	0.38
Liquor	1020	4.08	0.70	699	0.85	0.25
Small market	1578	4.55	1.13	799	0.86	0.26
Supermarket	594	4.90	1.02	98	1.12	0.23
Discount store	117	4.19	0.75	41	0.82	0.23
Gas kiosk	407	4.32	0.83	276	0.98	0.30
Tobacco shop/hookah bar	316	3.65	0.76	234	0.78	0.21
Other	168	6.06	1.78	27	0.95	0.28
Total	6711	4.33	0.97	3944	0.93	0.30

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Table 3. Multilevel Model of Cheapest Cigarette Pack (Before Sales Tax) as a Function of Store Type and Neighborhood Demographics: California, 2013[a]

	Unadjusted models		Multivariate model		Spatial model	
	Coef.	*p*	Coef.	*p*	Coef.	*p*
Level 1 (Store characteristics, *n* = 6687)						
Intercept			4.16	<.001	4.12	<.001
Store type						
Convenience	Ref	Ref	Ref	Ref	Ref	Ref
Pharmacy	0.05	.070	0.04	.133	0.06	.167
Liquor	−0.02	.448	−0.01	.837	−0.01	.868
Small market	0.42	<.001	0.44	<.001	0.44	<.001
Supermarket	0.77	<.001	0.75	<.001	0.77	<.001
Discount store	0.17	.016	0.21	.002	0.21	.006
Gas kiosk	0.16	<.001	0.13	.002	0.14	.002
Tobacco shop/hookah bar	−0.41	<.001	1.75	<.001	−0.37	<.001
Other	1.79	<.001	−0.40	<.001	1.73	<.001
Distance to nearest competitor (miles)	0.04	<.001	0.03	<.001	0.03	<.001
Level 2 (Tract characteristics, n = 1823)						
Race/ethnicity						
% African American	−0.04	.011	−0.01	.756	−0.02	.459
% Asian/Pacific Islander	0.03	.084	−0.04	.031	−0.05	.029
% Other/multiple race	0.02	.470	0.02	.319	0.02	.407
% Hispanic	−0.14	<.001	0.00	.904	−0.04	.113
Age						
% School-age youth (ages 5–17)	−0.20	<.001	-0.17	<.001	−0.12	<.001
% Young adults (ages 18–24)	−0.08	<.001	-0.03	.119	−0.02	.178
Household median income	0.22	<.001	0.22	<.001	0.12	<.001
Population density	0.03	.081	0.09	.003	0.00	.884
Tobacco retailer density (per 1000 residents)	0.00	.824	0.03	.102		

[a] Level 2 coefficients represent the change in price for one standard deviation increase in respective census measure.

not predict cigarette price in the adjusted model, and other neighborhood correlates of pack price did not persist.

There was significant variation in the price of one flavored Swisher Sweets cigarillo across census tracts (between tract variance = 0.011, *p* value <.001, ICC = 0.122; model not shown). Compared to the price in convenience stores, a flavored Swisher Sweets cost significantly more in pharmacies, supermarkets, and gas kiosks and significantly less in small markets and tobacco shops (see Table 4). In bivariate models, the product cost significantly less in tracts with higher proportions of African American and Hispanic residents, in tracts with higher proportions of school-age youth and young adults, and in tracts with higher population density. In a multivariate model that adjusted for store type, neighborhood income, and other tract demographics, the product cost $0.03 less for each SD increase in the proportion of school-age youth (equivalent to a 5.7 percentage point increase; $p < .001$). A flavored Swisher Sweets was also cheaper in low-income neighborhoods ($0.04 less with each standard deviation decrease in median household income, $p < .001$). However, no differences in cigarillo price by neighborhood race/ethnicity persisted in the adjusted model.

Price outcomes were consistently related to measures of localized competition at the store level (distance to nearest competitor) but not at the tract level (tobacco retailer density). In multivariate models, the price of the cheapest pack cost $0.03 more with each additional mile to the nearest competitor (see Table 3). A flavored Swisher Sweets cigarillo cost $0.01 more with each additional mile to the nearest competitor (see Table 4). Tobacco retailer density was not a predictor of these prices in either bivariate or multivariate models.

Accounting for spatial autocorrelation did not appear to alter the main findings about neighborhood correlates of price, although it did change the magnitude and significance of some predictors (see Tables 3 and 4). Specifically, a small negative association between cigarillo price and proportion of young adults that was significant in the multilevel model was not significant in the spatial regression model.

Discussion

This study documented the widespread availability of cheap combustible tobacco products in a state with low and stagnant tobacco tax at the time of data collection. In 2013, the average price for the cheapest pack of cigarettes in this California sample was $4.33, which is 20.8% less than the average pack price in the state,[10,28] 22.6% less than what California smokers reported paying without discounts, and 4.8% less than reported price including discounts.[29] On average, the cheapest cigarette pack cost less than the regional market basket prices for a pound of ground beef ($4.62), potato chips ($4.41), or roasted coffee beans ($4.81) and less than a half-gallon of ice cream ($4.60).[30] On average, a popular brand of flavored cigarillos (Swisher Sweets) cost $0.93 for a single unit, and it was available for less than $1 in 73% of stores that sold the brand. There was surprising variation in the price of cheap combustible tobacco products: The maximum price for the cheapest cigarette pack was 6.6 times the lowest price, and the maximum price for a single cigarillo was 10.5 times the lowest price for the same brand.

Variation in prices by neighborhood demographics is also a cause for concern. In California, the cheapest pack cost significantly less in

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Table 4. Multilevel Model of Single Swisher Sweets Cigarillo Price (Before Sales Tax) as a Function of Store Type and Neighborhood Demographics: California, 2013[a]

	Unadjusted models		Multivariate model		Spatial model	
	Coef.	*p*	Coef.	*p*	Coef.	*p*
Level 1 (Store characteristics, *n* = 3928)						
Intercept			0.93	<0.001	0.93	<0.001
Store type						
Convenience	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Pharmacy	0.48	<.001	0.48	<.001	0.48	<.001
Liquor	−0.08	<.001	−0.07	<.001	−0.07	<.001
Small market	−0.07	<.001	−0.05	<.001	−0.05	<.001
Supermarket	0.18	<.001	0.17	<.001	0.17	<.001
Discount store	−0.09	.022	−0.06	.156	−0.05	.209
Gas kiosk	0.05	.014	0.05	.013	0.05	.005
Tobacco shop/hookah bar	−0.14	<.001	−0.13	<.001	−0.13	<.001
Other	0.04	.517	0.04	.460	0.04	.435
Distance to nearest competitor (miles)	0.01	.011	0.01	.032	0.01	<.001
Level 2 (Tract characteristics, *n* = 1524)						
Race/ethnicity						
% African American	−0.02	<.001	−0.01	.093	−0.02	.032
% Asian/Pacific Islander	−0.002	.764	−0.01	.179	−0.01	.448
% Other/multiple race	0.004	.662	0.00	.577	0.01	.466
% Hispanic	−0.03	<.001	−0.01	.369	−0.01	.234
Age						
% School-age youth (5–17 yrs.)	−0.04	<.001	−0.03	<.001	−0.03	<.001
% Young adults (18–24 yrs.)	−0.03	<.001	−0.01	.050	−0.01	.077
Household median income	0.05	<.001	0.04	<.001	0.02	.013
Population density	−0.01	.019	0.00	.468	0.00	.881
Tobacco retailer density (per 1000 residents)	0.004	.423	0.01	.193		

[a]Level 2 coefficients represent the change in price for one standard deviation increase in respective census measure.

neighborhoods with a higher proportion of youth, which is consistent with previous research in this state[10] and in New York.[12] This is the first study that we are aware of to observe lower prices for cigarettes in neighborhoods with a higher proportion of Asian/Pacific Islanders. Asian men have among the highest smoking rates of any group in California, at 15.6%, with even higher rates for Vietnamese men (18.6%) and Chinese men (16.7%).[31]

Consistent with a previous study in Washington, DC,[20] a single cigarillo cost significantly less in neighborhoods with a higher proportion of African-American residents. In the current study, that difference persisted after controlling for median household income. The association was smaller in California than in the DC study, which may reflect differences between brands as well as population demography. In California, neighborhood variation in the price of cigarettes and a flavored cigarillo suggest that school-age youth, African Americans, Asian/Pacific Islanders, and residents of lower income neighborhoods have greater access to combustible tobacco products at significantly lower prices. The patterns are consistent with tobacco industry documents that describe research about geodemographic targeting of vulnerable populations.[7,32] The study results suggest that availability of lower-priced cheap combustible products may contribute to socioeconomic and racial/ethnic disparities in their use.[33,34]

The current study also found that cigarettes and cigarillos cost less as the distance to the nearest competitor decreased. These findings are consistent with the idea that localized competition promotes lower prices, although the association was small. Future research should consider how alternative measures of retailer density (e.g., gravity-based measures) or other features of the environment (e.g., retailer proximity to schools, arterial roadway location, whether the store sells gasoline) also explain variation in tobacco prices.

Strengths of this study are the large, representative sample of licensed tobacco retailers, and the availability of data for comparable prices from nearby stores. One limitation of the study is that price at nearby competitors was bounded by zip code, therefore nearby competitors in unobserved zip codes were not considered. Because we did not collect brand information about the cheapest pack, we cannot know the extent to which this factor explains variation in price, or may be related to other predictors in the model. Given concerns about the use of menthol cigarettes by youth and disadvantaged populations, future research should record whether the cheapest cigarettes were available in a menthol variety and assess whether it cost the same or less than a nonmenthol variety of the same brand.

Other limitations of the current study are that cigarillo price was limited to a single brand and nearly half of stores did not sell the brand or single-packaged variety. Because cigarillos vary in length, shape, weight, and pack material, even among "single sticks," we did not impute a single-stick price from multiunit packs or record the cheapest cigarillo regardless of brand. Among other reasons to implement product standardization, such regulation would ensure that neighborhood variations in price for multiple brands reflect price differentials for truly equivalent products.

The study findings have implications for federal, state, and local strategies to decrease the affordability and availability of cigarettes and flavored cigarillos that may deter youth uptake of tobacco and reduce tobacco-related disparities. The US Food and Drug Administration has the authority to establish a minimum pack size for cigarillos, establish a minimum price for all tobacco products, and ban flavored tobacco altogether.[35,36] State and local governments also have legal authority to establish minimum price and pack size for cigarillos and little cigars.[17,37–39] In addition, more than 50 cities

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or counties adopted sales restrictions on flavored tobacco that withstood legal challenges.[40] In Boston, Massachusetts, for example, a city-wide regulation significantly reduced neighborhood disparities in the retail availability of single, flavored cigars per 100 youth.[41] Finally, this study and others suggest that restrictions to limit the quantity of tobacco retailers and increase the distance between them may decrease competition and serve to increase the price of tobacco products.[42] The impact of such policies on disparities in the availability and price of cigarettes, cigarillos and other tobacco products warrants further study.

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Declaration of Interests

None declared.

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Tobacco industry use of flavours to recruit new users of little cigars and cigarillos

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ABSTRACT

Objective While flavoured cigarettes were prohibited in the USA in 2009, flavoured little cigars and cigarillos (LCCs) remain on the market. We describe the evolving strategies used by tobacco companies to encourage uptake of flavoured LCCs and industry research findings on consumer perceptions of flavoured LCC products.

Methods Analysis of internal tobacco industry documents was triangulated with data from tobacco advertisement archives, national newspapers, trade press and the internet.

Results Flavoured LCC products were associated with young and inexperienced tobacco users, women and African-Americans. Internal industry studies confirmed that menthol and candy-like flavours (eg, vanilla and cherry) increased LCC appeal to starters by masking the heavy cigar taste, reducing throat irritation and making LCC smoke easier to inhale. To appeal to new users, manufacturers also reduced the size of cigars to make them more cigarette-like, introduced filters and flavoured filter tips, emphasised mildness and ease of draw in advertising, and featured actors using little cigars in television commercials. RJ Reynolds tried to capitalise on the popularity of menthol cigarettes among African–Americans and marketed a menthol little cigar to African–Americans.

Conclusions Tobacco companies engaged in a calculated effort to blur the line between LCCs to increase the appeal to cigarette smokers, and the use of flavours facilitated these efforts. Bans on flavoured cigarettes should be expanded to include flavoured LCCs, and tobacco use prevention initiatives should include LCCs.

INTRODUCTION

Tobacco companies have used flavours to market their products to new users,[1 2] and accordingly, fruit, candy and alcohol characterising flavours were prohibited in cigarettes by the 2009 Family Smoking Prevention and Tobacco Control Act.[3] Declines in cigarette consumption have been accompanied by sharp increases in the consumption of cigarette-like small cigars and pipe tobacco (up 482% from 2000 to 2011), which can be used for roll-your-own cigarettes.[4] The US Food and Drug Administration (FDA) proposed rule in April 2014 to regulate cigars and little cigars/cigarillos did not include any limitations on flavours.[3]

Little cigars resemble cigarettes but are wrapped in tobacco leaf rather than paper (and weigh less than £3/1000 cigars). Cigarillos are longer, slimmer versions of a large cigar (and weigh £3–£10/1000 cigars).[5] Cigar smoking was the second most common form of tobacco use among youth in 2012: 13.1% of high school students currently smoked cigars (17.8% of boys; 8% of girls).[4] In a 2011 national survey, ever cigar use was reported by 37.9% of young adults, and of the cigar smokers, 21.5% had used little cigars and cigarillos (LCCs).[6] The 2009–2010 National Adult Tobacco Survey revealed that young adults aged 18–24 had the highest use rates, and 57.1% of young adult cigar smokers used flavoured cigars.[7] In 2013, cigars and cigarillos were more available in predominantly African-American neighbourhoods.[8] In 2010–2011, youth, young adults, females, blacks, cigarette smokers and blunt users were significantly more likely to report a usual cigar brand that was flavoured. Flavoured cigar brand preference decreased significantly with age.[9]

We analysed previously secret tobacco industry documents from RJ Reynolds (RJR), Philip Morris (PM), British American Tobacco, Lorillard and U.S. Smokeless Tobacco Company (USST, formerly United States Tobacco Company) on the development and marketing of flavoured non-cigarette combustible products to determine not only the purpose of flavoured additives in LCCs, but also what role flavours played in LCC product use.

METHODS

We searched the University of California, San Francisco Legacy Tobacco Documents Library (legacy.library.ucsf.edu), between November 2010 and August 2013; cigarette companies produced LCCs and archived research on competing cigar producers, including Consolidated Cigar Corporation and General Cigar Company (GC) (see online supplementary appendix for details). Search terms included 'flavor', 'flavor*', 'other tobacco products', 'flavored cigar*', 'new users', 'starters' and 'youth'. We reviewed the documents, retained the documents related to flavoured cigars, organised them chronologically and thematically, and identified common themes. This analysis is based on a final set of 251 industry documents. Research memos were reviewed, and questions were resolved by collecting additional data. Information from industry documents was triangulated with data from brand websites between 2012 and 2013 and materials archived at the Rutgers Trinkets and Trash and Stanford University SRITA tobacco advertisement collections, government websites, news stories in trade press and national newspapers.

RESULTS

'New cigar philosophy'

Strategic use of flavours to attract new cigar users followed the release of the 1964 Surgeon General's Report on Smoking and Health.[10] The report

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emphasised the harms of cigarette smoking, with cigar smoking having 'little significance' compared with cigarettes.[11] After the report's release, major cigar manufacturers and several cigarette companies planned to take advantage of the fact that cigars were perceived as a safer product.[12–15] In 1969, the President of Consolidated Cigar Corporation (currently Altadis), Ed Kelley, told the trade magazine *Tobacco Reporter*, "We imply cigars are better for your health than are cigarettes and that you'll enjoy them more."[14]

Cigar manufactures planned to target young people, especially young males, with flavoured little cigars. In 1968, the Cigar Institute, an industry trade organisation, promoted slimmer cigars as a new trend among youth in a *Life* magazine ad campaign (figure 1).[16] In 1970, Ted Cott, executive director of the Cigar Institute, described the 'new cigar philosophy' in a *Los Angeles Times* article titled 'Cherry or Lime. Stogie Gives Way to Mod Cigar Look':

> What this country needs is a good small cigar. It should be thin. It should be the size of a cigarette. It should sometimes have a plastic mouthpiece. It should be mild. It shouldn't emit too much smoke and *it should come in a selection of flavors*. Whenever possible, it should sell for less than a nickel [emphasis added].[17]

Consistent with this 'new philosophy' between the 1960s and 2014, flavour additives in LCCs served *four major functions*: (1) masking the harsh properties of cigar tobacco to make it more palatable to new users; (2) increasing attractiveness to younger users; (3) increasing acceptance among women and recruiting women as new users of LCCs; (4) targeting minorities, specifically African-American users. These tactics resulted in altered consumer perceptions of LCCs, including confusing the products with cigarettes.

Product development and targeting

Use of flavours to make LCC smoke milder

Since the 1960s, tobacco industry researchers recognised that flavours could increase the appeal to initiates by helping mask the bitterness of tobacco leaves, throat burn and the heavy cigar taste. Fruit flavours (eg, cherry) as well as menthol were particularly popular.[18 19] In 1966, FJ Triest, the President of the Fries & Brother Flavor Specialists Company, stated:

> Natural flavoring of non-tobacco origin includes plant materials of aromatic properties. These products … act as masking agents against objectionable off-flavors. This group of flavoring materials includes: vanilla beans … peach, apricot, licorice, cocoa and many others … Sugar-deficient leaf can be improved through the addition of sucrose, glucose or any other variation of sugar.[20 21]

Since the alkaline smoke from traditional cigars is usually not inhaled, using flavours in LCCs made smoke more tolerable and facilitated inhalation.[22] In addition to adding flavours, tobacco companies reduced the nicotine level,[23] reduced the size of cigars,[24] and added plastic or wooden filter tips[25–27] and charcoal or other types of filters[25 28] to make cigars more palatable to new users.

Introduction of flavoured LCCs by cigar companies

In the late 1960s, numerous flavoured 'small cigars' were introduced; these cigars were larger in diameter than cigarettes but shorter than regular cigars. Consolidated introduced one of the first flavoured small cigars, CigarLet, in 1964.[29] Consolidated subsidiary Muriel Cigars's Tipalet followed with cigars in cherry, burgundy and natural (tobacco) flavours. The 1968 Tipalet promotional campaign on college campuses targeted young adults.[30] In 1970, Consolidated president Kelley told the *Los Angeles Times* that the company was experimenting with cola, root beer, carnation, honey, strawberry and mint flavours to decide which flavours to bring to the marketplace.[17]

In 1969, GC introduced Tijuana Smalls little cigars, featuring cherry flavour, using television commercials stating "you do not have to inhale them to like them," although the actors were depicted inhaling the smoke.[31] USST introduced Tall N' Slim menthol cigars in 1969, rum-flavoured Wolf Brothers in 1969 and Zig-Zag Little Cigars in 1971–1972[13 23] in regular and menthol flavours.[32] In addition to a variety of flavours, USST little cigars had relatively low nicotine content.[33] Tall N' Slim was advertised as 'the cigar for cigarette smokers' with 'more flavor' and less nicotine.[23]

Introduction of flavoured LCCs by cigarette companies

In 1970, PM's Director of Research Center Operations recommended producing flavoured little cigars, creating a mild smoke utilising 'air dilution' and the 'masking effect of the Cherry and Menthol flavors'.[24] Another memo to PM's Director of Development specified that the circumference of the new cigar should be the same as that of Virginia Slims cigarettes: "We are to make a 100 mm product of slim circumference (22.8 mm) using either cigaret or cigar filler and producing a mild smoke. This should be as close to a cigaret as possible."[24] This decision was made based on prior PM research on Tijuana Smalls which concluded, 'the only way to achieve high volume of sales' for small cigar products was to make them similar to cigarettes.[25] Tijuana Smalls and Marlboro were to be 'comparison products'.[34] The little cigars were to be packaged in packs of 20,[34] and the company planned to add a 'cigarette-type' filter or cork, smooth plastic filters.[25 28]

Flavours in filters and filter tips

PM evaluated two categories of little cigars: four regular and four aromatic (produced with a 'cigaret-like' blend of tobacco) in 1970.[26] Flavours such as vanillin were added 'to enhance smoke taste' but did not have any distinctive taste or aroma.[27] The low vanillin flavoured sample differed from the low vanillin regular sample "only by virtue of its flavoured plastic tip."[26]

In 1971, RJR introduced its first little cigar, Winchester,[35–37] which quickly became the largest selling brand of little cigars.[22] Winchester was the size and shape of a cigarette, sold in packs of 20, filter-tipped and could 'easily be inhaled'.[22] Product introduction resulted in 'the Winchester Little Cigar Controversy' when, in 1972, the Federal Trade Commission (FTC) called for additional evidence to determine whether, "in actual use by consumers, small cigars are inhaled in the same manner as cigarettes."[38] According to Jesse Steinfield, the Surgeon General at the time, it was "conceivable that the design, blend, flavorings, and filters and not least, the advertising support being given the new little cigars, is resulting in more smokers inhaling than formerly."[39] In 1973, health advocates called for warning label and advertisement regulation.[22 40] In 1973, the US Congress extended the broadcast ban on cigarette advertising to include little cigars.[41] The FTC did not add warning labels to cigars until 2001.[42]

In 1965, Lorillard introduced Omega filter-tipped little cigars;[43] in 1971, the company launched their Stag tipped menthol and cherry-flavoured little cigars,[44 45] and in 1972 they promoted cherry and menthol Omega Slim 100s.[43 44] A 1972 Lorillard market research report noted that "about the most important single factor in placing [smoked] product types and brands on [a product] continuum is perception of the strength

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Figure 1 Life Magazine Print Advertisement by the Cigar Institute highlighting cigar use among younger smokers, emphasising the slimmer (smaller) size as a driver of this trend, 1968. The text includes, "If you think you've noticed that cigars are getting slimmer these days, it isn't your imagination at work. It's today's younger smokers at work. Maybe it's because slimmed down cigars look better with slimmed down clothes. Maybe it's because slim cigars are easier to carry around. Maybe it's because slim cigars are simply more casual. We don't really know but these gentlemen may be on to something. Maybe you ought to see what it's all about. The Cigar Institute."[16]

of flavor" and that mildness was crucial in attracting new users to the category.[46]

According to a 1992 Euromonitor Market Direction Report on Cigars, Cigarillos and Tobacco, the 'bad publicity' of cigarettes and the shift towards milder cigar types helped create a 'mini-boom' in cigar sales by the mid-1980s.[47] In the early 1990s, however, cigar sales started to decline due to restrictions on advertising, growing prices and younger people not taking up the 'old-fashioned habit'.[47 48]

Between 2000 and 2014, tobacco companies continued to increase the use of sweet flavours, resulting in a proliferation of flavoured line extensions. In 2011, a senior manager for cigar manufacturer Swedish Match explained that the flavour trend 'took off' in the early 2000s because flavours helped make smoke smoother, tasting and smelling better.[49] In 2014, Black and Mild cigars produced by Middleton (an Altria subsidiary) and mild White Owl cigarillos produced by White Owl came in a variety of fruit and candy flavours.[49]

Flavoured cigars facilitated targeted marketing to youth, women and minorities

Using flavours in LCCs to appeal to youth and young adults

In the 1960s, the major tobacco companies started to explore the potential of flavoured LCCs to expand their youth consumer base.[50] The trend towards milder, smaller, more inexpensive cigars was consistent with the cigar companies' emphasis on

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youth.[51 52] A 1969 report prepared for ABC Television network stated:

> Consolidated Cigar has introduced two new cigars aimed directly at youth. Elite Cigars "for today's young, contemporary smokers" and Tipalets, a burgundy flavored "new thing in smoking."… Both Consolidated and Bayuk Cigars are complementing their youth-oriented campaigns with record albums and other premium offers.[51]

USST internal memos in 1972[50] and its internal magazine in 1973[53] discussed the importance of the youth market to tobacco industry growth. In 1975, the USST president explored having its subsidiary, House of Windsor, develop a new cigar product 'designed to invade the youth, pipe and cigarette smokers markets' with a 100% Borkum Riff (Bourbon) tobacco filler and sweetened wrapper,[54] and a smaller, slimmer 'panatela' shape than regular cigars. We were unable to determine if this plan was implemented, but House of Windsor produced Javelin Candela panatela-shaped cigars[55] and rum-flavoured little cigars, including Wolf Brothers Little Nippers in 1968[56] and Wolf Brothers Crooks and Crookettes in 1968.[57]

In 1972, RJR's marketing research found that describing menthol Winchester Little Cigars as having a 'frosty-new taste' would intrigue younger respondents.[58] RJR expected Winchester to appeal to young smokers, women, those accustomed to cigarette brands with a stronger tobacco taste and menthol cigarette smokers. The mint and menthol flavours appealed to novices but were 'not appealing to cigar connoisseurs'.[58]

Raising acceptance among women and targeting women as new users

Cigar companies tried to achieve female acceptance with flavours, slimmer cigar shapes and milder tobaccos.[51] In 1966, GC launched the "Should a gentleman offer a lady a Tiparillo?"campaign to win "female acceptance rather than female consumption" of Tiparillos and maintain the cigar as a symbol of masculinity.[51 59] The advertisements did not depict women smoking the product (figure 2).[60] In 1969, GC's Tipalet (cherry and burgundy flavours) advertising emphasised mildness and acceptability among women to appeal to young men: "Blow in her face and she'll follow you anywhere. Hit her with tangy Tipalet Cherry, Or rich, grape-y Tipalet Burgundy … It's new. Different. Delicious in taste and aroma. A puff in her direction and she'll follow you, anywhere."[61]

However, women also began to be portrayed as cigar smokers: an advertisement for Wolf Brothers Cherry-Flavoured Little Cigars, introduced in 1969, claimed, "She'll like them too,"[18] and in 1974, women were shown to be smoking Tiparillo cigars (figure 2).[60] In 1970, the vice-president of the Cigar Institute gave *The Financial Post* the following reasons for the steady cigar sales growth since 1967:

> The market is responding to longer, thinner, more elegant cigars and new flavors, such as rum, sherry, burgundy, coffee, mint, wild berry, and natural. Greater demand among young people helped along by greater acceptance among women.[62]

In the 1970s, celebrity actresses and singers were used as spokespeople; Susan Anton, an actress and singer, sang in Muriel commercials, "Muriel air-tips drive me mild, with the easiest taste they could've found."[63] RJR's internal research also found that a menthol and mint combination little cigar would appear to have the best chances of success by appealing to women as well as to men and the younger cigarette smokers.[58]

Targeting minority groups

In 1972, RJR researchers interviewed Salem and Kool cigarette smokers to test Winchester Menthols, and found that use of menthol increased perceptions of mildness and coolness.[58] RJR introduced Winchester Menthol nationally in 1974.[64] RJR's marketing plan anticipated menthol growth especially among the low-to-middle-income 18–34-year-old African-American males.[64] The company planned to run 'special Negro advertising' for 2 months in those areas which had 'high Negro concentrations'.[65 66]

In 1975, American Tobacco planned to publish promotions for menthol-flavoured little cigars branded Long Johns[67 68] in 'Negro' newspapers:

> It is proposed that a special advertising … campaign be directed at the Black Market to generate awareness and trial of Long Johns Filter and Menthol 120's in this important segment of the market. We recommend a 13-week campaign consisting of one 500 line Black and White insertion each week in the Negro newspapers located in open areas … The newspaper campaign will effectively supplement our Outdoor and Transit schedules in these markets…[67]

Consumer response studies

Consumer research on flavoured LCCs conducted by RJR and Lorillard in the 1970s and, recently, in 2000 confirmed that the tobacco companies were able to achieve several of their objectives to increase appeal to younger users and initiates when designing or advertising flavoured cigars. Consumers perceived mint and menthol cigars to be less harsh and more acceptable to smokers. RJR's 1969 focus groups on cigars[58 69–72] found that:

> Most men (and women) inhaled their first puffs of [the] new product … because the product seemed like a cigarette in terms of size and shape and because the filter suggested that it could be smoked just like a cigarette. (… many said they could not imagine giving up inhaling under any circumstances.)[69]

Focus group results also demonstrated that these little cigars "seemed surprisingly 'mild;' it wasn't thought to be as strong or rough as a small cigar … It even compared favorably in this respect to a cigarette."[69]

In 1972, RJR researchers conducted interviews with Salem and Kool (both RJR brands) cigarette smokers to test Winchester Menthols, and confirmed that consumers perceived menthol cigars as acceptable, milder and cooler than non-menthol cigars.[58] They recommended that Winchester marketing emphasise mild flavours and a 'frosty new taste' to increase trials among younger smokers.[58 66]

Tobacco companies also found that consumers confused little cigars and cigarettes. Focus group research conducted by RJR in 1971 evaluating a television commercial for Winchester little cigars found that it successfully evoked cigarette associations, "Almost everyone recalls and comments on the fact that the girl smokes the product. Additionally, many seem to remember that she actually inhales it … In a more subtle way, the whole mode of execution suggests the traditional cigarette commercial."[73]

The researchers identified the following elements of the commercial that appeared to evoke cigarette associations:

> Copy ("It's not a cigar" "It's a whole 'nother smoke" "It's somethin' else"); Girl seems to inhale product which communicates cigarette-like mildness; The feminine way girl handles product as she "tries it on", Packaged like cigarettes. Twenty in a pack; Has filter and looks like a cigarette (except for brown "paper"); "Subconscious slips of the tongue" (Several refer to Winchester as "cigarettes").[73]

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Figure 2 Role of Women in Little Cigar Advertisement Campaign. The goal of the earlier advertisements (top row) was female acceptance, "Should a gentleman offer a Tiparillo to a lady?" (1968) campaign by General Cigar. It did not feature women handling the cigars; the goal of the subsequent advertisement (bottom row) was recruiting women as users: Winchester (1974) campaign by RJR featured women holding or smoking cigars.[60]

Lorillard internal research on cigars in 1971 confirmed that flavour was the prime factor for cigar product preference and concluded that any flavour could mask out cigar-like taste characteristics.[74] In 1970, Lorillard conducted consumer research on little cigars[75–77] including male and female cigar, LCC and cigarette smokers, including recent quitters for several reasons:

> Although it is felt that current female cigarette smokers may represent a potential for new product development, the recent quitters may be even better prospects and should be included … We feel the attitudes of women toward cigar smoking, not simply as possible consumers of little cigars, but, as strong influences upon male smoking of all types of cigars is important. Inclusion of cigarette quitters is also important because, to some extent the current trend away from cigarette smoking represents a potentially profitable void which, properly positioned, little cigars can fill very well.[75]

Children above 16 years of age were included in the study.[78] The study led to the 1971 'Cigar Segmentation Study', which classified cigar smokers into five segments based on smoking attitudes or needs: Social Smokers; Casual Smokers; Inveterate Smokers; Worried Inhalers; Adjusted Inhalers.[79] The researchers identified seven benefits of cigarillos, including being inoffensive, mild/refreshing, flavour, male success.[79]

In 1972, Lorillard used these five segments in a national study to determine product perceptions among male LCC non-users and users.[80] They found that consumers perceived little cigars and tipped cigarillos as 'positioned' closer to cigarettes than cigars. Furthermore, tipped LCCs excited more purchase interest and offered similar perceived benefits: health, change of pace, easy draw, good taste, lack of irritation, relaxing, pleasing aroma, enjoyable without inhaling, pleasant in the mouth, helped cut down smoking, and low in tar and nicotine.[80] LCCs also tended to be held by participants in a similar manner as cigarettes.[80]

In 1972, Lorillard conducted research to determine consumer perceptions of their Stag Tipped Little Cigar and response to a television commercial promoting Stag[44 81] as masculine, active and youthful.[44] Respondents found Stag less irritating and milder than the comparison product, Tiparillo.[44] In 2000, Roper Starch conducted qualitative interviews with cigarette and LCC users for Lorillard, which showed that flavoured LCCs were popular among younger women and those trying to quit cigarettes, and that LCC users inhaled cigar smoke:

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A. Cigars are booming. You don't even know how many women are smoking cigars. It's insane.

Q. Oh, really? They're going for the flavored cigars?

A. Flavored cigars, yeah. I just got both my sisters hooked, which is terrible. They won't quit smoking cigarettes, but they're hooked on cigars. They like the vanillas and the cherries. They're smoking the filtered ones."… "My sisters both started smoking them because the[y] quit smoking cigarettes"… "My goofy sisters are inhaling cigars … They probably think they are less addicted. They probably think it's a temporary thing…"[82]

Another interviewee was not able to differentiate between little cigars and cigarettes and called little cigars "little flavor-tip cigarettes."[83]

In 2005, PM conducted 'Project Door' to explore cigar smokers' perceptions of the leading mass market cigar brands (including Swisher Sweets, Phillies, Black & Mild, Dutch Masters, White Owl, Garcia Y Vega) and brand selection criteria.[84 85] Most of the Project Door documents are withheld due to claims of confidentiality.[84–90]

DISCUSSION

The marketing of flavoured LCCs began 50 years ago, and in 2014 a variety of fruit and candy flavours, including chocolate, cherry and vanilla, were still available,[91] including flavours tobacco companies identified as attractive to youth. These flavours, both characterising and non-characterising, in combination with colourful and stylish packaging, mask the harsh and toxic properties of tobacco. Cigar manufacturers (many now owned by cigarette companies) continue to use flavours and media channels accessible to youth. For example, underage visitors of the splitarillos.com website are redirected to the Splitarillos Facebook page,[92] circumventing the website age restrictions. Furthermore, the company uses models, music and flavours appealing to youth (figure 3).[60 92 93]

Characterising flavours are banned in cigarettes, but in 2014 flavoured LCCs remain available and unregulated in the USA with a few local exceptions. We found that like flavoured cigarettes, flavoured LCCs appeal to youth. In addition, flavours facilitated consumers handling cigars in the same manner as cigarettes, evoking mildness, masking the strong cigar taste, and making it easier to inhale the smoke.

Furthermore, to appeal to new users, little cigar manufacturers reduced the size of cigars to make them more cigarette-like, introduced filters and flavoured filter tips, emphasised mildness and ease of draw, evoked associations with cigarettes, and featured actors inhaling little cigar smoke in television commercials. Flavoured products enhanced tobacco companies' calculated efforts to blur the line between little cigars and cigarettes to appeal to cigarette smokers. In addition, RJR tried to capitalise on the success of menthol cigarettes among African-Americans to market menthol little cigars. In 2014, LCCs are promoted by hip-hop and rap singers, DJs and in music videos.

For example, the Executive Branch cigarillo was endorsed by the famous singer Snoop Lion (aka Snoop Dogg) in 2012. The singer placed cigarillo advertisements in his music videos on YouTube; one video featuring the ad had over 51 million views as of 2014.[94] This strategy is similar to cigarette campaigns targeting African-American youth, such as the 2004 Kool Mixx cigarette campaign by Brown & Williamson (figure 4),[60 92 95 96] which resulted in protests[97 98] and an eventual recall.[99]

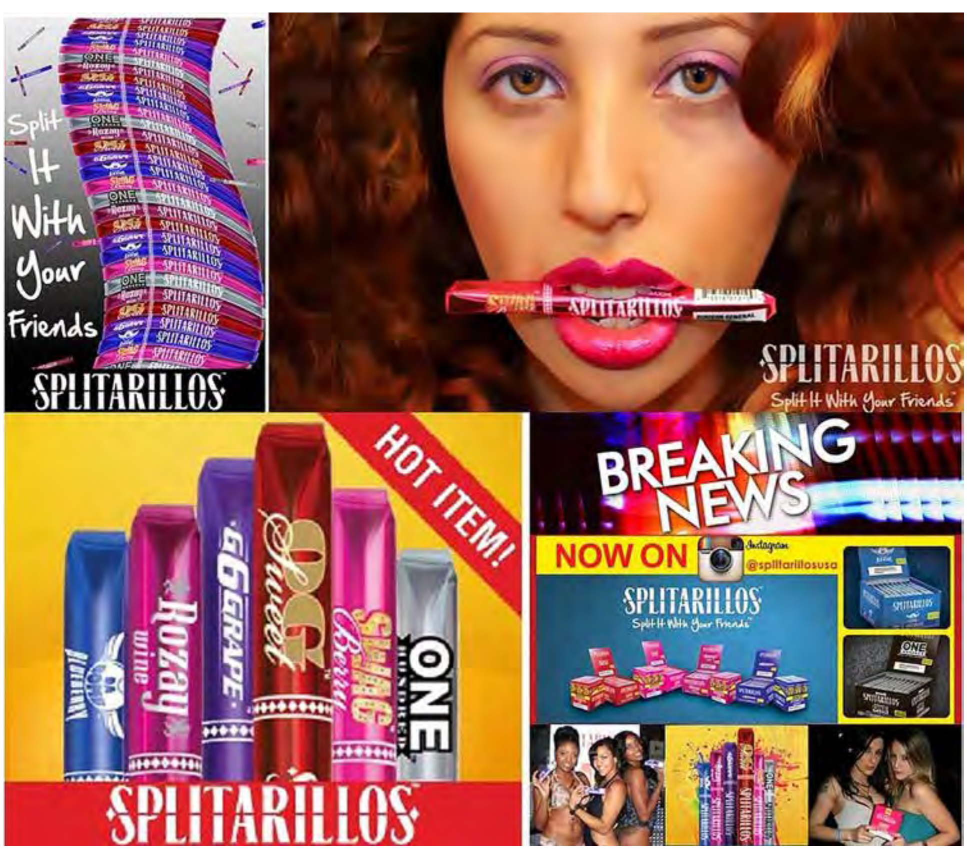

Figure 3 Splitarillo (2012–2014) promotion of flavoured cigarillos appealing to youth, prominently featuring sweet, grape and wine flavours, candy-like packaging, youthful models, sex appeal and the peer oriented slogan "split it with your friends."[60 92 93]

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Figure 4 African–American Musicians featured in advertising for Executive Brand Cigarillos (2014) and Hunid Racks Cigarillos, showing imagery similar to the 2004 Kool Cigarettes Promotion (lower right) that was withdrawn after public health and African-American groups raised concerns about the campaign's youth appeal.[60 95 96 98]

Cigar manufacturers targeted women by reducing the cigar size and using flavours, 'purse' packs, decorative tips and celebrities in advertising. This targeting continues (see online supplementary appendix). In a January 2014 news article, Avanti cigar company spokeswoman Elaine Ferri stated that Avanti began selling its new cafe mocha Estilo cigar in three-pack pouches which 'women like to slip into a purse or pocket'.[100] Avanti was also launching a new line of decorative tips and flavours in February 2014, and Ferri commented "Women absolutely are a growing market in the cigar industry and they prefer flavoured and small cigars."[100]

There have been few studies on the promotion of LCCs. A 2001 content analysis of two cigar 'lifestyle' magazines found that cigar promotions helped promote the industry, normalise smoking and positioned cigar use as a socially welcome relief from restrictions.[101] Our study extends the findings to LCCs. Our findings also confirm a content analysis of YouTube user videos promoting LCCs, which showed that candy flavours were one of the most common themes.[102] Prior research showed that celebrities and women were used in cigar advertising to appeal to young men; we found that similar tactics were used to increase appeal to LCCs.[103] Delnevo and Hrywna[104] discussed RJR's efforts to make little cigars as close to cigarettes as legally possible, including consumer perceptions of non-flavoured little cigars. Our study adds the role of flavours in the promotion of LCCs.

The study's limitations are that the archives of the industry documents are incomplete and some relevant documents may not have been found or were not available. However, the consistency of these findings over time and across multiple tobacco companies, and the continuation of these strategies in 2014, increases our confidence in the findings.

Since the marketing of flavoured products adversely affects public health by promoting youth initiation, FDA and authorities in other countries should prohibit flavoured LCCs. In addition, use of flavoured products may contribute to dual use of cigarettes and other tobacco products among those who are trying to quit smoking and those who do not differentiate among cigarettes and little cigar products.[3] FDA should immediately establish a product standard prohibiting flavours in LCCs, e-cigarettes and all other covered tobacco products. Elimination of all flavoured tobacco products would benefit public health by helping reduce youth initiation of tobacco and dual use of tobacco products.[9]

What this paper adds

What is known about this topic?

- While cigarette use is declining, cigar use has been increasing. Prior studies demonstrated that tobacco companies have undertaken marketing tactics to increase the appeal of cigars to young men, to normalise smoking, and to portray cigar use as socially acceptable. However, prior studies have not specifically addressed little cigars and cigarillos, and the role of flavour additives in these efforts.

What does this paper add?

- This is the first study addressing the role of flavouring in the marketing of little cigars and cigarillos (LCCs). We found that flavour additives were used to make LCCs more palatable to new users; make LCC products more attractive to younger users; increase acceptance of LCCs among women, and to target minorities, specifically African-American users.
- The promotion of flavoured LCCs resulted in altered consumer perceptions; LCCs were perceived as milder, easier to smoke, more appealing to non-users and more similar to cigarettes than to traditional (large) cigars. Consumers referred to LCCs as cigarettes, and handled LCCs such as cigarettes, including inhaling the smoke.
- These findings suggest that restrictions on cigarette marketing strategies and the use of fruit, candy and alcohol flavours should be applied similarly to LCCs. Menthol and mint flavours serve the same function as other flavours, and should similarly be prohibited.

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Data sharing statement All documents that constitute the data for this study are freely available to the public at the UCSF Legacy Tobacco Documents Library.

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Disparities in tobacco marketing and product availability at the point of sale: Results of a national study

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ABSTRACT

Objective. Neighborhood socioeconomic and racial/ethnic disparities exist in the amount and type of tobacco marketing at retail, but most studies are limited to a single city or state, and few have examined flavored little cigars. Our purpose is to describe tobacco product availability, marketing, and promotions in a national sample of retail stores and to examine associations with neighborhood characteristics.

Methods. At a national sample of 2230 tobacco retailers in the contiguous US, we collected in-person store audit data on: Availability of products (e.g., flavored cigars), quantity of interior and exterior tobacco marketing, presence of price promotions, and marketing with youth appeal. Observational data were matched to census tract demographics.

Results. Over 95% of stores displayed tobacco marketing; the average store featured 29.5 marketing materials. 75.1% of stores displayed at least one tobacco product price promotion, including 87.2% of gas/convenience stores and 85.5% of pharmacies. 16.8% of stores featured marketing below three feet, and 81.3% of stores sold flavored cigars, both of which appeal to youth. Stores in neighborhoods with the highest (vs. lowest) concentration of African-American residents had more than two times greater odds of displaying a price promotion (OR = 2.1) and selling flavored cigars (OR = 2.6). Price promotions were also more common in stores located in neighborhoods with more residents under age 18.

Conclusions and relevance. Tobacco companies use retail marketing extensively to promote their products to current customers and youth, with disproportionate targeting of African Americans. Local, state, and federal policies are needed to counteract this unhealthy retail environment.

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1. Introduction

Despite recent progress in reducing overall tobacco use, disparities by socioeconomic status and race/ethnicity persist (Centers for Disease Control and Prevention, 2013). Data from the 2013–2014 National Adult Tobacco Survey indicate that about 32% of adults without a high school degree or who earn less than $20,000 per year used some form of tobacco, compared to about 10% of college graduates and 12% of people with annual incomes of $100,000 of more (Hu et al., 2016). In 2015, current tobacco use among middle school students was higher for Hispanic students (10.6%) compared with Non-Hispanic White (6.3%) or Black students (6.6%) (Singh et al., 2016).

Furthermore, use of specific tobacco products is growing, especially among youth. The 2014 National Youth Tobacco Survey found that 63.5% of current adolescent smokers used flavored little cigars, and 53.6% used menthol cigarettes (Corey et al., 2015). In 2015, cigar use was highest among Black high school students compared with both White and Hispanic students (Singh et al., 2016). An estimated 5.6 million youth under age 18 in the United States (US) will die prematurely from tobacco-related illnesses if present adolescent smoking trends continue (USDHHS, 2014).

The retail environment provides the tobacco industry with extensive opportunities to market current and emerging products to adults and youth. In 2014, the largest US cigarette and smokeless tobacco companies spent $8.2 billion in marketing and promotion at the point of sale (91% of annual marketing dollars), with the majority of this spending on promotions to reduce the price of tobacco products (Federal Trade Commission, 2016a; Federal Trade Commission, 2016b). In the National Youth Tobacco Survey, 76.2% of US students in grades 6–12 reported

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seeing tobacco advertising in stores (Agaku et al., 2013). Among youth, greater exposure to cigarette advertising is associated with more positive attitudes toward smoking (Kim et al., 2013), greater susceptibility to smoking (Paynter and Edwards, 2009), and smoking initiation (Paynter and Edwards, 2009; Henriksen et al., 2010). Among adults, exposure to point of sale (POS) marketing is linked to greater cravings among current smokers (Paynter and Edwards, 2009), and smokers who quit are more likely to relapse if they live near a tobacco retailer (Reitzel et al., 2011). Almost 20% of current smokers use promotions or coupons to reduce cigarette prices (Xu et al., 2013), and these price minimizing behaviors are associated with fewer quit attempts and lower rates of quitting smoking (Choi et al., 2013; Choi et al., 2011; Licht et al., 2011).

Tobacco industry documents illustrate marketing strategies to target racial and ethnic minorities (Balbach et al., 2003) and youth (Perry, 1999) by exploiting the retail environment as the main channel to communicate with consumers (Lavack and Toth, 2006). More POS tobacco advertising has been documented in predominantly African-American (Cantrell et al., 2013; Lee et al., 2015; Moreland-Russell et al., 2013) and low-income neighborhoods (Lee et al., 2015; John et al., 2009; Laws et al., 2002; Siahpush et al., 2010), near high schools with higher proportions of African-American (Henriksen et al., 2012), Hispanic and low-income students (Henriksen et al., 2008) and in neighborhoods with a higher proportion of youth (Henriksen et al., 2012; Waddell et al., 2016). These studies, however, are based on store samples from single cities or states, or focus primarily on marketing for a specific tobacco product. A recent systematic review (Lee et al., 2014) of tobacco retail studies found only four that included measures of cigar availability.

This is the first national study to estimate POS marketing and promotions for both cigarettes and other tobacco products (e.g. cigars, e-cigarettes, smokeless tobacco), as well as the availability and marketing of products with youth appeal such as flavored cigars and advertising near candy. We also explore whether previous observations of marketing disparities observed in cities occur on a national level. The purpose of this paper is to (1) report the amount and types of tobacco marketing materials and promotions overall and by store type in a representative sample of US stores in the contiguous US that sell cigarettes and (2) examine whether tobacco marketing, promotions and flavored cigar availability are associated with neighborhood sociodemographic characteristics.

2. Methods

This study used data from Advancing Science and Policy in the Retail Environment (ASPiRE), funded by the National Cancer Institute's State and Community Tobacco Control Research Initiative. ASPiRE is a consortium of researchers from the Center for Public Health Systems Science at Washington University in St. Louis, the Stanford Prevention Research Center, and the University of North Carolina Gillings School of Global Public Health.

2.1. Sample

2.1.1. Selection of counties

To obtain a representative sample of tobacco retailers in the contiguous US, we employed a two-stage sampling design. In the first stage, we selected counties with minimal replacement using a probability proportionate to size (PPS) method developed by Chromy (Chromy, 1979). We used 2010 Census data to identify all 3109 counties and selected 100 with a probability of selection proportional to county population. In the final sample of 100 counties, 97 were unique.

2.1.2. Random selection of stores

The US does not have a mandatory licensing system for selling tobacco products; therefore no national sampling frame exists. To create a sampling frame, we purchased lists from two secondary data sources, ReferenceUSA and the North American Industry Classification System (NAICS), which provided a list from Dun & Bradstreet, Inc. We then processed these lists using an approach validated in our previous study (D'Angelo et al., 2014). Using NAICS codes, we selected ten store types that accounted for 98% of tobacco product sales in payroll establishments in the 2007 Census of Retail Trade (i.e., tobacco stores; supermarkets and grocery; convenience stores; gas stations with convenience stores; other gas stations; warehouse clubs and supercenters; news dealers and newsstands; beer, wine and liquor stores; pharmacies; discount department stores) (Census Bureau, 2010).

Before sampling, we excluded chains known not to sell tobacco products (e.g., Target, Whole Foods). Pilot testing in a previous study (D'Angelo et al., 2014) showed that only Wal-Mart among the discount department stores, and only chain/retail stores among pharmacies were likely to sell tobacco products; therefore we included only Wal-Mart and the top 50 retail pharmacies in these categories. The resulting lists from the two secondary sources were merged and de-duplicated. Based on our power analysis, our goal was to complete audits in at least 2000 stores. We randomly selected up to 55 stores in each of our selected counties, and called the list in order until we verified addresses and cigarette availability in 24 per county. Stores that could not be reached after three attempts, or that did not sell cigarettes, were deemed ineligible. Seven counties produced fewer than 24 verified stores even after calling all likely retailers in the county, resulting in a final sample of 2346.

2.1.3. Data collection

Following general recommendations by Lee and colleagues (2014), our trained data collectors used standardized approaches to conducting exterior and interior audits of tobacco marketing materials and promotions as well as tobacco product availability and placement. Data for each store were collected in person by a trained auditor using an electronic audit form designed for this study and programmed onto Apple iPads© using iSurvey©. Prior to conducting audits, 13 data collectors received a 5-hour in-person training that included field practice. All audits were conducted between June and October 2012. The University of North Carolina Office of Human Research Ethics determined that the study did not constitute human subjects research (12-0765).

Fig. 1 shows that exterior audits were completed at 2230 stores, and among those, interior audits were completed at 2163 stores (97.0% of eligible stores). Interior audits were not completed when store clerks refused permission to complete the audit or when the store was temporarily closed. Analyses of exterior characteristics use the larger sample ($n = 2230$), and all other analyses use stores with complete data for interior and exterior ($n = 2163$). On average, there were 22.3 complete stores successfully audited per county (min = 6, max = 67 where a county was sampled three times).

2.2. Measures

2.2.1. Tobacco marketing materials

Data collectors counted and coded branded signs (professional signs that include any imagery and font associated with tobacco company brand insignia), branded displays (portable units that hold tobacco products and can be moved easily), branded shelving units (large shelving units or power walls with a header display that are typically affixed to the wall or floor), and branded functional items (industry produced items with a brand or company logo that serve a functional purpose in addition to advertising the product, such as a Marlboro trash can). Data collectors recorded whether each marketing material was: 1) specific to cigarettes or other non-cigarette tobacco products (NCTP), such as cigarillos, smokeless tobacco, and e-cigarettes, and 2) located on the interior or exterior of the store, including in the parking lot. Total marketing materials measures the sum of interior and exterior.

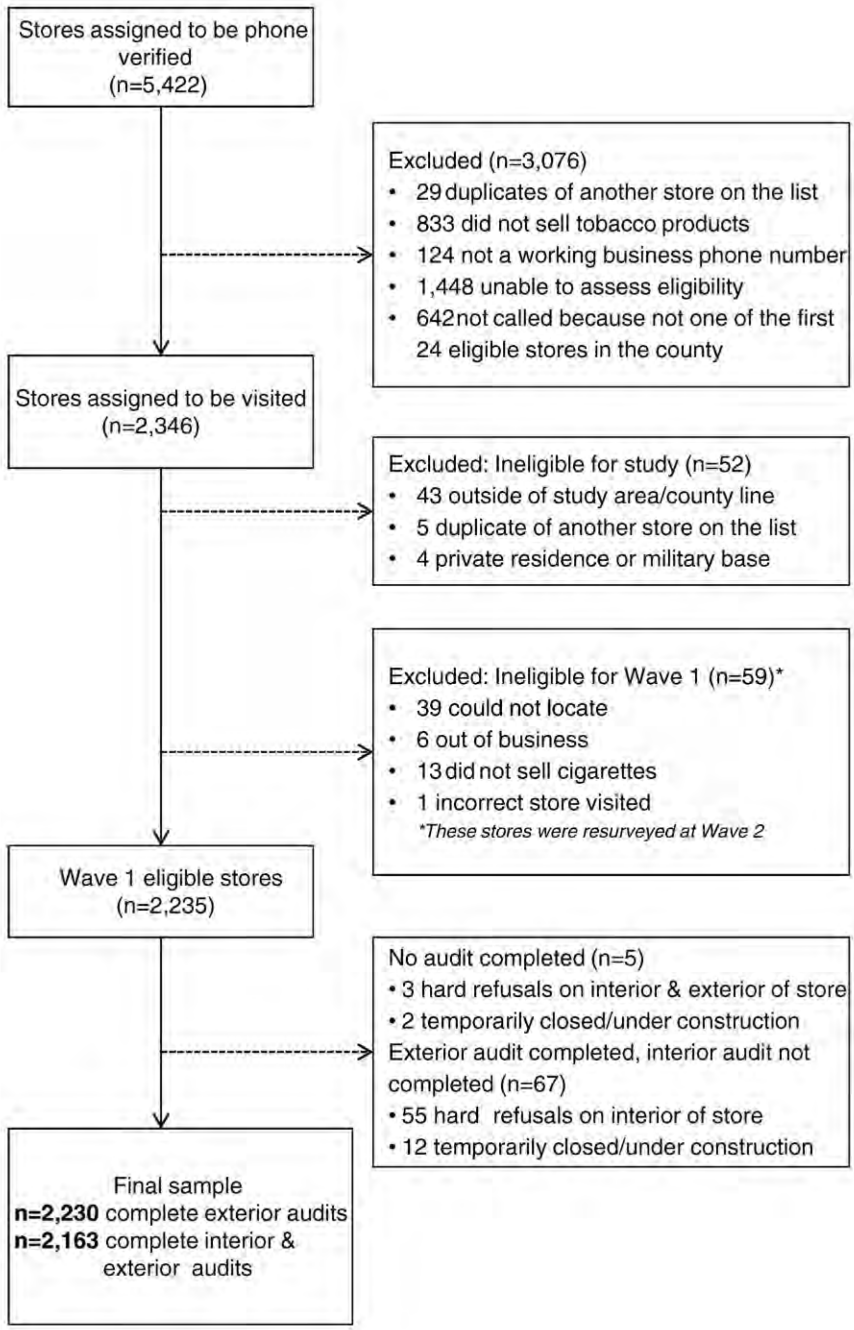

Fig. 1. Sampling diagram, ASPiRE study, 97 countries in the contiguous US (data collected 06/2012–10/2012).

2.2.2. Tobacco price promotions

Price promotions were defined as any multi-pack special (e.g., buy one get one free) or special price (e.g., $1.00 discount), and these were coded by product type and location (interior/exterior).

2.2.3. Tobacco products and marketing with youth appeal

We created five dichotomous indicators: 1) flavored cigar availability; 2) single cigar availability; 3) flavored and unflavored smokeless product availability (including snus); 4) tobacco products displayed near (i.e., within 12 in. of) candy, and 5) interior marketing materials placed at or below three feet. Cigars were defined to include cigarillos, little cigars, and large cigars. We considered flavors to include any flavor except tobacco or menthol/mint, which matches Food and Drug Administration's Center for Tobacco Product definitions.

Inter-rater reliability was assessed at 165 stores visited twice within an average of 30 days (range 6 to 49 days) in a convenience sample of 6 counties. Reliability for marketing materials was calculated using an intraclass correlation coefficient (ICC), and was 0.77 for total, 0.77 for interior, and 0.57 for exterior. Inter-rater reliability for any price promotions and flavored cigars sold was calculated using Cohen's kappa and was 0.41, and 0.63, respectively.

2.2.4. Countermarketing

We observed whether stores displayed an interior graphic health warning sign.

2.2.5. Store type

We assessed whether marketing and product availability differed by type of store, and included it as a covariate to ensure that differences by neighborhood demographics did not simply reflect the types of stores in the neighborhood. Each store was categorized in the field using one of ten North American Industry Classification System (NAICS) codes, or as 'other' if no code seemed appropriate. We consolidated store types into seven categories: supermarket/grocery stores; gas station with or without convenience store (gas/convenience); convenience store (without a gas station); pharmacy/drug store; warehouse club/supercenter (including Wal-Mart); liquor store, and other (e.g., newsstands and other store types).

2.2.6. Store neighborhood characteristics

Using the latitude and longitude recorded by iSurvey©, stores were joined to their corresponding census tract using ArcGIS and Tiger/Line® Shape files from the 2010 US Census. Four measures for the store's census tract were used to assess neighborhoods demographics: median household income (grouped into tens of thousands), percent of the population that is Non-Hispanic Black (identifying as one race only), Hispanic, and under age 18. These measures were obtained from the 2011 American Community Survey 5-year estimates (GeoLytics, Inc.). Race and ethnicity distributions were categorized into quartiles to ease interpretation of differences by neighborhood demographics. A Census indicator of region (West, South, Northeast, and Midwest) was also included as a control variable in multivariate analyses.

2.3. Statistical analysis

We created national estimates of tobacco marketing materials, promotions and products by applying sampling weights that accounted for both county and store selection in the sampling design and non-response. We used mixed-effects modeling using HLM 7 (HLM 7.00 for Windows, 2011) to examine 1) whether store and neighborhood characteristics were associated with four outcomes: total tobacco marketing materials, price promotion availability, flavored cigar availability, and smokeless product availability; and 2) whether any observed relationships were maintained after controlling for store type because store type distributions are often related to neighborhood demographics. Of the youth appeal indicators, we chose to model neighborhood effects for flavored cigars, given the growing popularity of these products. A mixed-effects linear model was used for the continuous outcome (total marketing materials) and a generalized mixed-effects model was used for the dichotomous outcomes (presence of price promotion and availability of flavored cigars and smokeless). The mixed-effects models accounted for the clustering of stores (level 1, $n = 2163$) within counties (level 2, $n = 97$) that resulted from our sampling design (total marketing materials, ICC = 0.18; any promotion, ICC = 0.13; flavored cigars, ICC = 0.11; smokeless, ICC = 0.11) (Merlo et al., 2006). Clustering of stores in tracts was minimal: 80% had only one observed store. All models employed both store- and county-level weights. Median household income was log transformed and continuous variables were grand mean centered.

3. Results

Estimates of tobacco marketing at stores that sell cigarettes in the contiguous US are presented in Tables 1 and 2. Table 1 provides descriptive statistics of marketing materials and promotions (interior and exterior) for cigarettes and NCTP, and Table 2 specifies marketing materials, promotions, and youth appeal indicators by store type.

3.1. Marketing materials

Stores had an average of 29.5 (95% CI = 28.3, 30.7) total marketing materials, with more materials on the interior than the exterior and more for cigarettes than NCTPs (Table 1). Among these, interior signs were the most common (cigarette 12.3, 95% CI = 11.9, 12.7; NCTP 6.6, 95% CI = 6.2, 7.0) followed by NCTP displays (4.3, 95% CI = 3.8, 4.7) and cigarette shelving units (1.6, 95% CI = 1.5, 1.7). Functional items were uncommon, as were graphic health warning signs.

Table 2 shows that nearly all (95.1%) of the stores displayed tobacco marketing materials on the interior, exterior or both (95% CI = 94.0%, 96.1%). Not surprisingly, tobacco stores contained the most marketing materials (mean = 76.7, 95% CI = 62.0, 91.4), followed by gas/convenience stores (mean = 39.5, 95% CI = 37.9, 41.2) and convenience stores (mean = 28.0, 95% CI = 25.0–31.0). More than half of all gas/convenience stores, convenience stores, and tobacco stores marketed tobacco products outside, whereas just under a quarter of supermarkets, and fewer than 2% of pharmacies or warehouse clubs did.

3.2. Price promotions

Three quarters of stores displayed at least one tobacco price promotion (95% CI = 73.0%, 77.1%); 71.2% displayed special prices (95% CI = 69.1%, 73.3%) and 35.8% indicated multi-pack offers, such as buy one pack, get one free (95% CI = 33.6%, 38.0%) (Table 2). Price promotions were common at all store types. Nearly 9 out of 10 gas/convenience stores and pharmacies, 8 out of 10 tobacco stores, and 7 out of of 10 convenience stores offered special prices or multipack discounts. Promotions were also present at more than half of supermarkets, warehouse clubs, and liquor stores.

3.3. Youth appeal

Flavored cigars were sold in 81.3% of stores (95% CI = 79.4%, 83.2%), and single cigars (flavored or unflavored) were sold in 77.5% of stores (95% CI = 75.5%, 79.5%); both products were widely available across store types.

Overall, 16.8% of stores displayed tobacco ads below 3 ft (95% CI = 15.1%, 18.5%) and 10.0% (95% CI = 8.6%, 11.3%) displayed tobacco

Table 1
Estimates of branded tobacco marketing materials and promotions at tobacco outlets in the contiguous US ($N = 2230$)[a], 2012.

	Cigarettes				Non-cigarette tobacco products				Total ($n = 2163$)	
	Interior		Exterior		Interior		Exterior			
Number of marketing materials, mean (95% CI)	14.5	(14.0, 15.0)	2.5	(2.3, 2.7)	11.7	(10.9, 12.4)	0.9	(0.8,1.0)	29.5	(28.3, 30.7)
Signs	12.3	(11.9, 12.7)	2.4	(2.2, 2.6)	6.6	(6.2, 7.0)	0.9	(0.8, 0.9)	22.2	(21.3, 23.0)
Functional items	0.2	(0.2, 0.2)	0.07	(0.05, 0.09)	0.14	(0.1, 0.2)	0.03	(0.02, 0.04)	0.5	(0.4, 0.5)
Displays	0.4	(0.3, 0.4)	na		4.3	(3.8, 4.7)	na		4.6	(4.2, 5.1)
Shelving units	1.6	(1.5, 1.7)	na		0.66	(0.6, 0.7)	na		2.3	(2.2, 2.4)
Any price promotions, % (95% CI)									75.0	(73.0, 77.1)
Special price	66.2	(64.0, 68.4)	23.3	(21.4, 25.2)	28.8	(26.6, 30.9)	3.7	(2.8, 4.5)	71.2	(69.1, 73.3)
Multi-pack discount	24.6	(22.7, 26.5)	6.6	(5.6, 7.7)	17.8	(16.1, 19.5)	2.5	(1.8, 3.1)	35.8	(33.6, 38.0)
Stores with graphic health warning signs, % (95% CI)									0.2	(0.0, 0.4)

[a] N for interior and total measures is 2163; N for exterior measures is 2230. All estimates are weighted.

Table 2
Branded tobacco marketing materials and indicators or youth appeal by store type at tobacco retailers in the contiguous US ($N = 2230$)[a], 2012.

Store type	n[b]	Marketing materials				Youth appeal			
		Total marketing materials	Any exterior marketing	Any interior marketing	Any price promotion	Flavored cigars sold	Single cigars sold	Any interior marketing below 3 ft.	Any product within 12 in. of candy
		Mean (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Gas stations with or without convenience store	945	39.5 (37.9, 41.2)	76.2 (73.1, 79.2)	99.3 (98.7, 99.8)	87.2 (84.7, 89.8)	92.8 (90.9, 94.7)	90.2 (87.9, 92.2)	20.2 (17.3, 23.0)	13.4 (11.0, 15.8)
Supermarkets & other grocery	399	15.9 (14.0, 17.8)	22.7 (17.8, 27.6)	90.0 (86.8, 93.2)	57.4 (51.8, 63.0)	61.4 (55.8, 66.9)	54.5 (48.9, 60.2)	12.9 (9.5, 16.3)	4.1 (2.2, 6.1)
Convenience stores (without gas)	258	28.0 (25.0, 31.0)	64.4 (58.1, 70.6)	93.8 (90.5, 97.2)	73.2 (67.0, 79.4)	84.4 (79.3, 89.4)	81.0 (75.8, 86.3)	17.3 (12.3, 22.2)	11.4 (7.1, 15.8)
Pharmacy and drug stores	236	16.0 (14.7, 17.2)	1.4 (0.0, 3.1)	98.9 (97.4, 100.0)	85.5 (80.3, 90.6)	90.3 (86.2, 94.5)	87.7 (83.1, 92.3)	0.0	1.2 (0.0, 2.6)
Beer, wine, and liquor stores	224	13.6 (11.3, 15.9)	37.9 (30.7, 45.0)	83.6 (76.9, 90.2)	50.9 (43.4, 58.5)	51.3 (43.7, 59.0)	53.3 (45.6, 60.9)	14.1 (9.1, 19.1)	10.5 (6.2, 14.7)
Tobacco stores	93	76.7 (62.0, 91.4)	81.1 (72.0, 90.0)	95.2 (89.8, 100.0)	79.4 (70.2, 88.5)	98.0 (95.2, 100.0)	96.8 (92.2, 100.0)	59.4 (48.1, 70.8)	26.5 (16.0, 36.9)
Warehouse clubs, supercenters and Walmart	56	19.2 (15.1, 23.3)	1.2 (0.0, 3.5)	95.2 (89.8, 100.0)	51.5 (37.6, 65.4)	79.3 (68.1, 90.5)	43.1 (29.4, 56.8)	5.1 (0.0, 10.9)	0.0
Other establishment type	16	6.4 (1.9, 10.9)	27.4 (3.7, 51.2)	77.5 (56.8, 98.2)	33.2 (6.5, 59.9)	29.6 (4.4, 54.7)	35.6 (9.6, 61.7)	18.0 (0.0, 37.2)	0.0
All stores	2230[c]	29.5 (28.3, 30.7)	51.5 (49.3, 53.9)	95.1 (94.0, 96.1)	75.1 (73.0, 77.1)	81.3 (79.4, 83.2)	77.5 (75.5, 79.5)	16.8 (15.1, 18.5)	10.0 (8.6, 11.3)

[a] n for interior and total measures is 2163, N for exterior measures is 2230.
[b] Unweighted count of store type, all other data are weighted.
[c] Stores do not sum to 2230 because 2 stores were missing store type.

products near candy. Rates were similar or slightly higher in store types that adolescents are likely to visit (Sanders-Jackson et al., 2015) such as gas/convenience and convenience stores.

3.4. Associations of neighborhood characteristics with tobacco marketing materials, promotions and products

Table 3 shows the results for four outcomes: total number of tobacco marketing materials, any price promotions, any flavored cigars sold, and any smokeless sold, each modeled as a function of neighborhood demographics and region. Each outcome was modeled with and without store type as a covariate. For all four dependent variables, adding store type to the model (Models 2, 4, 6 and 8) results in a statistically significant improvement in model fit over Models 1, 3, 5 and 7 respectively as determined by using a log likelihood ratio test ($p < 0.01$ for each model comparison, Table 3).

3.4.1. Marketing materials

Stores located in neighborhoods in the third quartile of percentage of non-Hispanic Black residents displayed significantly more marketing materials than stores in neighborhoods with the lowest percentage of non-Hispanic Black residents when store type was added to the model (Table 3, Model 2) ($B = 8.6$, $p = 0.02$).

3.4.2. Price promotions

The odds of displaying a promotion were 1.8 times higher (95% CI = 1.2, 2.7) in stores located in neighborhoods with the highest vs. lowest percentage of non-Hispanic Blacks (Table 3, Model 3). After adjusting for store type, the association persisted (OR = 2.1, 95% CI = 1.3, 3.4) (Table 3, Model 4). Stores located in neighborhoods with a higher proportion of youth had greater odds of featuring price promotions (OR = 1.03, 95% CI = 1.00, 1.05). Neither the percentage of Hispanic residents nor median household income was associated with a price promotion being displayed. All store types had significantly lower odds of displaying a promotion compared with gas/convenience stores, except pharmacies, which did not differ significantly from gas/convenience stores (Table 3, Model 4).

3.4.3. Flavored cigar availability

Similar to the findings for price promotions, stores in the second and fourth quartile of the percentage of non-Hispanic Black residents had significantly higher odds of selling flavored cigars compared to stores in the first quartile (OR = 1.5 and 2.0, respectively), (Table 3, Model 5). After adjusting for store type, the association was significant for these quartiles, with stores in quartile 4 having 2.6 times greater odds of flavored cigar availability compared to stores in quartile 1 (95% CI = 1.3, 5.1), (Table 3, Model 6). Stores in quartile two for percent of Hispanic residents, as well as stores in areas with higher median household incomes, had significantly lower odds of selling flavored cigars (OR = 0.6, 0.9 respectively) but these associations were non-significant after adjusting for store type (Table 3, Models 5–6). The percentage of the population under age 18 was not associated with flavored cigar availability. All store types had significantly lower odds of selling flavored cigars compared with gas/convenience stores, with the exception of tobacco stores and pharmacies, which did not differ significantly from gas/convenience stores.

3.4.4. Smokeless product availability

The odds of a store selling smokeless tobacco products (including snus) was lower in neighborhoods in the highest quartile of Hispanic residents, compared with the lowest (OR = 0.5, 95% CI = 0.3, 0.8) There were no significant associations with the percentage of Black residents, median household income, or the percentage of population under age 18 (Table 3, Models 7–8).

Table 3
Store and neighborhood predictors of tobacco product marketing materials, price promotions, and flavored cigars at tobacco outlets in the contiguous US ($N = 2163$), 2012.

	Total marketing materials				Any price promotion				Flavored cigar availability				Smokeless availability			
	Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7		Model 8	
	β	(95% CI)	β	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Intercept	**19.7**	**(10.6,28.9)**	**28.7**	**(20.2, 37.2)**	**1.8**	**(1.2,2.9)**	**4.4**	**(2.4,7.9)**	**5.5**	**(3.1,9.6)**	**15.7**	**(7.7,32.4)**	**2.9**	**(1.9,4.4)**	**8.8**	**(5.4,14.1)**
Level 1 (n = 2163 stores)																
Store type																
Gas station with or without convenience store (ref)			Ref				Ref				Ref				Ref	
Supermarket & other grocery			**−22.3**	**(−29.6, −15.0)**			**0.1**	**(0.1,0.2)**			**0.1**	**(0.09,0.2)**			**0.2**	**(0.1,0.2)**
Convenience store (without gas)			**−9.1**	**(−14.4, −3.8)**			**0.4**	**(0.3,0.6)**			**0.6**	**(0.3,0.9)**			**0.3**	**(0.2,0.4)**
Pharmacy and drug stores			**−24.2**	**(−27.7, −20.7)**			1.0	(0.7,1.6)			0.8	(0.5,1.3)			**0.4**	**(0.3,0.6)**
Beer, wine, and liquor stores			**−24.3**	**(−29.5, −19.2)**			**0.1**	**(0.1,0.2)**			**0.1**	**(0.1,0.1)**			**0.1**	**(0.1,0.1)**
Tobacco store			**61.8**	**(27.8, 95.7)**			**0.4**	**(0.2,0.9)**			3.5	(0.6,21.5)			**0.5**	**(0.3,1.0)**
Warehouse clubs, supercenters and Walmart			**−22.0**	**(−27.5, −16.6)**			**0.1**	**(0.1,0.3)**			**0.3**	**(0.1,0.6)**			0.8	(0.3,2.5)
Other establishment type			**−40.4**	**(−50.5, −30.3)**			**0.03**	**(0.0,0.1)**			**0.02**	**(0.0,0.1)**			**0.03**	**(0.01,0.1)**
Neighborhood (tract) characteristics																
Hispanic, %																
Q1: <2.02% (ref)	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Q2: 2.02–5.98%	1.0	(−6.9, 9.0)	−0.3	(−7.1, 6.6)	0.9	(0.6,1.2)	1.1	(0.7,1.7)	**0.7**	**(0.4,1.0)**	0.8	(0.5,1.3)	**0.6**	**(0.4,0.9)**	0.7	(0.5,1.1)
Q3: 5.98–16.8%	−3.8	(−9.6, 2.1)	−4.0	(−9.5, 1.5)	1.1	(0.7,1.6)	1.2	(0.7,2.0)	0.8	(0.5,1.3)	0.8	(0.5,1.4)	0.8	(0.6,1.2)	0.8	(0.5,1.2)
Q4: >16.8%	−3.0	(−10.8,4.8)	−3.4	(−10.5, 3.7)	0.8	(0.5,1.3)	1.0	(0.6,1.6)	0.7	(0.4,1.1)	0.8	(0.3,1.3)	**0.4**	**(0.3,0.7)**	**0.5**	**(0.3,0.8)**
Non-Hispanic Black, %																
Q1: < 1.01% (ref)	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Q2: 1.01–4.96%	2.9	(−0.4, 6.2)	3.0	(−1.4, 7.3)	**1.7**	**(1.2,2.4)**	**1.8**	**(1.2,2.6)**	**1.5**	**(1.1,2.2)**	**1.6**	**(1.0,2.4)**	1.2	(0.8,1.8)	1.2	(0.8,1.9)
Q3: 4.96–15.8%	7.7	(−0.1,15.5)	**8.6**	**(2.5, 14.8)**	**1.7**	**(1.1,2.4)**	**1.6**	**(1.0,2.3)**	1.4	(1.0,2.1)	1.3	(0.8,2.2)	1.2	(0.8,1.6)	1.1	(0.8,1.6)
Q4: > 15.8%	1.3	(−4.1, 6.8)	5.2	(−2.4, 12.8)	**1.8**	**(1.2,2.7)**	**2.1**	**(1.3,3.4)**	**2.0**	**(1.2,3.5)**	**2.6**	**(1.3,5.1)**	**0.7**	**(0.5,1.0)**	0.7	(0.5,1.0)
Median household income, $10,000	−0.2	(−1.6, 1.1)	0.6	(−0.8, 2.1)	1.0	(1.0,1.1)	1.0	(1.0,1.1)	**0.9**	**(0.9,1.0)**	0.9	(0.9,1.0)	1.0	(1.0,1.1)	1.0	(1.0,1.1)
Population under age 18, %	0.2	(−0.2, 0.6)	−0.2	(−0.5, 0.1)	**1.0**	**(1.01,1.04)**	**1.0**	**(1.01,1.05)**	1.0	(1.0,1.0)	1.0	(1.0,1.1)	1.0	(1.0,1.01)	1.0	(1.0,1.01)
Level 2 (n = 97 counties)																
Region																
West (ref)	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Northeast	11.8	(−4.1,27.7)	8.6	(−5.0, 22.3)	1.8	(1.0,3.3)	**2.2**	**(1.1,4.4)**	**0.5**	**(0.3,0.9)**	**0.5**	**(0.3,0.9)**			**0.5**	**(0.3,0.9)**
Midwest	**10.1**	**(1.0, 19.2)**	7.9	(−0.1, 15.8)	**2.2**	**(1.2,3.9)**	**2.2**	**(1.1,4.1)**	0.7	(0.4,1.3)	0.6	(0.3,1.2)			1.0	(0.5,2.2)
South	**15.9**	**(6.1,25.7)**	**11.7**	**(2.5, 20.9)**	1.5	(0.9,2.4)	1.2	(0.7,2.1)	1.7	(1.0,2.9)	1.4	(0.7,2.7)			1.0	(0.5,2.0)
Bold indicates significance at $p < 0.05$																
AIC		20,626		19,768		6218		5960		5870		5600		6148		5894
χ^2		872				272				284						254
p value (for model comparison)		<0.01				<0.01				<0.01						<0.01

Significance at p < .05 is indicated by bold text.

4. Conclusion

This is the first study to comprehensively examine retail marketing and promotions for cigarettes and other tobacco products by neighborhood characteristics in a representative sample of tobacco retailers in the contiguous US. Retail tobacco marketing was omnipresent. Stores featured nearly 30 tobacco product marketing materials on average, 75.1% featured one or more price promotions, and 81.3% sold flavored cigars. Stores in neighborhoods with a higher proportion of non-Hispanic Black residents were more likely to feature a price promotion or sell flavored cigars. Price promotions were also more common in stores located in neighborhoods with a greater proportion of youth. Taken together, these findings suggest that tobacco products, along with their advertising and promotions, are widely available in stores across the country and that tobacco companies appear to be targeting their products, including candy and fruit flavored products, by offering price promotions in neighborhoods with more youth and non-Hispanic Black residents.

A greater presence of tobacco marketing in Black/African American neighborhoods has been found in other studies (Henriksen et al., 2012; Widome et al., 2013) and systematic reviews (Lee et al., 2015; Primack et al., 2007). Of these, the study most similar to ours documented a 9% increase in the number of marketing materials for every 10 percentage point increase in the proportion of a store neighborhood that is Black/African American in Minneapolis (Widome et al., 2013). Based on our regression model we find that on average, stores in quartiles 3 (4.96–15.8% non-Hispanic Black) have more marketing materials than stores in quartile 1 (<1% non-Hispanic Black).

To our knowledge, this is the first national study to find more price promotions in neighborhoods with more children. Studies in California (Henriksen et al., 2012) and New York (Waddell et al., 2016) found that stores in neighborhoods with a higher proportion of youth had more price promotions for menthol cigarettes. Our results suggest that the presence of price promotions for *any* tobacco product increased with the proportion of youth in the store neighborhood. We also found that products that appeal to youth are particularly prevalent in the types of stores that youth visit most frequently (Sanders-Jackson et al., 2015). Flavored cigars, in particular, were available in >80% of gas stations, convenience stores and pharmacies. Nearly half of all adolescents visit convenience stores at least once a week, and the odds of visiting are nearly double for African-American youth (Sanders-Jackson et al., 2015). The patterns of marketing and product availability are troubling given that point of sale tobacco marketing is related to increased youth initiation and tobacco use (Paynter and Edwards, 2009; Henriksen et al., 2010; Robertson et al., 2014).

Similar to other studies (Siahpush et al., 2010; Widome et al., 2013), we find no association between the proportion of Hispanic residents and any measures of marketing or product availability, with the exception of smokeless products, which were less likely to be available in the predominantly Hispanic areas. Perhaps the industry does not explicitly target Hispanic populations because they smoke at lower rates than other ethnic groups, or perhaps stores (e.g., tiendas) in Hispanic neighborhoods are smaller and less likely to feature marketing, have large tobacco product assortments, or offer price promotions. We also did not find differences between neighborhood income levels and measures of marketing or product availability. Lower levels of neighborhood income in both Oklahoma County, Oklahoma and Omaha, Nebraska were associated with more tobacco marketing materials and promotions (John et al., 2009; Siahpush et al., 2010), but in Minneapolis, larger proportions of the population using public assistance or living below 150% of the poverty level was only associated with menthol advertising, and not with overall number of marketing materials (Widome et al., 2013). Evidence that the amount of marketing materials, price promotions, and flavored products were related to several store neighborhood characteristics emphasizes the utility and importance of store environment assessments.

Our findings suggest that additional policies are needed to counteract this unhealthy retail environment, particularly for youth and for African American residents. The widespread availability of flavored cigars and single cigars should be addressed. The Family Smoking Prevention and Tobacco Control Act (FSPTCA) (Ribisl, 2012) restricted the sale of flavored cigarettes, but the US Food and Drug Administration (FDA) did not restrict flavors in cigars as part of their "deeming" rules. This would be important for a future regulation as African Americans smoke cigars at higher rates than whites (Anon., 2013; Agaku et al., 2014). Local jurisdictions are implementing flavor restrictions and minimum pack size restrictions (Lange et al., 2015) and these efforts should accelerate in the absence of federal rules. Given that the FDA flavored cigarette restriction appears to have contributed to lower youth tobacco use (Courtemanche et al., 2017), communities may want to enact restrictions on other flavored products.

Tobacco product price promotions are particularly appealing to youth (Pierce et al., 2005) and to low-income tobacco users (Cornelius et al., 2015). The tobacco industry significantly increased its use of price promotions after the 1998 Master Settlement Agreement (Loomis et al., 2006). Jurisdictions such as Providence, RI, and New York City, NY have restricted tobacco industry price promotions including coupon redemption, special price discounts, and buy one get one free specials (McLaughlin et al., 2014). These restricitions on price promotions appear to be on solid legal grounding based on recent court decisions, although comprehensive restrictions on tobacco advertising are unconstitutional (Lange et al., 2015). Similar restrictions should be implemented at other local, state, and federal levels. In spite of the large quantity of tobacco marketing materials in stores, policies to restrict advertising are less likely to survive legal challenges than policies that restrict selling of a type of product (e.g., menthol), or regulating the manner (e.g., self-service displays) and location (e.g., prohibiting sales in pharmacies and near schools) of sale (Lange et al., 2015).

Study strengths include a large representative sample of US stores, making this one of the few national studies of point-of-sale marketing. The current study used best practices for store audit data collection (Lee et al., 2014), included multiple tobacco products, and focused on youth appeal. A limitation is that we did not measure the size or prominence of marketing materials. Although the data collection protocol was standardized, these two measures had low reliability, making it more difficult to detect associations with store type and neighborhood demographics (Lee et al., 2014). The exclusion of Alaska and Hawaii from our sample due to the impracticably high cost of data collection beyond the contiguous United States limits the generalizablity of the sample. We also lumped all types of cigars together for parsimony, however, the use patterns of cigarillos vary from large cigars.

Future studies should identify the impact of programs and policies to curtail targeted marketing of tobacco products to vulnerable populations. The tobacco industry has a long history of targeting youth, racial/ethnic populations, and low-income individuals, and these practices continue. Given that most tobacco control interventions do little to reduce or eliminate disparities in tobacco use (Hill et al., 2014), finding such policy levers is essential.

Conflict of interest

Dr. Ribisl has served as an expert consultant in litigation against cigarette manufacturers and Internet tobacco vendors. Dr. Ribisl and Ms. Feld have a royalty interest in a mobile store observation system owned by UNC-Chapel Hill. This system is not described or mentioned in this paper.

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Changes in the prevalence and correlates of menthol cigarette use in the USA, 2004–2014

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ABSTRACT

Introduction National data from 2004 to 2010 showed that despite decreases in non-menthol cigarette use prevalence, menthol cigarette use prevalence remained constant in adolescents and adults and increased in young adults. The purpose of the current study was to extend these analyses through 2014.

Methods We estimated the prevalence of menthol cigarette smoking in the USA during 2004–2014 using annual cross-sectional data on persons aged ≥12 years from the National Survey on Drug Use and Health. Self-reported menthol status for selected brands that were either exclusively menthol or non-menthol were adjusted based on retail sales data. Data were weighted to provide national estimates.

Results Although overall smoking prevalence has decreased, the proportion of past 30-day cigarette smokers using menthol cigarettes was higher (39%) in 2012–2014 compared to 2008–2010 (35%). Youth smokers remain the most likely group to use menthol cigarettes compared to all other age groups. Menthol cigarette prevalence has increased in white, Asian and Hispanic smokers since 2010. Menthol cigarette prevalence exceeded non-menthol cigarette prevalence in youth and young adult smokers in 2014. Among smokers, menthol cigarette use was positively correlated with co-use of cigars. Menthol cigarette and smokeless tobacco co-use also increased from 2004 to 2014.

Conclusions The youngest smokers are most likely to use menthol cigarettes. Among smokers, increases in overall menthol cigarette use and menthol cigarette use in whites, Asians and Hispanics since 2010 are of concern. There is tremendous urgency to limit the impact of menthol cigarettes on public health, particularly the health of youth and young adults.

INTRODUCTION

National data from 2004 to 2010 showed that despite decreases in non-menthol cigarette use prevalence, menthol cigarette use prevalence remained constant in adolescents and adults and increased in young adults.[1] This was consistent with trends in non-menthol and menthol cigarettes in the USA over this time period.[2] While population data have shown significant declines in cigarette use among youth[3] and adults[4] in recent years, findings from the 2013–2014 wave of the Population Assessment of Tobacco and Health (PATH) Study indicate that 59.5% of youth smokers report using menthol cigarettes in the past 30 days.[5]

Evidence syntheses highlight greater experimentation with cigarettes and nicotine dependence among youth menthol cigarette smokers compared to non-menthol cigarette smokers.[6–8] Studies documenting the differential impact of menthol cigarettes (vs non-menthol cigarettes) on subsequent smoking outcomes among youth and young adults highlight the role of menthol cigarettes in facilitating increased smoking and progression to regular smoking in youth and young adults.[9 10] Recent studies have also documented the high proportion of polytobacco use in youth[11] and young adults,[12 13] though few studies have examined the relationship between menthol cigarette use and other tobacco use.

The 2009 Family Smoking Prevention and Tobacco Control Act required the US Food and Drug Administration (FDA) to ban fruit, candy and clove characterising flavours in cigarettes in September 2009 but did not extend that ban to menthol characterising flavours in cigarettes. FDA's recently issued deeming regulations also failed to propose a ban on menthol in cigarettes or other tobacco products. Since then, several countries have passed bans on menthol cigarettes, including the European Union, and many have implementation dates in 2020.[14] Local action has occurred more quickly with implementation of menthol cigarette sales bans in several Canadian provinces in 2015 and 2016[14] and the city of Chicago's 2014 ban on the sale of flavoured products (including menthol cigarettes) within 500 feet of schools.[15] The tobacco marketplace continues to evolve and the largest US cigarette manufacturers have renewed efforts to increase menthol's market share in their portfolios.[16 17] The purpose of this study was to extend our trend analyses through 2014, determine whether there were differences in the distribution of menthol cigarette users from 2008–2010 to 2012–2014 and examine correlations between menthol cigarette use and other tobacco product use over time.

METHODS

National Survey on Drug Use and Health

The National Survey on Drug Use and Health (NSDUH) is a nationally representative survey that assesses tobacco, alcohol and drug use behaviours in the US civilian, non-institutionalised population. Respondents are aged 12 years and older. NSDUH respondents were selected using a multistage probability sample. Respondents include persons living in households in addition to residents of non-institutional group quarters, such as college students living in dormitories, civilians residing on military bases and persons living in group homes, shelters and rooming houses. The sample excludes members of the active-duty military and individuals in institutional group quarters. Racial/ethnic minorities and persons aged 12–25 years were oversampled.

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Cross-sectional surveys were administered annually from 2004 to 2014. Most interviews were conducted in the respondents' homes by trained interviewers. To increase measurement accuracy, drug use questions—including tobacco questions—were administered by audio computer-assisted self-interviews (A-CASI). The overall response rate from 2004 to 2014 ranged from 58.3% to 70.0%.

Measures

Current cigarette smoking in the NSDUH was assessed by asking respondents who had ever smoked whether they had smoked part or all of a cigarette in the previous 30 days. Those who responded affirmatively were subsequently asked to report the brand of cigarettes they smoked most often. They were able to select and verify their usual brand from 2 lists with a total of 57 (60 in 2004) brand names that were presented on-screen. Once respondents selected and verified one of the brands on the screen, they were subsequently asked, "Were the <CIGFILL> cigarettes you smoked during the past 30 days menthol?" (note: '<CIGFILL>' was replaced by the computer programme with the name of the brand the respondent had previously reported and verified as having smoked most often). In 2014, ~94% of smokers selected a brand from the lists offered. The remaining 6% were asked, "Were the cigarettes you smoked during the past 30 days menthol?"

Owing to concerns about misclassification, especially among adolescents, we examined Nielsen market scanner data to classify major brands for which at least 99% of sales were menthol or non-menthol. Incorporating a method of Hersey *et al*,[18] if a respondent reported usually smoking Kool and also reported on the menthol question that the usual brand was non-menthol, the respondent's response to the menthol variable question was recoded as menthol. A similar adjustment was made for exclusively non-menthol brands.

Analyses used imputed values for age, gender, race and income available in the data sets. To aid comparison with our previous analyses,[1] age was categorised as 12–15, 16–17, 18–21, 22–25, 26–34 and 35 years and older. For estimating trends in menthol prevalence over time, age categories were collapsed into three groups: 12–17, 18–25 and 26 years and older. Race/ethnicity was grouped into Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic Asian, non-Hispanic more than one race and non-Hispanic other. Total family income was separated into three groups: <US$10 000–US $29 999, US$30 000—$74 999 and US$75 000 or more. Number of days smoked per month among past 30-day smokers was categorised as 1–5, 6–29 and 30 days. Past 30-day cigar use was ascertained by the question: "During the past 30 days, that is, since [DATEFILL], on how many days did you smoke part or all of a cigar?" Past 30-day use of snuff was measured by the item: "During the past 30 days, that is, since [DATEFILL], on how many days did you use snuff?" Similar item wording was used to measure past 30-day use of chewing tobacco: "During the past 30 days, that is, since [DATEFILL], on how many days did you use chewing tobacco?" We combined use of snuff and/or chewing tobacco into one variable measuring past 30-day use of smokeless tobacco. Data were missing for fewer than 2% on tobacco use items across all NSDUH waves.

Statistical analyses

Three types of analyses were carried out. For assessing changes in use of menthol cigarettes between 2008–2010 and 2012–2014, we duplicated table 1 in Giovino *et al*.[1] For this phase of the analysis, NSDUH cross-sectional surveys administered annually from 2008 to 2010 were combined for analysis, as were annual surveys conducted from 2012 to 2014. Brand choices for 2008–2010 respondents were adjusted for 100% menthol based on 2012–2014 sales data. This provided comparisons

Table 1 Prevalence (%) of menthol cigarette use among past 30-day smokers, by age and gender, race/ethnicity, household income and the number of days smoked/month in the USA, 2008-2010 and 2012–2014

	2008–2010						2012–2014					
	All Ages	12–17	18–25	26–34	35–49	50+	All Ages	12–17	18–25	26–34	35–49	50+
Overall	34.7	52.5	43.6	34.6	30.3	30.6	**38.8**	53.9	**50.0**	**43.9**	**32.3**	32.9
Gender												
Male	30.9	49.8	40.6	32.5	24.9	25.6	**34.8**	50.8	**45.9**	**39.8**	**29.2**	26.7
Female	39.1	55.5	47.4	37.3	36.3	35.7	**43.5**	57.6	**55.9**	**49.3**	35.9	39.1
Race/Ethnicity												
Non-Hispanic white	25.6	49.5	36.1	23.6	20.0	22.5	**28.9**	51.6	**41.7**	**33.4**	20.9	24.0
Non-Hispanic black	86.0	74.2	85.7	91.3	89.0	80.4	84.6	71.3	84.3	90.5	87.2	79.8
Non-Hispanic other	45.1	56.0	56.1	38.7	48.5	31.6	46.7	52.6	54.4	51.6	41.9	41.8
Non-Hispanic Asian	30.3	58.5	48.1	27.0	24.9	17.0	**38.0**	**39.5**	54.3	**42.5**	25.2	**27.4**
Non-Hispanic more than one race	41.1	54.8	50.2	30.4	47.5	33.7	38.1	57.4	57.5	**52.5**	**30.0**	23.7
Hispanic	37.1	53.3	45.4	40.0	31.2	26.8	**46.9**	56.7	**57.5**	**51.2**	**41.7**	33.0
Household income												
<US$10 000 (including loss)–US$29 999	38.6	53.1	43.8	42.4	36.7	32.1	**43.7**	54.3	**50.8**	**51.0**	39.2	**37.0**
US$30 000–US$74 999	33.2	53.3	43.4	32.8	27.9	30.2	**37.2**	57.0	**49.9**	**42.1**	30.7	30.7
US$75 000 or more	30.5	50.9	43.3	24.8	25.8	28.4	32.1	48.7	**48.2**	**33.8**	24.9	28.3
Number of days smoked per month (days)												
1–5	37.7	51.2	40.8	32.4	33.4	39.1	**41.4**	55.3	**50.0**	**42.3**	34.3	32.3
6–29	40.5	55.5	45.2	37.7	36.8	38.6	**45.7**	55.7	**52.4**	**49.0**	41.1	39.2
30	31.8	50.5	44.0	34.1	27.7	27.7	**35.4**	48.5	**48.3**	**42.2**	29.3	**31.2**

Source: National Survey on Drug Use and Health. Self-reported menthol status was adjusted if necessary using retail checkout scanner data. Sample size=35 320.
Bolded percentages indicate statistically significant change from 2008–2010 to 2012–2014 ($p<0.05$).

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between time periods in the prevalence of use of menthol cigarettes. Multivariable logistic models were used to estimate odds ratios (ORs) of menthol cigarette use among past 30-day cigarette smokers, adjusted for age, gender, race/ethnicity, income and number of days smoked; listwise deletion was used to handle respondents with item-level missing data.

Next, we estimated time trends in the use prevalence of menthol and non-menthol cigarettes. Annual prevalence estimates for the use of each type of cigarette were calculated for 2004 to 2014. Regression lines were fitted to the prevalence estimates using piecewise linear regression[19] in which the dependent variable was the annual prevalence estimates. Differences in the variances of the annual prevalence estimates were accounted for using weighted regression. Separate lines were fitted for menthol and non-menthol prevalence by age (12–17, 18–25 and 26 years and older). An inflexion point was included that allowed the slopes of the lines to change at year 2010 based on visual examination of the raw data, the last year of our previous analyses and the first full year in which other flavoured cigarettes were no longer on the market. Statistical tests were carried out to assess differences in the slopes of menthol and non-menthol regression lines and, within each type of cigarette, differences in slopes between two time periods: 2004–2010 and 2010–2014.

The third analysis investigated the use of cigars and smokeless tobacco among past 30-day cigarette smokers. Prevalence estimates for past 30-day cigar and smokeless tobacco use were compared for past 30-day menthol and non-menthol cigarette smokers by gender and age. Multivariable logistic models were used to estimate ORs for cigar and smokeless tobacco use between menthol and non-menthol cigarette smokers, adjusted for gender and age. For this analysis, NSDUH annual surveys were combined into three time periods: 2004–2007, 2008–2011 and 2012–2014. Changes over time in the odds of smoking cigars or using smokeless tobacco for menthol cigarette smokers compared with non-menthol cigarette smokers were also assessed. The top brands of cigars and smokeless used by menthol and non-menthol cigarette smokers were identified.

SAS V.9.4 was used for all analyses. The SAS survey procedures took into account NSDUH's complex survey design. Survey weights were used to adjust for different probabilities of selection and for non-response, producing estimates representative of the US population.

RESULTS

Change in prevalence of use of menthol cigarettes between 2008–2010 and 2012–2014

Table 1 compares the prevalence of use of menthol cigarettes among past 30-day smokers between two time periods: 2008–2010 and 2012–2014. Overall, the percentage of menthol cigarette smokers increased 4.1 percentage points between 2008–2010 and 2012–2014. Menthol prevalence increased for all age groups. The largest increase (9.3 percentage points) occurred among smokers aged 26–34 years. Youth smokers aged 12–17 years were more likely to use menthol cigarettes than smokers in any other age group in both time periods. This was true for male and female smokers.

By race, black smokers continued to smoke menthol cigarettes at higher rates than smokers of any other race. However, from 2008–2010 to 2012–2014, the prevalence of menthol cigarette use in black smokers declined 1.4 percentage points. This decline in menthol use occurred among black smokers of all ages, ranging from 0.6 percentage points among those ages 50 years and older to 2.9 percentage points among those who were 12–17 years old. In comparison to black smokers, white, Hispanic, Asian and non-Hispanic other races increased use of menthol cigarettes. The largest increase was found among Hispanic smokers. Overall, between 2008–2010 and 2012–2014 the percentage of Hispanic smokers using menthol cigarettes rose 9.8 percentage points. The next largest increase was found for Asian smokers for which the menthol prevalence increased 7.7 percentage points. White smokers also increased the use of menthol cigarettes by 3.4 percentage points between 2008–2010 and 2012–2014. The largest increase was found among white smokers aged 26–34 years where the menthol percentage increased 9.8 percentage points.

Multivariable analyses

Online supplementary table S1 presents the adjusted odds of menthol cigarette use among past 30-day smokers. Consistent with our earlier analyses, the odds of menthol cigarette use are at least three times higher among the youngest smokers (ages 12–15 and 16–17) compared to smokers aged 35 and above. Female and black smokers remained significantly more likely to smoke menthol cigarettes than male and white smokers, respectively. Higher use of menthol cigarette use in women held for blacks and whites when examined separately, with the female/male difference in menthol prevalence being more pronounced for whites (OR=1.8; $p<0.01$) than for blacks (OR=1.4; $p<0.05$; see online supplementary table S2). There were no differences in the odds of menthol cigarette use among smokers by income, but menthol cigarette smokers were significantly less likely to smoke infrequently (1–5 days per month) than non-menthol cigarette smokers (OR=0.90; $p<0.05$).

Trends in the prevalence of use of menthol compared with non-menthol cigarette use 2004–2014

Figure 1A–C and tables 2 and 3 show estimated time trends in the prevalence of using menthol and non-menthol cigarettes in the full sample from 2004 to 2014 using piecewise linear regression. Two straight lines with intersection at year 2010 were fitted to each time series for menthol and non-menthol cigarette prevalence. Separate lines were estimated for each age group. Note that the denominator here is all individuals in the relevant age groups, not just cigarette smokers. The fit of the piecewise linear regression models was adequate for menthol and non-menthol trends in all three age groups. Non-menthol prevalence decreased over time for all three age groups and both time periods. The non-menthol prevalence slope decreased most quickly among 18–25 year-olds in the 2004–2010 time period. Menthol prevalence increased among 18–25 year-olds in the first time period (0.5 percentage points per year; $p<0.01$) and among persons aged 26 years and older in the second time period (0.1 percentage points per year; $p<0.05$).

In 2004, 4.9% of youth smoked menthol cigarettes and this prevalence declined to 2.5% in 2014 (figure 1A). The rate of decline was significantly greater after 2010 ($p<0.01$; table 2). Similarly, non-menthol smoking declined among youth, from 6.3% in 2004 to 2.2% in 2014. The slopes of the non-menthol lines were not significantly different between 2004–2010 and 2010–2014. The slopes of the non-menthol and menthol lines were significantly different during 2004–2010 (table 3; $p<0.01$). After 2010, the menthol and non-menthol prevalence lines declined at about the same rates ($p=0.08$). By 2014, smoking rates among youth were low and about the same for menthol and non-menthol cigarette smoking.

Among young adults aged 18–25 years, non-menthol smoking prevalence declined over the study period, from 26.9% in 2004

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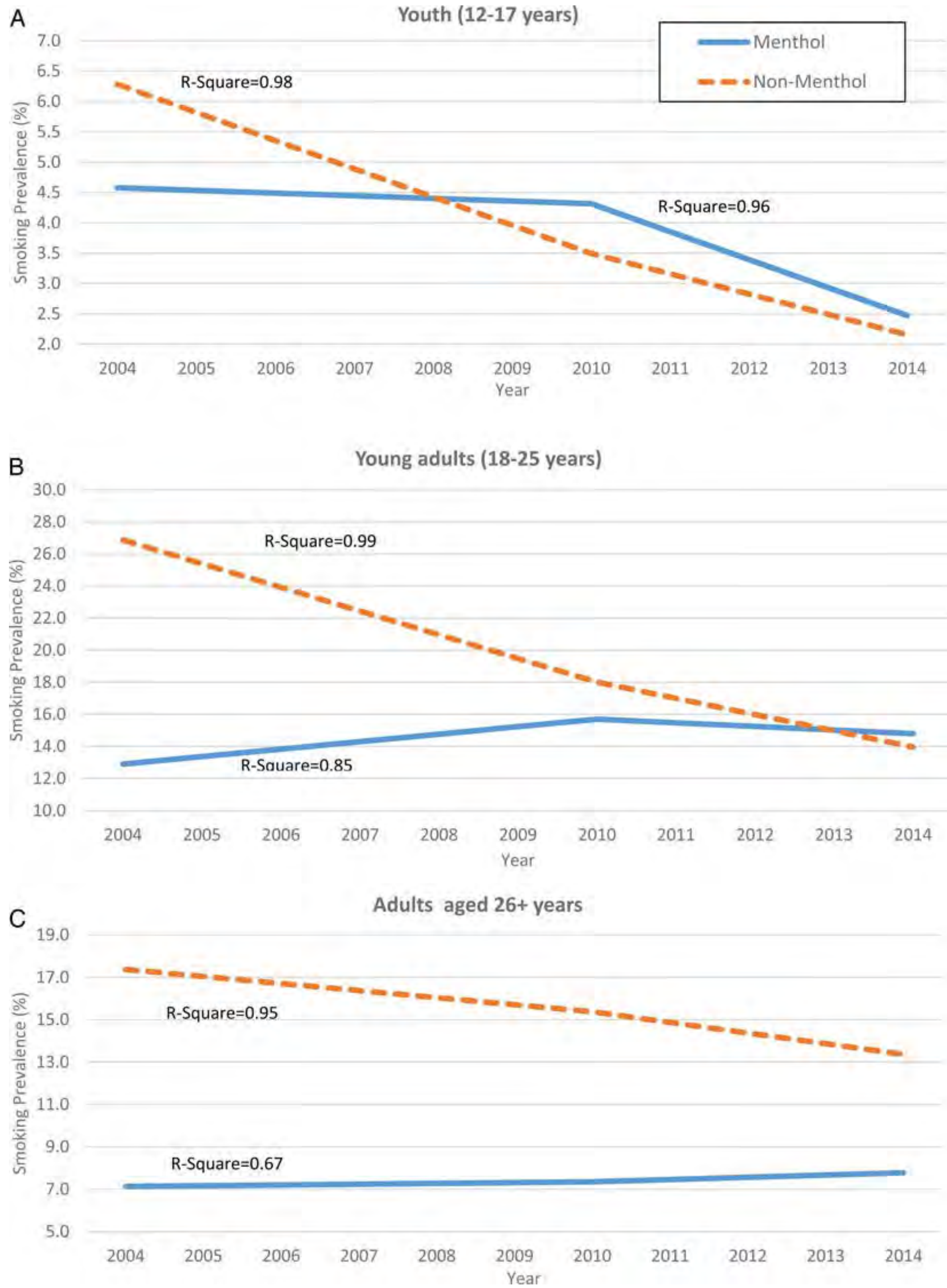

Figure 1 Trends in the prevalence of menthol and non-menthol cigarette smoking (%) by age in the US population, National Survey on Drug Use and Health, 2004–2014.

to 14.0% in 2014 (figure 1B). From 2004 to 2010, the rate of decline was about 1.5 percentage points per year. After 2010, the decline lessened to about 1 percentage point per year. The rates of decline were statistically significant for both time periods ($p<0.01$), and the change in slopes at 2010 was statistically significant (table 2; $p<0.05$). Menthol smoking prevalence among persons aged 18–25 years increased at a rate of about 0.5 percentage points per year during 2004–2010. After 2010, menthol prevalence declined at about 0.2 percentage points per year. The change in slopes across the two time points was statistically significant ($p<0.01$). The slopes of the non-menthol and menthol lines were significantly different during 2004–2010 (Table 3; $p<0.01$), and they were significantly different after 2010 ($p<0.01$). Although menthol prevalence at the beginning of the time series was lower than non-menthol prevalence, by 2014, menthol prevalence was higher.

Among adults aged 26 and older, menthol prevalence was constant during 2004–2010 and increased slowly (slope=0.1 percentage points per year; $p<0.05$) after 2010 (figure 1C). Non-menthol prevalence decreased over the entire study period though the non-menthol slopes were not significantly different between time periods (table 2). The slopes of the non-menthol

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Table 2 Estimated trends* in the prevalence of cigarette smoking by type of cigarette and age, 2004–2014

	Prevalence (%)†			Estimated slopes‡				Test for difference in slopes 2004–2010 vs 2010–2014
				2004–2010		2010–2014		
	2004	2010	2014	Slope	p Value	Slope	p Value	p Value
12–17 years								
Menthol	4.6	4.3	2.5	−0.04	0.28	**−0.46**	<0.01	**<0.01**
Non-menthol	6.3	3.5	2.2	**−0.46**	<0.01	**−0.33**	<0.01	0.13
18–25 years								
Menthol	12.9	15.7	14.8	**0.47**	<0.01	−0.23	0.13	**<0.01**
Non-menthol	26.9	18.0	14.0	**−1.48**	<0.01	**−1.01**	<0.01	**<0.05**
26+ years								
Menthol	7.1	7.3	7.8	0.04	0.28	**0.11**	<0.05	0.34
Non-menthol	17.4	15.4	13.4	**−0.33**	<0.01	**−0.50**	<0.01	0.26

*Time trends estimated using piecewise linear regression with one inflexion point at year 2010.
†Prevalence estimates are predicted from model.
‡Slopes measure the percentage point change in prevalence per year. Bolded slopes indicate statistically significant change between 2004 and 2010 and 2010–2014 (p<0.05).

and menthol lines were significantly different during 2004–2010 and after 2010 (table 3; both p<0.01).

Past 30-day use of cigars and smokeless tobacco among smokers of menthol cigarettes

Past 30-day use of cigars varied by menthol cigarette use status (table 4). Cigars included big cigars, cigarillos and little cigars, flavoured and non-flavoured. In order to assess changes over time, the total time series was separated into three periods: 2004–2007, 2008–2011 and 2012–2014. Over all three time periods, the prevalence of cigar use among menthol cigarette users remained approximately the same. However, menthol cigarette smokers were more likely to use cigars than non-menthol cigarette smokers. In 2012–2014, ∼12.9% of menthol cigarette smokers used cigars compared with 10.6% of non-menthol cigarette smokers. This difference was statistically significant for all three time periods. Higher cigar prevalence was seen for male and female menthol cigarette smokers compared to non-menthol cigarette smokers. Online supplementary table S3 shows the cigar brand smoked most often by past 30-day cigar users, by cigarette menthol smoking. Black & Mild cigars were the most highly used among co-users of cigars and cigarettes, with higher prevalence of use among menthol cigarette smokers than non-menthol cigarette smokers across all time periods. In 2012–2014, 43.6% of menthol cigarette smokers who also used cigars preferred Black & Mild compared to 30.4% of non-menthol cigarette smokers.

Over all three time periods, use of smokeless tobacco increased from 3.3% to 5.0% in past 30-day menthol cigarette smokers and from 6.0% to 6.5% in past 30-day non-menthol cigarettes smokers (table 4). While the odds of using smokeless tobacco remained lower among menthol compared to non-menthol cigarette smokers over time, the prevalence of smokeless use among menthol cigarette smokers approached that seen in non-menthol cigarette smokers in the 2012–2014 period (OR=0.8) compared to the earlier time points (OR=0.5 in 2004–2007 and OR=0.6 in 2008–2011). The higher smokeless tobacco prevalence among non-menthol cigarette smokers was observed for most age groups. Men who smoked non-menthol cigarettes used smokeless tobacco at higher rates than male menthol cigarette smokers. Approximately 6.2% of male menthol cigarette smokers used smokeless tobacco between 2004 and 2007. This prevalence increased to 9.4% in 2012–2014 and was statistically significant (p<0.01). Among male non-menthol cigarette smokers, there was no statistically significant increase in smokeless use between 2004–2007 and 2012–2014. Unlike cigars, there was not a consistent pattern of brand preference for smokeless products (see online supplementary table S4). In 2004–2007, Skoal was the top smokeless brand identified by cigarette smokers and menthol cigarette smokers reported a higher prevalence of Skoal use than non-menthol cigarette smokers. In the latter two time periods, Grizzly became the top brand, with relatively equal proportions of menthol and non-menthol cigarette smokers using this brand.

DISCUSSION

Findings from this study highlight five key points: first, although overall smoking prevalence has decreased, the prevalence of menthol cigarette use among past 30-day cigarette smokers

Table 3 Change in slopes of linear regression lines comparing rates of change in menthol and non-menthol smoking prevalence, by time period*

Age		Slopes		Difference in slopes	
		Menthol	Non-menthol	(Non-menthol—menthol)	p Value for different slopes
12–17	2004–2010	−0.04	−0.46	−0.42	**<0.01**
12–17	2010–2014	−0.46	−0.33	0.13	0.08
18–25	2004–2010	0.47	−1.48	−1.94	**<0.01**
18–25	2010–2014	−0.23	−1.01	−0.79	**<0.01**
26+	2004–2010	0.04	−0.33	−0.37	**<0.01**
26+	2010–2014	0.11	−0.50	−0.61	**<0.01**

*Slopes measure the percentage point change in prevalence per year. Bolded p values indicate statistically significant difference between menthol and non-menthol cigarette smoking during the time period noted (p<0.05).

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Table 4 Past 30-day use (%) of cigars* and smokeless† and non-menthol cigarette smokers, by gender and age, USA, 2004–2014

Cigars*

	2004–2007 (N=57 451)				2008–2011 (N=53 961)				2012–2014 (N=35 296)			
	Menthol smoker	Non-menthol smoker	OR (menthol vs non-menthol‡)	p Value	Menthol smoker	Non-menthol smoker	OR (menthol vs non-menthol‡)	p Value	Menthol smoker	Non-menthol smoker	OR (menthol vs non-menthol‡)	p Value
Overall	13.5	11.5	**1.2**	<0.01	13.9	10.7	**1.4**	<0.01	12.9	10.6	**1.3**	<0.01
Gender												
Male	20.6	16.7	**1.3**	<0.01	20.6	15.1	**1.5**	<0.01	19.5	14.7	**1.4**	<0.01
Female	7.0	4.8	**1.5**	<0.01	7.9	4.9	**1.7**	<0.01	6.8	5.0	**1.4**	<0.01
Age												
12–17	25.1	27.8	**0.9**	<0.05	26.7	26.8	1.0	0.96	22.3	25.0	0.9	0.19
18–25	23.3	20.6	**1.2**	<0.01	22.1	19.7	**1.2**	<0.01	20.1	20.1	1.0	0.99
26–34	15.1	12.0	**1.3**	<0.01	15.3	10.8	**1.5**	<0.01	14.2	12.2	1.2	0.16
35–49	8.7	8.6	1.0	0.88	9.7	8.6	1.1	0.19	11.1	7.8	**1.5**	<0.05
50+	5.7	5.8	1.0	0.88	6.0	6.1	1.0	0.92	5.4	7.0	0.8	0.09

Smokeless tobacco†

	2004–2007 (N=57 514)				2008–2011 (N=54 016)				2012–2014 (N=35 320)			
	Menthol Smoker	Non-menthol smoker	OR (menthol vs non-menthol§)	p Value	Menthol smoker	Non-menthol smoker	OR (menthol vs non-menthol§)	p Value	Menthol smoker	Non-menthol smoker	OR (menthol vs non-menthol§)	p Value
Overall	3.3	6.0	**0.5**	0.01	4.4	6.7	**0.6**	<0.01	5.0	6.5	**0.8**	<0.01
Gender												
Male	6.2	10.0	**0.6**	0.01	8.2	11.3	**0.7**	<0.01	9.4	10.8	**0.9**	<0.05
Female	0.6	0.6	0.9	0.74	0.9	0.6	1.4	0.06	0.9	0.7	1.2	0.28
Age												
12–17	8.2	13.8	**0.6**	<0.01	12.1	15.0	**0.8**	<0.01	15.7	18.7	0.8	0.13
18–25	5.9	10.6	**0.5**	<0.01	8.1	12.4	**0.6**	<0.01	8.6	13.2	**0.6**	<0.01
26–34	3.8	7.4	**0.5**	<0.01	4.2	9.2	**0.4**	<0.01	5.4	10.2	**0.5**	<0.01
35–49	1.7	4.5	**0.4**	<0.01	2.5	5.5	**0.4**	<0.01	3.7	5.1	**0.7**	<0.05
50+	0.9	1.9	0.5	0.07	0.9	2.1	**0.4**	<0.05	1.2	1.9	0.6	0.18

*Includes big cigars, cigarillos and little cigars.
†Includes chewing tobacco or snuff or both.
‡Estimated OR comparing past 30-day cigar prevalence among menthol cigarette smokers with past 30-day cigar prevalence among non-menthol cigarette smokers. Bolded ORs indicate statistically significant differences between menthol and non-menthol cigarette smokers.
§Estimated OR comparing past 30-day smokeless prevalence among menthol cigarette smokers with past 30-day smokeless prevalence among non-menthol cigarette smokers. Bolded ORs indicate statistically significant differences between menthol and non-menthol cigarette smokers.

increased significantly from 35% in 2008–2010 to 39% in 2012–2014. Second, youth smokers remain the most likely group to use menthol cigarettes compared to all other age groups and there were significant increases in menthol cigarette use among adults ages 18–25, 26–34 and 35–49 between the two time periods. Third, while menthol cigarette prevalence has remained constant among black smokers, it has increased in white, Asian and Hispanic smokers. Fourth, dramatic reductions in youth and adult cigarette smoking in recent years have resulted in decreases in menthol cigarette prevalence in youth and young adults, but those declines have not occurred as rapidly as in non-menthol cigarettes. Menthol cigarette prevalence now exceeds non-menthol cigarette prevalence in youth and young adult smokers. Finally, among past 30-day smokers, menthol cigarette use is positively correlated with co-use of cigars, another harmful combustible product. There has also been an increase in co-use of menthol cigarettes and smokeless tobacco over time. Both are possibly due to the pervasiveness of characterising flavours, including menthol, in these products.[20 21]

Tobacco companies have noted that the menthol segment of the market continues to grow.[16] The 2015 merger of Lorillard and Reynolds American tobacco companies[22] has resulted in a strategic push to accelerate the retail impact of the Newport brand,[17] the top menthol brand in the USA, which has resulted in strong growth of the Newport market share in 2016. Philip Morris USA also continues to expand their menthol distribution, including new brands such as Marlboro Midnight menthol which were rolled out nationally in November 2015.[16]

This study is limited in several ways. First, the definition of menthol use is based on brand preference. We did not estimate the number of menthol and non-menthol cigarettes smoked during a period of time by each smoker. Rather, we estimate the menthol status of the brand smoked most often. Second, we measured prevalence of use and not incidence of initiation. However, prevalence in young people is largely driven by initiation rather than migration, cessation or death. Third, we did not assess sales data prior to 2008. Nevertheless, brands such as Kool, Newport and Salem have long been classified as menthol brands.[23] In the latter years, we were unable to recode Newport as menthol due to the increasing prevalence of Newport non-menthol cigarettes in the market. Finally, our data (table 1) indicate that the use of menthol cigarettes among older smokers was less common than among adolescent and young adult smokers. It is impossible to discern with serial cross-sectional data from 2004 to 2014 whether smokers switched away from menthol cigarettes as they aged. The findings might simply indicate higher rates of menthol use among more recent birth cohorts. Cohort surveys with appropriate age groups like the PATH Study will facilitate the study of switching behaviours.

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As in our earlier analyses,[1] younger age, female gender and black race were significant correlates of menthol cigarette use among past 30-day smokers even after controlling for potential confounders. The age gradient in menthol use persists, such that the youngest smokers are the most likely to use menthol. Increases in overall menthol cigarette use and among white, Asian and Hispanic smokers over a 5 year period are of concern. Similarly, dramatic reductions in cigarette smoking at the population level have been reflected in continued declines in non-menthol cigarette use, but mixed changes in menthol cigarette use in the full sample. The data presented in this study highlight that menthol cigarette prevalence has increased among smokers in recent years and that menthol cigarette use now exceeds non-menthol cigarette use in youth and young adults. Given that cigarettes are the dominant product used in the USA and the most harmful, there is tremendous urgency to enact large-scale efforts at FDA and in state and local policy to limit the impact of menthol cigarettes on public health, particularly the health of youth and young adults.

What this paper adds

The data presented in this study highlight that among smokers, menthol cigarette prevalence has increased overall since 2010, that age remains inversely associated with menthol cigarette use and that there is co-use of menthol cigarettes with other tobacco products likely to be flavoured (ie, cigars and smokeless tobacco). In 2014, past 30-day menthol cigarette use exceeded non-menthol cigarette use in youth and young adults.

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Contributors All authors conceived of the study. ACV and PDM wrote the initial draft of the manuscript. PDM conducted the data analysis. ACV, PDM, CDD, RSN, DBA and GAG contributed to the analysis, interpretation of the data and to the review, revision and approval of the final article.

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Competing interests The authors have read and understood Tobacco Control's policy on declaration of interests and declare that they have no competing interests.

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A study of pyrazines in cigarettes and how additives might be used to enhance tobacco addiction

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ABSTRACT

Background Nicotine is known as the drug that is responsible for the addicted behaviour of tobacco users, but it has poor reinforcing effects when administered alone. Tobacco product design features enhance abuse liability by (A) optimising the dynamic delivery of nicotine to central nervous system receptors, and affecting smokers' withdrawal symptoms, mood and behaviour; and (B) effecting conditioned learning, through sensory cues, including aroma, touch and visual stimulation, to create perceptions of pending nicotine reward. This study examines the use of additives called 'pyrazines', which may enhance abuse potential, their introduction in 'lights' and subsequently in the highly market successful Marlboro Lights (Gold) cigarettes and eventually many major brands.

Methods We conducted internal tobacco industry research using online databases in conjunction with published scientific literature research, based on an iterative feedback process.

Results Tobacco manufacturers developed the use of a range of compounds, including pyrazines, in order to enhance 'light' cigarette products' acceptance and sales. Pyrazines with chemosensory and pharmacological effects were incorporated in the first 'full-flavour, low-tar' product achieving high market success. Such additives may enhance dependence by helping to optimise nicotine delivery and dosing and through cueing and learned behaviour.

Conclusions Cigarette additives and ingredients with chemosensory effects that promote addiction by acting synergistically with nicotine, increasing product appeal, easing smoking initiation, discouraging cessation or promoting relapse should be regulated by the US Food and Drug Administration. Current models of tobacco abuse liability could be revised to include more explicit roles with regard to non-nicotine constituents that enhance abuse potential.

INTRODUCTION

Tobacco dependence is understood to be a complex process that is primarily caused by the pharmacological effects of nicotine which activate nicotinic acetylcholine receptors in the brain leading to release of the neurotransmitter dopamine into the mesolimbic area, corpus striatum and frontal cortex.[1–6] Dopamine release induces rewards, including pleasure, arousal, mental acuity and modulation of mood.[1] Since the 1980s, nicotine is believed to play a central role in biological reinforcement, tolerance and physical dependence, and withdrawal symptoms on discontinuation of intake.[7] However, substantial evidence exists to suggest that nicotine's reinforcing effects alone are not sufficient to account for the intense addictive properties of tobacco smoking and the high relapse rates among smokers after quitting even when provided nicotine in forms other than tobacco.[8–16] Further evidence that tobacco dependence entails more than addiction to nicotine includes the drug's limited ability to induce self-administration in animals;[17 18] lack of positive mood effects of pure nicotine in abstinent smokers;[19–21] lack of findings that nicotine in any other form than tobacco was preferred to placebo in normal smokers;[22 23] de-nicotinised cigarettes were as effective as regular cigarettes, and more than nicotine in any other delivery mode, in relieving withdrawal and craving;[24–27] and essential role of non-nicotine factors in cigarette addiction.[24 28]

The release of tobacco industry documents in the 1990s and investigation by the US Food and Drug Administration (FDA) brought to light tobacco manufacturers' research and development of the use of additives and ingredients besides nicotine which led to the increased appeal, attractiveness and addictiveness of products.[3–5 29] Independent scientific evidence has demonstrated that conditioned cues produced by tobacco non-nicotine ingredients and smoke constituents are instrumental in maintaining tobacco use.[6 7 16 22 28 30–35] Therefore, current models of tobacco product abuse potential recognise nicotine as the primary drug of addiction, and that non-nicotine tobacco constituents and sensory stimuli from packaging and environmental cues also contribute to tobacco dependence.[36]

Two major determinants of abuse potential are (A) dynamic pharmacokinetics of nicotine delivery and (B) learned behaviour effects triggered by sensory cues associated with use.[36 37] A smoker may feel the need to puff in order to attain threshold doses of nicotine and elicit the hedonic effects attributable to dopaminergic system reward pathways.[38] Nicotine delivery and its perception may be related to ease of the drug's administration and the 'impact' of tobacco smoke on posterior pharynx nociceptors, which is proposed to occur primarily by free nicotine.[39 40] Puff volume, speed of delivery, lung deposition, frequency of dosing, arterial absorption and other parameters affect the efficiency of nicotine delivery.[41]

Tobacco manufacturers modified the design of products by directly adding constituents to cigarettes that stimulate gustatory, tactile and olfactory nerve receptors and create chemosensory effects that could enhance elasticity in nicotine dosing as well as strengthen sensory cueing to optimise the 'pleasure' in smoking.[38 42–51] Pyrazines, a class of chemosensory agents, comprise 15 of the 599 compounds on the list of cigarette ingredients

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provided by manufacturers to the US Department of Health and Human Services in 1994,[52] 8 of the compounds on the list of additive ingredients provided by manufacturers to the FDA in 2011[53] and 10 of the compounds presently listed on cigarette manufacturers' website as cigarette ingredients"[54–56] (box 1). The present study explores tobacco industry research that first identified pyrazines in tobacco smoke and was followed by the introduction of pyrazines in 'light' cigarettes and subsequent incorporation into Marlboro Lights and eventually in many other cigarette brands. It further examines their possible role in abuse potential.

METHODS

More than 7 000 000 tobacco industry documents have been disclosed by the major tobacco companies during litigation processes and made public as a result of the Minnesota Tobacco Trial and the Master Settlement Agreement of 1998.[57 58] We searched online internal tobacco industry document databases housed at Tobacco Documents Online (http://www.tobaccodocuments.org), the British American Tobacco Document Archive (http://bat.library.ucsf.edu) and the Legacy Tobacco Documents Library (http://legacy.library.ucsf.edu). Standard methods used for document analysis have been described in detail elsewhere.[59 60] Document identification was performed using an index-based word search of titles, authors, recipients and other document characteristics (such as date, document type, original file location), as well as keywords and abstracts. Whenever available, full-text optical character recognition was also used.

We used a snowball sampling method to first search the databases using an initial set of key words (eg, pyrazines, flavorant, flavoring, flavor, chemosensory, sensory, low-tar, stimulation, attributes, perception, effects, taste, smoothness and product development) and relevant combinations of these terms, and to generate further search terms from the documents identified. Relevant documents were abstracted and indexed. The resulting document set was surveyed for recurring authors, keywords, codes or project names that would suggest further avenues for retrieval.

A number of unique difficulties associated with the use of internal industry documents as a source of scientific information must be considered. Industry research was not generally subjected to careful peer review, and details regarding the experimental methods used and the resulting quality of the data are often unavailable, making it difficult to assess the reliability of the science. In addition, the available documents do not always represent the totality of the internal research that was conducted on a particular topic—as indicated by the existence of many partial reports and memos. Finally, within each given company, the documents are authored by numerous different researchers from a range of departments over tens of years, and so findings are sometimes inconsistent and occasionally even contradictory. Comparisons of the documents reveal real company-to-company differences in approach to the engineering of tobacco product design, a finding that must be taken into account. For these reasons and to inform the findings in internal industry documents, we conducted this research in conjunction with a systematic review of evidence from the current scientific literature indexed in databases including PubMed (http://www.pubmed.gov) and Web of Science (http://thomsonreuters.com/web-of-science) using the same search strategies.

Box 1 Pyrazine compounds in manufacturers' reports of cigarette ingredients

2-acetyl-3-ethylpyrazine,[52]
Acetylpyrazine,[52 53 55 56]
2,3-diethylpyrazine,[52–55]
2,3-dimethylpyrazine,[52]
2,5-dimethylpyrazine,[52–55]
2,6-dimethylpyrazine,[52]
2-ethyl(or methyl)-(3,s and 6)-methoxypyrazine,[52]
2-ethyl-3,(s or 6)-dimethylpyrazine,[52 53 55 56]
2-ethyl-3-methylpyrazine,[52 53 55]
2-isobutyl-3-methoxypyrazine,[52]
Methoxypyrazine,[52]
2-methylpyrazine,[52 53 55 56]
(Methylthio)methylpyrazine,[52]
2,3,5,6-tetramethylpyrazine,[52–56]
2,3,5-trimethylpyrazine,[52–56]
Methoxymethylpyrazine,[52 54 56]
[52]Manufacturers' 1994 cigarette ingredients report,
[53]Manufacturers' 2011 report to the Food and Drug Administration (FDA),
[54]Philip Morris, Inc. web site,
[55]Lorillard, Inc. web site,
[56]R.J. Reynolds Tobacco Company web site.

RESULTS

Introduction of pyrazines in cigarettes

The first US Surgeon General Report in 1964, which greatly increased concerns about the dangers of smoking, and the decline in cigarette sales beginning for the first time since World War II gave a major impetus to the tobacco industry's efforts to increase product appeal.[61] Tobacco manufacturers introduced new cigarette brands in response to these concerns, using filter ventilation, which lowered tar and nicotine yields or altered ratios measured under a standardised machine-based testing protocol.[38] The 'low-tar' cigarettes were found to have diminished taste, aroma and flavour and a weaker impact on receptors in the throat.[62 63] Facing a decrease in smoking and continuing 2% annual decline in cigarette sales, Philip Morris (PM) endeavoured to develop cigarettes with even lower tar yields, yet with taste and flavour that would satisfy smokers' 'palates and needs'.[62]

PM achieved a major breakthrough in this area by developing a 'full-flavour, low-tar product', marketed under the MERIT brand, which was the first 'light' cigarette.[62] The company accomplished this by first selecting out components of the volatile fraction of the particulate phase that contributed the greatest odour intensity from among the multitudes of aromatic chemicals and substances in tobacco smoke.[62] The gas chromatographic fractions of approximately 100 distinctive tobacco smoke flavourants were selected on the basis of high odour intensity as perceived by human participants using vapour dilution olfactometry.[62] The molecular structures of these compounds were then tentatively identified by high resolution mass spectrometry and by comparing the 'cracking', a term used by PM for fragmentation patterns, with known reference spectra. PM then incorporated the flavourants of highest intensity into the variety of compounds to be added to the reconstituted tobacco sheet. The reformulated cigarette flavour systems provided the taste, flavour and aroma qualities of the low-tar delivery cigarettes.[62] Finally, the company used panels of trained

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flavour experts to evaluate the smoke flavour of prototypes. PM's research and development resulted in a cigarette yielding less than 9 mg tar with a smoke flavour of much higher tar yielding products.[62]

An extensive consumer testing programme of the new MERIT product was conducted, including blind interviews with nearly 3000 smoker panellists.[62 64] The majority of consumer participants reported that the new MERIT was equal or superior in taste to brands that delivered 60% more tar. Advertisements touted the product's 'enriched flavor' and described, "After twelve years of intensive research, Philip Morris scientists isolated certain key ingredients in smoke that deliver taste way out of proportion to tar." [65] (figure 1). This brand went on to capture a significant share of the low-tar cigarette market following its national launch in 1976.[62]

PM called the new flavour formulation 'Super Juice', which contained 2,6-dimethyl pyrazine, tetramethyl pyrazine and trimethyl pyrazine as well as acetic acid, cyclotene, maltol, isobutyric acid and 1-methyl indole.[66] Reverse engineering and research by British American Tobacco of PM products, MERIT, MERIT Menthol, Marlboro and Marlboro Lights identified at least six pyrazines: 2-methylpyrazine, methylethylpyrazine, dimethylethylpyrazine, 2,3-dimethylpyrazine, 2,6-dimethylpyrazine, trimethylpyrazine and tetramethylpyrazine, and found that pyrazines contribute to the burley flavour, which is a common characteristic of many PM brands (isomers noted only where referenced in document).[67] In the USA in the late 1970s, 'Super Juice'-like compounds were added to Marlboro Lights, which is now called 'Marlboro Gold'. Ingredients also included essential oils, inorganic acids and other constituents, added to a reconstituted tobacco sheet with diammonium phosphate, which appears to have allowed better control of constituent release.[68] Marlboro Lights have since become the leading selling cigarette brand.

Pyrazine flavour profiles

Pyrazines are heterocyclic aromatic organic compounds with the underlying chemical formula $C_4H_4N_2$. They are formed under pyrolytic conditions (temperatures ≥100°C) via the Maillard Browning reaction between amines and carbonyl compounds (generally sugars)[69 70] (figure 2), which occurs during the curing of tobacco leaf and during the smoking process.[71 72] Numerous pyrazine compounds have been detected in foods, which arise from the common practice of heating and Maillard

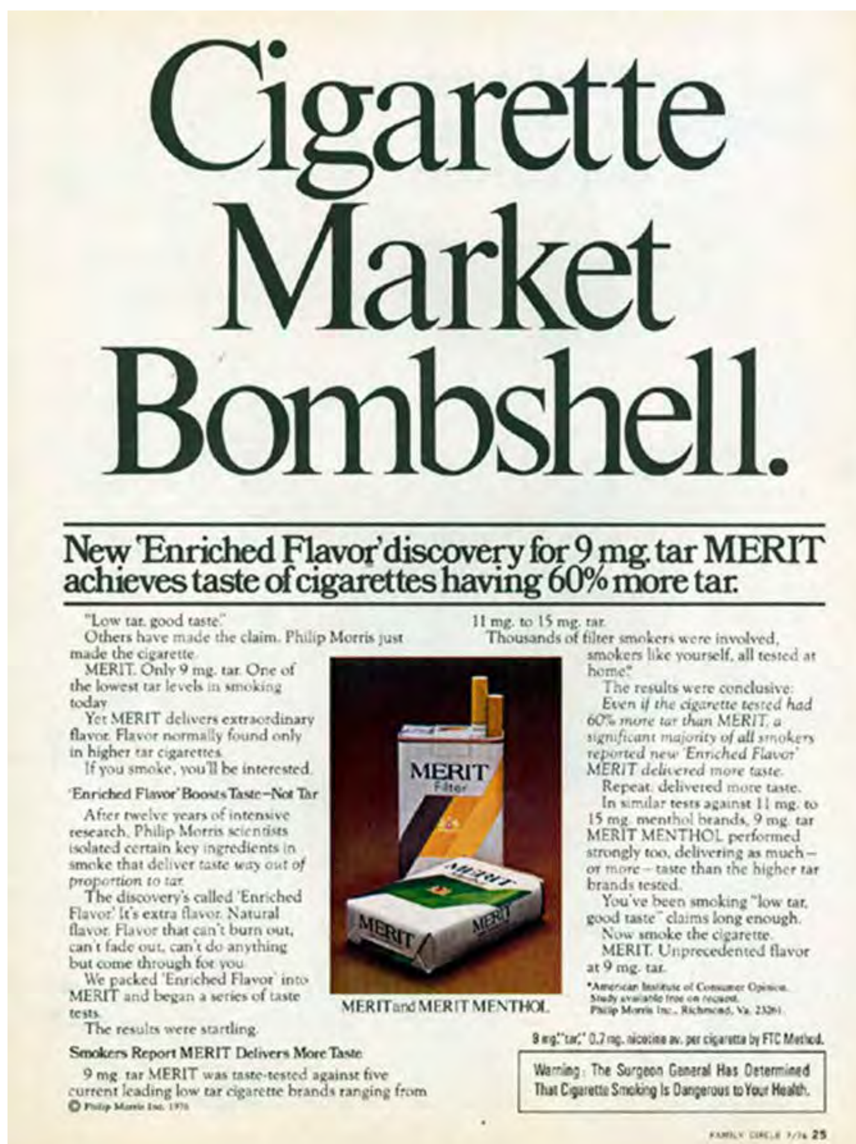

Figure 1 Advertisement for new 'Enriched Flavor' MERIT cigarettes (1976).

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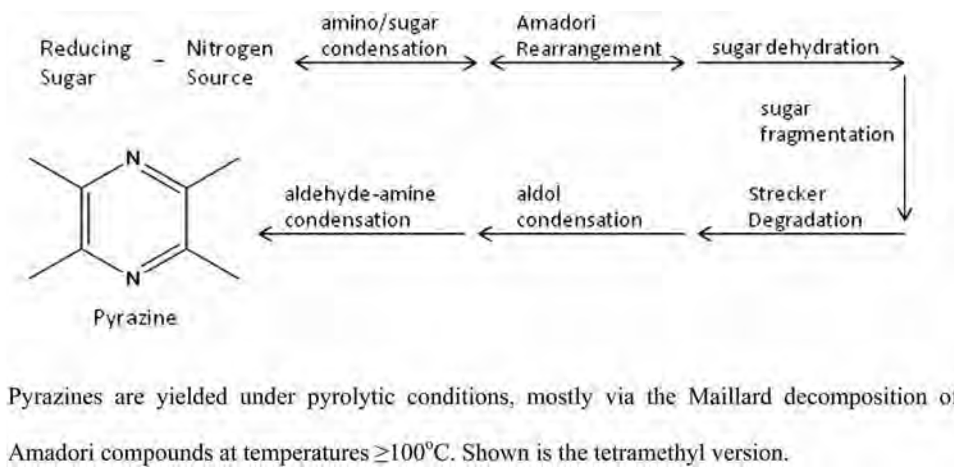

Figure 2 Graphic representation of the Maillard Browning reaction in the formation of pyrazines.

Browning reaction of sugars with protein and ammonia, providing a distinctive flavour. Other pyrazine compounds have been synthesised and promoted as flavouring agents because of their unique organoleptic properties and flavour and aroma profiles.[73–77] Pyrazines are 1 of 18 chemical classes of flavouring materials used in combustible tobacco products as described by Leffingwell *et al*.[78] They have been said to be among the most important compounds characterising the aroma and flavour of tobacco and tobacco smoke, contributing the 'brown notes' in general, and at least in some cases the cocoa, nutty or popcorn-type flavour notes.[79]

Chemosensory effects

Pyrazines are known to act on chemoreceptors, sensory receptors that transduce chemical signals into *action potentials*.[80] In addition to conveying the classical senses of taste and smell in humans, the mouth, nose and airways also contain chemosensory nerve endings of the trigeminal nerve.[81] These can be activated by physical stimuli as well as by a large array of chemical agents, leading to sensations such as burning, cooling and tingling, and contributing to flavour even in the absence of an olfactory percept.[82] Chemosensory effects of some other additives to cigarettes have been described, including essential oils (eg, menthol)[83] and organic acids (eg, levulinic acid).[84]

A report by the Tobacco Product Scientific Advisory Committee to the FDA described menthol's actions on transient receptor potential (TRP) channels, in particular TRPM8, which produce cooling and analgesia at low doses, irritation and pain at high doses, and desensitisation of the receptors with prolonged stimulation.[85] The report described how the addition of menthol in cigarettes creates perceptions of smoothness at low levels and analgesia at high levels and reduces the discomfort of smoking in long-term users. Results of population studies cited in the report showed youth being more likely to initiate smoking with a low menthol brand (eg, Newport), and older adults being less likely with a high menthol brand (eg, Kool).[85] An earlier review of internal tobacco industry documents reported the addition of levulinic acid to cigarettes to increase nicotine yields while enhancing perceptions of smoothness and mildness.[84 86]

Important chemosensory effects of pyrazines identified by the industry include smoothing, which may enhance the ease of inhalation and nicotine deposition by reducing the harshness and irritating effects of nicotine and other tobacco smoke constituents in the airways.[87] PM's internal documents of 1990 pertaining to the company's chemical senses research programme describe how a "chain of events from stimulation in the mouth, the throat and at the olfactory level leads to transmembrane electrical signals which are integrated in the brain."[88] According to these documents, diffusion and binding of constituents to receptors at sites of action, generation of action potentials, transmembrane signalling and integration of the diverse stimulus signals result in percepts (perceptions), which the company attempted to balance in order to promote high consumer acceptance and continued use as opposed to rejection of the product.[89]

Pyrazines and learned behaviour

Pyrazine stimulation of olfactory receptors may enhance learned behaviour, either by acting alone or in combination with other sensory modality stimuli.[90 91] Human responses to chemosensory and olfactory effects that are associated with emotionally significant experiences can become constitutional through neuroplastic changes in the olfactory pathways to the limbic system as well as other areas of the brain associated with hedonic perception.[92 93] Such events can reinforce smoking through associative learning and become cues for increased hedonic valence of stimuli[94] and motivate increased desire or wanting, or even unrestrained consumption.

DISCUSSION

This is the first report to document the tobacco industry's incorporation of pyrazine compounds into cigarettes since the early 1970s which appear to contribute to the products' appeal and abuse potential. Effects of pyrazines in cigarettes as described in industry documents reflect a range of processes by which such non-nicotine constituents might increase tobacco product abuse potential.[84] Pyrazines may act in concert with nicotine either by chemosensory effects that reduce noxious sensations such as irritation in the upper ways and ease nicotine uptake and entry into the lung. They may also act by chemosensory effects that reinforce the learned behaviour of smoking, enhance elasticity and help optimise nicotine dosing to achieve a desired delivery to the brain and satisfy a smoker's need for the drug based on mood and circumstances.[95] Several pyrazine derivatives have also been found to potentiate 5-HT binding to receptors in the central nervous system, which results in enhanced dopamine release independently of nicotine.[96–98]

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Chemosensory effects such as perceived smoothing and coolness (tactile) are associated with decreased aversion to smoking from the harshness and irritation of initial exposure to nicotine among novice smokers.[99 100] Similar effects have been described for menthol.[84] These effects might be a factor in smokers switching to 'low-tar' brands as an alternative to quitting smoking, going beyond the cognitive perception of reduced disease risk, to the emotive, physical perception that the smoke is 'smoother' and thus less harmful. Further, an RJR 1986 brand report describes the company's targeting of males 18–24 years of age by increasing the smoothness and masking the harshness and irritation of tobacco smoke.[101] The observed effects of pyrazines on secondhand smoke (SHS) demonstrate that these compounds were also used to reduce the irritation from SHS among non-smokers.[102] If non-smokers exposed to SHS perceive less risk due to lower irritation, without an actual reduction in their toxic constituents and effects, pyrazines might be classifiable as 'potentially hazardous constituents' under Section 904 of the Family Smoking and Tobacco Prevention Act of 2009 (FSPTCA).

Although independent research has been conducted on the effects on tobacco use of distal cueing from visual exposure to tobacco advertising and from social stimuli, little attention outside of tobacco manufacturers has previously been given to the more proximal cues that directly stimulate receptors of the head and neck.[89] The sensory inputs of pyrazine flavour additives might also provide cues for reward-related learned behaviours and could play a critical role in the development, maintenance and relapse of tobacco dependence. They could increase the attractiveness of smoking, particularly among youth.[103] Substantial evidence exists to suggest that flavour ingredients are used in cigarette 'starter' products, which increase cigarette experimentation and may help establish smoking behaviours that could lead to a lifetime of addiction.[103]

The FSPTCA explicitly bans the use of additives in cigarettes that are 'characterising flavours', which as defined by FDA food regulations are those that have taste or gustatory (eg, sweet, salt, sour, bitter) effects and are used in labelling, such as 'chocolate' flavoured cigarettes. However, a 'characterising' gustatory flavour may have relatively little significance if the major effect of an additive is on the olfactory and tactile receptors. British-American Tobacco concluded from research conducted that the prime sensorial experiences of smoking are associated with chemosensory flavour (odours, aroma) and irritation (tactile) sensations, whereas the gustatory qualities were found to be relatively less important for product attractiveness and appeal.[104] Flavour ingredients such as cocoa, licorice or vanilla have remained present in major cigarettes brands since prior to the ban's implementation,[54] which raises questions about the efficacy of the ban on the use of flavour ingredients and their consequential effects. When defining 'characterising' flavours for combusted tobacco products, the FDA Center for Tobacco Products should consider the distinction between flavours whose effects are primarily gustatory and flavours with olfactory or tactile effects.

Experimental use of electronic nicotine delivery systems (ENDS) has been rapidly increasing among teens.[105–108] Not surprisingly, the liquid flavour fluid formulations of ENDS include pyrazine additives such as 2,3,5,6-tetramethyl-pyrazine (0.9–1.5%), 2,3,5-trimethylpyrazine (0.3–4.5%) and acetylpyrazine (0.4–1.6%),[109] which also appear on the aforementioned lists of cigarette additives. Taken together, pyrazines appear to increase product appeal and make it easier for non-smokers to initiate smoking, more difficult for current smokers to quit, much easier for former smokers to relapse into smoking, and may mask the risks of both active and passive smoking.

The present findings should be interpreted in the context of the unique challenges of tobacco document research and known limitations with respect to documents availability. Access to the most recent industry documents is limited; use of terminology, practices and methods varies between companies and over time; and industry documents pertaining to pyrazines since the 1990s are largely unknown. Research conducted by industry is for business and commercial purposes, has not been peer reviewed and cannot be considered to be conclusive, absent independent confirmation. Therefore, a larger body of evidence should be considered with respect to the implications of these findings for public health and policy.

Future studies could focus on understanding the pivotal roles of pyrazines, their derivatives and other 'flavour' additives that stimulate neural receptors in neurobiological pathways, and actions in areas of the brain that affect abuse liability. Research could be conducted to examine the physiological and pharmacological actions of pyrazines and provide insight into the transduction mechanisms, receptor structure and chemical structure-activity relationships. Electrophysiological responses to chemosensory stimulants using radioactive labelled pyrazines and functional MRI and EEG could highlight specific areas of the brain stimulated by pyrazines.

The tobacco industry has long been interested in maximising the attractiveness, appeal, ease-of-use and low health-risk perceptions of tobacco products in a highly competitive and unregulated market in order to increase sales and market share.[29 36–38] To that end, manufacturers have researched and designed cigarettes with constituents that act independently of as well as synergistically with nicotine and may enhance abuse potential. The findings that are provided by these and other reports may help enable regulators such as the FDA, Health Canada, European Union and the WHO to develop standards to reverse these actions and reduce the addictiveness of tobacco products.

What this paper adds

- ▶ Nicotine is known as the drug that is responsible for the addicted behaviour of tobacco users, but it has been argued that non-nicotine factors are also essential to account for the intense addictive properties of tobacco smoking and high relapse rates among smokers after quitting.
- ▶ This study reveals how some tobacco manufacturers innovated with the use of pyrazines as additives. Pyrazines have been reported to have chemosensory and pharmacological properties and appear to be widely used now in cigarette brands.
- ▶ Pyrazines may help to optimise nicotine delivery and dosing, and promote addiction through cueing, learned behaviour and/or direct effects.

Disclaimer This research was conducted by the authors while at the Harvard School of Public Health. Dr Connolly is now Professor of Research at Northeastern University.

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Brief Report

High-Intensity Sweeteners in Alternative Tobacco Products

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Abstract

Introduction: Sweeteners in tobacco products may influence use initiation and reinforcement, with special appeal to adolescents. Recent analytical studies of smokeless tobacco products (snuff, snus, dissolvables) detected flavorants identical to those added to confectionary products such as hard candy and chewing gum. However, these studies did not determine the levels of sweeteners. The objective of the present study was to quantify added sweeteners in smokeless tobacco products, a dissolvable product, electronic cigarette liquids and to compare with sweetener levels in confectionary products.
Methods: Sweetener content of US-sourced smokeless tobacco, electronic cigarette liquid, and confectionary product samples was analyzed by liquid chromatography-electrospray ionization–mass spectrometry (LC-ESI-MS).
Results: All smokeless products contained synthetic high intensity sweeteners, with snus and dissolvables exceeding levels in confectionary products (as much as 25-fold). All snus samples contained sucralose and most also aspartame, but no saccharin. In contrast, all moist snuff samples contained saccharin. The dissolvable sample contained sucralose and sorbitol. Ethyl maltol was the most common sweet-associated component in electronic cigarette liquids.
Discussion: Sweetener content was dependent on product category, with saccharin in moist snuff, an older category, sucralose added at high levels to more recently introduced products (snus, dissolvable) and ethyl maltol in electronic cigarette liquid. The very high sweetener concentrations may be necessary for the consumer to tolerate the otherwise aversive flavors of tobacco ingredients. Regulation of sweetener levels in smokeless tobacco products may be an effective measure to modify product attractiveness, initiation and use patterns.
Implications: Dissolvables, snus and electronic cigarettes have been promoted as risk-mitigation products due to their relatively low content of nitrosamines and other tobacco toxicants. This study is the first to quantify high intensity sweeteners in snus and dissolvable products. Snus and dissolvables contain the high intensity sweetener, sucralose, at levels higher than in confectionary products. The high sweetness of alternative tobacco products makes these products attractive to adolescents. Regulation of sweetener content in non-cigarette products is suggested as an efficient means to control product palatability and to reduce initiation in adolescents.

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Introduction

In the United States, the Family Smoking Prevention and Tobacco Control Act (FSPTCA) restricts the sales of flavored cigarettes, with the exemption of menthol cigarettes. These restrictions do not apply to smokeless tobacco products, cigars, and electronic cigarettes. These products are available in a wide range of flavors with novel flavor combinations introduced almost daily. The presence of characterizing flavor additives is expected to attract both smokers and non-smokers, and especially adolescents.[1–3] Previous studies have noted similarities in the content of flavor chemicals in tobacco products and confectionary products such as hard candy, mints, and chewing gum.[4,5] Tobacco flavorants include many of the esters, alcohols, terpenes, and aromatic chemicals added to foods. For example, benzyl alcohol is used as a flavoring both in cherry candies and cherry-flavored tobacco products.[5] Electronic cigarette liquids also contain a wide range of known flavor chemicals used in the food industry.[6]

In contrast to these aroma flavorings, only limited information is available about the presence of sweeteners in the currently marketed smokeless tobacco products and electronic cigarette liquids. Traditionally, chewing tobacco and moist snuff have been sweetened either with table sugar (sucrose), causing documented oral health problems in users, or with saccharin.[7,8] Tobacco Industry Documents list sweetener contents in some products, however, this information is likely outdated and new sweeteners and product categories have been introduced.[9,10] For currently marketed products manufacturers list sweeteners as ingredients, including saccharin and sucralose, high intensity sweeteners several hundred times sweeter than sucrose.[10–16] The quantities and types of sweeteners contained in individual products, and how these compare to confectionary products, are unknown.

Sweeteners have powerful psychophysical effects and are known to mask the unpleasant taste of tobacco constituents and reduce oral aversion to nicotine in animals.[17,18] Analogous to candies and sweetened beverages designed to appeal to teenagers and young adults, addition of sweeteners to tobacco products might promote product uptake and determine preference and use patterns.[19,20]

In the present study, 18 tobacco products, including snus, moist snuff, dissolvable tobacco, and electronic cigarette liquids marketed in the United States were analyzed by liquid chromatography–mass spectrometry [LC-MS], to determine levels of natural and high-intensity sweeteners. Sweetener contents in representative confectionary products and soda were analyzed and compared.

Methods

Product Samples

Sixteen tobacco products were purchased from stores in the New Haven, CT, area including four snus products, five moist snuffs, five electronic cigarette cartridges, and two electronic cigarette refill liquids. One electronic refill liquid was purchased online from the manufacturer (V2), and one dissolvable tobacco product was procured from an out of state online vendor. For comparison with other high-intensity sweetened products, four sugar-free confectionary products of different brands and two sugar-free beverages of different brands were bought from area stores (Supplementary Table 1).

Chemical Analysis

Levels of synthetic high-intensity sweeteners (sucralose, cyclamates, saccharin, aspartame, acesulfame potassium), bio-derived high-intensity sweeteners (stevioside, glycyrrhizin), sugar alcohols, natural sugars, and other constituents were determined by a modified LC-MS method previously used in our laboratory for the analysis of sweetener content in environmental samples[21] (Supplementary Methods). This technique provides a conservative estimate of sweetener levels; in some samples the tobacco matrix may cause minor suppression of MS response.[22]

Results

All tested products contained no or only very small amounts of the sugars, glucose (<0.072 % w/w) or sucrose (<0.024 % w/w). As expected, the high-intensity sweeteners, sucralose, or aspartame, were detected in the soda and confectionary products (Table 1). The bulk of all mint lozenge products consisted of the sugar alcohol, sorbitol. Sucralose was detected in all snus products at high levels, with three of the four snus products also containing aspartame (Table 1). Saccharin was only detected in the moist snuff products. Snuff products contained no aspartame and only one contained a comparably small amount of sucralose (Skoal mint Xtra). No high-intensity sweeteners were detected in the electronic cigarette liquids tested (Table 1). Two of the liquids contained traces of sorbitol (<0.003 % w/w). Ethyl maltol was detected in six of the eight liquids. All the E-liquids had glycerol as carrier, three of them also contained propylene glycol (Supplementary Table 2). The dissolvable product consisted of a large percentage (59.0 ± 3.0 % w/w) of sorbitol, and contained a high amount of sucralose, but no aspartame or saccharin (Table 1).

The average total amount of sucralose per product unit (piece, lozenge, or strip) was calculated for the sucralose-containing confectionary and smokeless tobacco products (Figure 1). Amounts of sucralose per unit were much higher in the snus products (>6 mg/unit, one product > 11 mg/unit) than in the confectionary products (<0.4 mg/unit). The single snuff product containing sucralose had <1 mg/unit. Sucralose content in the dissolvable product was higher (4.48 mg/unit).

Among the nine snus and moist snuff products, seven were in the form of small pouches. The content of sweeteners in the pouch material, comprising about 10% of total product weight, followed distributions in the bulk products, but concentrations were all lower (Supplementary Tables 3–5).

Discussion

In the present study, all the tested snus and moist snuff products contained high-intensity sweeteners. All tested moist snuff products contained saccharin as the sole added synthetic sweetener with one exception containing roughly equal amounts of both saccharin and sucralose. Manufacturers have been adding saccharin to smokeless tobacco products since 1891, when R. J. Reynolds introduced saccharin-sweetened chewing tobacco.[7] In fact, the tobacco industry was the first to license synthetic high-intensity sweeteners to add to consumer products, likely to improve shelf stability, product uniformity and create brand identity.[7] The majority of the moist snuff products investigated here were brought to market prior to introduction of sucralose in 1999.[10] Saccharin, in addition to being perceived as sweet, has a bitter taste, a property not shared by sucralose and aspartame that have replaced saccharin in most high-intensity sweetened food products.[3] It is possible that tobacco manufacturers did not replace saccharin in snuff products because long term users have

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Table 1. Sweetener Levels in Alternative Tobacco Products, Soda, and Confectionary Products

Category	Product	Sorbitol	Aspartame	Saccharin	Sucralose	Ethyl maltol
Soda	Cherry Limeade				0.0145 ± 0.0022	
	Waist Watcher diet				0.0143 ± 0.0023	
Candy	Jelly Belly sugar free	0.0388 ± 0.0004			0.0369 ± 0.0113	
Mint lozenge	Life Savers sugar free	85.3 ± 0.8	0.270 ± 0.003			
	Ice Breakers sugar free	96.7 ± 0.71	0.820 ± 0.002			
	Altoids smalls peppermint	38.9 ± 1.18			0.023 ± 0.006	
Gum	Trident white peppermint	0.375 ± 0.016	0.132 ± 0.004		0.0132 ± 0.0014	
Snus	Camel mint	<0.001	0.00932 ± 0.00021		1.12 ± 0.06	
	Camel mellow		0.0128 ± 0.0002		1.26 ± 0.06	
	Marlboro mint				1.32 ± 0.07	
	Marlboro mellow		0.00759 ± 0.00080		0.690 ± 0.035	
Moist snuff	Kodiak mint			0.0895 ± 0.0131		
	Kodiak wintergreen			0.0457 ± 0.0006		
	Skoal mint classic			0.0563 ± 0.0030		
	Skoal mint – Xtra			0.0593 ± 0.0033	0.0519 ± 0.0010	
	Skoal classic straight			0.0587 ± 0.0042		
E-cigarette	Blu classic tobacco	<0.003				<0.0003
	Blu magnificent menthol	<0.0005				0.00133 ± 0.00005
	Blu vanilla					0.00908 ± 0.00045
	Finiti rich tobacco					
	Finiti cool menthol					
	CT menthol					0.00311 ± 0016
	CT packed					0.00338 ± 0.00017
	V2 red					0.0890 ± 0.001
Dissolvable	Arriva	59.0 ± 3.0			1.79 ± 0.09	

Data are stated as % w/w of product unit as received; means from three samples each, with standard error; blank fields indicate nondetected (n.d.)

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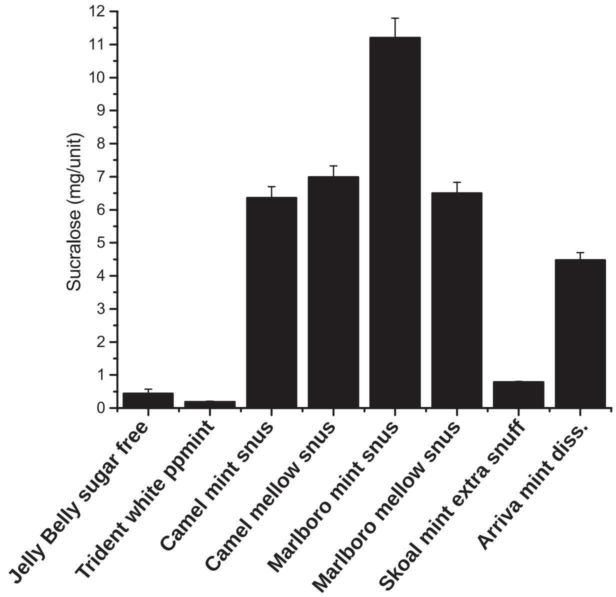

Figure 1. Comparison of sucralose content in product units of confectionary products and snus. Average content of sucralose in mg per piece or pouch is displayed. Data derived from Table 1.

been habituated to its taste profile and would disapprove of a change to other sweeteners. This view is also supported by the observation that saccharin content in the currently marketed products analyzed here did not differ much from levels determined in snuff products more than 20 years ago.[9] The lower price of saccharin compared to sucralose may also explain its continued use in the product category.

In contrast, all four snus products tested here contained sucralose, most in combination with aspartame. Snus products were introduced to the US market in 2006 when sucralose was already widely used in food products.[23] Sucralose content in the tested snus products, both % w/w and weight per product unit, exceeded the levels in any of the other solid confectionary products (candy, mint lozenges, chewing gum). The absolute amounts of sucralose in snus were 14- to 25-fold higher than the highest content found in a candy product. The bulk of some of the confectionary products consisted of a high percentage of sorbitol, a sugar alcohol with a sweetness lower than table sugar (sucrose). Together with sorbitol, smaller amounts of sucralose and aspartame are likely sufficient for these products to reach the desired level of sweetness. Intriguingly, the dissolvable tobacco product tested here also contained substantial amounts of sorbitol with sucralose added at an amount approaching that found in the snus products.

Six of the eight E-cigarette liquids contained ethyl maltol, known to be a sweet taste potentiator and previously reported in E-liquids.[5,6,24] Propylene glycol and glycerol, the major constituents of the E-liquids tested, are lightly sweet. Their sweetness may be enhanced by ethyl maltol and other popular sweet-associated flavorings.[25,26] Ethyl maltol was awarded GRAS status (Generally Recognized As Safe) from the Flavor & Extracts Manufacturers Association (FEMA) for the intended use as a food additive. Some E-liquids vendors advertise the GRAS label as supportive of safety for the flavorants added to their products. However, FEMA has repudiated these claims since GRAS status only applies to use in food and not in E-cigarettes for inhalational delivery.[27] It is unknown whether ethyl maltol is chemically stable in E-liquids, and when these are heated and vaporized.

High-intensity sweeteners were not detected in the E-liquids tested suggesting that the major manufacturers of E-cigarettes and -liquids do not include high-intensity sweeteners in their E-liquid formulations. However, online vendors currently offer sucralose liquids for sale to customers to mix with their E-liquids. While sucralose is an FDA-approved food additive, its health effects and metabolic fate when delivered by E-cigarette are unknown.

In summary, the current findings suggest that US-marketed new smokeless tobacco products, snus and dissolvables, are more highly sweetened than confectionary products. With sucralose perceived as 600 times sweeter than sugar, and added aspartame, the sweetness of snus and dissolvable products exceed the sweetness of their unit (pouch or lozenge) weight in sugar. Optimal sweetener levels were likely determined in tests by company-internal panelists and consumer groups, suggesting that higher levels of sweetness are required to establish palatability and liking of these tobacco-containing products. The intense sweetness may be necessary to mask the adverse taste and sensory effects of the processed tobacco that contains irritating and bitter nicotine and other tobacco constituents with adverse tastes. Sweeteners are known to suppress the perception of bitter taste and to inhibit the sensation of irritation.[28] While sucralose uptake from snus alone is unlikely to exceed the FDA-determined acceptable daily intake (ADI), daily repeated use of snus together with consumption of other sucralose-sweetened products such as soda, sweetener packets and food products may lead to continuous high exposure. Recent studies revealed that high-intensity sweeteners affected metabolic signaling in pancreatic beta cells and changed the composition of the gut microbiome, potentially contributing to metabolic dysregulation.[29]

Dissolvables and snus have been promoted as risk-mitigation products due to their relatively low content of nitrosamines and other tobacco toxicants. While not as popular, these products may increase the risk of polytobacco use and their intense sweetness is of concern since it may appeal especially to adolescents who initiate tobacco product use.[30,31] In addition to E-cigarettes, other sweet flavored tobacco products such as small cigars have made rapid inroads among adolescent populations and remain unregulated.[32,33] Among the wide variety of flavors offered intense sweetness appears to be a common denominator in the majority of the newly introduced products. Thus, the regulation of sweetener content may represent an efficient means to control palatability of a wide range of products and to reduce tobacco product use initiation.

Supplementary Material

Supplementary Tables 1 to 5 and Supplementary Methods can be found online at http://www.ntr.oxfordjournals.org

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Declaration of Interests

The authors declare no competing interests.

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Review

Sugars as tobacco ingredient: Effects on mainstream smoke composition

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Abstract

Sugars are natural tobacco components, and are also frequently added to tobacco during the manufacturing process. This review describes the fate of sugars during tobacco smoking, in particular the effect of tobacco sugars on mainstream smoke composition. In natural tobacco, sugars can be present in levels up to 20 wt%. In addition, various sugars are added in tobacco manufacturing in amounts up to 4 wt% per sugar. The added sugars are usually reported to serve as flavour/casing and humectant. However, sugars also promote tobacco smoking, because they generate acids that neutralize the harsh taste and throat impact of tobacco smoke. Moreover, the sweet taste and the agreeable smell of caramelized sugar flavors are appreciated in particular by starting adolescent smokers. Finally, sugars generate acetaldehyde, which has addictive properties and acts synergistically with nicotine in rodents. Apart from these consumption-enhancing pyrolysis products, many toxic (including carcinogenic) smoke compounds are generated from sugars. In particular, sugars increase the level of formaldehyde, acetaldehyde, acetone, acrolein, and 2-furfural in tobacco smoke. It is concluded that sugars in tobacco significantly contribute to the adverse health effects of tobacco smoking.
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Keywords: Tobacco; Additives; Sugar; Pyrolysis; Smoke; Addiction

Contents

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1. Introduction

Tobacco smoke constitutes the most significant cause of morbidity and mortality in the world (WHO, 2000). In 2000, an estimated 4.8 million premature deaths in the world were attributable to tobacco smoking due to cardiovascular diseases (~35%), chronic obstructive pulmonary disease (~20%), and various types of cancer, in particular lung cancer (~18%) (Hoffmann and Hoffmann, 1997; Hoffmann et al., 2001; Ezzati and Lopez, 2003; Byrd, 2004). Upper limits for the most harmful components in tobacco smoke are expected to be set in the near future in an attempt to decrease the negative impact of smoking (Bates et al., 1999b; IARC, 2004; Henningfield et al., 2004).

The composition of tobacco smoke depends on the chemical nature of natural tobacco, the various ingredients added to tobacco, and the design characteristics of the product. Since consumer acceptance of tobacco smoke is, amongst others, proportional to the sugar level in tobacco (Shelar et al., 1992; Rodgman, 2002), manufacturers select natural high-sugar tobaccos or add sugars during tobacco manufacturing.

Sugars are generally recognized as being safe (GRAS) when used in food products, but this recognition does not imply their safety as tobacco additive. In burning tobacco, sugars are pyrolyzed, which results in a large number of highly toxic or even carcinogenic degradation products (Vleeming et al., 2005). In addition, compounds are generally more toxic via the inhalatory route as compared to their toxicity following ingestion, because the respiratory system largely lacks the detoxifying metabolic pathways of the digestive system (Bates et al., 1999a; Fowles, 2001; Vleeming et al., 2005).

This paper reviews the generation of heating/combustion products from sugars in tobacco (naturally present and/or intentionally added), which serve to mask the adverse taste of tobacco smoke and enhance its addictiveness.

2. Sugars in tobacco products

2.1. Amounts and identity of sugars in tobacco products

Sugars like glucose, fructose and sucrose, are natural components of tobacco (Fox, 1993; Leffingwell, 1999). Sugars in tobacco are formed via enzymatic hydrolysis of starch during the period after priming (harvesting) and the early stages of the curing process (Leffingwell, 1999). The sugar content of tobacco types is highly variable, but primarily depends on the method of curing (Leffingwell, 1999). For instance, sugars are largely metabolized during air-curing (Burley, Maryland and cigars) (Elson et al., 1972; Fox, 1993; Leffingwell, 1999; Seeman et al., 2003). By contrast, flue- and sun-cured tobaccos contain higher sugar levels because the metabolizing enzymes are rapidly inactivated at the relatively high temperatures employed during this curing process (Elson et al., 1972). The latter curing process results in sugar levels of over 20 (flue-cured, like Virginia) and 10 (sun-cured, like Oriental) weight percent of dried tobacco, respectively (Elson et al., 1972; Fox, 1993; Leffingwell, 1999; Seeman et al., 2003). A typical American blended product contains approximately 25–35% of both flue-cured and air-cured tobaccos, and 3–15% of Oriental tobacco, together with smaller amounts of other tobaccos (Fisher, 1999). Its sugar content is about 12%, of which 8% is of natural origin (Fox, 1993).

During the manufacturing process of a tobacco product, up to 13% w/w of sugars and sweeteners are intentionally added to tobacco (Leffingwell, 1999; Fowles and Bates, 2000; Rodgman, 2002; Seeman et al., 2003). Sugars used as cigarette additive include glucose, fructose, invert sugar (glucose/fructose mixture), and sucrose (Leffingwell, 1999; Seeman et al., 2003). In addition, many tobacco additives contain high amounts of sugars, e.g. fruit juices, honeys, molasses extracts, corn and maple syrups, and caramel (Fox, 1993; Rustemeier et al., 2002; Seeman et al., 2003).

Table 1 lists the amounts and functions of several carbohydrate additives as reported by five major tobacco manufacturers on their websites. These manufacturers do not report the amount of added sugar per brand, but give the so-called quantities not exceeded (QNEs). The QNE is the highest level of an ingredient that a manufacturer adds to any single brand, and is expressed as the percentage by weight (% w/w) of the additive in the tobacco blend (including moisture). Table 1 shows that all manufacturers add invert sugar (QNE-value typically 2%) and sucrose (QNE-value typically 3%).

In addition to mono- and disaccharides, natural tobacco contains considerable amounts of polysaccharides, such as cellulose, pectins, and starch (Schlotzhauer and Chortyk, 1987; Fox, 1993; Rodgman, 2002; Seeman et al., 2002). Some of these polysaccharides, like cellulose, are used as tobacco additive (see Table 1) (Fox, 1993). Typical blended cigarettes contain about 10% of cellulose, 10% of pectins, and 2% of starch (Fox, 1993; Leffingwell, 1999; Seeman et al., 2002). Thus, carbohydrates may comprise over 40% of the tobacco and accordingly largely determine the chemical composition of tobacco smoke (Leffingwell, 1999; Weeks, 1999; Rodgman, 2002). Although this review primarily focuses on mono- and disaccharides, the differences in pyrolyzation of polysaccharides and simple sugars will be addressed to estimate their relative contribution to mainstream smoke.

2.2. Function of sugars in tobacco

The tobacco companies claim that ingredients are added to tobacco products to aid the production process or to realize brand specifications (Vleeming et al., 2005). For instance, the website of BAT states: “Food-type ingredients and flavorings are added to balance the natural tobacco taste, to replace sugars lost in the curing process, and to give individual brands their characteristic flavor

Table 1
Amounts and functions of sugars, sugar containing additives and polysaccharides added to tobacco as reported by five major tobacco manufacturers on their websites (market in brackets)

Additive	Quantities not exceeded (% w/w) and function of sugar				
	BAT (Dutch)	PM (Dutch)	RJRT (World)	Gallaher (World)	JTI (Europe)
Glucose	0.005(a)	–	<0.001(a)	2.6(a)	0.7(a),(b)
Fructose	–	–	–	2.6(a)	0.0001(a),(b)
Invert sugar	3.2(c)	1.9(a),(b)	0.003(a)	2.4(a),(b)	1.5(a),(b)
Sucrose	0.84(c)	3.4(a),(b)	3.0(c)	3.0(a),(b)	4.0(a),(b)
Brown sugar	1.3(c)	–	3.0(c)	–	–
Honey	0.8(c)	–	2.3(c)	0.1(a)	0.1(a)
Glucose (corn) syrup	1.2(c)	–	3.8(a)	0.1(a)	0.4(a),(b)
Molasses, sugar cane	0.3(c)	–	–	0.1(a)	0.3(a)
Fig juice	0.04(a)	–	0.3(c)	0.1(a)	0.03(a)
Prune juice	1.4(c)	–	0.5(c)	0.1(a)	0.3(a),(d)
Cellulose	1.3(e)	–	3.6(f)	4.8(e)	1.5(f)

Selection of sugars was based on: (1) reported by at least two manufacturers, and (2) reported QNEs over 0.1% for at least two manufacturers or over 1% for at least one manufacturer.
(a) Flavor; (b) humectant; (c) casing ingredient; (d) plum juice; (e) Binder; (f) formulation aid.
BAT: British American Tobacco (British American Tobacco, 2004), PM: Philip Morris (Philip Morris International Inc., 2004), RJRT: R.J. Reynolds Tobacco Company (R.J. Reynolds Tobacco Company, 2005), Gallaher: Gallaher Group Plc. (Gallaher Group Plc., 2005), JTI: Japan Tobacco International (JT International, 2005).

and aroma. Other ingredients have more technological functions such as to control moisture, to protect against microbial degradation, and to act as binder or filler." (British American Tobacco, 2004). According to five main tobacco manufacturers, sugars serve as binder, casing ingredient, flavor, formulation aid or humectant (see Table 1).

Indeed, sugars are important for tobacco smoke flavoring (Leffingwell, 1999; Weeks, 1999; Seeman et al., 2003), considering for instance the differences in smoke flavor between flue-cured, bright tobaccos (high-sugar levels) and air-cured, Burley tobaccos (virtually no sugars) (Schlotzhauer and Chortyk, 1987). The tobacco industry probably also adds sugars to mask the bad harsh taste and the irritability of tobacco smoke. Finally, and not mentioned by tobacco companies, sugars are pro-addictive compounds. These consumption-enhancing effects of sugar will be addressed in Section 6.

3. Fate of sugars upon combustion

Due to the high content of sugars in tobacco products, their fate during smoking has been thoroughly investigated. As most of the naturally present sugars are non-volatile, only minor amounts of sugars (approximately 0.5% of glucose and sucrose) are transferred unchanged into the mainstream smoke (Gager et al., 1971a,b; Fox, 1993; Rodgman, 2002; Byrd et al., 2004). The larger part of the sugars will combust, pyrolyze or participate in pyrosynthesis processes (Schlotzhauer and Chortyk, 1987; Fox, 1993; Baker, 1999; Byrd, 2004).

Upon pyrolysis, sugars caramelize and break down into a mixture of organic acids and a variety of aldehydes (Creighton and Hirji, 1988; Shelar et al., 1992). The reactions involved, varying from chemical degradation and polymerization to condensation, are complex and the chemical identity of the final reaction products is poorly known (Tomasik, 1989). First, thermally induced enolization and dehydration reactions generate osuloses (α-dicarbonyl compounds), the key intermediates of thermal caramelization (Fig. 1) (Tomasik, 1989; Ledl and Schleicher, 1990; Hollnagel and Kroh, 2002). These osuloses may cyclise to furan derivatives (Tomasik, 1989). The principal degradation product in caramel is 5-hydroxymethyl furfural (an intramolecular condensation product of deoxyhexosulose) (Fadel and Farouk, 2002). The formed osuloses may also decompose into acids and aldehydes (Tomasik, 1989; Ledl and Schleicher, 1990).

Tobacco contains a variety of amines (ammonium compounds, amino acids, proteins) that are naturally present or have intentionally been added in considerable amounts (Leffingwell, 1999; Britt et al., 2004; Indiana Prevention

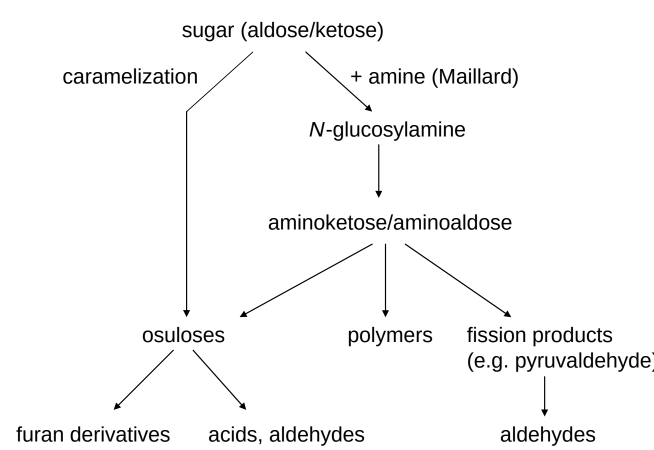

Fig. 1. Products formed from sugars via caramelization and via reaction with amines (Maillard reaction).

Resource Center, 2005). In addition to thermal caramelization, reducing sugars participate with such amines in a complex set of reactions that are collectively known as the Maillard reaction (Tomasik, 1989; Fadel and Farouk, 2002). Like in food processing, during smoking sugars react with amines to yield brown-colored Maillard reaction products that 'improve' the taste of tobacco smoke (Ledl and Schleicher, 1990; Coleman and Perfetti, 1997; Rodgman, 2002; Britt et al., 2004). In tobacco, Maillard reactions result in 1.5–2.0% w/w amino-sugar compounds (Leffingwell, 1999; Britt et al., 2004).

The initial step in the Maillard reaction involves condensation of a carbonyl group of a reducing sugar with an amino group, and results in *N*-substituted glycosylamines (Fig. 1). These compounds are thermally unstable and quickly undergo isomerization by Amadori rearrangement (if the sugar is an aldose) or Heynes rearrangement (if the sugar is a ketose) to give aminoketoses and aminoaldoses, respectively (Ledl and Schleicher, 1990; Coleman and Chung, 2002). Various compounds are formed from these aminoketoses and aminoaldoses (Tomasik, 1989; Ledl and Schleicher, 1990; Coleman and Perfetti, 1997), for example osuloses (as described above), melanoidin polymers, and fission products, such as diacetyl (2,3-butanedione), acetol (1-hydroxy-2-propanone) and pyruvaldehyde, which can react further to other aldehydes (Tomasik, 1989; Fadel and Farouk, 2002). In the following sections, the effects of the addition of sugars to tobacco on mainstream smoke, smoking behavior and consumer's health will be described.

4. Combustion of tobacco sugars: pyrolysis and products in mainstream smoke

Three methods are usually employed to investigate the identity of the compounds formed during the combustion process of a tobacco additive (Fox, 1993; Byrd, 2004; Byrd et al., 2004):

(1) Pyrolyzation of a single additive in absence of tobacco and subsequent analysis of the pyrolysis products. This technique is useful as a first screening of potential pyrolysis products, their thermal stability and the temperature at which they are formed (Baker and Bishop, 2004). However, the pyrolysis conditions only approximate the burning cigarette with regard to temperature and atmosphere and make no allowance for the presence of other tobacco and/or smoke components that may interact with the sugars (Fox, 1993; Byrd, 2004; Byrd et al., 2004).

(2) Burning (smoking) the tobacco that contains a specific amount of the additive and subsequent analysis of selected smoke components. The substantial loading of tobacco with the additive that is mostly required to obtain significant results may, however, affect the burning characteristics of the tobacco (Fox, 1993; Byrd, 2004; Byrd et al., 2004). Also, this method cannot determine whether the additive is a precursor or an enhancer of a certain smoke component (Torikaiu et al., 2005). These problems can be circumvented by:

(3) Burning the additive in the tobacco matrix, but labeled as radioactive isotope. The low quantities used here do not affect the burning characteristics of the tobacco (Byrd, 2004; Byrd et al., 2004), but the method is sophisticated and expensive (Fox, 1993).

4.1. *Pyrolysis of single ingredients and simple mixtures*

Table 2 describes the results of pyrolysis studies (two of the studies have been performed by tobacco companies). Pyrolysis of sugars or sugar-amino acid mixtures was performed at one temperature, often in inert atmospheres. Such study designs poorly reflect the conditions of burning cigarettes with oxygen levels ranging from 0% to 14% and the temperature in the burning zone ranging from ambient temperature to 900 °C (Stohs et al., 1997; Stotesbury et al., 1999; Baker and Bishop, 2004; Torikai et al., 2004). Since each entry reflects only part of the actual pyrolyzation process in cigarettes, it is important to consider a range of measurements that have been performed at different temperatures.

Various sugar pyrolysis products are reported with yields that depend on the pyrolysis temperature. Typical high temperature pyrolysis products are the polyaromatic hydrocarbons (PAHs) (Sanders et al., 2003). Indeed, PAHs are detected in the studies performed at >650 °C, but not in those performed <460 °C (see Table 2). In the lower temperature range, sugars degrade less vigorously, resulting in pyrolyzation products that resemble more closely the original sugar structure (Table 2).

With increasing temperature, less furan, furfural and 5-hydroxymethylfurfural is formed, whereas the yields of aliphatic aldehydes (such as acetaldehyde and acrolein) increase. Glucose, fructose and sucrose result in the same pyrolysis products, but the yields are different, e.g. fructose yields more furfural than glucose or sucrose, whereas glucose yields relatively more 5-hydroxymethyl furfural.

A large variety of products, including aldehydes, ketones, acids, pyrazines and pyridines, results from the Amadori reaction between sugars and amino acids. For instance, acrylamide is generated from asparagine and glucose (Friedman, 2003; Yaylayan et al., 2003), and furfural is generated from alanine and glucose (Yaylayan and Keyhani, 2000). The products from sugar-amine pyrolysis partly overlap with those of simple sugar pyrolysis, because the Maillard reaction includes catalyzed caramelization of sugars (Tomasik, 1989; Ledl and Schleicher, 1990; Fadel and Farouk, 2002).

The pyrolysis products of polysaccharides and simple sugars are similar, but their yields differ (Fox, 1993; Rodgman, 2002; Seeman et al., 2002; Sanders et al., 2003). As compared to cellulose, pyrolysis of simple sugars yields

Table 2
Pyrolysis products of sugars and sugar-amino acid mixtures (i.e. no tobacco matrix)

Sugar	Pyrolysis conditions and major products (yield in mg/g sugar or otherwise as indicated)
Fructose	840 °C in N_2 (Higman et al., 1970). Benzene 5.3; phenol 4.8; toluene 2.8; furfural 2.4; indene 2.1; styrene, xylenes 1.4; naphthalene 1.1; *p*-methylstyrene 0.7; ethylbenzene 0.7; alkyl-naphthalene 0.4; *o*-cresol 0.3; *m*-cresol, *p*-cresol 0.3; 5-methylfurfural 0.2; B[*a*]P 0.1 800 °C in N_2/air (Schlotzhauer et al., 1982). Furfural 38.6; 5-hydroxymethylfurfural 19.5 Rapidly heated to 650 °C in N_2 (Gilbert and Lindsey, 1957). Main PAHs (μg/g): acenaphthylene 1.0; fluorene 1.2; anthracene 1.4; pyrene 0.4; fluoranthrene 1.1; 3-methylpyrene 0.1; 1:2-benzanthracene 1.2; 3:4-benzpyrene 0.3 Heated to 900 °C at 6 °C/min. in He (Burton, 1976). Rel. amount (temperature of max. formation): formaldehyde 1680 (225 °C); acetaldehyde 96 (325 °C); acrolein 480 (425 °C); acetone 176 (325 °C); 2-butanone 188 (325 °C)
Glucose	Heated at 460 °C for 5 s; Curie-point pyrolysis[a] (Ohnishi and Kato, 1977). 1,6-Anhydro-β-D-glucopyranose (levoglucosan) 23; 1,6-anhydro-ß-D-glucofuranose 12; 5-hydroxy-methylfurfural 11; furfural 8 840 °C in N_2 (Higman et al., 1970). Phenol 6.2; benzene 4.6; toluene 2.6; naphthalene 1.4; furfural 1.3; styrene, xylenes 1.3; *m*-cresol, *p*-cresol 1.2; indene 1.1; *o*-cresol 1.1; ethylbenzene 0.8; *p*-methylstyrene 0.8; alkyl-naphthalene 0.6; 5-methylfurfural 0.4; acenaphthylene 0.2; B[*a*]P 0.05 Rapidly heated to 650 °C in N_2 (Gilbert and Lindsey, 1957). PAHs (μg/g): acenaphthylene 1.3; anthracene 0.4; pyrene 0.7; fluoranthrene 0.5; 1:2-benzanthracene 0.4; 1:2-benzpyrene 0.1; 3:4-benzpyrene 0.3 Heated to 250, 350 and 500 °C in stationary He (Kato, 1967). Relative amount of product at 250, 300 and 500 °C: acetaldehyde: 1.8, 5.2, 5.6; acetone: 1.7, 2.6, 3.1; furan: 2.1, 2.9, 1.1; diacetyl: 0.5, 1.0, 2.0; propionaldehyde: 0.8, 1.0, 1.5; furfural: 11.7, 12.5, 3.3; acrolein: 0.7, 1.5, 4.3; 5-methylfurfural: 1.9, 1.9, 0.5 Heated to 900 °C at 6 °C/min. in He (Burton, 1976). Rel. amount (temperature of max. formation): formaldehyde 238 (225 °C); acetaldehyde 255 (375 °C); acrolein 800 (400 °C); acetone 830 (400 °C); 2-butanone 875 (400 °C)
Sucrose	800 °C in N_2/air (Schlotzhauer et al., 1982). Furfural 27.7; 5-hydroxymethylfurfural 19.5 700 °C for 10 s in N_2 (Schlotzhauer et al., 1985). Total volatiles from pyrolysate (%): 2-fural-dehyde 67%; 5-methyl-2-furaldehyde 4%; 3-methylfuran 3%; 1,3-cyclo-pentane-dione 2%; 2-furan-methanol 2%; furancarboxylic acid methyl ester 2% Rapidly heated to 650 °C in N_2 (Gilbert and Lindsey, 1957). PAHs (μg/g): acenaphthylene 0.2; fluorene 0.1; anthracene 0.7; pyrene 0.2; fluoranthrene 0.4; 3-methylpyrene 0.2; 1:2-benzanthracene 0.4 Heated for 10 s at different *T*'s in N_2 (Schlotzhauer et al., 1986). 5-Hydroxymethylfurfural formed: 61 (350 °C); 83 (450 °C); 76 (550 °C); 66 (650 °C); 47 (750 °C) and 37 (850 °C) Heated to 900 °C at 6 °C/min in He (Burton, 1976). Rel. amount (temperature of max. formation): formaldehyde 920 (200 °C); acetaldehyde 140 (375 °C); acrolein 148 (325 °C); acetone 270 (425); 2-butanone 250 (375 °C)
Glucose-amino acids	Glucose-Ala heated to 210 °C at 50 °C/ms for 20 s (Yaylayan and Keyhani, 2000). Glycolaldehyde, pyruvaldehyde, furanmethanol, acetol, furfural, 2,3-pentanedione, 3-hydroxy-2-butanone, 2,3-butanedione Glucose-Asp to 300 or 700 °C at 10 °C/min in air[a] (Coleman and Perfetti, 1997). Ketones, furans, acetic acid, pyrroles, pyridines, methylpyridines, pyrazines Glucose-Leu to 300 or 700 °C at 10 °C/min in air[a] (Coleman and Perfetti, 1997). Ketones, 3-methyl-butanal, furans, acetic acid, pyrazines, 3-methylbutanoic acid, pyrroles Glucose-Pro 840 °C in He (Britt et al., 2004). mg/g mixture: pyrrole 6.4; benzene 5.8; benzonitrile quinoline 2.1; isoquinoline 0.49; phenanthracene 0.45 Glucose-Thr to 300 or 700 °C at 10 °C/min in air[a] (Coleman and Perfetti, 1997). Ketones, furans, acetic acid, pyridines, pyrazines, propanoic acid, pyrroles Glucose-Val to 300 or 700 °C at 10 °C/min, air[a] (Coleman and Perfetti, 1997). Ketones; 2-methyl-propanal; furans; pyrazines; 2-methylpropanoic acid

[a] TC: study sponsored by tobacco company.

more (substituted) furfurals and less anhydrosugars, like levoglucosan (Ohnishi and Kato, 1977; Schlotzhauer et al., 1982, 1985; Evans et al., 1996; Sanders et al., 2003). In addition, it seems that simple sugars generate more formaldehyde (Burton, 1976), but less acetaldehyde, acetone (Kato, 1967; Burton, 1976), and acrolein (Burton, 1976). It is difficult to estimate the difference in total yield of pyrolysis products of simple sugars versus polysaccharides, because the few comparative studies available report only part of the products. Since conclusive studies[1] on the effect of (labeled) polysaccharides on the composition of cigarette mainstream smoke are also not available, the relative contribution of pyrolyzation products of sugars versus other carbohydrates to the composition of tobacco smoke cannot be properly evaluated.

4.2. Combustion products of sugar additives in mainstream smoke

Burning the (labeled) additive in the tobacco matrix in a smoking machine and subsequent analysis of the mainstream smoke components gives more accurate information on the actual pyrolysis process than the pyrolysis studies on a single ingredient (see Section 4.1). One

[1] Only one study ((National Cancer Institute, 1980) cited in (Paschke et al., 2002)) gives detailed information on the effect of added cellulose on mainstream smoke.

should, however, realize that the data thus obtained do not imply that the detected products solely originate from sugars.

Table 3 (mainly based on studies performed by tobacco companies) shows that the addition of sugars to tobacco primarily enhances the level of aldehydes and ketones, especially formaldehyde, acetaldehyde, acetone, acrolein, 2-furfural and other furans. For instance, as compared to the Burley reference cigarette, the addition of 12% w/w of sugar (a representative concentration in tobacco, see Section 2.1) to a Burley tobacco increased (depending on the type of sugar and tobacco) the mainstream smoke levels of formaldehyde (40–148%), acetaldehyde (6–36%), acetone (11–52%), acrolein (20–73%), and total carbonyl (14–36%) (Shelar et al., 1992). Precursor–product relationships of these components are described in Section 5. Studies with mixtures of additives on smoke components support the observation (Table 3) that the addition of sugars to tobacco significantly increases the pyrolytic formation of formaldehyde. Baker and co-workers reported statistically significant increases (up to 73%) in formaldehyde levels in mainstream smoke for all mixtures containing over 1% w/w sugars (but not in corn syrup) (Baker et al., 2004a,b,c). Similarly, a 60–65% increase in the concentration of formaldehyde in mainstream smoke was observed following the addition of a corn syrup sugar mixture containing 4.2–6.3% w/w sugar (Rustemeier et al., 2002; Baker et al., 2004b).

Table 3 further shows that the addition of sugars to tobacco enhances the concentration of total acids in mainstream smoke. This is in agreement with the results obtained by Elson et al. (1972), who showed that the smoke pH-value of a cigarette containing 17.8% of sugar ranges around 4.0, whereas the smoke pH of a cigarillo containing only 0.5% of sugar exceeds the value of 8.5. As a result of the lower pH, mainstream smoke of tobacco enriched with sugars will contain lower levels of free-base nicotine (see Table 3 and Section 6.1) (Willems et al., 2006). Finally, Table 3 indicates that sugar combustion products have primarily been found in sidestream smoke. As specific data on sidestream smoke components are not available, the effect of combustion/pyrolysis of sugars on the composition of sidestream smoke is not further addressed.

Table 3
Effect of added sugars on the composition of cigarette mainstream smoke (MSS)

Sugar	Amount added (% w/w), type of tobacco and selected MSS components (mg/cig; % difference from control)
Fructose	12.8, Burley[a] (Thornton and Massey, 1975). Total nicotine alkaloids 2.2 (−30%); total carbonyls 4.4 (+10%); volatile carbonyls 2.2 (+16%); volatile aldehydes 0.53 (−12%); 2-furfural 0.089 (+68%); total acids 2.7 (+14%); volatile acids 1.2 (+17%) 12, low-mid stalk Burley tobacco[a] (Shelar et al., 1992). Formaldehyde 0.025 (+53%); acetaldehyde 0.57 (+13%); acetone 0.35 (+32%); acrolein 0.16 (+37%); total carbonyl 1.1 (+22%); volatile nicotine 0.083 (−30%) 12, mid-upper stalk Burley[a] (Shelar et al., 1992). Formaldehyde 0.020 (+80%); acetaldehyde 0.64 (+10%); acetone 0.34 (+12%); acrolein 0.14 (+20%); total carbonyl 1.1 (+13%); volatile nicotine 0.20 (−29%)
Glucose	10.5, Burley[a] (Thornton and Massey, 1975). Total nicotine alkaloids 2.6 (−2.0%); total carbonyls 4.2 (+5.0%); volatile carbonyls 2.0 (+5.3%); volatile aldehydes 0.50 (−17%); 2-furfural 0.067 (+26%); total acids 2.5 (+6.9%); volatile acids 1.1 (+5.7%) 16.8, Burley[a] (Thornton and Massey, 1975). Total nicotine alkaloids 2.2 (−35%); total carbonyls 4.3 (+7.5%); volatile carbonyls 2.1 (+10%); volatile aldehydes 0.54 (−10%); 2-furfural 0.080 (+51%); total acids 2.5 (+6.0%); volatile acids 1.2 (+11%) 16.1, air-cured[a] (Thornton and Massey, 1975). Available ^{14}C-nicotine directed into MSS: 37% (−15%) 12, low-mid stalk Burley[a] (Shelar et al., 1992) Formaldehyde 0.028 (+72%); acetaldehyde 0.646 (+26%); acetone 0.41 (+52%); acrolein 0.16 (+36%); total carbonyl 1.2 (+36%); volatile nicotine 0.090 (−23%) 12, mid-upper stalk Burley[a] (Shelar et al., 1992) Formaldehyde 0.020 (+80%); acetaldehyde 0.78 (+36%); acetone 0.43 (+40%); acrolein 0.16 (+36%); total carbonyl 1.4 (+37%); volatile nicotine 0.19 (−33%) ^{14}C-glucose in Burley[a] (Gager et al., 1971b). ^{14}-C pyrolysis products (%) in MS gas phase 4.7 (acetone 0.08; acetaldehyde 0.05; 2-methylfuran 0.02; 2-butanone 0.02; furan 0.01; propionaldehyde, acrolein, crotonaldehyde, benzene < 0.01); MS TPM 1.7; SS gas phase 45.8; SS TPM 3.7; butt 41.0
Invert sugar	5.4, tobacco blend[b] (National Cancer Institute, 1977 cited in Paschke et al., 2002). Nicotine 1.8 (−3.6%); acetaldehyde 1.26 (+0.6%); acrolein 0.11 (+0.2%); isoprene 0.46 (−9.5%); HCN 0.34 (−8.5%); formaldehyde 0.03 (+22%); NO_x 0.44 (+5.8%) 5.4, Burley blend (National Cancer Institute, 1977 cited in Paschke et al., 2002). Nicotine 2.9 (−19%); phenol 0.11 (−33%); acetaldehyde 1.1 (−0.9%); acrolein 0.08 (−0.2%); isoprene 0.47 (−5.4%); HCN 0.33 (−13%); formaldehyde 0.02 (−10%); NO_x 0.63 (−11%) 5.1, 1R1 Kentucky Ref[a] (Jenkins et al., 1980). ^{14}-C pyrolysis products (%) in MS gas phase 13.6; MS TPM 9.1; SS gas phase 63.8; SS TPM 7.8; butt 5.7
Sucrose	12, low-mid stalk Burley[a] (Shelar et al., 1992). Formaldehyde 0.023 (+40%); acetaldehyde 0.55 (+9%); acetone 0.35 (+31%); acrolein 0.20 (+73%); total carbonyl 1.13 (+25%); volatile nicotine 0.075 (−36%) 12, mid-upper stalk Burley[a] (Shelar et al., 1992). Formaldehyde 0.028 (+148%); acetaldehyde 0.62 (+6%); acetone 0.34 (+11%); acrolein 0.18 (+52%); total carbonyl 1.2 (+14%); volatile nicotine 0.18 (−36%) ^{14}C-sucrose in Burley blend[a] (Gager et al., 1971b). ^{14}-C pyrolysis products (%) in MS gas phase 5.9 (acetone 0.1: 2,5-dimethylfuran 0.07; acetaldehyde 0.06; acetonitrile 0.04; 2-methyl-furan 0.03; 2-butanone 0.03; 2,3-butanedione 0.01; furan 0.01; propionaldehyde, acrolein, benzene, 3-buten-2-one, crotonaldehyde < 0.01); MS TPM 3.0; SS gas phase 51.6; SS TPM 3.8%; butt 40.6

[a] TC: study sponsored by tobacco company.
[b] Flue-cured, Burley, Maryland, Turkish, reconstituted sheet.

5. Relation between the sugar content of tobacco and smoke composition

In addition to the previously mentioned studies where one specific amount of sugar was added to tobacco, others have investigated the effect of increasing amounts of sugar in tobacco on the mainstream smoke level of several aldehydes. This is important since the precursor–product relationships between ingredients and smoke components should be clearly established before measures can be taken to diminish the concentration of toxic ingredients in the frame of tobacco control. Benchmark studies are mainly performed to assess the effect of sugars in various tobacco brands on the smoke components generated. Such studies, however, neglect that the level of smoke components also depends on the type of tobacco. This can be circumvented by testing the effect of different amounts of sugar added to a single type of tobacco (preferably Burley that contains virtually no natural sugars). The results of these approaches for aldehydes are discussed below.

A benchmark study by Seeman et al., sponsored by Philip Morris, on a large number of commercial US cigarettes suggested that the concentration of reducing sugars in the tobacco was not correlated to the concentration of acetaldehyde in mainstream smoke (Seeman et al., 2003). The authors proposed that mainstream smoke acetaldehyde was mainly derived from naturally occurring polysaccharides, such as cellulose, since the pyrolysis of cellulose generates larger amounts of low molecular weight aldehydes than the pyrolysis of reducing sugars (see Section 4.1). The lack of a correlation between the tobacco sugar content and the concentration of aldehydes in mainstream smoke was confirmed by the Imperial tobacco company in a benchmark study of forty different cigarette brands (Phillpotts et al., 1975).

In contrast to these benchmark studies, Zilkey et al. (1982), using 25 cigarettes that were blended from several types of bright and Burley tobacco (no sugar added), showed clear relations between sugar levels in tobacco and the concentration of aldehydes in mainstream smoke. In this study, the reducing sugars in tobacco ranged from 0% to 20%, whereas the range of the mainstream smoke level (μg/cig) of acetaldehyde, acrolein and total aldehydes was 163–1003, 14–75 and 303–1292, respectively. Using these data, the coefficient of determination (i.e. r^2-value) of the association between reducing sugars and acetaldehyde, acrolein and total aldehydes was 0.53, 0.46, and 0.55, respectively. After exclusion of the three data points of cigarettes that were equipped with a charcoal filter (instead of a cellulose acetate filter), the r^2-value of the associations increased to 0.61, 0.59, and 0.64, respectively. This indicates that, in addition to the tobacco type, the design characteristics of the cigarette determine the chemical composition of mainstream smoke. In contrast to the proposition of Seeman et al. (see above), the concentration of cellulose in tobacco was not correlated to smoke levels of acetaldehyde, acrolein and total aldehydes (r^2-values of 0.05, 0.002, and 0.1, respectively).

Studies performed by R.J. Reynolds Tobacco confirm that sugar in tobacco increase the level of tobacco smoke aldehydes (Shelar et al., 1992). Fructose, glucose, and sucrose were added in increasing amounts (4%, 8%, 12%, and 16% w/w) to either low-mid stalk Burley tobacco (K1) or mid-upper stalk Burley tobacco (K2). The results show significant correlations between the levels of fructose, glucose, sucrose in tobacco and the smoke level of formaldehyde, acetaldehyde, acetone, and acrolein (see Table 4). As the sugars in this study were all tested in the same tobacco type, the calculated correlation coefficients were higher than those obtained from the data of Zilkey et al. (1982).

In summary, conflicting results have been reported on the relation between the concentration of sugars in tobacco and mainstream smoke aldehyde levels. Clearly, the study with different types of tobacco (but no additives or differences in cigarette design) gives better correlations than the benchmark studies, and those studies using increasing amounts of sugars tested in one type of tobacco give the best correlations. It is therefore concluded that benchmark studies, with their variety in both tobacco composition and design characteristics of the cigarettes, are not optimal to study the effect of the combustion of particular ingredients. When increasing concentrations of sugars are tested in one type of tobacco, significant linear increases of several aldehydes are clearly established.

Table 4
Correlations (expressed as r^2-values) between levels of sugars in tobacco and smoke components calculated from the data of Shelar et al. (1992)

Tobacco type/sugar (range in % w/w)	Correlation between sugar and smoke component (r^2-value)			
	Formaldehyde	Acetaldehyde	Acetone	Acrolein
K1/fructose (0.1–12.4)	0.93	0.68	0.88	0.95
K2/fructose (0.1–10.0)	0.93	0.85	0.88	0.92
K1/glucose (0.1–15.6)	0.95	0.95	0.97	0.90
K2/glucose (0.0–13.6)	0.68	0.69	0.45	0.47
K1/sucrose (0.1–14.2)	0.95	0.36	0.59	0.98
K2/sucrose (0.0–13.2)	0.97	0.66	0.68	0.90

K1: low-mid stalk Burley tobacco; K2: mid-upper stalk Burley tobacco.

For K1: increase (μg/cig) per weight percent of sugar added: 0.8–1.2 (formaldehyde; control 16.0), 3.3–10.5 (acetaldehyde; control 506.7), 6.4–11.2 (acetone; control 268.9), and 3.8–9.1 (acrolein; control 117.5). For K2, increase (μg/cig) per weight percent of sugar added: 0.6–1.8 (formaldehyde; control 11.2), 13.0–20.5 (acetaldehyde; control 577.6), 7.4–11.5 (acetone; control 306.3), and 3.7–7.9 (acrolein; control 117.8).

6. Effects of tobacco sugars on tobacco consumption

The toxicity of certain smoke compounds, generated upon combustion/pyrolysis products of sugars in tobacco is generally known. Two other specific effects of sugars that are related to the facilitation of tobacco use are less known and will be addressed in this section in more detail.

6.1. Masking of tobacco smoke harshness

Volatile basic components, such as ammonia, nicotine and other tobacco alkaloids give tobacco smoke a harsh taste, which keeps smokers from inhaling (Hoffmann and Hoffmann, 1997). During smoking, sugars generate acids that decrease smoke pH (Section 4.2), which in turn decreases the free-base nicotine level in mainstream smoke. As a result, the impact, ''nicotine strength'', harshness and irritation of the smoke will decrease as well (Elson et al., 1972; Creighton and Hirji, 1988; Shelar et al., 1992; Leffingwell, 1999; Rodgman, 2002), which is especially important for naïve smokers, as it will encourage them to develop a smoking habit. Throat impact and harshness decrease as the sugar level increases, until a plateau value of around 10% (Shelar et al., 1992). The optimum sugar to nicotine ratio in tobacco for developing smooth products was determined to be 3.3 (Shelar et al., 1992). A major drawback of the lower content of nicotine in smoke is that smokers increase their smoking frequency and inhale the smoke more deeply to enable a higher absorption of nicotine in the airways (Elson et al., 1972; Hoffmann and Hoffmann, 1997). This obviously leads to a higher exposure of smokers to toxic and carcinogenic agents.

Furthermore, combustion/pyrolysis of sugars generates caramel flavors in tobacco smoke, which give it a sweet taste that is appreciated in particular by adolescents. This sweeter taste masks the adverse bitter taste of cigarette smoke. As a result of the lower adverseness of tobacco, people (in particular adolescents, Bates et al., 1999a; Fowles, 2001; Vleeming et al., 2005) start smoking earlier, continue smoking for longer periods, and increase their tobacco use. Smoking panels confirmed that consumer acceptance of cigarette mainstream smoke is proportional to the sugar level in the tobacco (Rodgman, 2002).

6.2. Pro-addictive properties of sugar in tobacco

Although sugars have no addictive potential *per se*, sugars in tobacco act pro-addictively, because they generate acetaldehyde in tobacco smoke. Acetaldehyde and nicotine act, via a still unknown mechanism, synergistically with respect to the addictive effect of nicotine in rodents (Bates et al., 1999a; Gray, 2000; Henningfield et al., 2004; Belluzzi et al., 2005). It has been speculated that acetaldehyde reacts with biogenic amines to condensation products that inhibit monoamine oxidase, an enzyme that degrades biogenic amines, like dopamine and noradrenalin (Villegier et al., 2003; Jamal et al., 2003; Belluzzi et al., 2005). The brain levels of these aminergic neurotransmitters, known to be involved in drug addiction (Koob, 1992), increase as a result of the inhibition of monoamine oxidase.

In summary, the addition of sugars to tobacco can enhance tobacco use in at least two ways: (1) neutralization of the harsh taste of cigarette smoke and (2) generation of acetaldehyde, which increases the addictive effect of nicotine. Philip Morris and BAT, however, reject the allegations that some of their additives increase the addictive nature of cigarettes (British American Tobacco, 2004; Philip Morris International Inc., 2004).

7. Conclusions

Sugars (naturally present and/or intentionally added) have a significant effect on mainstream smoke composition, as they are one of the main ingredients of tobacco. Depending on the type of curing, sugars are regularly present naturally in levels up to 20% w/w. In addition, various sugars, particularly sucrose and invert sugar, as well as sugar mixtures (syrups, honey) are added to tobacco in amounts up to 4% w/w for each sugar.

Five major tobacco manufacturers claimed that sugars are added either as flavor, casing or humectant. The addition of sugars, however, also promotes tobacco use as certain combustion/pyrolysis products of sugars neutralize the adverse tobacco taste or even have addictive properties (acetaldehyde). Apart from the adverse health effects that result from increased tobacco consumption, high-sugar tobaccos also yield elevated levels (increases of up to 150% were reported) of toxic components in mainstream smoke. For instance, formaldehyde, acetaldehyde, acetone, acrolein, 2-furfural and other furans are very toxic or even carcinogenic.

As the combustion products of sugars appear mainly in the sidestream smoke, the sugar level in tobacco may be relevant for passive smokers as well. Further research to the effect of sugars on main- and side-stream smoke is therefore highly recommended. Also, additional comparative data are necessary to estimate the relative contribution to mainstream smoke of sugars compared to polysaccharides. Such information is essential to estimate the impact of the adverse health effect of sugars, which is important in ingredient regulation issues.

In summary, sugars in tobacco have a negative health impact on the smoker. This is an important issue for tobacco ingredient regulation and may restrict the use of sugars as additives. Furthermore, as the type of curing largely determines the final sugar level of tobacco products, the impact of such methods should also be considered when regulation measures on sugar ingredients are issued.

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Industry research on the use and effects of levulinic acid: A case study in cigarette additives

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Public health officials and tobacco researchers have raised concerns about the possible contributions of additives to the toxicity of cigarettes. However, little attention has been given to the process whereby additives promote initiation and addiction. Levulinic acid is a known cigarette additive. Review of internal tobacco industry documents indicates that levulinic acid was used to increase nicotine yields while enhancing perceptions of smoothness and mildness. Levulinic acid reduces the pH of cigarette smoke and desensitizes the upper respiratory tract, increasing the potential for cigarette smoke to be inhaled deeper into the lungs. Levulinic acid also may enhance the binding of nicotine to neurons that ordinarily would be unresponsive to nicotine. These findings held particular interest in the internal development of ultralight and so-called reduced-exposure cigarette prototypes. Industry studies found significantly increased peak plasma nicotine levels in smokers of ultralight cigarettes following addition of levulinic acid. Further, internal studies observed changes in mainstream and sidestream smoke composition that may present increased health risks. The use of levulinic acid illustrates the need for regulatory authority over tobacco products as well as better understanding of the role of additives in cigarettes and other tobacco products.

Introduction

In response to growing public health concerns in the 1950s and 1960s, tobacco manufacturers recognized the need for cigarettes that provided reduced "tar" delivery. A number of major cigarette modifications, including the introduction of filters, ventilation, and processed tobaccos, resulted in lower machine-measured tar and carbon monoxide levels. Ventilation in particular became a primary technique for decreasing smoke yield; however, ventilation also reduced levels of nicotine, smoke strength, and tobacco taste, and left the smoker with a sensation of thinness and dryness (Hale, Kroustalis, Lin, Raymond, & Spielberg, 1990a; Kozlowski & O'Connor, 2002). Reduced smoke nicotine delivery was of particular concern to manufacturers because a high level of nicotine "contributes to smokers' physiological and also sensory satisfaction" (Hale et al., 1990a).

Manufacturers turned to chemical additives to accommodate the need for lower tar delivery with sustained smoking satisfaction. Cigarette additives may be used to offset the unpleasant taste associated with lower-tar products, alter product chemistry, and create the sensations of a full-flavor cigarette (Bates, McNeill, Jarvis, & Gray, 1999; Hurt & Robertson, 1998; Wells, 1995). Manufacturers today publicly acknowledge the use of hundreds of additives in their products. The modern U.S.-style cigarette generally contains about 10% additives by weight, mostly in the form of sugars, humectants, ammonia compounds, cocoa, and licorice (Browne, 1990). Most other additives are used in very small amounts—less than 0.01% of total weight. However, little is known about the role and effects of most individual additives. Federal law requires manufacturers to report the names of additives to the U.S. Department of Health and Human Services, but information is not provided for specific cigarette brands or for levels of use.

Internal tobacco industry documents made publicly available as a requirement of the 1998 Master

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Settlement Agreement provide an important resource for evaluating tobacco industry knowledge and practices. Although the tobacco industry has denied that use of additives has any known effect on the pharmacological properties or addiction potential of cigarettes, published research using industry documents suggests otherwise. An example is smoke pH, which is a measure for whether nicotine in smoke is found in its free-base or protonated (bound) form. Tobacco manufacturers used ammonia in the early 1970s to manipulate smoke pH levels, based on their belief that a higher smoke pH would increase the impact of nicotine and the rate at which inhaled nicotine is absorbed into the bloodstream (Henningfield, Pankow, & Garrett, 2004; Hurt & Robertson, 1998). Similarly, to increase product appeal among young adult users, R. J. Reynolds used additives in combination with other product changes in its Camel cigarette brand to increase smoothness and reduce irritation, while maintaining or increasing nicotine delivery in smoke (Ferris Wayne & Connolly, 2002). The industry has also used numerous additives to reduce sidestream irritation and odor, thereby lessening the perception of second-hand tobacco smoke and its associated risks (Connolly, Wayne, Lymperis, & Doherty, 2000).

In this industry document–based study, we sought to identify the potential pharmacological and behavioral effects that result from the use of one known additive in cigarettes, levulinic acid. We cataloged the internal industry use of levulinic acid in brand development and other product research. Our findings confirm that levulinic acid can play an important role in product delivery as well as influence smoke perception and the bioavailability of other constituents (including nicotine). Further, our findings demonstrate the unique importance of levulinic acid in the internal development of some low-yield and so-called reduced-exposure products. We conclude that use of additives, in particular levulinic acid, may result in significant unmeasured changes to product delivery, potentially increasing overall addictiveness or toxicity of the tobacco product.

Method

More than seven million tobacco industry documents discovered through ongoing trial litigation have been made publicly available as a result of the 1998 Master Settlement Agreement between the state attorneys general and major U.S. tobacco manufacturers (Philip Morris, R. J. Reynolds, Brown & Williamson, and Lorillard). These documents are now widely accessible via the Internet through archival databases such as those maintained at Tobacco Documents Online (tobaccodocuments.org) and the Legacy Tobacco Documents Library (legacy.library.ucsf.edu). Document identification and retrieval is performed using an index-based word search of titles, authors, recipients, and other document characteristics (such as date, document type, original file location) as well as key words, abstracts, and in many cases full-text optical character recognition of scanned document images.

In the present study, our goal was to provide a comprehensive assessment of industry studies addressing the intended use or role of levulinic acid in product research and development. Initial searches were conducted to assess areas of internal discussion. For example, a search on Tobacco Documents Online for the term *levulinic acid* yielded 2,797 documents (as of January 15, 2004) and for *nicotine levulinate* (the nicotine salt of levulinic acid) yielded 674 documents. From these documents, relevant ones were identified based on whether they described (a) historical measures or assessments of levulinic acid in commercial brands, (b) the additive's effects on product delivery, perception, or bioavailability, or (c) its use in product development and internal research projects. The documents identified as relevant were abstracted and indexed. These documents were surveyed for key words or projects that might suggest further avenues for retrieval. A final set of 284 documents (of which 51 are directly cited here) was cataloged for the present study. A full set of these documents, ranging in dates between 1968 and 1993, can be accessed and viewed at http://tobaccodocuments.org/product_design/list.php?field_id=7&resource_id=20926.

We believe the collection of documents identified in the present study is sufficient to draw general conclusions regarding industry testing and use of levulinic acid. It should be noted that the document collections are gathered from different manufacturers, spanning a number of distinct eras, and representing the findings and opinions of many different authors. In the present study, a majority of the relevant findings were obtained from a single manufacturer (R. J. Reynolds). Thus our findings should be interpreted not as representative of the entire tobacco industry but rather as instructive regarding the character of internal research on additives, assessment of their potential effects, and the use of this knowledge in product development.

Results

Historical use of organic acids in cigarettes

Organic acids have been used since the 1950s to improve smoothness of cigarettes, typically at low levels in top dressings, that is, sprayed onto the shredded tobacco (R. J. Reynolds, 1991b). Philip

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Morris tested organic acids in its Marlboro cigarettes in the 1970s and found that lactic acid decreased harshness and bitterness, and produced a sweeter flavor (Vinals, 1971). Other internal studies confirmed a smoothing effect when lactic acid was added to tobacco filler, with reduced smoke impact (Cipriano, Kounnas, & Spielberg, 1975), as well as a slight reduction in nicotine and tar deliveries (Meyer, 1963). Citric additives have been used not only for reduced harshness and flavor modification but also to reduce smoke pH, to "neutralize" nicotine impact, and to enhance sheet formation in reconstituted tobacco (Philip Morris, 1989). Tartaric and lactic acids likewise caused reductions in the pH of smoke (Backhurst, 1968). All of these organic acids increased smoothness but were associated with a decrease in nicotine impact.

A number of internal studies have explored the use of organic acids for manipulation of nicotine delivery in cigarette smoke. In 1978, an R. J. Reynolds author speculated that sorbic acid was being used in Philip Morris cigarettes for nicotine reduction (Thacker, 1978). The authors of a 1980 Lorillard study (Hurst & Slaven, 1980) reported that acid-impregnated papers (including lactic, citric, and malic) influenced migration of nicotine to the periphery, which elevated mainstream smoke nicotine delivery without affecting other smoke constituents. Another Lorillard study (Sudholt, 1985a), seeking to produce an increased impact in ultra-low-tar cigarettes, proposed cigarettes made with malic acid filters to test the migration of nicotine from tobacco to the filter. Despite an initial fourfold increase in the rate of migration (Sudholt, 1985a), the author later concluded that malic acid was not useful for promoting migration under typical construction and storage procedures (Sudholt, 1985b).

Philip Morris initiated a study of organic acids in 1975 to evaluate the contribution of individual acids to subjective acceptability, particularly in the development of low-delivery cigarettes (Cipriano et al. 1975). In one finding, the addition of formic acid produced "a distinct sour effect" and otherwise failed to improve subjective performance. However, the researchers observed an unexpected 25% increase in smoke nicotine delivery in cigarettes injected with formic acid. This nicotine increase did not correspond to an increase in perceived impact, and in fact appeared to reduce impact—a finding attributed by the authors to a likely reduction in free nicotine delivery consistent with a reduction in smoke pH. The authors concluded: "Perhaps another non-volatile acid can be found which might contribute to increased nicotine delivery without itself distilling through the rod and affecting either basic taste sensations or smoke pH" (Cipriano et al., 1975).

Indeed, in the late 1980s, R. J. Reynolds scientists discovered that when levulinic acid, another organic acid, was applied to high-nicotine blends of tobacco, harshness was reduced without a decrease in smoke nicotine delivery or unpleasant taste. Furthermore, the nicotine salt of levulinic acid, nicotine levulinate, decreased harshness as expected but also increased smoke nicotine delivery. A summary of this research commented, "Numerous…organic acids were evaluated at varying application levels but none were found to work as effectively as levulinic acid" (R. J. Reynolds, 1991b).

On December 24, 1987, R. J. Reynolds filed for a patent for incorporating levulinic acid as an additive into cigarettes. The principle of the invention was to increase the smoke impact strength by raising the delivered nicotine in smoke, while reducing the inherent harshness of nicotine through levulinic acid or nicotine levulinate (Hale et al., 1990a). The patent application claimed that cigarettes "composed of high nicotine tobaccos and levulinic acid and cigarettes having a salt such as nicotine levulinate incorporated therein can exhibit low U.S. Federal Trade Commission (FTC) 'tar' to nicotine ratios while providing a smooth, palatable and flavorful taste" (Lawson, Bullings, & Perfetti, 1987).

Properties and effects of levulinic acid

According to the standard tobacco industry monograph on additives, levulinic acid is used in cigarettes as a flavorant because of its sweet caramel taste and body (Leffingwell, Young, & Bernasek, 1972). But results from various internal projects (discussed in detail below) indicate that levulinic acid has been used by manufacturers to improve sensory character (smoothness) of smoke and raise delivered nicotine. Further, this internal research suggests that levulinic acid may enhance the binding of nicotine to neurons that ordinarily would be unresponsive to nicotine. This combination of effects corresponds to increased levels of plasma nicotine in smokers of cigarettes treated with levulinic acid, particularly when applied to lower-yield and reduced-exposure products. Table 1 summarizes the effects of levulinic acid as a cigarette additive, and these effects are each described in turn below.

Alters sensory perception of smoke. R. J. Reynolds began evaluating the addition of levulinic acid to tobacco in an effort to address harshness issues encountered in the development of low-tar cigarettes. Researchers had observed that levulinic acid reduced throat irritation from cigarette smoke (Santambrogio, 1991). Subjective reports indicated that overall sensitivity to cigarette smoke constituents was decreased in the upper respiratory tract

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Table 1. Summary of effects of levulinic acid when used as an additive in cigarettes.

Potential effect	Measure used	Objective	Outcome
Sensory perception (Steele, 1989)	Subjective consumer panel testing of treated cigarettes	Offset harshness and irritation in development of low-yield cigarettes	"…physiological clues are being blocked, since people smoked the test cigarettes essentially the same as the control, even though more nicotine was obtained"
Smoke pH (Stewart & Lawrence, 1988)	Electrode-based measure of smoke pH of machine-smoked cigarettes	Offset harshness and irritation in development of low-yield cigarettes	Decreased smoke "pH" in Camel Light when used alone or added as nicotine levulinate
Nicotine delivery in smoke (Steele, 1989)	Puff profiles of smokers, followed by yield measures based on Human Mimic Smoking Machine	Increase smoke nicotine delivery of low-tar cigarettes relative to higher tar controls	Smoke nicotine delivery increased in a number of tested brands, including Camel Light, Vantage Ultra Light, and NOW
Plasma nicotine (Steele, 1989)	Plasma nicotine change from baseline measured comparing smokers of control and test cigarettes	Increase bioavailability of smoke nicotine in low-yield and low tar/nicotine cigarettes	Plasma nicotine for NOW about 6 ng/ml higher than the control (Winston King); for Winston Ultra Light, about 13 ng/ml higher than control
Tar/nicotine ratio (Steele, 1989)	Machine-measured smoke yields of tar and nicotine	Increase delivery of nicotine relative to tar in low-yield cigarettes	Levulinic acid alone had little effect; nicotine levulinate decreased tar and nicotine by half in Winston Ultra Light and NOW
Receptors in brain (Steele, 1989)	In vitro studies on binding of radiolabeled nicotine to pharmacological receptors in brain tissue	Determine whether levulinic acid affects nicotinic cholinergic receptors in the brain	Observed increased nicotine binding ranging from 20%–50%, with a mean value of around 30%; "…changes in receptor binding may lead to changes in physiological effects of nicotine…"

from the oropharynx to the trachea (R. J. Reynolds, 1990a). Consumer panel testing of levulinic acid–treated cigarettes showed a reduction in harshness but also revealed a decrease in strength (impact), taste, and consumer preference (satisfaction; R. J. Reynolds, 1990b). At high levels (3%–5%), the application of levulinic acid resulted in products that were "very smooth" but had an off taste (R. J. Reynolds, 1991b). Adding nicotine levulinate instead of the acid precursor produced cigarettes that were much smoother than expected, without a measurable deterioration in taste (R. J. Reynolds, 1991b).

A series of internal studies was conducted to measure the effects of levulinic acid on neural response. These included psychophysical and respiratory response studies conducted with anosmic human subjects (i.e., those without a sense of smell), measurement of peripheral sensory response in the trigeminal and olfactory nerve endings of pigeons, and physiological experiments on portions of the upper respiratory tract in dogs (Walker, 1990). An incremental increase in nerve activity was shown with the addition of a small concentration (1 ppm) of levulinic acid. This increase in activity was greatest for the lowest nicotine concentration and decreased as the nicotine concentration was progressively increased, suggesting increasing overlap between the neurons activated by these two compounds (Guy, Jennings, Morgan, & Walker, 1992). Pretreatment with levulinic acid significantly reduced the olfactory response to nicotine concentrations, consistent with these findings (Walker, 1991). Figure 1 illustrates the effect of levulinic acid on the olfactory nerve response in an effort to modify perceptual responses to cigarette smoke.

The mechanism of action for these effects was a subject of some internal debate (Best, 1992). Some researchers speculated that levulinic acid may restrict chemoreceptor stimulation in the upper airway and thereby decrease the permeability of nicotine through the epithelia and nasal cavity, blocking the physiological clues for the delivery of nicotine (R. J. Reynolds, 1990a). Other researchers hypothesized that levulinic acid may alter olfactory responses to nicotine by lowering the pH of the mucus overlying the olfactory receptor sheet. This lower pH would reduce the proportion of free-base nicotine that is available to interact with receptor olfactory neurons (Jennings et al., 1992). Indeed, according to data taken from a separate study of nicotine transport, the addition of levulinic acid measurably reduced the amount of nicotine in the vapor phase of smoke, presumably making the nicotine less available to receptors that respond to irritating compounds in the throat or upper airways (Dufour, 1991).

Alters smoke pH. The tobacco industry has an established history of manipulating the pH levels of tobacco and smoke (Connolly, 1995; Hurt & Robertson, 1998; Pankow, 2001). Cigarette smoke pH is ordinarily slightly acidic (about 6), and as a result nicotine in smoke exists mainly in the salt

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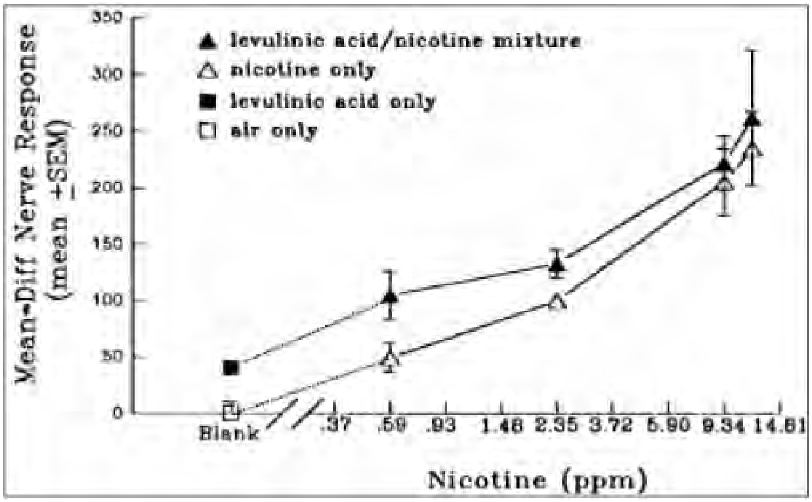

Figure 1. An illustration of the effect of levulinic acid on olfactory nerve activity for increasing levels of nicotine. From an R. J. Reynolds internal report, "Modification of olfactory nerve response to nicotine by levulinic acid experiment" (Jennings et al., 1992).

(protonated) form. When pH is elevated (7–12), nicotine moves to its free-base form, in which it is more readily absorbed into the lungs and provides a stronger sensory impact in the mouth and throat. Higher rates of free nicotine may increase the potential for addiction but also can be experienced as too harsh and having too strong an impact (Hale, Kroustalis, Lin, Raymond, & Spielberg, 1990b). Thus a reduction in smoke pH may be desirable for cigarettes exhibiting higher smoke delivery, whereas increased pH may compensate for reduced delivery.

As the level of levulinic acid in tobacco is increased (from 0% to 5%), the pH of tobacco smoke decreases, consistent with the acidic nature of the additive itself (Cook, 1987). In one series of studies, R. J. Reynolds researchers determined that a 3:1 molar ratio of levulinic acid to nicotine resulted in a decrease in the smoke pH of Camel Light 85 cigarettes from 6.25 to 5.38 (R. J. Reynolds, 1988a). Tests comparing combinations of added levulinic acid, nicotine levulinate, and a "soup" of levulinic acid and "SDK-22" tobacco essence indicated that levulinic acid decreased smoke pH values more than either nicotine salt preparation. But high doses of nicotine levulinate and the mixture of levulinic acid and tobacco essence were effective in decreasing smoke pH as well, lowering the pH value by 0.52 units and 0.74 units, respectively, from the control value of 6.12 (Figure 2) (Stewart & Lawrence, 1988).

Increases smoke nicotine delivery and absorption. High-nicotine tobaccos treated with levulinic acid or nicotine levulinate delivered an increased dose of nicotine to the smoker across a range of experiments, including low-tar (Camel Light 85) and ultra-low-tar (Vantage Ultra Light 85) configurations, and across a variety of tobacco types (Montoya & Best, 1987; Perfetti, 1989; Powell, Redding, & Stewart, 1988). For example, smoke nicotine levels (as measured using a Human Mimic Smoke Machine, which adjusts for differences in inhalation behaviors) for the brand NOW 85 were doubled for test cigarettes treated with nicotine levulinate (0.77 mg/cigarette for control vs. 1.68 mg for the test; Steele, 1989). The smoke nicotine delivery from the treated (test) cigarettes was considered remarkably high: The study authors noted that 1.19 mg is generally the upper limit of full-flavor Winstons and Marlboros (Steele, 1989). Subsequent research confirmed that smokers could get the same nicotine from lower-tar products treated with levulinic acid as from higher-tar controls. A study completed in 1991 used low tar/nicotine (T/N) prototypes including Dakota Lights base blend with G7-1 reconstituted tobacco at 5 mg tar and 0.47 mg nicotine (J. H. Reynolds, 1991). When modified by additions of nicotine and levulinic acid, the nicotine yield ranged from 0.73 mg to 1.02 mg. Although the majority of internal studies on nicotine yield were conducted using nicotine levulinate as the additive, and nicotine levulinate increased yields significantly more than levulinic acid alone, the nicotine yields from G7-1 treated with levulinic acid also were increased (Perfetti, 1989).

One noted advantage of levulinic acid was its ability to offset the harshness usually associated with an increase in smoke nicotine delivery, particularly in lower-yield cigarette brands (Hale et al., 1990b; R. J. Reynolds, 1988b). Biobehavioral studies confirmed that the NOW 85 test and control cigarettes described previously were smoked almost identically, "even though T/N was low enough in the test cigarettes to make them 'almost unsmokable' without the nicotine levulinate" (Steele, 1989). However, an internal harshness threshold study

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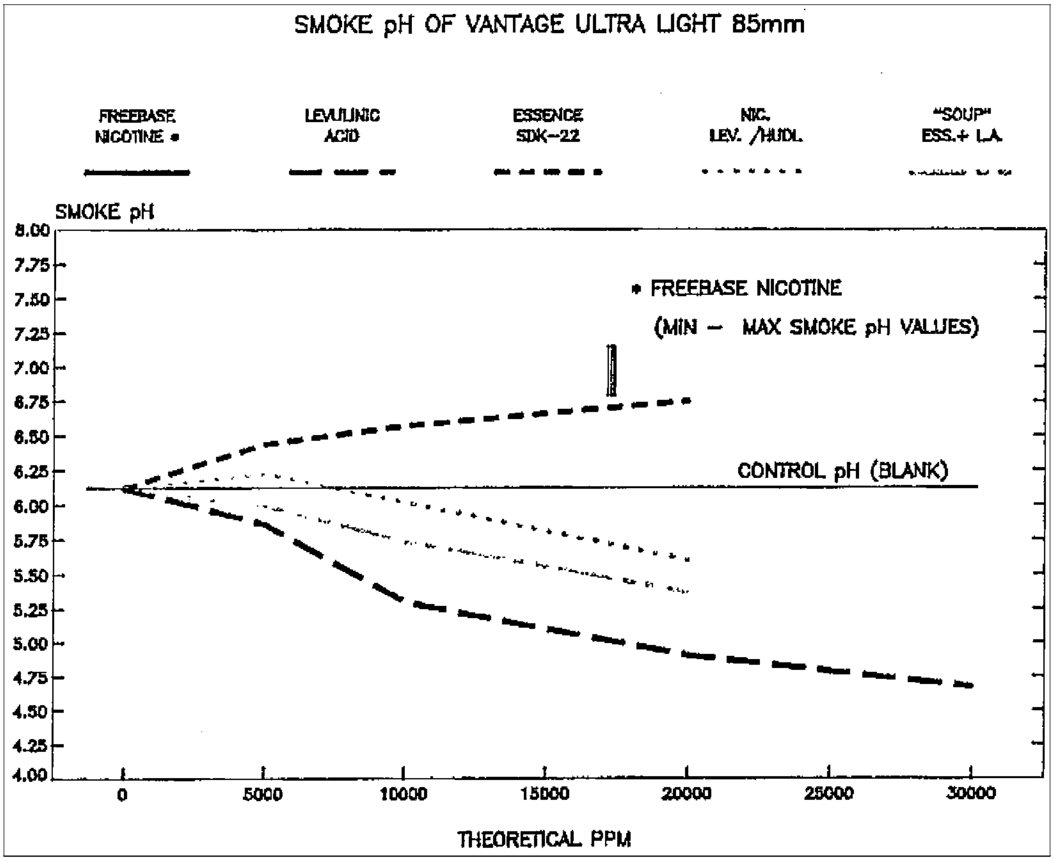

Figure 2. Effects of levulinic acid and other compound mixtures on smoke pH of experimental (Vantage Ultra Light) cigarette. From an R. J. Reynolds internal report on the development of Project XGT prototypes (Stewart & Lawrence, 1988).

demonstrated that for products with a high T/N ratio, levulinic acid can increase harshness (Perfetti & Wong, 1989). The authors cited further internal studies to suggest that a smoke aerosol high in organic acids and with low yields of nicotine is perceived as harsh, and will grow increasingly harsher following application of higher loads of the acid.

Increases peak plasma nicotine level. Higher smoke nicotine deliveries were ultimately reflected in plasma nicotine/cotinine changes from baseline among study subjects (R. J. Reynolds, 1990c). Researchers observed increased peak plasma levels of two times or greater in ultralight brands tested (R. J. Reynolds, 1987). The plasma nicotine for NOW 85 (treated with 10% nicotine levulinate) was approximately 6 ng/ml higher than for the control, whereas the Winston Ultra Light (5% nicotine levulinate) was about 13 ng/ml higher. In fact, the plasma nicotine levels for both brands proved higher than the Winston Full Flavor plasma nicotine rise (R. J. Reynolds, 1991b). This indicated that smokers had no problem inhaling smoke, even though the treated cigarettes contained higher nicotine and had lower T/N ratios. A separate document claimed that a 1- to 2-mg (nicotine) prototype had been developed internally that achieved higher blood nicotine levels than conventional 1- to 2-mg products (R. J. Reynolds, 1992).

Reduces tar/nicotine ratio. A primary goal in the design of lower-yield cigarettes is to increase the smoke delivery of nicotine relative to tar (Hale et al., 1990b). Although levulinic acid alone had little direct effect, nicotine levulinate proved particularly successful in reducing T/N levels (R. J. Reynolds, 1991b). When NOW 85s and Winston Ultra Lights were treated with nicotine levulinate (10% and 5%, respectively), FTC tar and carbon monoxide delivery were essentially unchanged for test and control cigarettes (Steele, 1989). But T/N ratios decreased by approximately one-half (9.1 and 4.97 for the control and test, respectively). Nicotine levulinate added to NOW 100s and Winston Ultra Light 100s was found to reduce T/N ratios and to significantly increase mainstream smoke yields of nicotine, further corroborating these findings (R. J. Reynolds, 1990c).

Enhances binding of nicotine in brain. Although research had originally focused on the interactions of nicotine and levulinic acid at sensory receptor

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sites, scientists at R. J. Reynolds conducted experiments beginning in 1989 to assess potential pharmacological interactions affecting the nicotinic cholinergic receptors in the brain (Lippiello, Fernandes, Reynolds, & Hayes, 1989). It had already been determined that some compounds enhanced the binding of nicotine to its receptors in brain tissue (Lippiello et al., 1989), although nicotine salts per se had not been investigated. Evidence indicated, however, that levulinic acid might interact with cholinergic systems by virtue of its ability to reverse acetyl cholinesterase inhibition (Lippiello et al., 1989).

Inhibition binding assays were conducted in vitro to test the effects of levulinic acid and nicotine levulinate on the binding of nicotine to pharmacological receptors in membrane preparations derived from rat brain tissue (Lippiello et al., 1989). The high-affinity sites present in the tissue were saturated (i.e., >90%) by a concentration of radiolabeled nicotine (30 nM), and the level of binding was arbitrarily taken to be 100%. Nicotine binding was then plotted as a function of increased concentrations of an unlabeled competitive inhibitor (such as nicotine salicylate or nicotine levulinate). The study results showed that the levulinic compounds significantly increased the amount of nicotine bound to nicotinic receptors above the expected control level. In the case of nicotine levulinate, observed increases ranged from 20% to 50%, with a mean value of around 30%, whereas enhancement was similar although somewhat less in the case of levulinic acid alone (Lippiello et al., 1989). A graph modeling enhanced nicotine binding in the presence of levulinic acid is presented in Figure 3.

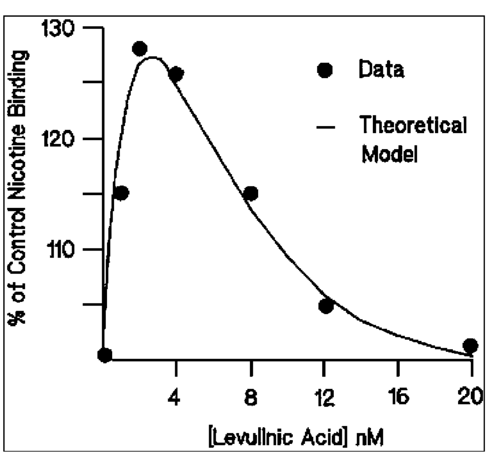

Figure 3. Theoretical curve for enhancement of [3H]-nicotine binding to nicotinic receptors. Cited in a 1989 R. J. Reynolds study on the effects of nicotine levulinate and levulinic acid on the binding of nicotine to nicotine receptors in rat brain tissue (Lippiello et al., 1989). nM, nanomoles per liter.

Lippiello et al. (1989) theorized that levulinic acid induces positive cooperativeness at an additional class of low-affinity receptor sites. Thus, in the presence of levulinic acid, nicotine binds to an additional set of receptors that would not ordinarily be responsive to the nicotine molecule. Although other organic acids were similarly tested, only levulinic acid demonstrated significant enhancement of nicotine binding, and it did so only in a narrow concentration range (Guy, 1990). At higher concentrations the effect was reversed, suggesting that levulinate also has a reasonable affinity for the nicotine binding sites and therefore eventually inhibits its own effect. Another study conducted at the University of Colorado using mouse brain tissue indicated a similar trend but with a lower magnitude of effect (i.e., maximum effect of approximately 10%–12%; as discussed in Steele [1989] and Lippiello et al. [1989]).

Application and smoke delivery of levulinic acid

Migration. Internal research suggests that use of levulinic acid may have produced unintended effects on product delivery and tobacco smoke exposure. For example, migration of levulinic acid within the cigarette was found to be a significant problem during toxicological tests conducted in 1989–1990, resulting in a significant change in the FTC tar and carbon monoxide values of test cigarettes. When levulinic acid was applied to the cigarette rod, it migrated heavily to the paper wrapper (50% after 4 months), regardless of wrapper type (Best, 1990), and not to the cellulose acetate filter (R. J. Reynolds, 1990d). The migration occurred radially, thereby decreasing the wrapper porosity. This in turn affected sidestream/mainstream ratios as well as the burn rate and puff count (R. J. Reynolds, 1989), and the amount of tobacco consumed during puff and smolder periods, resulting in more tobacco consumed during puffs (Best, 1990). These differences resulted in an increase in mainstream gases (particularly carbon monoxide and carbon dioxide) at the expense of sidestream gases. Process changes were used to arrest the migration in a later round of toxicological testing (Lloyd, 1992a), but internal analysis of these changes was not identified in the present study.

Mainstream and sidestream delivery. Levulinic acid has been reported in mainstream smoke at levels of 29–56 μg/cigarette and in sidestream smoke at 25–49 μg/cigarette (Kusama, Munakata, Ohsumi, Sakuma, & Sugawara, 1983). However, industry analysis of prototypes developed and tested internally demonstrated yields in some cases 10–100 times greater (J. H. Reynolds, 1991). Radiotracer studies performed at R. J. Reynolds found that 9% of the

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levulinic acid added to tobacco was transferred intact to mainstream smoke, with a further 3% transferred in mainstream smoke as pyrolysis products (R. J. Reynolds, 1990d). The transfer distribution between mainstream and sidestream vapor phases changed when using longer equilibration times or increasing application of levulinic acid to the wrappers, with mainstream smoke increasing and sidestream smoke decreasing (Best, 1990). Industry documents list a number of the pyrolysis products of levulinic acid and nicotine levulinate, including carcinogenic and toxic compounds such as styrene, trimethylbenzene, and naphthalene (Chung & Aldridge, 1990; Chung, Moore, & Aldridge, 1987). However, internal documents do not discuss the effects (actual or potential) of these products on the smoker.

Use of levulinic acid in commercial cigarette brands

In the late 1980s, R. J. Reynolds embarked on a series of research projects with the goal of developing a reduced-tar product with taste, impact, and satisfaction comparable with a higher delivery product (Table 2). Levulinic acid played a central role in this research. Physical, analytical, sensory, and behavioral effects were evaluated for levulinic acid, a nicotine extract ("KDN"), and various mixtures of the two, across a wide range of levels (R. J. Reynolds, 1991a). In addition to research conducted under projects targeting development of a successful ultralight brand, levulinic acid was incorporated into the development of the potentially reduced-exposure Premier prototype (R. J. Reynolds, 1990b). Internal research found that levulinic acid transferred to smoke from the Premier prototype substrate at a rate six to seven times greater, as measured by human smoking conditions, than with a standard FTC smoke-machine measure (Best, 1991).

Levulinic acid was included in a voluntary 1994 list of the 599 additives used by tobacco manufacturers in commercial cigarettes (Doull et al., 1994) and continues to be listed as an active ingredient on R. J. Reynolds's Web site (www.rjrt.com, accessed February 4, 2004). Although internal discussion of the use of additives in specific commercial brands is quite limited, the available evidence suggests that levulinic acid has been used at levels consistent with a significant role in cigarette design relative to other additives. For example, an internal commentary from 1991 noted, "Use of levulinic acid is proposed at levels which may place it within the top ten ingredients used by RJR" (Dube, 1991). The author observed the importance of obtaining further information "to identify potential concerns and defend its use" and recommended the development of a protocol for evaluation of use of this additive in commercial cigarettes. According to the list made publicly available by R. J. Reynolds's Web site, the current maximum level of levulinic acid used in any brand is 0.02%. This would equate to 200 μg in a typical (~1 g) cigarette. This level is greater than the amount common for most tobacco flavorants but below the levels typical of sugars, cocoa, licorice, and humectants. An internal file note from 1988 observed

Table 2. Series of R. J. Reynolds projects targeting use of levulinic acid.

Project	Objective	Use of levulinic acid	Outcome
Delta (Premier) (1986) (R. J. Reynolds, 1990b)	Develop cigarette that heats rather than burns tobacco (potential reduced-exposure product)	Explored ways to reduce harshness of cigarettes; organic acids evaluated for "smoothness"	Levulinic acid increased smoothness without off taste; suggests application in development of conventional (ultralight) brands considered
Project GT (1987) (R. J. Reynolds, 1990b, 1990e)	Develop product with reduced tar (ULT) comparable with full-flavor light	Explored the addition of nicotine levulinate to two ULT cigarettes, NOW and Winston Ultra Light 100s	Extremely low TN ratios, increased smoothness, low impact; no change in smoking behavior; increased nicotine delivery reflected in plasma concentrations
Project GTX (1990) (R. J. Reynolds, 1990b, 1990e)	Develop alternate methods/ sources for enhancing nicotine yields of low-tar products	Experimental nicotine levulinate sheet developed for sensory and biobehavioral testing	Concluded "ULT cigarettes with enhanced nicotine yields and good smoking characteristics can be produced"
Project XB (1991) (Lloyd, 1992b; R. J. Reynolds, 1990a, 1990e; Wilson, 1991)	Provide the taste and satisfaction of FFLT products at lower tar yields (1 mg)	"Breakthrough": when nicotine was added to levulinic acid to form nicotine levulinate, significant T/N reductions achieved with products much smoother than expected	Proposed further exploration of psychophysical and respiratory effects among normal and anosmic human subjects
KDN extract (1991) (Lloyd, 1992b; R. J. Reynolds, 1991c)	"need an in-process source of nicotine because we couldn't achieve a consumer acceptable low T/N ratio product using construction variables…"	KDN extract identified as a source of nicotine for the synthesis of nicotine levulinate, supporting use of nicotine levulinate in brand development	"Levulinic acid is what helps the KDN have a higher overall acceptance and closer subjective response to Marlboro Lights…"

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that "levulinic acid is currently used as a direct flavor additive in 12 RJRT brands at concentrations ranging from 0.040 to 154.8 μg/cigarette" (R. J. Reynolds, 1988b). Table 3 lists those cigarettes and their respective levels of levulinic acid (R. J. Reynolds, 1988c).

Discussion

Tobacco industry scientists generated considerable evidence that levulinic acid and nicotine levulinate decreased harshness and increased nicotine yield from tobacco smoke. Further, internal research demonstrated the capacity of levulinic acid to enhance the binding of nicotine in the brain, increasing its pharmacological effectiveness. The addition of levulinic acid also altered the composition of mainstream and sidestream smoke and introduced potentially toxic pyrolysis products to smoke. These combined effects could have significant implications for the increased addictiveness or toxicity of the cigarette and the progression of smoker behaviors including initiation and quitting. Measured increases in peak plasma nicotine levels among treated low-yield cigarettes confirm the importance of these internal findings in the assessment of brand deliveries.

Despite the potential health consequences, internal findings regarding the effects of levulinic acid as an additive were not reported to public health or other government agencies. Commercial products containing levulinic acid have been sold to smokers, but the relative amounts of the additive and its effects on smoke perception, behaviors, and bioavailability remain for the most part unknown. Based on recent internal industry projects, it seems likely that levulinic acid may have had particular impact in the development of so-called reduced-exposure products such as Premier and, later, Eclipse. Thus possible effects on smoker inhalation patterns or bioavailability of smoke constituents may present serious concerns regarding the evaluation of these nonconventional products, as well as conventional cigarettes. Although internal findings do not clearly indicate levels of the additive relevant for human exposure, they suggest the importance of further research in these areas.

Table 3. Levels of levulinic acid used in 12 commercial cigarettes.

Brand	Levulinic acid level (μg/cigarette)
More Light 100 Menthol Box	0.040
Salem Light 100 Custom Case Box	0.045
Century Light 100 Menthol	0.046
Salem Light 100	0.046
Vantage 85	1.407
Century 85	2.496
Magna 80 Box	2.565
Magna 85	2.584
Vantage Ultra Light 100	2.945
Winston Ultra Light 100	2.945
More 120	154.282
More Light 120	154.822

Source. R. J. Reynolds, 1988c.

Given the health risks of tobacco use and addiction, and the complicated array of additives commonly used in tobacco products, scientists and public health officials must continue to advance their knowledge of the function of additives and, ultimately, their effects. This investigation depends on adequate disclosure requirements and ongoing independent research. To date, the success of tobacco manufacturers at safeguarding the identity of the additives used in their products has prevented meaningful disclosure. Making this information available to appropriate regulatory agencies would allow researchers to assess interactions between additives and to evaluate their effects. Further, smokers would be given the opportunity to consider added chemicals and their byproducts inhaled in cigarette smoke.

A critical first step in the evaluation of the role of additives in tobacco products is the requirement of full and meaningful disclosure (by brand) to an appropriate regulatory agency, such as the U.S. Food and Drug Administration. In addition to questions of toxicity, the role of additives in controlling or altering pharmacological and sensory effects of smoke must be considered, particularly in the context of low-yield and reduced-exposure products. Future studies should include respiratory effects and bronchodilation, smoke perception, effects on absorption and receptor binding, and smoking topography. All internal toxicological and behavioral studies undertaken by manufacturers should be released to the public record, including methodologies used, data collected, and results. Finally, continuing independent public health research is needed, including product testing to identify and assess brand-specific design issues and to warn the public of potential harm.

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Pharmacological and Chemical Effects of Cigarette Additives

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We investigated tobacco industry documents and other sources for evidence of possible pharmacological and chemical effects of tobacco additives.

Our findings indicated that more than 100 of 599 documented cigarette additives have pharmacological actions that camouflage the odor of environmental tobacco smoke emitted from cigarettes, enhance or maintain nicotine delivery, could increase the addictiveness of cigarettes, and mask symptoms and illnesses associated with smoking behaviors.

Whether such uses were specifically intended for these agents is unknown. Our results provide a clear rationale for regulatory control of tobacco additives. (*Am J Public Health.* 2007;97:1981–1991. doi:10.2105/AJPH.2005.078014)

ACCORDING TO THE WORLD Health Organization, there were approximately 1.3 billion smokers worldwide in 2003, and that number is expected to increase to 1.7 billion by 2020.[1] It is estimated that about 1 billion people will die from smoking in the 21st century.[2] Research conducted over the past several decades indicates that tobacco companies have engaged in extensive efforts, including developing genetically engineered tobacco to enhance nicotine delivery[3–6] and using reconstituted tobacco and nicotine extracts, to manipulate cigarette nicotine levels and influence people's smoking behaviors.

Reconstituted tobacco, referred to as "sheet," is a major ingredient in modern cigarettes; sheet is manufactured from recycled stems, stalks, scraps, collected dust, and floor sweepings.[7] Those materials are ground up, nicotine is extracted from them, and chemicals, fillers, glue, and other agents are added to the slurry. The sheet is then pressed out and puffed, with the previously extracted nicotine sprayed onto it, and ground into tiny curls before being incorporated into cigarettes at the desired level.[7] Tobacco companies have studied nicotine extracts as a method to augment nicotine levels in cigarettes.[8–14]

In addition, tobacco companies have devoted a significant amount of research and development to the use and inclusion of additives in cigarettes, and the industry has acknowledged using 599 different cigarette additives.[15,16] According to various tobacco company documents, many of these additives are used to improve taste and decrease harshness.[17] We propose that, in contrast, tobacco companies have expended resources to exploit the pharmacological and chemical effects of cigarette additives.

The tobacco industry used few additives in US cigarettes before 1970.[18] However, current US-style cigarettes generally contain about a 10% level of additives according to weight, mostly in the form of sugars, humectants, ammonia compounds, cocoa, and licorice.[19,20] Most other additives are used in small amounts, less than 0.01% of total weight. There is evidence that the percentage of additives by weight may have increased in the 1990s, especially the use of sweeteners (which many researchers believe were added to entice younger people to smoke).[18] Those increases roughly coincided with the controversial Joe Camel cigarette advertising campaign initiated by RJ Reynolds in 1985.

Previous studies have reviewed the use of ammonia technology to increase levels of nicotine and free base nicotine in cigarette smoke[18]; the use of additives with additional or synergistic addictive potential, anesthetic properties, or bronchodilator effects; and the use of additives that decrease environmental tobacco smoke (ETS) odor, visibility, and irritation without equivalent efforts to decrease the harmful effects of ETS.[18,21,22] These tobacco industry practices, motivated by awareness of public concern regarding ETS, may have led to nonsmokers as well as smokers being unaware or less aware of the presence of hazardous substances associated with ETS.[23–27]

In this study, we examined the tobacco industry's use of additives that inhibit nicotine metabolism and increase the addictive potential of cigarettes, with a particular focus on the neurological techniques used by Philip Morris to assess the effects of additives on smokers' central nervous system functioning. We also explored the addition of antioxidants and mitigants to cigarettes in an attempt to prevent illness, genetic modifications of tobacco to increase levels of beta-carotene and incorporate molecules intended to decrease carcinogenic tobacco-specific nitrosamines, the use of other "beneficial" additives and specific chemical additives, and the tobacco industry's objections[17] to scientific discussions[18] about additives used for cigarette engineering and nicotine addiction.

METHODS

We used 5 primary sources of information for our review. First, we examined an Indiana University Web site aggregate list of 599 known cigarette additives (the industry does not specify which brands use particular additives).[15] In 1984, the US Department of Health and Human Services began requiring tobacco companies to submit annually a confidential, aggregated list of ingredients added to cigarettes manufactured in or imported into the United States. In 1994, National Public Radio reported on a number of these ingredients, which caused a public outcry. Subsequently, in that same year, the 6 major US tobacco companies made the list public. This was the only time the list was made public, and there is no current public list of tobacco additives.

Second, we reviewed documents from 2000 to 2005 housed in the Legacy Tobacco Documents Library ("Legacy Library") at the University of California, San Francisco.[28] The Legacy Library contains 7 million documents related to different practices associated with tobacco products. Visitors can search, view, and download these documents from the library Web site. Included are documents posted on tobacco industry Web sites as of July 1999 in accordance with the Master Settlement Agreement, documents added to those sites since that time, and the document collections from the Tobacco Control Archives maintained by the University of California, San Francisco. New documents are added monthly as they are collected from industry sites.

Initially, we searched for documents about additives on the Indiana University list, as well as keywords such as "additive" and combinations of keywords such as "additive" and "environmental tobacco smoke." To further our understanding of the use of additives, we employed snowball sampling methods wherein the content of the documents we reviewed (e.g., names, references to other documents, and important concepts) would then be searched in the Legacy Library. We followed these document leads in an effort to better assess industry efforts associated with tobacco additives. In all, we reviewed more than 10 000 documents.

Third, we reviewed a Memorial Sloan Kettering Cancer Center Web site that included science-based information on herbs and other supplements.[29] Fourth, we searched US Patent and Trademark Office Web site databases[30] in an attempt to gain an understanding of patents referenced by numbers and titles in Legacy Library documents. Finally, we used Internet searches and tobacco-related and other reference textbooks[2,31] to gain greater insight into previously reviewed material. Internet search engine technology was used to locate information not in the Legacy Library and to verify the information found therein.

RESULTS

Nicotine Metabolism and Addiction Potential

Numerous chemical agents, including gamma-heptalactone, gamma-valerolactone, gamma-decalactone, delta-decalactone, gamma-dodecalactone, delta-undecalactone, and gamma-hexalactone, are mild to weak inhibitors of coumarin-7-hydroxylases (also known as CYP2A5 and CYP2A6; these are enzymes within the P450 enzyme system that metabolize compounds in the body).[32] These 7 chemicals are among those found on the additives list. Because CYP2A6 is involved in the metabolism of nicotine, the presence of these chemicals could decrease smokers' metabolism of nicotine and maintain higher blood levels (thus increasing smokers' exposure to nicotine by slowing degradation of nicotine in the bloodstream). Furthermore, the inhibitory effect of these chemicals on CYP2A6, although relatively weak in isolation, might be greater when the chemicals act in combination.

If nicotine were the only addictive chemical affecting smoking behavior, then puffing should decrease as the amount of inhaled nicotine increases. However, this hypothesis does not account for the effects of other addictive substances in cigarettes. Acetaldehyde is formed in high concentrations when cigarette constituents, including sugars, are burned. Animal research conducted by Philip Morris demonstrated a synergistic interaction between nicotine and acetaldehyde: rats pressed a bar more for the combination than for either substance alone.[33,34] If these data generalize to humans, then smokers would puff more with the combination of nicotine and acetaldehyde. Industry data show that the combination of sugar, sorbitol, and diammonium phosphate (DAP) increases tar and nicotine levels and number of puffs taken.[35]

Neuropsychological Assessments

Philip Morris developed the science of nicotine delivery and measurement of the effects of nicotine far beyond what was known by the medical community. One goal of the Philip Morris Behavioral Research Lab, described in a 1981 document, was to identify responses of the human brain that change in a predictable and reliable manner as a function of cigarette smoking.[36] In research projects conducted by Philip Morris from 1982 to 1995 (e.g., Project 1620[37]), electroencephalography (EEG), pattern reversal evoked potential (PREP), and chemosensory event-related potential (CSERP) were used to measure physiological, sensory, and cognitive changes related to nicotine and to cigarette additives.[38]

Increases in tobacco filler pH increased the "impact" (a tobacco industry term for smokers' subjective awareness of the drug effects of nicotine) and decreased PREP P_1 latencies (an objective electrophysiological measure of brain activity).[39] Philip Morris's research demonstrated "a systematic relationship between increases in filler pH and increases in gas phase (presumably unprotonated) nicotine."[37] Philip Morris researchers noted a significant positive correlation between impact scores and P_1-N_2 amplitudes (another objective electrophysiological measure of brain activity), both of which were shown to increase with increased nicotine or menthol delivery. However, the effect of the interaction between nicotine and menthol levels on impact and P_1-N_2 was not a simple linear relationship; rather, it was found to be complex.[40] Further research by Philip Morris determined that the addition of other chemicals (e.g., pyrazine, vanillin, and propylene glycol) increased P_1-N_2 amplitudes.[41]

Sensory CSERP studies investigated whether given flavorants stimulated the olfactory nerve, the trigeminal nerve, or both.[38] Gullotta, one of the Philip Morris researchers, reported that CSERPs provided an objective measure of both impact and odor discrimination, in that different tobacco flavorants (e.g., natural vs synthetic menthol) affected CSERPs differently, even when smokers were unable to discriminate subjectively.[38] In effect, Philip Morris developed a putative method of objectively measuring and quantifying "impact."[40]

Addition of Antioxidants and Mitigants

RJ Reynolds investigated the addition of beta-carotene to cigarettes, including development of genetically engineered tobacco plants with genes inserted for beta-carotene production. RJ Reynolds's beta-carotene study group consisted of representatives from 15 different departments within RJ Reynolds.[42–45] Documents describing this group's activity were found for 1992 and 1993, but no subsequent documents were found to allow determination of how long the group continued to operate or whether it was disbanded or why.

It is unknown whether the 1994 *New England Journal of Medicine* report[46] suggesting that oral beta-carotene supplements might have harmful effects on smokers (e.g., increased frequencies of lung cancer and ischemic heart disease) affected this group's disposition. Its original vision statement was "to enhance natural tobacco components that may have potential to either reduce or mitigate the biological activity of tobacco-burning cigarettes."[43] This statement was later amended as follows: "to provide smokers with products which contain biological activity mitigants."[42] Biological activities targeted included reducing nitrosamine levels, nitric oxide levels, carbonyl groups, Ames activity (a measure of mutagenic and carcinogenic potential), ciliostatic and cytotoxic response, and possibly free radical concentrations.[44]

Numerous RJ Reynolds documents showed that the company considered adding mitigants, such as beta-carotene, to cigarettes.[42,47–56] Mitigants were defined as antioxidants and other compounds for free radical reduction (i.e., reduction of the concentration of free radicals)[57,58]; compounds "that combat the biological effect of some compounds in cigarette smoke," such as reducing oxidative stress[47]; and compounds that "may reduce the risk of developing alleged smoking-related illnesses."[45] RJ Reynolds catalogued and studied mitigants.[42,53] Many of these compounds can be found within plant additives or as direct chemical additives to cigarettes. Of 127 chemicals included on one RJ Reynolds list of mitigants,[42] 12 were direct chemical additives to cigarettes (e.g., beta-carotene, vitamin C, tannic acid, vanillin), and 40 were contained in botanical additives on the tobacco industry additives list[15] (Table 1).

Genetic Modification of Tobacco

In addition to Brown and Williamson's efforts to genetically manipulate nicotine levels of cigarettes sold in the United States (which have been documented in the media[6]), other companies in the industry also engaged in biotechnology development projects. Two examples were RJ Reynolds's development projects designed to incorporate the beta-carotene gene, control nicotine levels, and genetically modify the tobacco plant in other ways[97–100] and Philip Morris's development of specific molecules (antisense RNA) to decrease carcinogenic tobacco-specific nitrosamines.[101]

Use of "Beneficial" Additives

A 1981 surgeon general's report, *The Changing Cigarette*, expressed concern about cigarette additives causing additional or new health care risks.[102(pp6,8,51–52,99–100)] After the publication of that report, incorporation of "beneficial" additives into cigarettes was discussed at a pair of Philip Morris meetings in 1981.[103] In addition to scientists and other research and development personnel from Philip Morris, Hamish Maxwell, the CEO and president of Philip Morris, attended the meetings.

TABLE 1—Possible Pharmacological Effects of Selected Chemical Additives

Chemical	Possible Pharmacological Effects
Acetaldehyde[34,59–61]	Positive reinforcer that acts on the CNS, synergistic and enhanced reinforcing effects with nicotine, may contribute to addiction, carcinogen, production increased with increased use of sugars in cigarettes
Aconitic acid[17]	Unproven uses: treatment of neuralgia, serous skin inflammation, migraine, myalgia, rheumatism, pleurisy, mucosal diseases, pericarditis sicca, fever, anti-inflammatory, cardiac tonic (aconitin can trigger cardiac arrhythmia), and for disinfecting and wound treatment
Alpha-tocopherol [47,48,51–58]	Antioxidant/mitigant; extensively studied by RJR for addition to cigarettes for mitigant effect
Beta-carotene[47,48,51,58]	Antioxidant/mitigant; extensively studied by RJR for addition to cigarettes for mitigant effect
Benzyl salicylate[62]	Flavorant that is also anti-inflammatory, antipyretic, analgesic (partly to completely metabolized to salicylic acid)
Caffeic acid[51] (in botanical additives)	According to RJR, blocks the formation of nitrosamines in vivo, and "results of study suggest that dietary caffeic acid and ferulic acid may play a role in the body's defense against carcinogenesis by inhibiting the formation of N-nitroso compounds"[51]
Cocoa[13,63]	Contains theobromine, a bronchodilator; suspected to be added to entice young people to smoke
Chocolate[13,63]	Contains theobromine, a bronchodilator; suspected to be added to entice young people to smoke
Ethyl salicylate[62]	Flavorant, also anti-inflammatory, antipyretic, analgesic (partly to completely metabolized to salicylic acid)
Ethyl-vanillin[63]	Flavorant, subjectively experienced as similar to sugar
Eucalyptol (1,8-cineole)[64–68]	Antimicrobial, increases lung mucociliary clearance, suppresses arachidonic acid metabolism and cytokine production in human monocytes, anti-inflammatory activity in asthma patients; induction of apoptosis in human leukemia cell lines, antinocioceptive
Eugenol[31,69]	Used in cigarettes in 1970s and 1980s; a local anesthetic compound of interest to scientists because of potential CNS depressant effect that was possibly synergistic with barbiturates and alcohol, and because of a possible interaction of nicotine as a stimulant with eugenol as a depressant[31]; removed after possible hepatotoxic and carcinogenic effects of the compound were discovered.[70–74] An internal 1985 RJR document[69] indicated awareness of eugenol's pharmacological properties and stated that "eugenol is also used as a local anesthetic in temporary dental fillings and cements, as a fungicide in pharmaceuticals and cosmetics. . . . Pharmacologically, eugenol has been reported to exhibit antiseptic properties, analgesic action (local and general), spasmolytic and myorelaxant activities, parasympathetic effects (salivary gland secretion), and direct peripheral vasodilation."[69] RJR also knew that it was present in botanical agents. Although eugenol is no longer found in the list of additives, it is still present in many of the botanical agents that are used as additives, including basil, black pepper, Ceylon citronella, Ceylon cinnamon, lovage, licorice, mace, thyme, and other botanical additives
Farnesol[75]	Inhibits growth and viability of a variety of neoplastic cells
Ferulic acid[51] (in botanical additives)	According to RJR, blocks the formation of nitrosamines in vivo, and "results of study suggest that dietary caffeic acid and ferulic acid may play a role in the body's defense against carcinogenesis by inhibiting the formation of N-nitroso compounds"[51]
Glycyrrhizin, ammoniated[76–80]	Glycyrrhizin has anti-inflammatory, antiviral, and anti–gastrointestinal ulcer properties; may enhance interleukin 10 production
Isobutyl salicylate[62]	Flavorant, also anti-inflammatory, anti-pyretic, analgesic (partly to completely metabolized to salicylic acid)
Isovaleric acid[69,81,82,75–80,83]	Possible pheromone effect. Isovaleric acid is a component of the pheromones present in the vaginal secretions responsible in the female rhesus monkey for stimulating sexual behavior in the male. It is also found to be one of the major components of the subauricular gland secretion of the male pronghorn (antelope); its odor produces a strong response from the male as indicated by sniffing, licking, marking, and thrashing
Levulinic acid[19,84]	Nicotine levulinate and levulinic acid enhance the binding of nicotine to nicotinic receptors in rat and mouse brains. Levulinic acid also increases peak plasma nicotine levels while enhancing perceptions of smoothness and mildness; it desensitizes the upper respiratory tract, increasing the potential for cigarette smoke to be inhaled deeper into the lungs
D-limonene[29] (and its metabolites, perillic acid, dihydroperillic acid, perillyl alcohol, uroterpenol, and limonene1,2-diol)	Possible anticancer properties. May inhibit tumor growth via inhibition of p21-dependent signaling and apoptosis resulting from induction of the transforming growth factor beta-signaling pathway. D-limonene metabolites also cause G1 cell cycle arrest, inhibit posttranslational modification of signal transduction proteins, and cause differential expression of cell cycle–related and apoptosis-related genes. Animal studies show activity of D-limonene against pancreatic, stomach, colon, skin, and liver cancers. Data also indicate that D-limonene slows the promotion/progression stage of carcinogen-induced tumors in rats
Menthol[85]	Anesthetic action, complex interaction with nicotine, increase in P_1-N_2 amplitudes
Methyl salicylate[62]	Anti-inflammatory, antipyretic, analgesic, counterirritant (partly to completely metabolized to salicylic acid)

Continued

TABLE 1—*Continued*

Mitigants[15,42,86]	Of 127 chemicals on a list of mitigants,[42] 12 are direct chemical additives to cigarettes (beta-carotene, ascorbic acid/vitamin C, L-histidine, cinnamaldehyde, histidine, tannic acid, lauric acid, octanoic acid, oleic acid, vanillin, essential oils), and 40 are contained within botanical additives on the University of Indiana list of tobacco additives[15] (carotenoids, beta-carotene, ascorbic acid/vitamin C, bioflavonoids, catechin, myricetin, quercitin, isoquercitrin, quercitrin, rutin, kaemferol, naringenin, naringin, epigallocatechin gallate, caffeic acid, L-histidine, alpha-tocopherol/vitamin E, tryptophan, glutathionine, provitamin A, chlorophylls, chlorophyllin, cinnamaldehyde, curcumin, ellagic acid, eugenol, ferulic acid, gallic acid, histidine, tannic acid, chlorogenic acid, linoleic acid, linolenic acid, lauric acid, octanoic acid, oleic acid, vanillin, vitamin B2, polyphenols, essential oils)
Phenethyl salicylate[62]	Flavorant, also anti-inflammatory, antipyretic, analgesic (partly to completely metabolized to salicylic acid)
Propylene glycol[31]	Alters P_1-N_2 amplitude, an objective CNS activity measure correlated with favorable sensory characteristics of cigarettes
Pyrazine[31]	Alters P_1-N_2 amplitude, an objective CNS activity measure correlated with favorable sensory characteristics of cigarettes
Pyridine[13,87]	Has documented similar peripheral effects, but opposite CNS effects, to nicotine; has suspected synergistic CNS effects
Salicy-acetaldehyde[62,88]	Metabolized by oxidation to salicylic acid. Promotes wound healing and granulation when applied topically, and was shown in a rat study to be a less potent analgesic and anti-inflammatory agent. Equipotent with salicylic acid, methyl salicylate, and aspirin in hindpaw edema assay; equipotent with aspirin in acute inflammation
Thiamine hydrochloride	Vitamin B1
5,6,7,8-tetrahydroquinoxaline[89,90]	Tetrahydroquinolines, on the basis of experimental data, have been hypothesized to act as "false neurotransmitters" in catecholamine-containing neurons. In the 1960s, formaldehyde was shown to condense with endogenous catecholamines to form tetrahydroquinolines. That acetaldehyde is highly reactive with catecholamines was one of the reasons for DeNoble pursuing his research on the reinforcing effects of acetaldehyde.[91] Might serve as a "false neurotransmitter"[91] and might have an addictive effect
Valeric acid[92–96]	Flavorant. Chemical in botanical Valeriana officinalis, which is also a listed additive. Valeric acid has documented direct sedative effects and interactions with neurotransmitters such as GABA
Gamma-valerolactone[32]	Inhibits CYP2A6, a nicotine metabolizing enzyme, which could lead to higher nicotine blood levels. There are 20 known chemically related lactone compounds that are included on the University of Indiana list of additives and are known to inhibit CYP2A6. In addition, on the basis of a study noting that the level of inhibition of CYP2A6 varies by side chain substitutions, at least 14 other lactone compounds also on the University of Indiana list of additives may act as CYP2A6 inhibitors as well
Vanillin[31,63]	Flavorant. Also increases P_1-N_2 amplitude, an objective CNS activity measure correlated with favorable sensory characteristics of cigarettes, subjectively experienced as similar to sugar

Note. CNS = central nervous system; RJR = RJ Reynolds. This is not an exhaustive list of specific chemical additives with pharmacological effects; rather, it represents selected examples of additives with possible pharmacological effects.

The Philip Morris document summarizing these meetings defined "beneficial" as follows: (1) "creating more profit (sales) to Philip Morris"; (2) "creating a positive public image"; (3) "being safe, good for you as well as pleasurable"; and (4) "creating a favorable image with government agencies."[103] The document also stated that "rather than deliver a physiological effect directly we might incorporate an additive which causes the body to produce its own physiological agent. Thus, we could alleviate pain, increase sex drive, etc., without adding agents to do this but by adding a naturally occurring promoter."[103] Moreover:

> It was noted that one beneficial attribute ascribed to smoking is appetite suppressance [sic]. A thorough study of this effect and publication of the results may have a beneficial impact on the image of smoking. If particular compounds responsible for the effect can be found, it might be possible to enhance the effect in a cigarette aimed at people desiring help with weight control. Care must be taken not to make specific claims or to invoke a "drug additive" image.[103]

Finally, according to the document:

> Other factors were thought of (in addition to appetite suppression) that could be screened for beneficial effects of smoking. The idea again is to ascribe the effect to an additive that is already naturally occurring in tobacco, and then to possibly manipulate that additive: a) dental caries [tooth decay], b) reduction in constipation, c) heart rate regulation, d) effects in colds (i.e., mentholated brands), [and] e) anxiety reduction.[103]

No information is available on the extent to which Philip Morris engaged in subsequent action to study or incorporate the "beneficial" additives discussed at these meetings.

A separate Philip Morris document titled *Nontobacco Biological/Botanical Smoking Materials*[104] included a long list of patent numbers associated with specific plants (patents listed in reviewed documents were reviewed to gain additional insight into what the tobacco documents were discussing and research that specific tobacco companies were considering or pursuing). Several of those patents discussed direct "beneficial" physiological actions of botanical additives. In one US patent cited,[105] it was noted that nicotine in cigarettes has a deleterious vasoconstrictive effect on the cardiovascular system, particularly the blood vessels within and surrounding the heart. It was also noted that vaporized niacin in cigarette smoke has a vasodilating action that helps counteract the vasoconstrictive effect of nicotine. Furthermore, additional "beneficial" effects may be obtained when niacin is combined with rutin (a chemical found in botanicals), "which is considered effective in reducing and preventing capillary fragility."[105]

The patent went on to state that "niacin and rutin may also be incorporated in a smoking composition which is made from vegetable materials other than nicotine-containing tobacco and de-nicotinized tobacco."[105] It was noted that both compounds should be in the range of 0.1% to 2.5% by weight of the cigarette.[105] It is not known whether cigarettes were ever manipulated to have that concentration range of those chemicals. However, it is known that Philip Morris studied niacin in cigarettes,[106,107] investigated commercial production of niacin (i.e., nicotinic acid) and the cost associated with purchasing niacin in lots of 5000 or more kilograms,[108] and studied naturally occurring rutin in cigarettes.[109]

The patent listed 33 botanicals or vegetable materials, or compounds within them, that also appear on the tobacco industry cigarette additive list, including beets, carrots, chamomile, corn, eucalyptus, maple and maple syrup, menthe piperita, oak, patchouli, rose, and vanilla plantifolia. In its discussion of cigarette casing material, the patent listed caramel, licorice root, niacin, rutin, and glycerol as possible additives and noted that the following aromatics, flavoring agents, sweeteners, coloring agents, and humectants could be added or substituted in a vegetable material preparation that would naturally contain niacin and rutin: sage, honey, sucrose, vanillin, coumarin, vanilla bean, fruit flavors, molasses, propylene glycol, apple juice, apple cider, essential oils, anise, angelica, and prune juice. It is noteworthy that so many botanical agents listed in the patent are also mentioned on the tobacco industry's list of additives.[105]

Through the years, Philip Morris has maintained listings of patents on vitamins and therapeutic ingredients in cigarettes[110] as well as listings of patents on medicated cigarettes[111,112] The documents focusing on medicated cigarettes[111,112] discussed patents on cigarettes with therapeutic or anticarcinogenic additives and additives that relieve or treat bronchial irritation through means other than cigarette mentholation. Many of the ingredients were derived from pharmacologically active botanicals. However, as noted, it is not known how much effort Philip Morris engaged in to incorporate "beneficial" additives for the uses described in this section.

Other Specific Chemical Additives

Tobacco companies have added many other chemicals with a wide variety of possible effects (Figure 1). Table 1 includes a summary of chemical additives that may have pharmacological effects.[59–96,113]

Tobacco Industry Objections

Tobacco industry representatives attempted to refute the conclusions of Bates et al.[18] that cigarette additives were added to enhance nicotine addiction and induce other pharmacological effects. A 1999 industry statement denied that use of ammonia compounds increased the amount of ammonia in cigarette smoke, increased smoke pH, increased the amount of nicotine in smoke, or influenced nicotine yield as determined by the Federal Trade Commission/International Organization for Standardization method.[17] This refutation ignored tobacco industry documentation of extensive research on ammonia technology and its effect on nicotine form and physiology.[18,21]

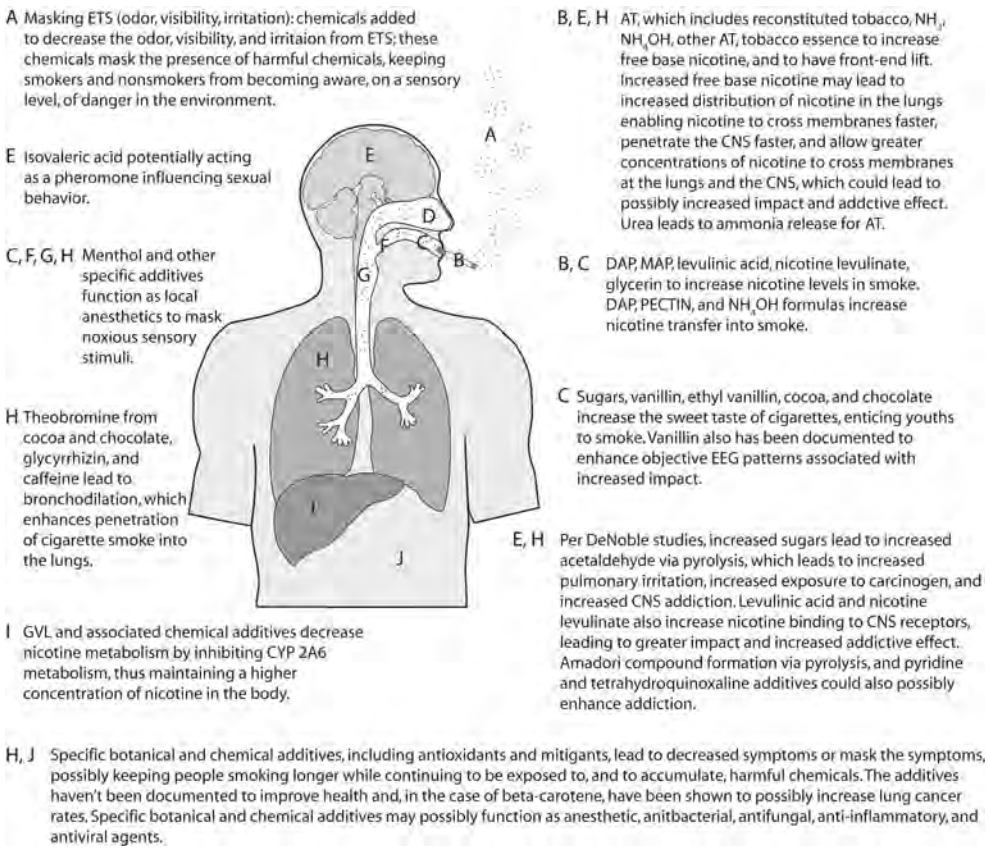
Also, the 1999 industry document just cited[17] stated that a synergistic effect of nicotine and acetaldehyde is unlikely.[17] However, Philip Morris research has clearly documented a synergistic effect on addictive behavior in rats. The document further stated that plasma levels of theobromine in smokers are far below the dose necessary for a pharmacological effect[17] and that glycyrrhizin is not transferred into mainstream smoke and has no bronchodilator effect.[17] Furthermore, the industry statement denied that levulinic acid and pyridine are used in the production of cigarettes.[17] However, levulinic acid and pyridine are on the list of additives prepared by the tobacco industry.[15] This industry statement emphasized that the additives discussed were used in casings or were used to enhance flavor.[17]

DISCUSSION

Increased knowledge about cigarette additives makes it clear that modern cigarettes are very different from cigarettes of the past, in that they have been extensively engineered to be delivery devices for nicotine and other ingredients. Evidence from tobacco industry documents indicates that additives have been used to increase free base nicotine and addiction potential and to mask and treat symptoms.

Free Base Nicotine and Addiction Potential

Previous research[18,21,114] makes it clear that the industry expended significant resources to develop and use methods to increase free base nicotine via ammonia technology and other methods. Industry research and development programs designed to develop methods to manipulate nicotine levels and forms (i.e., salt particulate, free base particulate, vapor free base) took place over 4 decades, starting in the 1960s. Increases in free base nicotine have been implicated in



Note. ETS = environmental tobacco smoke; GVL = gamma-valerolactone; AT = ammonia technology; NH_3 = ammonia; NH_4OH = ammonia hydroxide; CNS = central nervous system; DAP = diammonium phosphate; MAP = monoammonium phosphate.

FIGURE 1—Summary of pharmacological and chemical effects of cigarette additives.

increasing the addictive potential of cigarettes.[18,21,114]

The tobacco industry's scientific efforts were far more advanced compared with public scientific efforts to understand nicotine addiction. Philip Morris's research into EEG, PREP, and CSERP shows that the tobacco company attempted to quantify "impact" and to monitor the neurological effects of specific additives to maximize "cigarette acceptance" (which encompasses factors such as cigarette "satisfaction" and is influenced by a number of elements, including primary reinforcement [e.g., nicotine addiction] and secondary reinforcement[115]).

From a public health perspective, increasing the addictive potential of cigarettes with additives (e.g., via formulas including sugar, sorbitol, and DAP) increases the likelihood that new smokers will become addicted and that current smokers will have more difficulty quitting. Consequently, there will be greater levels of morbidity and mortality associated with smoking.

Masking and Treating Symptoms

The tobacco industry has stated that additives are used primarily for flavoring and "smoothing" the smoker's experience. However, a review of botanical medicine sources[103,116] indicates that many botanical and phytochemical additives have other properties, including anesthetic, antibacterial, anticancer, anti-inflammatory, antifungal, and antiviral properties. Industry documents[65,104,110–112] show awareness of and interest in these additional properties.

Unregulated botanical and chemical additives might have "multiple use" purposes, such as enhancing flavor and providing for a "smoother" smoking experience as well as preventing or masking symptoms associated with illnesses induced by smoking. Because inclusion of botanical and chemical additives could reduce, mask, or prevent smokers' awareness of the adverse symptoms caused by smoking (e.g., cough), smokers might continue to smoke even when they are ill, preventing reductions in cigarette consumption and sales revenues.

RJ Reynolds's addition of beta-carotene to cigarettes suggests that adverse health effects can occur even when a seemingly benign additive is used and points to the need for regulation by the Food and Drug Administration. Although the actions of beta-carotene and other additives may have decreased the carcinogenicity of cigarettes, their use may have unintentionally increased the risk for and rate of lung cancer in smokers.

A 1994 study concluded that there was no reduction in the incidence of lung cancer among male smokers after 5 to 8 years of oral supplementation with alpha-tocopherol or beta-carotene. That study raised the possibility that oral beta-carotene supplements might actually have harmful effects in smokers and might increase lung cancer rates.[46] A newer study[117] also has documented the possible adverse effects of oral beta-carotene on lung cancer. This is an example of the potential occurrence of unwanted and unanticipated dangerous effects if appropriate regulatory agencies do not monitor the use of additives.

Unresolved Issues

The actual composition of extracts used, the parts of plants used, and the physiological and pathological effects of these additives are unknown. It is not clear whether sufficient amounts of pharmacologically active chemicals derived from these additives remain after pyrolysis; no information is available on the effects of combustion of these compounds in cigarettes at the concentrations used, let alone whether the combustion products actually have any of the listed properties in vivo when smoked. For example, only scientific experimentation will be able to reveal whether theobromine, glycyrrhizin, and other cigarette additives induce a bronchodilator effect.

Conclusions

Modern cigarettes have been extensively engineered and optimized as nicotine delivery devices developed through major national and international research and development programs. The average smoker has been unaware of these efforts by the tobacco industry and of the extensive manipulation of cigarette chemistry.

Our results indicate that more than 100 of 599 documented cigarette additives have pharmacological actions. Previous research[18,21,22] has documented extensive efforts by the tobacco industry to use additives to mask the presence of ETS by reducing the visibility, odor, and irritability of tobacco smoke. Similar to the findings of previous studies, our results show that the tobacco industry used additives (1) that enhance or maintain nicotine delivery and could increase the addictiveness of cigarettes and (2) that mask symptoms and illnesses associated with smoking behavior.

To our knowledge, there has been no systematic evaluation of the public health effects of cigarette additives or their combustion products. The tobacco industry has actively manipulated cigarette content by using potentially hazardous chemical and phytochemical additives that should be regulated. Unregulated use of additives in tobacco products subjects billions of smokers and nonsmokers alike to an uncontrolled experiment with potentially devastating health effects. ■

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Contributors

M. Rabinoff was involved with all aspects of research, writing, and editing of the article. N. Caskey was involved in all aspects of editing and helped with research on many of the issues brought up during the review process. A. Rissling helped with most areas of research and did some writing for the initial version of the article. C. Park helped with research on numerous issues, especially on the topic of additives affecting environmental tobacco smoke.

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Human Participant Protection

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ORIGINAL INVESTIGATION

The Role of Cocoa as a Cigarette Additive: Opportunities for Product Regulation

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ABSTRACT

Introduction: The 2009 Family Smoking Prevention and Tobacco Control Act prohibited the use of characterizing flavors in cigarettes; however, some of these flavors are still used in cigarettes at varying levels. We reviewed tobacco industry internal documents to investigate the role of one of these flavors, cocoa, with the objective of understanding its relationship to sensory and risk perception, promotion of dependence, and enhancement of attractiveness and acceptability.

Methods: We used the Legacy Tobacco Documents Library to identify documents relevant to our research questions. Initial search terms were generated following an examination of published literature on cocoa, other cigarette additives, and sensory and risk perception. Further research questions and search terms were generated based on review of documents generated from the initial search terms.

Results: Cocoa is widely applied to cigarettes and has been used by the tobacco industry as an additive since the early 20th century. Cocoa can alter the sensory properties of cigarette smoke, including by providing a more appealing taste and decreasing its harshness. The tobacco industry has experimented with manipulating cocoa levels as a means of achieving sensory properties that appeal to women and youth.

Conclusions: Although cocoa is identified as a flavor on tobacco industry Web sites, it may serve other sensory purposes in cigarettes as well. Eliminating cocoa as an additive from tobacco products may affect tobacco product abuse liability by altering smokers' perceptions of product risk, and decreasing product appeal, especially among vulnerable populations.

INTRODUCTION

Cigarettes are highly engineered products that allow smokers to optimize their delivered dose of nicotine, the primary addictive agent in tobacco (Henningfield & Fant, 1999). In the United States, an estimated 45 million people smoke cigarettes, and 3,000 young people try smoking every day (Centers for Disease Control and Prevention [CDC], 2011; Substance Abuse and Mental Health Services Administration [SAMHSA], 2011). As the primary cause of preventable morbidity and mortality, cigarette smoking causes more than 440,000 deaths each year in the United States (CDC, 2008). In 2009, Congress passed the Family Smoking Prevention and Tobacco Control Act (FSPTCA), providing the U.S. Food and Drug Administration (FDA) with the unprecedented authority to regulate tobacco products (U.S. FDA, 2009). The law empowers the FDA to set standards for tobacco products in the interest of public health, defined in terms of likelihood of initiation, maintenance of use, and harm to nonusers (U.S. FDA, 2009). As a provision of the law, all cigarettes with "characterizing flavors" have been removed from the market in the United States (U.S. FDA, 2009).

Published reviews of internal tobacco industry documents have revealed that the tobacco industry altered cigarette design and additives to target groups such as young new smokers, women, racial/ethnic minorities, and health concerned smokers (Carpenter, Wayne, & Connolly, 2005; Ferris Wayne & Connolly, 2002; Kreslake, Wayne, & Connolly, 2008). Manufacturers modify additives, design features, and tobacco blends to attract target groups (Carpenter et al., 2005; Ferris Wayne & Connolly, 2002). One example is the development of brands that targeted young women using specific design features that increased smoke mildness and reduced tobacco taste (Carpenter et al., 2005). Some tobacco additives have been shown to increase tobacco products' attractiveness by ameliorating or masking the natural harshness of tobacco, thereby easing use (Kreslake

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et al., 2008). A clear understanding of product design and constituents associated with enhancing attractiveness and appeal is needed to establish a science base for regulation. Product design features and additives that are not pharmacologically active may still play a role in stimulating and facilitating trial and experimentation (Henningfield, Hatsukami, Zeller, & Peters, 2011; Scientific Committee on Emerging and Newly Identified Health Risks, 2010). Regulation of tobacco products that affects their attractiveness and appeal could reduce the public health impact of tobacco (McNeill, Hammond, & Gartner, 2012). Research is needed to determine how cigarette design increases appeal and attractiveness in order to inform product regulation.

American cigarettes are a blend of Virginia, Burley, Oriental, and reconstituted tobaccos (Abdallah, 2004). Tobaccos are blended to achieve specific sensory characteristics, which smokers experience as a combination of gustatory (taste), olfactory (smell), and tactile (feel) effects (Carpenter, Wayne, & Connolly, 2007). These effects arise from the physiological responses from the stimulation of the olfactory and trigeminal nerves and collectively make up the sensory perception of tobacco smoke flavor, according to Philip Morris (PM) (Philip Morris, 1999; Tobacco Products Scientific Advisory Committee [TPSAC], 2011). Flavorings are added to casings (the additive solution applied to tobacco blends), which are added both during leaf processing, and often to reconstituted tobacco sheets (Browne, 1990). In American blended cigarettes, additives represent up to 10% of cigarette weight (Scientific Committee on Emerging and Newly Identified Health Risks, 2010). The tobacco industry uses hundreds of different additives, some of which have effects at very low levels (Rabinoff, Caskey, Rissling, & Park, 2007). Internal tobacco industry documents show that flavors are commonly added to cigarettes to mask the harshness of smoke and increase product acceptability or attractiveness (Rabinoff et al., 2007). One common flavor additive in American blended cigarettes is cocoa.

Chocolate flavor may make cigarettes more palatable to younger, first time users and may indirectly facilitate dependence by providing enhanced flavor and mouth sensations, potentially serving as a cue for drug reward (Bates, Connolly, & Jarvis, 1999; Rambali et al., 2002; Scientific Committee on Emerging and Newly Identified Health Risks, 2010; World Health Organization [WHO], 2007). Cocoa includes a range of psychoactive constituents including caffeine and theobromine, which is part of a group of chemical compounds called xanthines (Rambali et al., 2002). Xanthines are characterized by their central nervous system (CNS) effects and their ability to relax smooth muscle and bronchodilate (Rambali et al., 2002). Unlike other xanthines, theobromine is not typically used in asthma medications, as a result of its comparatively weaker bronchodilatory effects (Rambali et al., 2002). Previous research has indicated that the amount of theobromine present in cigarettes (an estimated 0.19 mg per cigarette) is likely not sufficient to produce these effects (Rambali et al., 2002). Theobromine also tends to have substantially weaker CNS action than other xanthines (Rambali et al., 2002).

The FDA's Tobacco Products Scientific Advisory Committee (TPSAC) has not yet defined how the term "characterizing" applies to cigarette flavors. In the absence of a definition, tobacco manufacturers continue to add flavors at levels that may elicit a detectible difference in cigarette flavor that may not be recognizably attributable to a known and identifiable flavor. Although chocolate and cocoa flavored cigarettes are specifically banned in the FSPTCA, the PM (www.philipmorrisusa.com) Web site lists cocoa and cocoa products as flavors in its cigarettes (Philip Morris USA, 2012), and the RJ Reynolds (RJR) (www.rjrt.com) and Lorillard (www.lorillard.com) Web sites list cocoa and cocoa products as cigarette ingredients (Lorillard, 2011; RJ Reynolds, 2010).

The current study examined tobacco industry internal documents as a means of understanding the tobacco industry's historical use of cocoa in cigarettes, including cocoa's function, and if and how its chemosensory effects may serve to attract or retain nonsmokers, smokers, or specific target groups.

METHODS

Data Sources

As a result of the 1999 Master Settlement Agreement, millions of formerly secret internal tobacco industry documents have been made available to the public online. Relevant internal documents were identified using the Legacy Tobacco Documents Library (http://legacy.library.ucsf.edu/), a searchable online database. Additionally, the current Web sites of major U.S. tobacco manufacturers were reviewed for reports regarding cigarette constituents.

Data Extraction

A snowball sampling design was used, beginning with the search phrase "(Chocolate OR cocoa) AND cigarette AND additive." This phrase was intentionally broad to avoid the exclusion of any relevant documents or themes. Results were examined, and more specific search terms were generated from emerging themes. The initial search phrase yielded 12,026 documents, and 50 search terms, yielding 34,032 results. Documents were included for analysis if they answered one or both of the research questions (how and for what purpose is cocoa used in cigarettes, and what if any target markets for cocoa exist). Exclusion criteria for documents were as follows: (a) The document or a longer version of the document had previously appeared in search results; (b) Chocolate or cocoa was mentioned, but with no further information given; (c) Chocolate or cocoa is mentioned, but not as a tobacco additive (i.e., in describing differences in the diets of smokers vs. nonsmokers); (d) The document was written by parties outside of the tobacco industry, includes no relevant commentary from the industry, and is available for viewing either publicly or through scientific literature databases; and (e) The document was confidential or privileged and therefore publically inaccessible. After reviewing documents appearing under the secondary terms, additional search terms were added to further investigate specific unanswered questions. A final set of 179 documents that met the inclusion criteria was analyzed. Review was completed by a single researcher.

RESULTS

Historical Use of Cocoa in Cigarettes

Cocoa beans are derived from pods on a cocoa tree (*Theobroma cacao* L.) that are fermented, split open, dried, and roasted (Harllee & Leffingwell, 1979a). The fermentation process of the cocoa bean converts starches to reducing sugars, and proteins to free amino acid (Harllee & Leffingwell, 1979a). The process of heating cocoa helps develop cocoa flavor, and the

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roasting process reduces free amino acid and reducing sugars as a result of Maillard and Strecker Browning reactions (Harllee & Leffingwell, 1979a). These reactions produce compounds that contribute to cocoa aroma (Harllee & Leffingwell, 1979a). After they are roasted, the shell of the cocoa bean is opened, and the nib is sometimes alkali processed (Dutched) before it is ground and pressed, producing cocoa powder and butter (Harllee & Leffingwell, 1979a). For most products, cocoa powder (which retains between 11% and 23% cocoa butter) is reserved (Harllee & Leffingwell, 1979a). Cocoa powder is composed of crude protein, amino acids, polyhydroxy phenols, starch, sugars, theobromine, and caffeine (Leffingwell & Associates, 1991). Cocoa butter is nearly entirely composed of fatty acid triglycerides (Leffingwell & Associates, 1991).

Cocoa is one of the oldest tobacco additives and has been used in cigarettes since at least as early as 1932, when Souza Cruz (a Brazilian tobacco manufacturer and exporter owned by British American Tobacco) began adding cocoa powder with 10%–14% cocoa butter to its cigarettes (Pedreira, n.d.). Cocoa is generally incorporated into tobacco casing (Browne, 1990). Casings are typically applied to the air-cured portions of a cigarette's tobacco blend, as air-cured tobacco is generally lower in naturally occurring sugars and more absorbent than flue-cured tobacco (Browne, 1990). With sugars and humectants, cocoa is the most common casing ingredient (Browne, 1990).

Today, although cocoa is not used in every cigarette, it is widely applied, particularly in American blended cigarettes (Lorillard, 2011; Philip Morris USA, 2012; Reasor, 2000a, 2000b, 2000c; RJ Reynolds, 2010). A set of three Brown & Williamson Tobacco Company (B&W) documents, released in 2000, show the results of reverse engineering the company did to examine the design of the cigarette brands of their competitors (PM, RJR, and Lorillard) during 1998 and 1999 (Reasor, 2000a, 2000b, 2000c). Of the 107 cigarettes B&W tested for its presence in 1998, 80.4% contained cocoa (Reasor, 2000a, 2000b, 2000c). In 1999, cocoa was present in 81.2% of 138 cigarettes B&W tested (Reasor, 2000a, 2000b, 2000c). A 1991 B&W document identified that cocoa is generally applied to cigarettes at between 0.5% and 1.5% of tobacco weight (Leffingwell & Associates, 1991) (Table 1).

Chemosensory Properties of Cocoa in Cigarette Smoke

Enhancing or Improving Flavor or Aroma

Adding cocoa to cigarettes enhances and improves their taste and odor (e.g., Carmines, 1997; Lorillard, 1982; Pedreira, n.d.; Perfetti & Reynolds, 1996; RJ Reynolds, 1989). Cocoa powder contributes to a chocolate-like flavor in cigarette smoke, while its inherent sugars sweeten smoke (Bernasek & Woods, 1984; Brown & Williamson, n.d.-a; Harllee & Leffingwell, 1979b). Many cocoa volatiles (byproducts of burning cocoa) are identical to the volatiles produced by burning tobacco (Brown & Williamson, n.d.-b; Harlee & Leffingwell, 1979b). Therefore, when cocoa is added to cigarettes, it enhances what smokers perceive to be the tobacco flavor (U.S. Smokeless Tobacco, n.d.). One tobacco industry researcher hypothesized that the cocoa butter present in the cocoa used in cigarettes may enhance tobacco flavor by trapping tobacco volatiles in its aerosol droplets (Harllee & Leffingwell, 1979a).

> Cocoa has gained wide application in the tobacco industry since earliest times both as a sweetener and to add its own characteristic flavor. In recent years it has commonly been added to the burley tobacco of cigarette blends to enhance the cocoa-like aroma inherent in burley and, at the same time, suppress undesirable odors, thereby improving the smoking quality (Lorillard, 1982).

Increasing Smoothness or Decreasing Harshness

Cocoa affects tactile senses to reduce harshness and irritation caused by tobacco smoke. In one deposition, a former tobacco industry executive disclosed that the tobacco industry uses casing materials such as cocoa to produce acids in the smoke, which lowers smoke pH and reduces harshness (Rodgman, 1997). Tobacco smoke irritation is derived from the combustion or pyrolysis of cigarette constituents and is described as a sensation felt on the lips, tongue, mouth and back of the throat, and, rarely, in the chest, due to trigeminal nerve stimulation (Creighton, n.d.). Different cigarettes produce different levels of irritation, which are desirable to different smokers, and affect smoking topography and product satisfaction (Creighton, n.d.). Impact is another type of tactile sensation from tobacco smoke, similar to irritation, but much more immediately perceived and shortly lived, and directly related to the proportion of free nicotine available in the smoke, acting as a cue for nicotine reward (Creighton, n.d.). When sugars are heated, they become acids, which, when combined with nicotine, create nicotine salts that reduce impact and irritation (Brown & Williamson, n.d.-c). The triglycerides in cocoa also turn to acids when heated and combined with water, and in combination with nicotine also create nicotine salts to the same effect (Brown & Williamson, n.d.-c).

Table 1. Cocoa and Chocolate Ingredients in Cigarettes by the Top 3 American Manufacturers: 1998, 1999, and 2012

	Maximum level of use in any cigarette brand (%)			
Company	1998[b]	1999[b]	2012[a]	Stated function[a]
RJ Reynolds	1.13 (RJ Reynolds, 2010)	1.11 (RJ Reynolds, 2010)	1.84 (Reasor, 2000b)	Casing, flavor (Reasor, 2000b)
Philip Morris USA	0.81 (Philip Morris USA, 2012)	0.60 (Philip Morris USA, 2012)	0.50 (Reasor, 2000a)	Flavor (Reasor, 2000a)
Lorillard	0.00 (Lorillard, 2011)	1.04 (Lorillard, 2011)	[not given] (Reasor, 2000c)	[not given] (Reasor, 2000c)

[a]As reported on public company Web sites.
[b]Numbers obtained from reverse engineering done by Brown and Williamson in 2000. Cocoa levels are not available for all brands.

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> Natural cocoa has traditionally been used as a tobacco additive to enhance flavor and reduce the harshness of nicotine (Day, 1985).

When cocoa is not alkalized, cocoa with higher butterfat content reduces smoke harshness more significantly than cocoa with lower butterfat content (Frank, 1976). Dutched cocoas are less harsh than cocoas that are not Dutched; however, Dutching does not appear to be as effective in reducing harshness or increasing smoothness as increased butterfat (Frank, 1976). Internal documents also explain though that in Dutched cocoa, higher levels of butterfat actually decrease smoothness (Frank, 1976).

> Cocoa reduces harshness resulting in a smoother, fuller smoke. With normal processed cocoas, butterfat is the major factor: i.e. high butterfat cocoa is a more effective ameliorant than low butterfat cocoa. Dutch processed cocoas, while offering some amelioration, are not as effective as normal processed cocoas. They also do not follow the butterfat trend found with normal processed cocoas; high butterfat Dutch cocoa gives less amelioration than low butterfat Dutch cocoa (Frank, 1976).
>
> The new casing incorporated higher levels of cocoa (approximately 100% greater than current CAMEL Lt), high fructose corn syrup at levels to achieve sugar/nicotine balance, and removed licorice. This casing had a very significant effect on smoothness and acceptance (Smith, 1992).

Cocoa in Light Cigarettes

Tobacco manufacturers may have used cocoa to offset harshness from the lowered tar/nicotine (T/N) ratios in light cigarettes that resulted from filter ventilation. The cigarette T/N ratio is a crucial element of cigarette design because of tar's smoothing effect on the harshness and irritation caused by nicotine (Day, 1985). If nicotine is increased with decreased or maintained tar, a cigarette can become harsh (Day, 1985).

Some tobacco manufacturers who maintained nicotine levels in their products altered nicotine/sugar ratios in their products to increase smoothness (e.g., RJ Reynolds, 1994; Smith, 1992; Wolfe, 1983). One RJR project attempted to solve the problem of poor taste and low impact in light cigarettes by adding cocoa and sucrose to Burley, and heat treating the Burley (RJ Reynolds, 1994). This provided a lower T/N ratio (less tar compared to nicotine) but altered the sugar/nicotine ratio and produced better flavor (RJ Reynolds, 1994). RJR hypothesized that such products would have better taste, smoothness, and harshness compared to other low-tar products and could have lasting consumer appeal (RJ Reynolds, 1994). Another RJR document details 11 unique design features associated with a smooth tasting, low T/N cigarette, including increased sucrose, and the addition of cocoa at 0.78% of tobacco weight (Casey, 1994).

RJR's research of T/N ratios and sugar levels on cigarettes showed that certain T/N ratios require certain levels of sugar to maintain an acceptable level of smoothness (Wolfe, 1983). This research concluded that a relationship exists between the T/N ratio and sugar, having found that for a moderate level of harshness, a cigarette with a T/N ratio of 12 required 6.8% sugar, but an increase in nicotine for a T/N ratio of 11 required 8% sugar to achieve the same level of harshness (Wolfe, 1983). Blends with lower T/N ratios require more sugar for smoothness than blends with higher T/N ratios (RJ Reynolds, 1994; Smith, 1992; Wolfe, 1983).

Pharmacological and Physiological Activity

A 1969 document lists physiological activities of xanthines, including "central nervous system and respiratory stimulation, smooth muscle relaxation, skeletal muscle stimulation, coronary artery dilation, cardiac stimulation (including more efficient heart pumping), and diuresis" (Travers & Edmonds, 1968). The author of the document suggests determining the feasibility of engineering a product capable delivering xanthines in smoke for therapeutic effect, explaining that "coffee and/or cocoa may be used to balance or augment the flavor… …and afford additional Xanthine delivery" (Travers & Edmonds, 1968).

Although in one deposition, a former PM Vice President for Science and Technology agreed that PM used cocoa as a source of theobromine for bronchodilation, to increase the absorption of cigarette smoke constituents, in the lungs (Osdene, n.d.), internal documents examined did not reveal evidence that PM or other companies actually used cocoa explicitly for the pharmacological or physiological effect of theobromines. A number of industry documents investigated theobromine and determined that the levels present in cigarettes were not sufficient to produce physiological effects (e.g., British American Tobacco, 1999; Carchman, 1997; Philip Morris, 2001). Industry documents state that even at its maximum level in cigarettes, the amount of cocoa is not sufficient to produce a clinically effective dose of theobromine (e.g., British American Tobacco, 1999; Carchman, 1997; Carmines, 1997; Philip Morris, 2001).

Human Hedonic Research (Consumer Product Testing)

> A unique but subtle taste difference may be the key to broad acceptance of flavored cigarettes. Ideally, smokers would be able to recognize these cigarettes as delivering unique attributes and tastes but would not be able to specifically identify the flavor (Weber, 1983).

Results from hedonic research showed that although higher levels of cocoa in cigarettes increased acceptability (a global measure of consumer liking of and preference for a product), there was an "upper limit," with very high levels of cocoa actually decreasing product acceptability (Frank, 1976). One 1976 B&W study observed smoke quality improvements (in smoothness, irritation, and smoke character) after doubling levels of high-butterfat cocoa in one of their products but that these improvements dropped off after a 200% increase, with a 300% increase offering little or no improvement (Frank, 1976). The same study found that a 300% increase in low-butterfat cocoa resulted in decreased smoke quality, creating a cigarette that was less acceptable than the control (Frank, 1976). Researchers concluded, "there is an upper limit of the nonbutterfat material that is acceptable on tobacco unless accompanied by a proportionately greater increase in butterfat" (Frank, 1976).

RJR conducted a series of consumer testing initiatives in the 1980s to determine the feasibility of marketing cigarettes with varying levels and types of cocoa, including ones with discernible chocolate flavor (e.g., Carol Bernstein Research, 1983a, 1983b; Marco, 1993; Smith, 1992). Results from the testing

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of one of these products (a chocolate-mint-flavored cigarette) revealed that consumers enjoyed the chocolate mint flavor, but preferred cigarettes with lower levels of this flavor, finding them more satisfying; however, the majority of smokers did not believe that they could smoke chocolate-mint-flavored cigarettes all the time, finding them to have too much or too sweet a taste for regular use (Carol Bernstein Research, 1983b; Cohen, 1983). It appears that this is an established pattern, not only for chocolate, but for other nonmenthol flavors as well. In a letter to an RJR executive in response to a suggestion of experimenting with flavored cigarettes, one RJR scientist wrote that although the company used some flavors at subliminal levels, RJR's experience had shown that with the exception of menthol, smokers did not want cigarettes with flavors that overpower tobacco taste and that brands that had experimented with flavored cigarettes (including chocolate flavor) had been marketplace failures (Brown & Williamson, 1992). Similarly, a PM document on low-tar cigarette flavor explains that flavors are added to tobacco to enhance tobacco smoke flavor and notes that "If the added flavors yield predominating nontobacco notes and become distinctive, they are not desirable for American cigarettes. The only exception is mentholated cigarettes" (Hale, Kroustatis, Lin, & Wynn, 1990).

> We do, in fact, use a couple of the ingredients you suggested in our current formulations. However, their contribution to the overall flavor is at a subliminal level rather than the high level that would be needed to effect the response your suggestion includes. Our experience has shown that the smoker does not want a flavor which overpowers the tobacco taste in a cigarette (with the exception of menthol). A number of brands have been introduced by cigarette manufacturers over the years which have such a design, and all of them have been failures in the marketplace. Examples are Lyme (lime), Spring (lemon), and Chelsea (chocolate) (Brown & Williamson, 1992).

Target Markets

Documents reviewed showed that at least one tobacco company used cocoa as part of efforts to achieve product attributes that increased product appeal among young women and youth. RJR experimented with increasing cocoa as part of a project designed to increase their share of the young female market (Marco, 1993; Smith, 1992). This project, "Camel RU" (a product marketed as Camel Special Lights), aimed to develop a cigarette that was less strong, more smooth, and better tasting than a Camel Light, but stronger than a Camel Ultra-Light, to increase Camel's market share among young women and older smokers, while continuing to attract male smokers (Marco, 1993; RJ Reynolds, 1992a). Camel RU used increased sugar, high fructose corn syrup, and increased cocoa for improved casing and smoothness (RJ Reynolds, 1992b). Consumer research from this project showed that this casing composition had a major impact on perceptions of smoothness (Smith, 1992). Consumers preferred cigarettes cased with double the cocoa used in other Camel brands, finding them to taste better and be smoother, more satisfying, and more acceptable (Smith, 1992). Consumers further preferred high fat or Dutched cocoa over "F1" (the standard cocoa used in Camel brands at the time), perceiving products that contained either of these to be smoother than products containing F1 (Dube, Lloyd, & Burger, 1992).

> RJR is underrepresented among this smoker target group [18–34 year old women], especially among the 18–24 younger adult female smoker target subsegment… … priority aroma candidates have been identified on basis of smoker preference and perceived compatibility with cigarettes. Vanillin, toffee, coconut, chocolate, marshmallow… …vanillin and chocolate are currently most viable candidate. These two flavors' ability to impact a distinctive smoothness benefit may be large. However, their ability to impact pleasant aftertaste or crisp, refreshing taste is less assured (RJ Reynolds, 1986).
>
> Project RU (CAMEL Special Lights) is a lights proposition strategically focused toward broadening CAMEL's appeal beyond the current prime prospect smoker group (21–24 males) to include female and older smokers. RU is a milder, smoother, lighter tasting CAMEL that will feature a white tipping (Marco, 1993).

Another RJR project ("Project XG") sought to update Camel Filters 85s to "replace Marlboro as the key brand among younger adult smokers" based on the understanding that "product benefit" (taste, smoothness, and satisfaction) is necessary to attract younger smokers, regardless of product imagery, and increased cocoa in a number of prototypes (e.g., Alber, 1985; RJ Reynolds, n.d., 1984, 1985).

DISCUSSION

Cocoa has been widely used in American cigarettes. At least two tobacco companies continue to use cocoa as a cigarette additive at levels similar to those recorded in their internal documents. Documents revealed that cocoa has been used in cigarettes for its influence on sensory qualities. The tobacco industry has used cocoa to impact gustatory and olfactory perceptions by enhancing and sweetening tobacco flavor and aroma, and tactile perceptions by reducing smoke irritation. Documents showed the importance of cocoa in improving light cigarettes' acceptability by enhancing smoke flavor lost through ventilation, and smoothing smoke made harsh through lowered T/N ratios. Results from hedonic research indicated that cigarettes with higher levels of cocoa in their casing are more appealing and acceptable to smokers; however, studies also showed that consumers and researchers felt that when present at a level that would create a recognizable gustatory chocolate/cocoa flavor, the cigarette was no longer appealing for regular use. Although one document suggested that cocoa be investigated for use for physiological effects in future products (Yates-Evans, 1986), documents showed no indication that this project was carried out or that cocoa has any physiological effects at levels used in cigarettes. A report by Rijksinstituut voor Volksgezondheid en Milieu (RIVM) confirms this finding, and further finds the levels of all psychoactive compounds in cocoa found in cigarettes are insufficient to produce pharmacological effects (Rambali et al., 2002). RIVM does suggest, however, that one compound found in cocoa, phenylethylamine, could potentially serve as a cue for drug reward in cigarettes (Rambali et al., 2002).

Despite its other sensory properties, cocoa is identified only as a flavor on the Web sites of the three major U.S. tobacco companies (Lorillard, 2011; Philip Morris USA, 2012; RJ Reynolds, 2010). Although it is not the only product feature or

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additive with these functions (e.g., Carpenter et al., 2005, 2007; Ferris Wayne & Connolly, 2002; Ferris Wayne, Connolly, & Henningfield, 2006; Pritchard, Robinson, Guy, Davis, & Stiles, 1996), cocoa decreases sensory perceptions of cigarette smoke harshness, which ease or improve smoking, and prevent short-term adverse reactions to smoke inhalation. In particular, cocoa's smoothing properties may enhance product acceptability and attract certain subgroups of smokers such as women and young people (Henningfield et al., 2011; Scientific Committee on Emerging and Newly Identified Health Risks, 2010). Although research has shown that the compounds in cocoa with potential physiological activity likely have no effect on the development or maintenance of tobacco addiction (Rambali et al., 2002), one previous investigation of cocoa as a tobacco additive has indicated that cocoa, in addition to other similarly functioning additives, may play a role in dependence and addiction because of its sensory effects (WHO, 2007). Research has also shown that following the establishment of drug self-administration, sensory effects can function as reinforcing stimuli (e.g., Panlilio et al., 2005; TPSAC, 2011).

The FDA has defined "characterizing flavors" in food as those that are marketed in the labeling or advertising (U.S. FDA, 2011). Products so far affected by the ban on characterizing flavors in cigarettes have been ones that had a nontobacco, nonmenthol flavor designated in their marketing and recognizably attributable to a specific product flavor. This review presented tobacco industry research on cigarette flavoring from at least as early as 1976 showing that the consumers are not attracted to cigarettes with nonmenthol flavors at levels that are high enough to have been so far regulated as "characterizing." Further, sales data show that prior to the September 2009 ban, sales of flavored cigarettes made up less than 1% of the cigarette market (AC Nielsen, 2009), although it has been shown that cigarettes containing characterizing flavors were more popular among youth compared to adult smokers (Klein et al., 2008). Despite not imparting a characterizing "chocolate" flavor, at levels currently used in cigarettes, cocoa can alter cigarette flavor substantially and affect product acceptability. Cocoa plays a role in altering sensory perceptions of cigarette smoke, including by decreasing harshness and improving flavor. These altered sensory perceptions may impact smoker risk perceptions, particularly in regards to light cigarettes. Cocoa, at the low levels at which it is used in cigarettes, is of concern regardless of whether or not that level is considered to be characterizing.

Limitations

Due to the nature and quantity of available tobacco industry documents, and the inaccessibility of privileged and confidential documents, contents of this and any review of internal tobacco industry documents cannot be considered comprehensive. Further, because the documents reviewed were generally at least a decade old, findings from this review do not necessarily represent the current practices. However, according to the Web sites of two major tobacco manufacturers that list current maximum levels of cigarette ingredients by brand, current cocoa application appears to remain fairly consistent with historical standards cited in the older documents.

Section 904 of the FSPTCA requires tobacco manufacturers to disclose all cigarette additives (U.S. FDA, 2009). The FDA may also consider requiring manufacturers to disclose all intended and unintended functions of each cigarette ingredient to help better determine their appropriateness for continued use in cigarettes, given their impact on use behaviors. However, given the tobacco industry's history of a failure to fully disclose information about their products (USDCDC, 2006), independent internal documents investigation remains essential as a means of gaining a more holistic understanding of the intended purposes and functions of cigarette ingredients and components. Investigations of the tobacco industry documents may serve as an important means of identifying constituents for further regulatory research and action. In order to regulate cigarettes in the interest of public health, research is needed to investigate the relationships between noncharacterizing cigarette additives, perceptions of risk, and smoking behaviors.

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DECLARATION OF INTERESTS

None declared.

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The SECRET and SOUL of Marlboro

Phillip Morris and the Origins, Spread, and Denial of Nicotine Freebasing

| Terrell Stevenson, BA, and Robert N. Proctor, PhD

Philip Morris and other tobacco companies have been using ammonia in their manufacturing for more than half a century, and for a variety of purposes: to highlight certain flavors, to expand or "puff up" the volume of tobacco, to prepare reconstituted tobacco sheet ("recon"), to denicotinize (reduce the amount of nicotine in) tobacco, and to remove carcinogens.

By the early 1960s, however, Philip Morris had also begun using ammonia to "freebase" the nicotine in cigarette smoke, creating low-yield (reduced-tar or -nicotine) cigarettes that still had the nicotine kick necessary to keep customers "satisfied" (i.e., addicted). We show that Philip Morris discovered the virtues of freebasing while analyzing the impact of the ammoniated recon used in Marlboro cigarettes.

We also show how Marlboro's commercial success catalyzed efforts by the rest of the tobacco industry to discover its "secret," eventually identified as ammonia technology, and how Philip Morris later exploited the myriad uses of ammonia (e.g., for flavoring and expanding tobacco volume) to defend itself against charges of manipulating the nicotine deliveries of its cigarettes. (*Am J Public Health.* 2008;98:1184–1194. doi:10.2105/AJPH.2007.121657)

AMMONIA OCCURS NATURALLY in cured tobacco leaf, from close to 0% in some varieties up to about 1% (by weight) in the leaves used in some higher-quality cigars.[1] The compound is also commonly used as a tobacco additive, either in its native form as a clear, pungent gas (NH_3, an ingredient in smelling salts) or as an aqueous or solid ammonium salt (NH_4^+). Although toxic in large doses, ammonia is relatively easy to remove from processed tobacco leaves; the gaseous form is quite volatile, and the salt is easily neutralized by the addition of an acid.[2] The tobacco industry has for many years used ammonia as a relatively innocuous additive to augment certain flavors, to economize on costs by expanding or "puffing" the cured leaf, to denicotinize (reduce the amount of nicotine in) tobacco, and even to reduce some of the carcinogens in tobacco smoke.

By the early 1960s, however, Philip Morris scientists had discovered that ammonia could also be used to increase the free nicotine in cigarette smoke, providing a more powerful nicotine kick than the milder low-pH tobaccos traditionally used in American-blend cigarettes. The discovery seems to have come about by accident, in the course of exploring the properties of the ammoniated tobaccos used in the preparation of reconstituted tobacco sheet ("recon").

This freebased version of Marlboro cigarettes was one of the greatest triumphs in the history of modern drug design and one reason the brand became the world's most popular cigarette. Yet to this day, Philip Morris denies it has ever deliberately freebased tobacco to boost nicotine yields. The company recalls only the many innocuous uses of ammonia—as a "flavorant" or binder required for the manufacture of recon, for example. The industry reminds us that ammonia is naturally found in foods, fertilizers, and the very air we breathe.

We have analyzed internal documents of the tobacco industry to show that Philip Morris discovered ammonia's freebasing ability while attempting to understand the impact of the ammoniated tobacco sheet used in its Marlboro cigarettes. The archival record shows that ammonia technology eventually spread throughout the industry, but only after diligent efforts to reverse engineer the chemistry of Marlboros to discover their "secret." Philip Morris later exploited the alternate uses of ammonia—in flavoring, expanding, reconstituting, and denicotinizing tobacco—to defend itself against charges of having manipulated the nicotine in cigarettes. The tobacco industry is notorious for having manipulated science; it is now in the process of renarrating the history of science to defend itself against charges of having deliberately taken paths that led to massive death and disease.[3]

THE OMNIPRESENT ADDITIVE

Ammonia's capacity to improve tobacco smoke flavor has been recognized at least since the early 1950s, when Claude E. Teague Jr, an RJ Reynolds chemist who later became the company's director of research, found that ammonia gave smoke a richer, smoother, "chocolate-like" taste reminiscent of a burley blend, the most alkaline of the common varieties of tobacco leaf.[4] Philip Morris scientists also recognized this relationship between alkalinity and burley's rich taste, and in the late 1950s and early 1960s began using a range of bases, including ammonia, diammonium phosphate (DAP), and various ethanolamines and carbonates to "improve smoke flavor."[5]

In these early years, tobacco manufacturers were not sure why ammonia—most often regarded as an irritant—improved the taste of tobacco smoke. They eventually came to understand that there was a threshold level beyond which further additions of the compound would no longer improve flavor. In 1971, Philip Morris experimented on competitors' brands and found that ammonia added at 0.25% concentration created a taste that was "milder, more aromatic, sweeter, less harsh, and more like a Marlboro," whereas ammonia added at 0.50% concentration created an "off taste."[6] RJ Reynolds scientists later hypothesized that ammonia might improve tobacco smoke flavor by reacting with sugars to produce heterocyclic ring compounds known as pyrazines. Because pyrazines were already known for their vibrant flavors, RJ Reynolds scientists hypothesized (in documents marked "secret") that amino-sugars such as pyrazines might be the key to ammonia's ability to improve tobacco.[7]

Ammonia has also been used in a number of cost-saving processes, including the production of expanded or "puffed" tobacco. Increasing tobacco's volume was a priority in the 1970s, when tobacco companies first recognized that expanding a given volume of tobacco could increase its "filling power," thereby reducing the mass of leaf required to fill a cigarette of some fixed length and circumference. The reduced mass of tobacco per cigarette encouraged customers to smoke more to get their desired amount of "satisfaction," the industry's euphemism for nicotine.

There are a number of ways to expand tobacco. The most common today is the dry ice expanded tobacco (DIET) process, which uses carbon dioxide (CO_2) in solid form to freeze-dry and "puff up" the tobacco. In 1973, however, Philip Morris patented a puffing procedure that used ammonia in conjunction with CO_2. The cured leaf was treated with dry ice and ammonia—in liquid or gaseous form, as a hydroxide with CO_2 or as a carbonate or bicarbonate—followed by applications of heat.[8] This method was soon discontinued in favor of the DIET process,[9] apparently because of cost concerns. According to confidential Philip Morris records, it took 143 pounds of ammonia to make 2000 pounds of expanded tobacco[10]; dry-ice methods, by contrast, were relatively cheap.

Reconstituted tobacco has been a more enduring use of ammonia. Essentially a paper-making process, recon was developed in the 1930s and 1940s as part of an effort to salvage more of the tobacco leaf, including the stems or mid-ribs formerly thrown away as waste. To make these waste parts smokable, however, and to increase sheet strength, required the addition of a substance "to release the pectins in tobacco stems so they may form a gel which becomes the binder in the blended leaf sheet."[11] In the 1950s Philip Morris had begun exploring the use of diammonium phosphate (DAP) in recon and found it to be a successful pectin releaser and a potent flavor enhancer, masking the unpleasant taste of stem.[12] The company set up its first pilot plant for ammoniating tobacco (with DAP) in 1961, and 6 years later patented the "diammonium phosphate–blended leaf" (DAP-BL) process after realizing diammonium

> *"This freebased version of Marlboro cigarettes was one of the greatest triumphs in the history of modern drug design and one reason the brand became the world's most popular cigarette. Yet to this day, Philip Morris denies it has ever deliberately freebased tobacco to boost nicotine yields."*

phosphate's ability to increase free nicotine "delivery" in cigarettes.[13] The patent, interestingly, contains nothing about DAP's ability to freebase nicotine, citing only its importance as a pectin releaser.[14]

The tobacco industry also uses ammonia to remove nicotine from tobacco. The procedure is simple: Tobacco leaves are exposed to gaseous ammonia, which replaces nicotine in the salts that bind the alkaloid to the leaf. The ammonia and resulting nicotine are then removed by steam. This method of nicotine reduction gives tobacco manufacturers a degree of control over the amount of nicotine in a given tobacco blend.[15]

CANCER PREVENTION?

In the 1990s, Philip Morris and the other tobacco companies often mentioned these relatively innocuous uses of ammonia—in flavoring, expanding, and denicotinizing tobacco and in making reconstituted tobacco sheet—when defending themselves against charges of having used ammonia to freebase tobacco. Essentially, their argument was, how could we have done something insidious and underhanded with a molecule like ammonia that is so commonplace, public, and patented for use in so many different kinds of manufacturing processes?[16] Typical was a February 24, 1998, letter to the *New York Times* from Philip Morris's director of external relations that claimed that the company's use of ammonia in cigarette manufacturing "does not increase the amount of nicotine delivered to the smoker, does not increase the amount of nicotine absorbed in the lungs of the smoker, and does not affect the form of nicotine delivered to the smoker's brain."[17] The company was responding to a *New York Times* exposé on the industry's widespread use of ammonia technology.[18]

Prior even to the discovery of ammonia's ability to increase nicotine availability, however, tobacco companies were using the reagent in confidential experiments to reduce carcinogens in cigarettes. Throughout the 1950s and 1960s, industry scientists were researching the idea that certain ammonium salts, such as ammonium sulfamate and ammonium chloride, could reduce the levels of benzpyrene,[19] one of the forty carcinogens in cigarette smoke named by Helmut Wakeham, Philip Morris's director of research and development, in 1961.[20] This research on reducing benzpyrene was part of Philip Morris's Project 0107, the purpose of which was to develop cigarettes with "less tendency to cause lung cancer in smokers."[21] The Celanese Corporation in 1964 patented a tobacco substitute "in which ammonia salts are used to inhibit benz-a-pyrene formation,"[22] and in 1967 British American Tobacco researchers reported similar reductions with potassium carbonate.[23]

THE "SECRET" (AND SOUL) OF MARLBORO

Marlboro began in the 1920s as a women's cigarette. Advertisements called it "mild as May," and it was taken off the market during World War II because of a sales slump. In the mid-1950s, however, with growing public concerns about the link between smoking and lung cancer, Philip Morris decided to reintroduce the brand with a new and improved filter, a flip-top box, and a new masculine image.[24] This new version of Marlboro sold surprisingly well, and for an unanticipated reason.

Philip Morris researchers discovered that the reconstituted tobacco they were using to cut costs—the DAP-BL—had some fortunate side effects. Diammonium phosphate, which breaks down into ammonia when a cigarette is burned, improved the flavor of the smoke, giving it that smooth, "chocolate-like" taste, while also increasing the availability of nicotine in the smoke.[25] Soon thereafter Philip Morris began using diammonium phosphate and other forms of ammonia in its other cigarettes, including its health-conscious (low-tar) Merit brand. Merits were introduced in 1976 and within 3 years accounted for about 20% of Philip Morris's cigarette sales.[26]

How, though, did diammonium phosphate freebase the nicotine in cigarettes? Freebasing entered public consciousness in the mid-1980s, when a cheaper street version of cocaine known as "crack" came on the scene.[27] In point of fact, however, a kind of folk freebasing has been widely used in different parts of the world for many centuries. Archaeologists have found evidence of the use of lime or wood ash to freebase botanicals such as pituri (*Duboisia hopwoodii*), a nicotine-containing plant used by Australian aborigines to help them endure the harsh desert climate. Folk freebasing can also be found among traditional chewers of coca leaves, betel nuts, and tobacco.[28]

The chemistry of freebasing is not complex. A base, such as ammonia, accepts a proton from a positively charged nicotine carboxylic acid salt (e.g., a malate or a tartrate) found in tobacco. The ammonia (NH_3) is thereby transformed into a cation (NH_4^+), and the positively charged nicotine acid salt is deprotonated to become neutral. This neutral, deprotonated nicotine is "free" in that it is no longer bound to another molecule (or anion) in the form of a salt. Free nicotine is more volatile; James F. Pankow, of Oregon Health and Science University, stresses that "increasing the proportion of the particle-phase nicotine that is in the freebase form will . . . tend to drive more nicotine into the gas phase."[29] Gas-phase nicotine is able to deposit quickly and easily in the respiratory tract and, because of its freebase form, crosses the blood–brain barrier more readily ("moves easily into fatty tissues"[30]), making the nicotine more "available" to the smoker and therefore more potent.

Ammoniation increases nicotine's volatility. There is not universal agreement on whether ammoniation also increases the *rate* of nicotine delivery, but freebasing is widely thought to increase the *impact* of nicotine by increasing its efficiency of extraction during the smoking process.[31] Many tobacco industry documents mention augmentation of nicotine impact, and many of those also reveal a conviction that ammoniation was increasing the rate of nicotine delivery, causing a more immediate and profound "kick" to a smoker's central nervous system (Figure 1). Philip Morris admitted the increased rate of nicotine delivery in a 1989 interoffice memo, noting that "the CNS [central nervous system] effects obtained using the NC [nicotine citrate] cigarettes were approximately half the magnitude of those obtained with FB [freebase nicotine] and unextracted cigarettes."[33]

Many different terms have been used within the tobacco industry to describe this augmented impact, including *volatile nicotine, pH effect, amelioration, extractable nicotine, burley impact,* and *increased satisfaction* or *augmentation.*[34]

Channing Robertson, a Stanford chemical engineer, was barred from using the term *freebase nicotine* in his 1998 testimony for the plaintiffs in *Minnesota v. Philip Morris*, so he testified instead about what he called "crack nicotine."[35] Crucial for the tobacco industry, however, was that this augmented "kick" provided by ammoniation could offset declining levels of tar and nicotine in

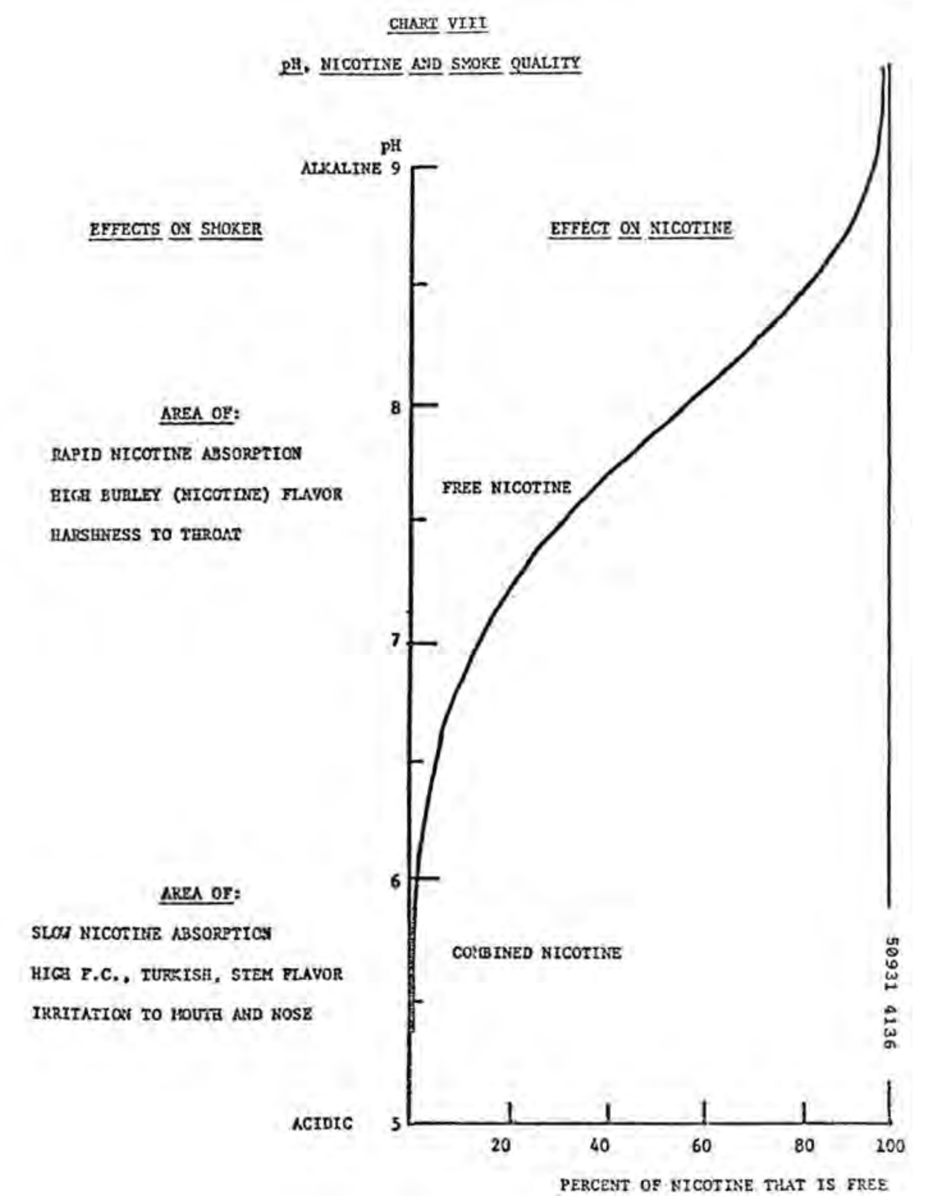

FIGURE 1—The chemistry of freebasing. The tobacco industry has long appreciated the importance of smoke pH for boosting nicotine's impact. This page, from a 1973 report by Claude E. Teague Jr of RJ Reynolds (*Implications and Activities Arising From Correlation of Smoke pH With Nicotine Impact*), shows how the freebase form of nicotine in smoke increases with increasing alkalinity. Although pH is a good indicator of relative freebase availability, it tends to underestimate the actual amount available. Other industry methods for measuring free nicotine—such as oil versus water partitioning or studies of nicotine volatility—reveal free nicotine levels much higher than those predicted from pH alone.[32]

Summary of Progress in 1971 on Project TE-5001

Title: DEVELOPMENT OF A CIGARETTE WITH INCREASED SMOKE pH

Prepared by: Robert E. Williams Section: Organic

Date: December 16, 1971 Checked by: [signature]

Notebook Ref. No.: FO-90A Approved by: [signature]

CHRONOLOGY

May-June - Tobacco treated with $Ca(OH)_2$ to increase smoke pH showed increased tobacco pH but no increase in smoke pH in handmade L+M cigarettes.

July-August - Tobacco treated with $Ca(OH)_2$ showed an increase in smoke pH if the cigarette was of the unfiltered type.

September-October - Sample cigarettes were made in the factory adding three levels of $Ca(OH)_2$. The project was turned over to Physical Section.

SUMMARY OF PROGRESS

Increasing the pH of a medium in which nicotine is delivered increases the physiological effect of the nicotine by increasing the ratio of free base to acid salt form, the free base form being more readily transported across physiological membranes. We are pursuing this project with the eventual goal of lowering the total nicotine present in smoke while increasing the physiological effect of the nicotine which is present, so that no physiological effect is lost on nicotine reduction.

Source. Reference 36.

FIGURE 2—The Industry's Rationale for Freebasing. Liggett and Myers in 1971 explained the rationale behind the company's experiments to increase the proportion of "freebase" nicotine as part of its multiyear "Project TE-5001."

cigarettes, which fell by more than half from the 1950s through the 1980s as the industry sought to reassure worried smokers. Freebasing meant you could maintain a high nicotine impact while lowering reported tar and nicotine levels. As one 1971 Liggett document states, "there could be a reduction in total nicotine in the smoke without a reduction in the physiological satisfaction associated with nicotine"[36] (Figure 2).

THE ORIGINS AND SPREAD OF AMMONIA TECHNOLOGY

Long before the widespread use of freebasing, tobacco industry scientists knew that nicotine deliveries were sensitive to pH manipulation (by adding acids or bases). Several documents from the 1930s and 1940s discuss how to *reduce* the amount of free nicotine in tobacco by adding an organic acid, which would combine with the free nicotine base to form a (bound) nicotine salt.[37] Free (vs "combined") nicotine in those early years was often characterized as "toxic,"[38] which made sense at a time prior to the push to reduce tar and nicotine in the "filter wars" and "tar derby" of the 1950s and 1960s. Many other industry documents from this earlier period describe the well-known art of denicotinization, which often used a base (such as ammonia) and steam to remove the offending alkaloid from tobacco. Denicotinization involves some of the same processes as freebasing, although the desired outcomes are different. Denicotinization involves the application of gaseous ammonia so that, upon addition of steam, the nicotine can be removed; freebasing impregnates tobacco with a salt (such as DAP) so that ammonia is released when the cigarette is lit, making nicotine more available to the smoker.

Tobacco chemists knew enough to freebase nicotine as early as the 1930s and 1940s,[39] but there was little reason then to manipulate cigarettes in this manner. Smoking was not yet widely accepted as a cause of lung and heart disease,[40] and most people still smoked cigarettes yielding very high levels of tar and nicotine. Only beginning with the "health scare" of the 1950s, and with increasing urgency in the 1960s and 1970s, did Philip Morris and the other manufacturers scramble to appease a rattled public by marketing cigarettes with lower levels of tar and nicotine, which is where the value of ammoniation came in.

It is difficult to say whether Philip Morris scientists expected diammonium phosphate to increase the availability of free nicotine in its new version of Marlboro, introduced in the mid-1950s. After all, the compound was largely being used as a pectin releaser and flavorant in reconstituted tobacco. Philip Morris chemists were, however, experts in pH manipulation, as were chemists more generally. Freebasing was not an unknown phenomenon, but there was not yet a practical need for it in the cigarette business.

In 1962, a Philip Morris study found diammonium phosphate products delivering 0.57 mg of nicotine per cigarette versus 0.44 mg in untreated tobaccos.[41] Keenly aware of the increasing demand for cigarettes low in nicotine,[42] Philip Morris later used its patented DAP-BL process to give its "low-yield" Merit brand an edge over its competitors. Merit cigarettes boasted a total nicotine yield (measured by Federal Trade Commission machines) only half of that found in Marlboros, but still managed to make available the same amount of free nicotine to smokers (about 0.33 mg in both instances). Brown and Williamson scientists reflected on this in 1980, commenting that "in theory a person smoking these cigarettes [Merit and Marlboro] would not find an appreciable difference in the physiological satisfaction from either based on the amount of free nicotine delivered."[43]

This was not the first time Brown and Williamson had pondered the value of freebasing. Its parent company, British American Tobacco, in the mid-1960s had recognized along with Philip Morris that the "strength" or "impact" of a cigarette was related not to the total nicotine content of the smoke but rather to the amount of "extractable" or "free" nicotine, which varied significantly with smoke pH.[44] Brown and Williamson in 1971 had given the code name UKELON to urea, an ammonia source that the company recognized as "a way of achieving normal impact from low tar cigarettes."[45] The same company's "Project LTS" (low "tar" satisfaction) acknowledged that free (unprotonated) nicotine was "more readily absorbed and thus has a decidedly satisfying effect on the smokers' taste receptors." The goal of LTS was a cigarette containing "greater levels of 'free' nicotine" in "an enhanced alkaline environment."[46] By 1980, the company had concluded that "we have sufficient expertise available to 'build' a lowered mg tar cigarette which will deliver as much 'free nicotine' as a Marlboro, Winston or Kent without increasing the total nicotine delivery above that of a 'Light' product."[47]

Apart from DAP-BL recon, Philip Morris experimented with other kinds of ammonia technology. As early as 1957, for example, the company came up with the economically unfeasible "New Idea No. 46"[48] to "soak stems in liquid ammonia," imparting to them greater "protein-like" material and "those properties now being produced by the aqueous NaOH, by virtue of its basic nature."[49] The ammonia was difficult to recycle, however, and the idea was quickly abandoned. A 1966 progress report on "nicotine and smoke pH" discussed the results of adding ammonium carbonate and oxalic acid to tobacco and concluded that nicotine deliveries could be "controlled via filler or smoke pH adjustment."[50] Throughout this time, from the mid-1960s through the 1970s and 1980s, the company kept a close eye on the pH levels of its major brands.[51]

THE STAMPEDE TO KEEP UP WITH THE MARLBORO MAN

Although some historians maintain that Philip Morris's rise to the top of the tobacco industry in the mid-1970s was because of its ingenious Marlboro ad campaign, featuring a ruggedly handsome cowboy in the beautiful and equally rugged West[52]—"Marlboro Country"—the makers of competitor brands could justifiably disagree. In the 1960s, with Philip Morris brands streaking ahead of the pack, RJ Reynolds, American Tobacco, Lorillard, Liggett, and Brown and Williamson all began investigations into what would later be called "the secret"[53] and eventually "the soul" of Marlboro.[54] All discovered the virtues of freebasing, but this didn't happen overnight.

Brown and Williamson and its parent, British American Tobacco, were apparently the first (after Philip Morris) to realize the importance of ammonia in increasing nicotine availability, but American Tobacco[55] and the other companies were not far behind. RJ Reynolds incorporated ammoniated sheet into Camel filters in 1974, allowing them to deliver 36 mg of ammonia per cigarette in the mainstream smoke.[56] Five years later, the company began using ammoniated sheet in its popular Winston brand.[57] Teague, in a 1973 report marked "secret," noted that Marlboro, in comparison with RJ Reynolds's own Winston, showed

> 1) higher smoke pH (higher alkalinity), hence increased amounts of "free" nicotine in smoke, and higher immediate nicotine "kick", 2) less mouth irritation, less stemmy taste and less Turkish and flue-cured flavor, and 4) [sic] increased burley flavor and character.[58]

Teague then went on to point out that cigarettes with rising sales, especially Philip Morris brands, all showed evidence of pH manipulation. Another RJ Reynolds document from 1973 (aimed at targeting the youth market) stated that "for public relations reasons it would be impossible to go back all the way to the 1955 type cigarettes"—high in tar and nicotine—but took comfort from the fact that "still, with an old style filter, any desired *additional* nicotine 'kick' could be easily obtained through pH regulation."[59]

Sometime during the 1980s, Lorillard caught up with Philip Morris and began using ammonia technology in its own cigarettes, by which time British American Tobacco had initiated Project AMTECH to investigate "the potential benefits of ammonia technology."[60] By the end of the 1980s, five of the "big six" of the industry (all but Liggett, which had researched but apparently never commercialized a freebase concept using calcium hydroxide)[61] were using a total of 10 million pounds of ammonia per annum, amounting to about 10 mg per cigarette. RJ Reynolds alone released 900 000 pounds of ammonia in 1989 from its factory in North Carolina.[62]

British American Tobacco and Brown and Williamson held the first of several ammonia technology conferences in the spring of 1989 to enhance "rapid commercial application" of ammonia technologies and to provide a forum to discuss "research strategies and priorities." Here we find an acknowledgment that ammonia technology was "the key to competing in smoke quality with [Philip Morris] worldwide"[63]; we also find a discussion of the different ways ammonia was being used to achieve the freebasing effect. Philip Morris was using DAP recon and urea; RJ Reynolds was using ammonia gas; American and Lorillard were using DAP recon; and Brown and Williamson itself was using DAP recon and urea, code-named QUELAR and UKELON.[64] At the second Annual Ammonia Technology Conference one year later, the opening statement affirmed that "ammonia technologies have been developed in the group to the stage where US blended products can be manufactured with comparable smoking quality to Marlboro."[65] A Brown and Williamson strategy document from 1991 concluded that ammonia technology was "the key factor" and "critical to the taste, character and delivery of Marlboro."[66]

Of course, the joy felt by Brown and Williamson and the other tobacco companies after uncovering "the secret of Malrboro" was matched by disappointment at Philip Morris, which had enjoyed this advantage over its competitors for years. William A. Farone, director of Applied Research at Philip Morris from 1976 to 1984, recalls that "when Winston started increasing their level of ammonia we had, you know—the roof fall down on us from [corporate headquarters in] New York City."[67]

THE OUTSIDE WORLD LEARNS THE TRUTH

Philip Morris's use of ammonia to freebase nicotine remained essentially a company secret until the 1970s and an industry secret until the 1990s. With access to documents produced in litigation, however, groups outside the industry began to catch on. Alix M. Freedman broke the story in a Pulitzer Prize–winning article for the *Wall Street Journal* in 1995,[68] based partly on documents unearthed through Commissioner David Kessler's investigations at the FDA. In 1996, in its regulations restricting the sale and distribution of cigarettes, the FDA noted that "compounds in free or unbound forms are vaporized more readily than compounds bound together in salts," giving both nicotine and cocaine as examples. The FDA went on to note that cigarette manufacturers had provided no evidence to rebut charges that "the conversion of nicotine from its bound form to its free form increases the transfer of nicotine to smoke."[69] One year later, James F. Pankow published a paper describing how ammonia increased nicotine volatility and availability in cigarette smoke, comparing this to the "immediate and intense high" produced by the freebasing involved in the making of crack cocaine.[70]

The industry's response was quick and characteristically dismissive. In 1998, Philip Morris lawyers deposed Pankow, questioning not just the details of his experimental design but also his professional ethics.[71] The company also criticized his assertion of a similarity between the tobacco industry's use of ammonia and the freebasing of cocaine.[72] Philip Morris lawyers also used the 1979 surgeon general's report to help them debunk the charge of freebasing. According to this report, produced under Surgeon General Julius B. Richmond, "the percentage of nicotine present as the free base is .40 at pH 5.35, 1.7 at pH 6, 15 at pH 7, 64 at pH 8, and 85 at pH 8.6."[73] Philip Morris maintained that because its cigarettes had a pH of about 6, nearly 99% of its nicotine was in the form of a protonated salt. So whatever effect ammonia might be having on the percentage of freebase nicotine, and thus the rate of nicotine "delivery," would be trivial.

From experiments performed by other companies, however, we know that even very slight increases in pH can have a significant effect on the availability of freebase nicotine in smoke. Recall Brown and Williamson's 1980s demonstration that Merit cigarettes had only half the total nicotine of Marlboro cigarettes while still delivering the same amount of free nicotine, thanks to only a 0.5 increase in pH. The companies were also aware that pH provides only an imperfect estimate of free nicotine availability.[74] Wayne, Connolly, and Henningfield have reviewed the industry's internal documents on freebasing and shown that free nicotine levels of Philip Morris's and other companies' cigarettes were significantly higher than those predicted from pH values alone.[32]

Company officials also argued that while ammonia might well increase the rate of nicotine delivery, the same total amount of nicotine was delivered nonetheless. Rate of nicotine delivery, though, is a key aspect of addiction. That is one reason nicotine gums and patches usually cannot deliver the same "satisfaction" as smoking: lung deliveries are far more intense, and freebasing only heightens this effect. A 1994 draft report on experiments conducted at Philip Morris's secret research center (INBIFO) in Cologne, Germany, conceded that when subjects inhaled the same amount of nicotine at different pH levels, those who inhaled at higher alkalinity experienced faster rates of entry of nicotine into the bloodstream.[75]

DISGUISING THE USE OF AMMONIA AS A FREEBASING AGENT

In their attempts to defend against charges of freebasing, Philip Morris and the other companies took advantage of ammonia's innocuous uses to draw attention away from its freebasing ability. Tobacco executives argued: how could ammonia, a natural compound found in tobacco, food, fertilizer, pesticides, and many other everyday products, have this secret ability to control nicotine levels? In a 1994 Tobacco Institute response to FDA Commissioner David Kessler we find such arguments, along with the claim that ammonia's most important use was in reconstituted tobacco, "so the blended leaf sticks together."[76] This same document suggests that the idea of the FDA regulating tobacco was ludicrous, making no more sense than the FDA regulating coffee or beer. (Philip Morris has since reversed course and now argues in favor of FDA regulation, hoping this regulation will help preserve its position as the nation's number one cigarette maker.)

There are many other industry pronouncements from the 1990s that attempt to draw attention away from ammonia's freebasing function. A 1994 Brown and Williamson document (prepared for use in public relations or litigation) points out that ammonia and its many derivatives are found in everyday foods: ammonium bicarbonate in baked goods; ammonium hydroxide in cured pork; diammonium phosphate in dough, ice cream, and gelatin; and ammonium sulfide in baked goods and meats. And ammonia itself is found in human breath.[77] An RJ Reynolds document insists that the industry's uses of ammonia "are similar to many of the applications commonly used in the food industry."[78]

Philip Morris has also tried to exonerate ammonia by emphasizing its roles as a flavorant and pectin-releaser.[79] In *Iron Workers v. Philip Morris*, Harold G. Burnley Jr, the company's former vice president of operations, was asked, "Is it true that Philip Morris uses ammonia for the purpose of increasing a nicotine kick?" He answered, "No, sir . . . it was used really initially in BL [blended leaf] to hold the sheet together, and it was used as a flavorant in RL [reconstituted leaf]."[80] In 1997, Philip Morris lawyers interrogated their company's former director of applied research about his claim that ammonia was used to increase nicotine availability, asking, in so many words: how do you know it's not just a flavor thing?[81] Pankow was questioned along similar lines in *Washington v. American Tobacco Co*, with lawyers for the defense asking how he could be sure that the increase in nicotine delivery was from the ammonia added and not the ammonia already present in the tobacco.[82] Similar rationalizations were put forward at the industry's second Annual Ammonia Technology Conference, where we hear that ammonia simply "enhances processes that occur *naturally* during tobacco and cigarette aging and during combustion."[83]

Philip Morris and the other tobacco companies also split chemical hairs by denying they had ever used gaseous ammonia to achieve any kind of freebasing effect.[84] A small truth here hides a larger deception, because it is true that the freebasing effect is not ordinarily achieved by using ammonia in gaseous form. The more usual practice is to use nitrogen-containing compounds such as proteins and amino acids (e.g., lysine) and ammonium salts such as DAP and ammonium tartrate, carbonate, and citrate along with ammonium hydroxide and urea, all of which readily transform into ammonia upon the addition of heat (as when a cigarette is lit). Tobacco manufacturers have also freebased using weakly basic substances that, when heated, convert into more-alkaline compounds (sodium carbonate produces sodium oxide, for example, which turns into sodium hydroxide in the presence of water).[85] Philip Morris in 1994 claimed that even if it *had* been adding ammonia (in a volatile gaseous form) to cigarettes the compound would simply evaporate away, reducing the pH to its normal level before the cigarette was even shipped.[86] That, however, is why most companies use nonvolatile ammonium salts such as DAP as their freebasing reagents: ammonium salts break down into ammonia, increasing the pH of the tobacco and deprotonating the nicotine in the process, but only after the cigarette has been lit.

CRACK NICOTINE?

In the mid-1990s, FDA Commissioner Kessler was using the tobacco companies' recently discovered manipulation of nicotine to argue for the regulation of tobacco.[87] The industry knew that any admission of using ammonia to increase the availability of nicotine would be an admission that nicotine is the addictive sine qua non of smoking, and tobacco manufacturers did not want to have cigarettes compared to crack cocaine. (According to Farone, the industry made a conscious effort in the 1980s and 1990s to avoid the term *freebasing* in any documents or statements because it didn't want to be associated with cocaine.[88]) With so much at stake, it is not surprising that the industry attempted to cover up its use of ammonia as a freebasing reagent.

It is important to keep in mind that the ammonia cover-up is only one of dozens of similar cover-ups, part of the industry's calculated disregard for human health.[89] The industry has tried to efface the truth in depositions and even in internal documents, but the facts are clear: Philip Morris by the early 1960s had realized ammonia's ability to augment the potency of nicotine and then used this knowledge to develop cigarettes that were nominally low in tar and nicotine while still having a powerful nicotine kick. Sales of Philip Morris products skyrocketed as a result, spiking the company to the top of the market charts. And the other manufacturers took notice: RJ Reynolds, American Tobacco, Brown and Williamson, Liggett, and Lorillard all worked hard to figure out Marlboro's secret and by the 1970s and 1980s had developed their own versions of ammonia technology, which all but Liggett implemented commercially.

It should also be noted that freebasing represented a reversal of a decades-old effort to make cigarettes "milder." The first major US cigarette brand, Camel, introduced in 1913, succeeded on the basis of its use of a flavored blend of oriental, burley, and flue-cured Virginia tobaccos, producing a milder and more inhalable smoke than previous generations of tobacco products. Flue-cured "bright" tobacco blends were less alkaline and therefore easier to inhale than traditional varieties, notably those used in the pipe and cigar trade, where tobaccos were typically high in pH (circa 8) but generally too harsh to inhale. Cigarette makers modified the chemistry of tobacco throughout the 1930s and 1940s, seeking to produce an ever-milder smoke that could be inhaled without stimulating coughing. When demand for lower-tar and lower-nicotine cigarettes arose in the 1950s and 1960s, however, the industry realized there were limits to how low nicotine levels could go without "weaning"[90] smokers from their habit. Cigarette manufacturers worried about producing an "emasculated"[91] cigarette devoid of flavor and missing the grip of addiction. Freebasing solved a big part of this problem, because tar and nicotine levels could now be lowered—up to a point—without the risk of losing customers. Teague at Reynolds in 1973 summarized the achievement: "As a result of its higher smoke pH, the current Marlboro, despite a two-thirds reduction in smoke 'tar' and nicotine over the years, calculates to have essentially the same amount of 'free' nicotine in its smoke as did the early WINSTON."[92]

It is not yet clear to what extent manufacturers in other parts of the world—for example, China and Japan—use ammonia in the manufacture of their cigarettes; this topic deserves further study. Diammonium phosphate is not legal for use in cigarettes in Austria, Germany, or Spain:[93] does this mean that freebasing is achieved by other means? Nicotine yields of American cigarettes have risen steadily over the past few years[94]: could this mean a retreat from the practice of ammoniation in favor of other methods of nicotine manipulation?

What is not in doubt is that the continued pull of nicotine has generated a global epidemic of lung and heart disease. Tobacco has become the world's single largest preventable cause of premature death, accounting for about 5 million fatalities per annum, a number expected to grow to about 10 million per year over the next couple of decades.[95] There is also tragedy, though, in the fact that so many scholars have helped to perfect and enhance this terrible technology of mortality. Tens of billions of dollars have been spent by the industry on tobacco chemistry[96] in the decades since British and American scientists followed the Germans in proving that smoking could cause lung cancer and heart disease.[97] Cigarettes are among the most carefully (and craftily) designed small objects on the planet, but they also cause more death and disease than any other invention since humans first learned how to spark fire from stone and metal. We should not be so surprised that the industry has manipulated cigarette chemistry to keep people smoking; what is surprising, though, is how easily they have gotten away with it. ■

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Scientific Committee on Emerging and Newly Identified Health Risks

SCENIHR

Addictiveness and Attractiveness of Tobacco Additives

SCENIHR approved this pre-consultation opinion for public consultation by written procedure on 6 July 2010

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ABSTRACT

The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) has been asked to evaluate the role of tobacco additives in the addictiveness and attractiveness of tobacco products.

The criteria for dependence established in humans indicate that tobacco has a high addictive potential, but it remains difficult to assess the addictiveness of individual additives. In animal studies the addictive potency of the final tobacco product cannot be assessed. The reinforcing potency of drugs is measured after intravenous injections and suggests that the addictive potential of pure nicotine is weak. The currently used methods to define addictiveness of nicotine and additives are thus not considered adequate.

In humans, the positive correlation between tobacco consumption and dependence suggests that individuals with high nicotine levels in their blood are more dependent. In animal studies using self-administration, an inverted U-shaped dose-response curve has generally been revealed suggesting that the addictiveness of nicotine is not directly linear with the dose. There is however substantial variation in the response to nicotine in both animals and humans, and genetic factors probably play an important role.

No tobacco additives, which are addictive by themselves, have so far been identified. However, sugars, which are present in high quantities in most tobacco products, give rise to acetaldehyde in tobacco smoke. Acetaldehyde given intravenously is addictive and enhances the addictiveness of nicotine in experimental animals. Additives that facilitate deeper inhalation (e.g. menthol) or inhibit the metabolism of nicotine may enhance the addictiveness of nicotine indirectly. Substances such as ammonia that increase the pH of the tobacco and the smoke, result in higher amounts of uncharged nicotine. However, it is uncertain if more nicotine is absorbed with higher smoke pH. For smokeless tobacco it seems that an increased pH enhances nicotine absorption in the mouth.

The methods used to quantify the addictive potency of additives have limitations because of technical challenges in experimentally manipulating the presence or absence of an additive in a tobacco product. Such experiments require large technical and financial resources. In addition, there are ethical issues if testing in humans is considered. Due to these limitations, the available methodologies are not considered adequate.

A number of technical characteristics of cigarettes (ventilation, packing, geometry) influence the content of different substances in the smoke and the size of smoke particles. Many smokers compensate for a lower dose of nicotine by increasing puff volume and frequency, and by deeper inhalation. The particle size of the smoke aerosol does not seem to substantially influence the exposure to nicotine.

Attractiveness is defined as the stimulation to use a product. The attractiveness of tobacco products may be increased by a number of additives but is also influenced by external factors such as marketing, price etc. Animal models do not currently exist for the assessment of attractiveness. In humans, the attractiveness of individual tobacco products may be compared in panel studies, surveys, and by experimental measures. Another method is to experimentally adjust tobacco products to exclude or include individual additives and test responses to them. However, this type of research is difficult nowadays due to ethical considerations that will usually preclude human testing.

The use of fruit and candy flavours seems to favour smoking initiation in young people. Menthol also attracts a number of smokers (in particular African Americans). Some additives decrease the harshness and increase the smoothness of the smoke. Certain additives yield a full and white smoke and other additives reduce the lingering odour of the smoke in order to favour the acceptability of smoking to people around.

Additives considered attractive may in principle lead to brand preference or a higher consumption of tobacco products. However, it remains difficult to distinguish the direct effects of these additives from indirect effects such as the marketing towards specific groups.

Keywords: addictiveness, additives, attractiveness, cigarettes, cigars, nicotine, SCENIHR, smokeless tobacco, smoking, target groups, tobacco, waterpipe

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EXECUTIVE SUMMARY

The Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) has been asked to evaluate the role of tobacco additives in the addictiveness and attractiveness of tobacco products. A summary of the answers are presented below.

1. Criteria which will define whether an additive or a combination of additives increases the addictive potency of the final tobacco product

In human studies there are clinical criteria for dependence, laboratory measures of self-administration, as well as preference studies. These criteria indicate that tobacco in humans has a high addictive potential, but they have limitations when assessing the addictiveness of individual additives in the final tobacco product. There is no widely-agreed universal standard for human studies and as a result various possible endpoints exist. In addicted individuals a modified regulation of neural networks exists, and the potential to induce such modifications should be the criteria used to define the addictive potency of a product.

In animal studies the reinforcing potency of a drug is used as a criterion for the addictive potential. However, self-administration studies indicate that pure nicotine could have a weak addictive potential. An evaluation of the role of additives has not yet been done in animals.

2. Methods currently used for assessing the addictive potency of a substance

Many different methods are used in humans, but there is a lack of consistency between them. Human studies have limitations in design (e.g. the use of conditioned cues, and the need to work with smokers). Furthermore, ethical issues may arise when testing substances in humans.

There is currently no animal model to assess the addictive potency of the final tobacco product; however, pure nicotine has been studied extensively. The experimental animal models are mainly based on self-administration in rodents, usually rats. The evaluation of addictiveness is based on the re-inforcing properties of the drug. However, there is no consensus on the predictive validity for the addictiveness of tobacco products in humans. In animal studies pure nicotine is injected intravenously and shows only a weak addictive potential whereas in humans, tobacco is used differently (e.g. inhalation, oral consumption) and is highly addictive. No method currently used to define addictive potency of a compound can therefore be considered as adequate.

3. Dose-dependency of development of nicotine addictiveness

In humans, there are little data available on pure nicotine use. However, tobacco consumption (e.g. number of cigarettes smoked per day) is positively correlated with dependence. This suggests that individuals who maintain higher nicotine levels in their blood are more dependent than individuals who maintain low levels.

In animal studies, an inverted U-shaped dose-response curve has generally been revealed suggesting that the addictiveness of nicotine is not directly linear with the dose. As mentioned before, pure nicotine is only weakly addictive in animal studies.

There is substantial variation in the response to nicotine and its addictive potential in both animals and humans, and genetic factors probably play an important role.

4. Additives in tobacco products that are addictive by themselves

No tobacco additives, which are addictive by themselves, have so far been identified. However, sugars which are added in high quantities to most tobacco products, give rise to acetaldehyde in tobacco smoke and acetaldehyde given intravenously is self-administered by animals and thus may be considered addictive.

Experiments using denicotinised cigarettes show that besides nicotine, other factors in cigarette smoke probably play an important role in craving and reinforcement. Although these unknown factors do not have pharmacologic effects similar to nicotine and are probably not addictive, they definitely play a role in smoking behaviour

5. Additives that enhance the addictiveness of nicotine

Sugars or their derivatives produce numerous substances upon heating. One of these is acetaldehyde, which enhances the addictiveness of nicotine when injected into experimental animals, probably by inhibiting monoamine oxidase (MAO) in the brain. Smokers have decreased levels of MAO in the brain. However, there is no proof that acetaldehyde in the smoke contributes significantly to blood levels of acetaldehyde. On the other hand, acetaldehyde generates in the smoke the compounds harman and norharman which may also inhibit MAO.

Additives that facilitate deeper inhalation (e.g. menthol) may enhance the addictiveness of nicotine indirectly. Other substances may enhance the addictiveness of nicotine by inhibiting its metabolism. Substances such as ammonia that increase the pH of the tobacco (and the smoke) result in higher amounts of uncharged nicotine that is more easily absorbed by the cells. However, due to the high buffer capacity of the lining fluid in the lungs it is uncertain if more nicotine is absorbed with higher smoke pH. For smokeless tobacco it has been shown that more nicotine is absorbed in the mouth when the pH of the product is increased.

6. Methods to quantify the potency of additives in enhancing the addictiveness of nicotine

The methods used to quantify the potency of additives in enhancing the addictiveness of nicotine or tobacco products are described above. The limitations of these methods arise from technical challenges in experimentally manipulating the presence or absence of an additive in the tobacco products used in these experiments. Such experiments have probably been carried out by the tobacco industry for some additives, especially sugars and their derivatives, but they require large technical and financial resources. In addition, there are ethical issues if testing in humans is considered. Because of these limitations, the available methodologies are not considered adequate.

7. Technical characteristics that enhance the addictive potential of tobacco products

A number of technical characteristics of cigarettes influence the content of different substances in the smoke and the size of smoke particles. The so-called TNCO values (tar, nicotine and carbon monoxide (CO)) are determined by, amongst other things, ventilation (paper, filter), the packing of the tobacco and the geometry of the cigarettes. Many smokers compensate for a lower dose of nicotine by increasing puff volume and frequency, and by deeper inhalation. Based on the limited publicly available information, it seems that exposure to nicotine cannot be substantially increased by altering the particle size of the smoke aerosol.

8. Criteria for considering an additive or a combination of additives as attractive

The criterion for attractiveness is the stimulation to use the product. Attractiveness of additives refers to factors such as taste, smell and other sensory attributes. In addition, a number of external factors (e.g. ease of use, flexibility of the dosing system, cost etc.) contribute to the attractiveness of the product.

The attractiveness of tobacco products may be increased by a number of additives that create a specific taste/flavour in order to attract certain target groups. An attractive effect may be obtained by changing the appearance of the product and the smoke, decreasing the harshness of the smoke, and inducing a pleasant experience of smoking.

In order to make smoking more acceptable to other people nearby, some additives reduce lingering odour or side-stream smoke visibility.

9. Methods currently used for assessing attractiveness

Animal models do not currently exist for the assessment of attractiveness.

In humans, the attractiveness of individual tobacco products may be compared with other tobacco products by panel studies and surveys, and by experimental measures. When examining what is known about the additive content of these products, judgements can be made as to the role of individual additives in the overall attractiveness of the product.

Another method is to experimentally adjust tobacco products to include or exclude individual additives and test responses to them. In addition, the quantity of the additive can be varied to assess dose response and whether there is a threshold below which any impact is not observed.

However, this type of research is difficult nowadays due to ethical considerations that will usually preclude human testing of different tobacco products, particularly among non-users or children. The methods currently used are thus not adequate.

10. Additives that increase attractiveness of tobacco products

Numerous additives are used in order to increase the attractiveness of tobacco products but it is very difficult to identify the role of individual additives in enhancing attractiveness.

Various sugars constitute a large proportion of additives, and the sweetness of the product is an important characteristic. The use of fruit and candy flavours in high amounts seems to favour smoking initiation by young people. Menthol also attracts a number of smokers (in particular African Americans) maybe due to its action on sensory nerve endings, resulting in a cooling effect.

Some additives decrease the harshness and increase the smoothness of the smoke. The harshness depends partly on the tar/nicotine ratio, but may also be decreased by additives such as propylene glycol and glycyrrhizin, a substance in liquorice.

Certain additives yield a full and white smoke (e.g. magnesium oxide, magnesium carbonate, sodium acetate, sodium citrate, calcium carbonate). Other additives reduce the lingering odour of the smoke in order to favour the acceptability of smoking to people around (e.g. acetylpyrazine, anethole, limonene, vanillin, and benzaldehyde).

In several countries there is a growing trend of using “natural” tobacco products advertised as containing no additives.

11. Association between additives and tobacco consumption – target groups

Additives considered attractive may in principle lead to brand preference or a higher consumption of tobacco products although it is difficult to distinguish the direct effects of these additives from indirect effects such as marketing towards specific groups. In the USA, the consumption of menthol cigarettes is relatively high among African Americans. Cigarettes with certain flavours (e.g. fruit, candy) appear to be developed to target young people.

Additives and design characteristics may modify consumption patterns. However, in spite of the many additives commonly used, tobacco products overtly marketed as containing additives (e.g. menthol cigarettes) command a relatively small market share in EU countries and there is presently a trend in several countries to use products labelled “without additives”.

It is notable that waterpipe smoking is becoming increasingly popular in some EU countries (and elsewhere), potentially due to the flavoured tobaccos used and the mild/cool smoke that may facilitate the inhalation of large volumes into the lungs. Smokeless tobacco products have gained increased interest from the industry because they may be used in places where smoking is prohibited.

1. BACKGROUND

Some 72-92% of adult cigarette smokers meet the criteria for dependence[1]. While nicotine is recognised as an addictive substance in the tobacco leaf, the risk of addiction to pure nicotine products is very low compared to cigarettes[1]. Currently, it is being discussed in the public health community whether lowering the levels of nicotine in tobacco products would make people less addicted and accordingly reduce the consumption of tobacco products.

Tobacco additives were hardly used before 1970, but today they represent up to 10% of the cigarette weight. By altering the taste and smell of cigarettes the products are made more attractive and the smoke more palatable which leads to an increase of smoking initiation. At present, the role of additives in enhancing the addictiveness of tobacco products is not clear.

In order to make tobacco products more attractive, design features are introduced, e.g. package design and cigarette form. In addition, these features are used to undermine the effect of the maximum limits set by the Tobacco Products Directive 2001/37/EC on tar, nicotine, and carbon monoxide (CO) yields in cigarettes.

<u>Legal background</u>

Article 13 of the Tobacco Products Directive (2001/37/EC)[2] stipulates that Member States can keep or introduce, in accordance with the Treaty, more stringent rules concerning the manufacture, import, sale, and consumption of tobacco products which they deem necessary in order to protect public health. Member States may prohibit the use of ingredients which have the effect of increasing the addictive properties of tobacco products.

Article 12 of the Tobacco Products Directive invites the Commission to submit a proposal providing a common list of ingredients authorised for tobacco products, taking into account, *inter alia*, their addictiveness.

In its comments to the Green Paper *Towards a Europe free from tobacco smoke: policy options at EU level*[3], the European Parliament invited the Commission to propose, by 2008 if possible, an amendment to the Directive including an evaluation and authorisation procedure for tobacco additives and an immediate ban on all additives that are addiction-enhancing[4]. In its 2nd Report on the implementation of the Tobacco Products Directive[5] the Commission stresses the need for further work on the addictiveness of tobacco additives.

DG SANCO wishes to have a better understanding of the criteria based on which an additive can be considered (classified) as an addictive and/or attractive substance, the role of additives in tobacco products and the role of design features in the attractiveness and addictiveness of a tobacco product.

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[4] http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+REPORT+A6-2007-0336+0+DOC+PDF+V0//EN

[5] http://ec.europa.eu/health/ph_determinants/life_style/Tobacco/Documents/tobacco_products_en.pdf

2. TERMS OF REFERENCE

In the light of the most recent scientific information, the Scientific Committee is requested to answer the following questions:

1. Which are the criteria which will define whether an additive or a combination of additives increases the addictive potency of the final tobacco product?
2. What are the methods currently used for assessing the addictive potency of a substance and are they considered adequate?
3. Is the development of nicotine addictiveness dose-dependent?
4. Which additives are addictive themselves in tobacco products?
5. Which additives enhance the addictiveness of nicotine and how?
6. Which are the methods used to quantify the potency of additives in enhancing the addictiveness of nicotine and are they considered adequate?
7. Which technical characteristics enhance the addictive potential of tobacco products?
8. Which are the criteria based on which an additive or a combination of additives can be considered (classified) attractive?
9. What are the methods currently used for assessing attractiveness and are they considered adequate?
10. Which additives increase attractiveness of tobacco products?
11. What is the association between additives and tobacco consumption (independent of any addictive potential they might have)? Which additives are used to target specific groups?

3. SCIENTIFIC RATIONALE

3.1. Introduction

According to a report from WHO (2008), about 100 million people died in the 20th century from tobacco use. The number of deaths in 2007 due to tobacco related diseases was about 5.4 million and if current smoking patterns continue, more than 8 million deaths are expected to occur each year due to tobacco smoking by the year 2030. In the EU, about a third of the adult population are smokers. The number of deaths from smoking per year is currently about 500,000 in the EU and more than 1.5 million in the whole European region (WHO 2007a). The vast majority of smokers use cigarettes, while other ways of smoking are less frequent (e.g. cigars, pipes, waterpipes). Apart from smoking tobacco, other tobacco forms (i.e. smokeless tobacco) may also have deleterious public health effects (SCENIHR 2008). In addition, exposure to tobacco smoke in the environment, so-called “passive smoking” or “second-hand smoking”, is an important cause of excess mortality and morbidity. Passive smokers have a significantly increased risk for several diseases such as lung cancer (IARC 2004), respiratory diseases (Jaakkola and Jaakkola 2002a, Jaakkola and Jaakkola 2002b) and cardiovascular diseases (Whincup et al. 2004).

The addictiveness of nicotine is enforced by substances in tobacco leaves that inhibit the action of monoamine oxidase (MAO) in the body (Berlin and Anthenelli 2001). Apart from naturally occurring substances in tobacco leaves, a number of ingredients in the final product may create or increase dependence. The tobacco industry has admitted the use of 599 different cigarette additives in the United States (US), which are claimed to improve taste and reduce harshness of the smoke (Rabinoff et al. 2007). Current US-style cigarettes contain about 10% of additives by weight; mainly sugars, humectants, cocoa and liquorice. Most other additives are used in small amounts. As discussed later in this opinion, cigars, pipe tobacco and smokeless tobacco generally contain fewer additives than cigarettes. Tobacco used in water pipes is characterised by a high content of water and various sugars.

Certain flavours (e.g. candy and fruit) have been used largely to make tobacco products more appealing to children (called “young adults” by the tobacco industry). In order to decrease the appeal of cigarettes to children, the US Food and Drug Administration (FDA) banned the use of a number of flavours as additives in cigarettes in September 2009 (http://www.fda.gov/TobaccoProducts/GuidanceComplianceRegulatoryInformation/FlavoredTobacco/default.htm). Menthol is not one of the banned additives, but is currently being evaluated by the Tobacco Products Scientific Advisory Committee of the FDA. In other parts of the world (e.g. Canada, Australia, New Zealand), legal measures on additives are established or are in preparation. In Europe, some countries, such as Germany, United Kingdom, Austria, Romania and France, use positive and/or negative lists which respectively allow or prohibit the use of specific compounds as tobacco additives, whereas other countries do not have such a regulation.

It is the purpose of the present opinion to examine the criteria for classifying tobacco additives as addictive or attractive, and to evaluate their role for the creation or maintenance of dependence on tobacco products. This would serve as the scientific basis for regulation of the use of additives in order to reduce the toxicity and the addictiveness of the final tobacco product. An important question is whether some additives are addictive by themselves or if they act by increasing the addictiveness of nicotine. The different methods of assessing addictiveness of an additive, alone or in combination with other substances, will be reviewed. In addition to the interactions between additives and constituents of tobacco, the burning of tobacco creates other complex chemical substances that may be toxic or favour addiction. An example of this is acetaldehyde, formed by the pyrolysis of various sugars in the tobacco (see section 3.8.1.4.). The technical characteristics of tobacco products, in particular of cigarettes, may also influence their addictive potential. A number of additives favour attractiveness of tobacco products, and may thus promote smoking initiation. In this context special attention will be paid to how additives may be used to target specific groups.

3.2. Methodology

A public call for information[6] was launched in November 2009, giving all stakeholders the opportunity to submit relevant scientific information concerning tobacco additives. The information asked for concerned: 1) details about the manufacturing process of tobacco products; and 2) methods applicable for assessment of attractiveness. A number of organisations and major tobacco companies responded. The information received has been evaluated carefully and was in many cases useful for writing the opinion. A particular problem in the area of tobacco products is that a number of studies relevant for this opinion have never been published but exist as internal documents of the tobacco industry. Some of the documents contain sensitive information showing health risks associated with smoking. In 1992, 60 documents were destroyed by Imperial Tobacco Canada in order to avoid exposure of the company to liability or embarrassment. Hammond et al. (2009a) have recently reviewed the contents of these documents that were recovered at the British American Tobacco headquarters in the United Kingdom and were released in 1998 through court disclosure in a trial in Minnesota. The author concludes that most of the studies that were carried out by researchers employed by the industry were scientifically valid. They gave evidence that cigarette smoke was carcinogenic and addictive. Since then, a great number of industry documents have become publicly available and can be found in two searchable databases, http://tobaccodocuments.org and http://legacy.library.ucsf.edu. The collections continue to be updated and currently contain more than 60 million pages in over 11 million documents.

Furthermore, a tobacco documents bibliography is also available which includes papers and publications based on documented research, broadly classified into several groups. Some examples of publications based on research of industry documents appearing under the heading of "Ingredients and Design" illustrate the tobacco industry research and development strategy on issues including: smoker preferences (Chaiton et al. 2005); smoking behaviour and product design (Hammond et al. 2006); targeting consumer groups with specific psychological needs (Cook et al. 2003); research on nicotine (Hurt and Robertson 1998); addictiveness (Scharfstein 1999, Slade et al. 1995, Stevenson and Proctor 2008, Vagg and Chapman 2005); manipulation/free base nicotine (Wayne et al. 2006, Wayne and Carpenter 2009); flavoured cigarettes (Lewis and Wackowski 2006); menthol (Kreslake et al 2008a, Wayne and Connolly 2004); youth targeting (Wayne and Connolly 2002); and particle size (Wayne et al. 2008a). Relevant publications are discussed in subsequent chapters of this opinion.

For the purpose of the present opinion, the health risks of tobacco products and additives have been investigated within different lines of evidence such as epidemiological studies, experimental studies in humans, experimental studies in animals, cell culture studies and in silico studies. To answer the questions in the Terms of Reference to this opinion, a weighted approach has been used, where data from all the available lines of evidence were integrated as appropriate. A more detailed description of how such weighting is performed is given in an earlier opinion of the SCENIHR (SCENIHR 2009). The primary sources for this opinion have been original scientific reports that are published in peer-reviewed scientific journals. In addition, the secondary sources used were the stakeholder information mentioned above and reports and opinions of other scientific committees as well as reports of various governmental bodies. In addition to the reports cited in the text and included in the list of references, various publications were noted but not considered appropriate for the purposes of developing the opinion.

[6] http://ec.europa.eu/health/ph_risk/committees/04_scenihr/scenihr_call_info_08_en.htm

3.3. Definitions

A number of terms related to tobacco products are explained below. For the list of abbreviations, see chapter 6. A full glossary can be found in chapter 8.

3.3.1. Technical characteristics

A wide variety of tobacco products are available worldwide such as cigarettes, cigars, pipe tobaccos, smokeless tobacco products etc. Each of these types is produced by using different tobaccos and additives and by using different manufacturing practices (Reviewed in IARC Monographs: 1985; 1986; 2004; and 2007).

Cigarette: The most common form of tobacco is the manufactured cigarette. Cigarettes are made from fine-cut tobacco leaves and are wrapped in paper or other non-tobacco material, filter–tipped or untipped, approximately 8 mm in diameter and 70-120 mm in length. Cigarettes are highly engineered, exquisitely designed “nicotine delivery devices”. Design features encompass a wide range of design variables such as tobacco type and blend, chemical processing and additives, and in addition, physical features such as paper, filter and ventilation. It is also important to consider factors such as tobacco weight or density, and cigarette geometry (circumference and length). Cigarette additives have a range of purposes; e.g. to facilitate manufacture, increase shelf life, control burn rates, nicotine delivery, flavour and harshness/irritation etc. The physical design characteristics of the tobacco product interact with its chemical composition to influence its function and effect (WHO 2001). For example, the size of the cuttings of the tobacco in cigarettes and non-combusted and non-heated tobacco, and its level of acidity (measured as pH), interact to influence the release of nicotine from the product (Callicutt et al. 2006, Stevenson and Proctor 2008). Cigarette ventilation designs also modify free nicotine levels in the smoke. Similarly, the physical and chemical characteristics of cigarettes interact to alter the size distribution of the aerosol particles that convey nicotine and other chemicals, and thus influence absorption (WHO 2007b).

Roll your own (RYO) tobacco denotes any tobacco product which, because of its appearance, type, packaging, or labelling, is suitable for use and likely to be offered to, or purchased by, consumers as tobacco for making cigarettes. RYO cigarettes are cheaper substitutes for commercially manufactured brands and have gained popularity worldwide.

A cigar is a roll of tobacco wrapped in leaf tobacco or any other substance containing tobacco. There are four main types of cigars: little cigars, small cigars (“cigarillos”), regular cigars and premium cigars. Little cigars contain air-cured and fermented tobacco and are wrapped either in reconstituted tobacco or in cigarette paper that contains tobacco and/or tobacco extract. Some little cigars have cellulose acetate filter tips and are shaped like cigarettes. Cigarillos are small, narrow cigars with no cigarette paper or acetate filter. Regular and premium cigars are available in various shapes and sizes and are rolled to a tip at one end.

Pipe tobacco can be a blend of as many as 20-25 different tobaccos, or made of Burley varieties only. Some pipe tobaccos contain midrib tissues, and casings and sauces are frequently added.

A water pipe is one of the ancient forms of tobacco use. Cut or shredded tobacco is smouldered inside the head, which is covered by a perforated aluminium foil on which the glowing charcoal is placed. The smoke is drawn through a tube inside the water pipe, filtered through water in a container and reaches the smokers' mouth via a long flexible tube. A great variety of tobaccos, or mixture of tobaccos with additives, is used in such pipes.

Smokeless tobacco is consumed without burning the product, and can be used orally or nasally. It comes in two main forms: snuff (finely ground or cut tobacco leaves that can be dry or moist, loose or portion packed in sachets, and administered to the mouth, or the dry products to the nose or mouth); and chewing tobacco (loose leaf, in pouches of tobacco leaves, "plug" or "twist" form). According to the Tobacco Products Directive (2001/37/EC) chewing tobacco is not included in the definition of "tobacco for oral use", the sale of which is banned in all EU countries except Sweden. Swedish-type moist snuff (snus) consists of finely ground dry tobacco (Kentucky and Virginia tobacco), mixed with aromatic substances, salts (sodium chloride), water, humidifying agents and chemical buffering agents (sodium carbonate). The large variety of smokeless tobacco products available worldwide has been described in detail elsewhere (SCENIHR 2008).

Electronic cigarettes, or e-cigarettes, are battery-powered devices that vaporise nicotine, flavouring, and other chemicals into an inhalable vapour (Pauly et al. 2007). Chemical analyses have detected tobacco-associated chemicals that may be harmful to humans, including known human carcinogens (Kuehn 2009). E-cigarettes have been marketed recently for a range of uses, including, as a cessation aid and as an alternative to cigarettes in smoke-free zones. The different brands vary greatly in content of nicotine and other chemicals, but the health risks or efficacy as cessation aids have not yet been sufficiently documented (Bullen et al. 2010).

3.3.2. Contents, ingredients, and additives

According to the terminology used in the WHO Framework Convention and the recommendation by the Scientific Advisory Committee in 2003, the term "contents" is used synonymously with the term "ingredients". Consequently, it means all product components, the materials used to manufacture those components, residual substances from agricultural practices, storage and processing, substances that can migrate from packaging into the product, as well as what may be termed "additives" and "processing aids" in some countries and regions (WHO 2007b).

Based on the 2nd Report on the Application of the Tobacco Products Directive (EC 2007b), the current definition of "ingredients" in Article 2 (5) covers any substance or constituent used in the manufacture or preparation of a tobacco product and still present in the finished product even if in an altered form, including paper, filter, inks and adhesives. It does not cover the tobacco leaf itself or other natural or unprocessed tobacco plant parts.

For the purpose of this report, we consider that the WHO definition is the most useful, as some of the added ingredients (e.g. different forms of sugar) are already present in the tobacco leaves. Tobacco leaves may also in some cases contain various toxic substances such as cadmium or radioactive isotopes. The possible presence of residual substances from agricultural practices will not be addressed in this report.

In order to avoid misunderstandings, the present report uses the term additives for added ingredients or substances. Additives are defined as any substance that is added, except water, during the course of manufacture of a tobacco product, including preservatives, humectants, flavours, and processing aids.

Natural or clean cigarettes are being marketed as having no chemicals or additives and the filters are made from natural cellulose. However, smoke from these cigarettes still contains all the carcinogens and toxins that come from the tobacco itself (Malson et al. 2002, McDaniel and Malone 2007).

Herbal cigarettes, although they may not contain tobacco, yield tar and carbon monoxide when smoked, and are thus also dangerous to health (Chen et al. 2007a, Gan et al. 2009).

3.3.3. Addiction and addictiveness

Addiction is the commonly used term referring to what is technically known as "dependence" and is widely employed to connote severe substance dependence, as has been demonstrated to occur in tobacco users. Dependence has been defined by the WHO

Expert Committee on Drug Dependence (WHO 2003) and The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines (WHO 1992).

Addictiveness refers to the pharmacological potential of a substance to cause addiction. Abuse liability of a drug is the likelihood that its use will result in addiction (dependence) and it can be assessed in laboratories by methods referred to as abuse liability testing. (Schuster and Henningfield 2003, Wayne and Henningfeld 2008b, WHO 2003).

The terms “dependence-causing” and “dependence potential” have been used as synonyms for “addictive” and “addictiveness”, respectively. In addition to the neurobiological characteristics of the substance itself, dependence potential is related to the dose, speed of absorption, metabolism, and to physical and chemical features of the formulation (WHO 2007b).

3.3.4. Attractiveness

According to the WHO, the terms “attractiveness” or “consumer appeal” refer to factors such as taste, smell and other sensory attributes, ease of use, flexibility of the dosing system, cost, reputation or image, assumed risks and benefits, and other characteristics of a product designed to stimulate use (WHO 2007b). Physical product characteristics are often integrated with marketing (WHO 2007b). For example, a flavour such as “menthol”, “mint”, or “cherry”, which is intended to appeal to a target population, may be incorporated into the product name or descriptors and marketed to reach out to that population (WHO 2007b). Attractiveness is also related to nicotine dosing characteristics, which is why smokeless tobacco product companies may include products ranging from lower dosing and slower onsetting “starter” products to higher dose maintenance products (FDA 1995, FDA 1996).

Although the risk of dependence on any substance is partially related to the attractiveness and/or ease of use of the delivery system, these features are not typically evaluated in dependence-potential testing but rather are generally described as factors affecting “consumer appeal” or “attractiveness”. Addictiveness and attractiveness go hand in hand as the real world liability for abuse of and addiction to a tobacco product is to a large extent also related to the attractiveness of the tobacco product.

Attractiveness is powerfully determined by imagery and cultural associations that are cultivated by the tobacco industry and effects may therefore be indirect. Attractiveness is also influenced by product sensory characteristics using flavours, and product characteristics (as well as marketing) that are intended to reduce concerns or undesirable features (e.g. reduce concerns about cancer with “light” branding, and reduce noxious throat burn with various chemicals and “smoke smoothers”) (Wayne and Henningfield 2008b).

3.4. Tobacco - manufacturing process

The manufacturing process for cigarettes has been described in several publications (Davis and Nielsen 2006, Hoffmann and Hoffmann 1997, IARC 2004, Wigand 2006). However, while the exact composition of each brand remains a trade secret, according to the Tobacco Products Directive (2001/37/EC) tobacco industries have to report the full list of additives in tobacco products, including the exact amount, to the competent authorities in the Member States.

Both the make-up of cigarettes and the composition of cigarette smoke have gradually changed in the last 50-60 years, including the use of a larger range of additives. The sales-weighted average “tar” and nicotine yields have declined. These changes have been primarily achieved by the introduction of filter tips, with and without perforation, selection of tobacco types and varieties, utilization of highly porous cigarette paper, and incorporation into the tobacco blend of reconstituted tobacco, opened and cut ribs, and "expanded tobacco" together with the use of a large number of additives/ingredients. At least four of the physical parameters of cigarettes have a decisive influence on smoke yields. These are the length of a cigarette, its circumference, the cut of the tobacco, and the packing density (Hoffmann and Hoffmann 1997). Agronomic factors such as production practices and soil characteristics, and environmental conditions such as rainfall, reportedly influence the accumulation of metals, including cadmium, beryllium, chromium, nickel and arsenic in the leaf.

Commercial tobacco products are predominantly produced from *Nicotiana tabacum*, while *Nicotiana rustica* is used on a limited commercial scale. Within the species *N. tabacum* one distinguishes four types: bright (Virginia), Burley, Maryland, and Turkish tobaccos. Bright tobacco is flue-cured by drying with artificial heat; Burley and Maryland tobaccos are air-cured; Turkish tobaccos are sun-cured. The properties of tobacco are based primarily on curing methods, locality of growth, position on the stalk from which the leaves have originated and factors such as colour quality and ripeness at harvest. Curing is the process for drying freshly harvested tobacco with partially or fully controlled temperature and moisture schedules. Freshly cured leaf is then threshed to separate stem from lamina, sometimes blended with other tobacco lamina and then re-dried to a uniform moisture level then packed into bales or hogsheads.

Virginia tobacco leaves contain a higher carbohydrate (e.g. sugars) level and lower nitrogen level than Burley leaves. The natural drying of the Burley leaves at relatively low temperatures allows plant respiration which continues to consume sugars during the process, leaving negligible sucrose and reducing sugars in the cured leaf. Burley leaves contain higher levels of nitrogen than Virginia leaves. The smoke of Virginia or flue-cured leaves is more aromatic and less alkaline than that of Burley tobacco, with a slight acidic taste resulting from the high levels of natural sugars. Burley tobacco produces a more alkaline smoke than flue-cured tobacco (Weeks 1999) and therefore imparts a bitter aroma and taste to cigarettes. Oriental leaves tend to have a low nitrogen content and moderate levels of carbohydrates, but fewer proteins, than the other varieties (Philip Morris 2010, Wolfe 1962).

A comprehensive integrated pest management programme is used to avoid insect infestation, e.g. chemical fumigation. The tobacco then undergoes aging and fermentation, usually for 1-3 years.

For the manufacture of cigarettes, specific tobacco blends utilizing desired tobacco types are prepared. Blending is the selection and thorough mixing of the tobacco-based components plus any associated casings, humectants and flavouring required for a particular product or brand. The tobacco based components may include the leaf lamina, cut and rolled stem, reconstituted sheet and expanded tobacco.

The tobaccos stored in bales are broken up, cut into specific dimensions, and combined with other blend components such as casing and top dressing, and adjustment of the moisture content. American blend cigarettes contain the four types of tobacco mentioned above plus reconstituted or homogenized sheet tobacco. This is made from tobacco dust, fines and particles, and leaf ribs and stems (IARC 2004). Reconstituted tobacco or homogenized sheet tobacco is a paper-like sheet approaching the thickness of tobacco laminae. It is made from tobacco dust, fines, and particles, and from ribs and stems; various additives may be incorporated. In the past, most of these "tobacco by-products" were wasted. The introduction of reconstituted tobacco or RECON, is the primary means by which ammonia chemistry and other chemicals are introduced into a cigarette. Expansion is a process which increases the shred filling power, e.g. puffed tobacco. Puffed, expanded, and freeze-dried tobaccos are modified preparations of cigarette tobacco and have up to twice the filling power, thus requiring less tobacco per cigarette. The principle applied here is to expand the tobacco cell walls by quick evaporation of water and other agents that readily volatilize.

Blending is carried out to achieve specific pH, taste, burning characteristics, and nicotine content. The pH strongly influences the concentration of free (i.e. non-protonated) nicotine in tobacco smoke, whereas the nitrate content influences the carcinogenic potential of smoke (IARC 2004).

Table 1 presents the classification of tobacco types based on curing methods and function.

Table 1 Classification of tobacco types based mainly on curing methods

Tobacco type	Characteristics / alternate names	Main use
Flue-cured	Leaves are yellow, blond, bright therefore also called Bright or Virginia	Cigarettes and also roll your own (RYO) cigarettes and pipe tobacco
Fire-cured	Light to dark brown cured over open fires (Kentucky)	RYO, chewing tobacco, cigars and smoking tobacco
Light air-cured	Burley (cured without supplementary heat) Maryland Perique	Mainly in cigarettes (also RYO, pipe tobacco and cigars) Cigarettes Pipe tobacco
Dark air-cured	Light to medium brown	Chewing tobacco and snuff, snus, dark cigarettes
Sun-cured	Oriental tobacco varieties Latakia	Turkish cigarettes (also RYO and pipe tobacco) Some pipe tobaccos
Cigar filler, **Cigar binder,** **Cigar wrapper**	Tobacco types for use as cigarfillers, binders and wrappers	Used for cigars

Ref: IARC Monograph 83 (2004), US Department of Agriculture (2001)

Two principal types of commercial cigarettes have traditionally been sold throughout the world: (i) American Blend cigarettes, which are made from a blend of Virginia, Burley and Oriental tobaccos, and (ii) Virginia cigarettes, which contain exclusively Virginia tobacco.

Casing refers to the sauce composed of a variety of ingredients such as humectants, sugars, cocoa, liquorice and fruit extracts (Hoffmann and Hoffmann 1997).

Casings are usually applied to tobacco strips or leaf early in the primary processing scheme to tone down or mute the strength or harshness of tobacco smoke, improve processibility of tobacco and add deep flavour notes to the smoke. Casings are traditionally added to US blended styles of product that contain significant proportions of Burley type tobacco blends. These casings are added to the Burley tobacco line through the means of the casing cylinder or Cased Leaf Dryer.

Ammonia technology has been used with US blended styles of products containing cased Burley tobacco. Ammonium salts could be added at the Cased Leaf Dryer (CLD) stage or with the manufactured reconstituted tobaccos.

There are no fixed rules as to where humectants, flavours and flavourings are added to the processed tobacco but generally the more volatile ingredients are added as late as possible during tobacco processing to prevent losses. Those tobacco blends that contain flavours and flavourings are usually held in a bin to allow for equilibration across the blend before it is passed to the making machine as the final blend. Top flavourings are generally applied to the total tobacco blend as one of the last steps in processing. They are usually carried in an alcohol base. They are used to improve quality of smoke, impart a pleasant pack aroma and side stream aroma. Menthol may be added at any of the following stages; spraying onto the final blend, through addition to the filter via a thread, or by application to the cigarette paper or the foil used to wrap the cigarettes. Due to the high level of volatility of menthol, different manufacturers have over the years developed a variety of methods for producing mentholated products that are as consistent as possible in terms of their finished product menthol levels (BAT 2010).

In cigarettes, flavours may be added to tobacco, cigarette paper, the filter, in a plastic pellet placed in the filter or the foil wrapper, in an attempt to enhance the tobacco flavour, mask unpleasant odour, and deliver a pleasant cigarette-pack aroma. Internal industry documents reveal additional flavour technologies such as flavour microencapsulation in the paper, carbon beads, and polymer-based flavour fibres inserted into the filter, flavoured tipping etc. (WHO 2007b).

As described above, the physical elements of the cigarette such as packing density, particle size distribution, rag cut per inch, colour appearance, resistance to draw, the appropriate paper, filter, tobacco type and the final tobacco blend, are carefully controlled (Wigand 2006). The final product is manufactured using high speed automated machines.

Over the years the tobacco industry has developed genetically modified (GM) tobacco plants with an aim, among others, to manipulate nicotine levels (Dunsby and Bero 2004). Reductions of nicotine levels have been in the range of 80-98%.

Philip Morris sought to use anti-sense biotechnology to disrupt enzymes involved in nicotine biosynthesis (US Patent 5684241). In 2003, Vector Tobacco began marketing a new cigarette that is produced from GM tobacco containing trace amounts of nicotine. The GM plant was produced by disrupting expression of the gene for quinolinate phosphoribosyl transferase, which encodes one of the rate-limiting enzymes in the nicotine biosynthetic pathway (Bonetta 2001). Vector Tobacco market Quest Cigarettes, which exist in three forms, ranging in nicotine content from 0.6 mg per cigarette to 0.05 mg per cigarette. They are marketed as a smoking cessation or reduction aid, with the manufacturer claiming that graded reduction of nicotine exposure through the gradual use of increasingly lower nicotine content cigarettes will lead to the eventual extinction of nicotine dependence and conditioned associations with related cues (Bonetta 2001).

Large scale field-trials have also been conducted despite consumer opposition and fear of tobacco growers that GM crops would be turned down by several countries.

3.4.1. Conclusions on manufacturing

Cigarettes, which are the predominant tobacco product, are highly engineered nicotine delivery devices that are mass produced by the major industries by integrated automation.

The properties of tobacco products depend on locality of growth, position of leaves on the stalk, ripeness and curing method. The different curing methods (drying procedures) determine the sugar content and colour of the tobacco leaves. During the manufacturing process of cigarettes, a number of substances are added at different stages for various reasons, such as providing consistency of the product, creating a unique brand, and promoting attractiveness.

3.5. Technical characteristics of cigarettes

Parts of cigarettes, like the paper and filter have technical features which affect the constitution of main-stream and side-stream smoke.

3.5.1. Introduction

Considering the natural origin of tobacco leaves, their content will, both qualitatively and quantitatively, depend on the season, local weather conditions and geographical origin. Consumers do not like to smoke a product that changes over time, i.e. smoking a constant product is preferred. In order to produce a constant product, i.e. to mask the batch to batch variation in taste, tobacco companies use a large variety of additives in the manufacture of tobacco products. In addition, the tobacco companies strongly prefer to maintain the same TNCO-values (tar, nicotine and carbon monoxide) of their products. To achieve consistency in TNCO values, tobacco producers change (amongst others) the ventilation of the products. The ventilation through the filter can be increased by punching more (or wider) ventilation holes. The ventilation of a cigarette can also be changed by using commercially available cigarette paper wraps with another grade of porosity.

Relevant technical characteristics of cigarettes are the following:

- Ventilation of the paper (paper porosity);
- Ventilation holes in the filter;
- Ventilation holes in the paper wrap;
- Packing of tobacco (dense or loose); and
- Geometry (length, diameter).

Ventilation

Large efforts have been made by the tobacco industry to investigate the effect of ventilation on the size distribution of the smoke aerosol. Depending on the size, the smoke particles enter and deposit at different levels of the airways (upper or lower airways). The purpose of this research was either to enhance the absorption of nicotine, to decrease the toxic potential of the product or to manipulate the taste of the smoke.

The main effect of ventilation is the dilution of the tobacco smoke. As such, the concentration of smoke components is reduced which not only leads to a lower dose of nicotine, but also to a lower concentration of other (toxic) components. It appears, however, that smokers compensate for the lower dose of nicotine per puff (due to increased ventilation) by increasing their puff volume, puff frequency, and deeper inhalation of the smoke (Jarvis et al. 2001, Scherer 1999). Many other smokers consciously or unconsciously block a part of the ventilation holes with their fingers so that more concentrated smoke is inhaled.

Another feature of ventilation is that it may affect the particle size and particle size distribution of the smoke aerosol, i.e. increasing the ventilation is supposed to decrease the mean particle size of the aerosol. It is difficult to assess whether an increase in ventilation indeed reduces the particle size, as only few studies are reported in publicly available literature.

3.5.2. Technical limitations

It is difficult to determine the size of the particles and their distribution in cigarette smoke, mainly because the half-life of the particles is very short (0.1-1 sec). Rapid ageing of the aerosol results in larger particles as they have time to coalesce, i.e. a secondary aerosol containing larger particles at the expense of smaller particles is rapidly formed (Harris and Kay 1959). Therefore, only sophisticated on-line sampling and detection allows a proper measurement of the particle distribution of the smoke aerosol. Obviously, these techniques require large financial resources and highly qualified technical personnel.

A number of variables other than ventilation may affect the particle size; moisture of the cigarette (relative humidity), puff volume, puff number (e.g. first or last puff), butt length, length of the cigarette, electrostatic charges, etc. Different unities are used in the studies to express the size of the particles (mean diameter, count median aerodynamic diameter, mass median aerodynamic diameter) which hampers quantitative comparison of the data. The aerosol is produced during burning, i.e. directly behind the burning cone at the tip of the cigarette the superheated vapour condenses and forms an aerosol; the longer the aerosol stays in the cigarette the larger the size of the particles.

Due to the number of different particle sizing methods, instrumentation and sampling and detection techniques applied, as well as differences in the cigarettes and smoking conditions, variable results are found and the results of different investigations are difficult to compare. Important limiting factors for many techniques are low time of resolution and the ageing of the smoke. Over time various methods have been developed to improve the accuracy of the measurements.

3.5.3. Smoke particles

Particle size may be relevant for the absorption of nicotine into the bloodstream.

Cigarette smoke particle size has generally been reported with MMD (mass median diameter) in the size range of 0.3-0.5 µm and CMD (count median diameter) in the range of 0.2-0.4 µm (Bernstein 2004, Wayne et al. 2008a). Particles larger than 1 µm are mostly trapped within the cigarette, whereas ultra-fine particles (less than 0.1 µm - nano-particle range) probably will adhere to the surface of the paper, tobacco and filter or coagulate into larger particles (Stratton et al. 2001), see section 3.5.4. Differences in particle size found in many studies were quite small and some internal tobacco documents concluded that the measurable influence of conventional design changes was insignificant (Philip Morris 1991, Wayne et al. 2008a). Of the four variables applied by Philip Morris to change the size of the particles (filler, filter, paper and ventilation) only ventilation had any significant effect (Cox et al. 1992). In addition, butt length and puff volume affect the size of the particles. There is a clear trend of decreased size of the particles at shorter butt lengths; the average size at 20 mm was 0.29 µm and at 55 mm it was 0.34 µm. Cox et al. (1992), taking all the variables mentioned above into account, reported deviations of about 10 to 30%. Surface mean diameter increased from 0.32 to 0.42 µm when the ventilation was increased from 0 to 60%. Based on their results, Cox et al. (1992) suggested that aerosol coagulation in the cigarette rod is the main mechanism for change in particle size.

Bernstein (2004) reviewed the available data of the tobacco smoke particulates which go back to 1950s. The main findings include:

- No difference in particle size between plain (non-filter) and filter cigarettes.
- Particle size depends on puff number (e.g. first vs. last puff).
- Relative humidity of the tobacco does not affect or only marginally affects particle size.
- Aged tobacco smoke contains larger particles than fresh smoke.

Over all the studies reviewed by Bernstein the size of the smoke particles range, roughly from 0.17 to 0.60 µm either expressed as CMD or MMD.

A study by McCusker et al. (1983) compares mass median aerodynamic diameter of ultra-low-tar, low-tar and medium-tar rated cigarettes (with and without filter). Particle size was less than 0.6 µm and not affected by the cigarette filters. Among the 10 brands tested ventilation ranged from 22 to 94%. The mass median aerodynamic diameter ranged from 0.36 µm to 0.56 µm, but did not correlate with ventilation efficiency. The number of particles was, however, reduced by 20–90% by applying the commercial filters and the particles were present in the higher puff numbers. Interestingly, blocking of the ventilation holes on the filters of ultra-low-tar cigarettes increased the particle concentration. This is explained by the longer residence time (longer transit time from cone to filter) of the newly formed particles in the cigarette rod.

As mentioned in section 3.5.2, only sophisticated on-line sampling and detection allows a proper assessment of the particle size and distribution. Moreover, the relevance of ultra-fine particles for nicotine absorption has only been taken seriously for the last two decades; therefore, most of the older studies did not focus on the presence of ultra-fine particles.

Recently, using on-line measurement of the particle size (range measured 5–1000 nm), Adam et al. (2009) reported that non ventilated cigarettes smoked under the intense regime, which includes blocking the ventilation holes resulted in count median diameter of 0.18 µm, whereas 70% ventilated cigarettes smoked under a milder standard smoking regime lead to a diameter of 0.28 µm. The particle size of mainstream smoke of Virginia cigarettes, smoked under a standard smoking regime, was 0.22 µm and 0.25 µm at 0 and 70% ventilation, respectively. For the intense smoking regime the respective particle sizes were 0.18 and 0.22 µm. Interestingly when the ventilation was increased from 0 to 70% the total number of particles decreased dramatically from 2.3×10^{12} to 0.3×10^{12}, and total mass of particles dropped from 17.2 to 2.3 mg (standard smoking regime). In another recent paper by Gowadia et al. (2009) the particle size (mass median aerodynamic diameter) was found to be approximately constant (0.9–1.0 µm) for three different puffing regimes. The smoke was collected in a conditioning chamber and the particle size distribution was determined by UV spectrometry.

Particle size of waterpipe smoke was shown to be somewhat smaller than that of cigarette smoke. Monn et al. (2007) reported waterpipe smoke particle median diameter in a full smoking set containing charcoal, tobacco and water, of 40 nm; the smoke of the heated tobacco alone ranged from 10 nm to 200 nm while the burning of charcoal was mostly responsible for the particles smaller than 50 nm. Fromme and colleagues found two phases of particle emission during a waterpipe session: when the charcoal was lit, the particle diameter was around 100 nm and during the smoking session it decreased to 17 nm (Fromme et al. 2009). Daher et al. (2010) found similar particle sizes to the Monn study in side-stream smoke from waterpipes, which was significantly smaller than particle sizes in side-stream smoke from cigarettes with a median diameter of 139 nm and a large number of particles smaller than 100 nm.

3.5.4. Deposition of particles

Although the size of the particle is an important factor for the deposition in the lung, the relationship between particle size and deposition in the lung is complex and factors other than size alone, such as respiration rate, depth of inhalation and flow rate, affect lung deposition (Sarangapani and Wexler 2000).

In figure 1 the relative deposition of particles (dependent on the aerodynamic diameter) in humans is depicted. Particles larger than 1 µm will mainly deposit in the extra-thoracic region. Smaller particles will deposit in different regions, but the general statement that smaller particles deposit deeper in the lung is not entirely true. Very small particles (a few nm) will mainly deposit in the extra-thoracic region. Peak alveolar deposition is around 30-20 nm and becomes less important at sizes less than 8-9 nm (ICRP 1994, Oberdörster et al. 2005). The question whether the ultra-fine particle size is relevant for mainstream tobacco smoke is unanswered. From a theoretical point of view removal of ultra-fine particles is to be expected due to adherence to the surface of the paper or to the tobacco and filter, or due to coagulation into larger particles (Stratton et al. 2001) (see section 3.5.3), however this needs to be confirmed experimentally.

Other points of concern in the inhalation of ultra-fine particles are the translocation of these particles: (1) from the lumen of the lung to the circulation; and (2) from the olfactory nerve endings in the nose to the brain. These two events have been described for several solid nanoparticles in the lungs of animals and humans (Kreyling et al. 2002, Nemmar et al. 2002,), and in the noses of rodents (Oberdörster et al. 2002). These phenomena have not been shown for tobacco smoke derived particles which are not solid nanoparticles (although combustion derived particles have been studied in the lung); therefore, only theoretical/hypothetical considerations can be made (which fall outside the scope of this opinion).

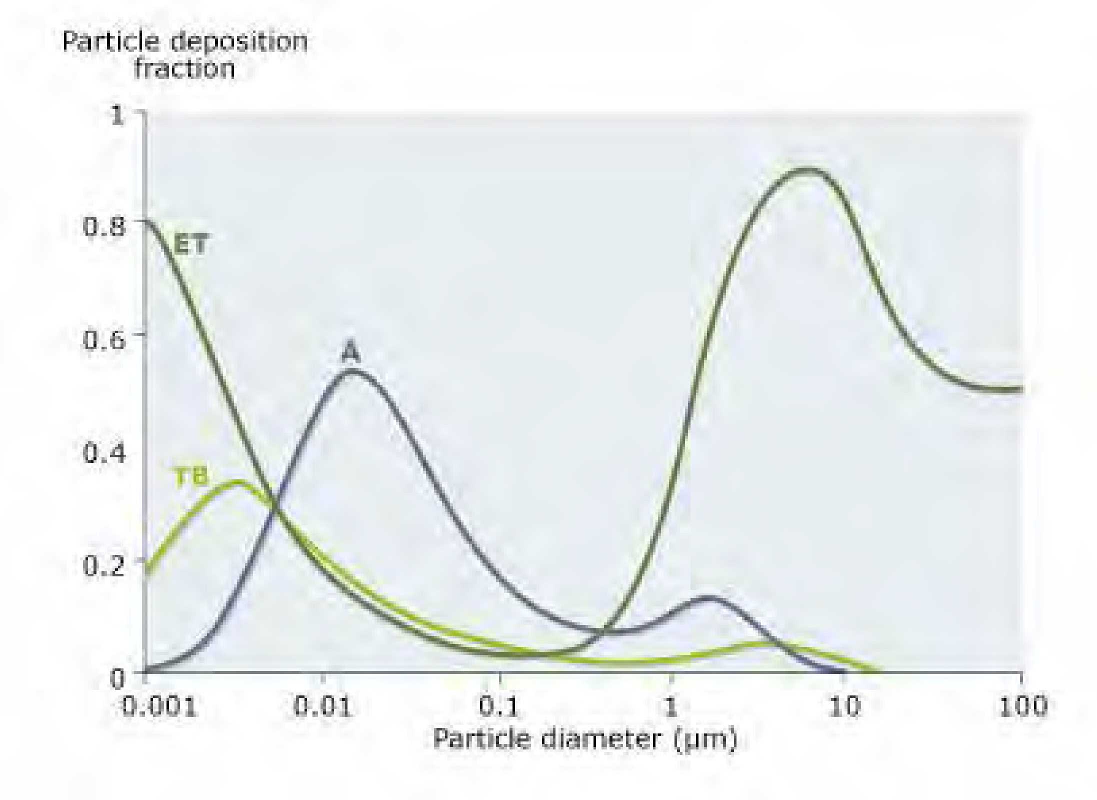

Figure 1 Predicted deposition of inhaled particles during nose breathing. Fractional deposition in: extrathoracic (ET); trachea-bronchial (TB); and alveolar (A) regions (adapted from ICRP 1994).

3.5.5. Light cigarettes as an example of cigarettes with high ventilation

The best known application of changing ventilation is the development of light cigarettes. Light cigarettes have been marketed as products with a lower health risk as they should deliver less tar and other toxic compounds in the smoke inhaled. As will be described in detail in section 3.10.1 many smokers of light cigarettes inhale the smoke deeper and increase the number of puffs, so the health risks are probably not lower than for smokers of regular cigarettes (Frost et al. 1995). Animal studies have shown that self-administration of a low dose of nicotine at a high frequency gives a more reinforcing effect as compared to self-administration of a higher dose at a low frequency (in this comparison total dose self-administered is the same) (Harris et al. 2008, Harris et al. 2009, O'Dell et al. 2007).

3.5.6. Conclusions on technical characteristics

A number of technical characteristics of cigarettes influence the content of different substances in the smoke and the size of smoke particles. The so-called TNCO values (tar, nicotine and CO) are determined by, amongst other things, ventilation (paper, filter), the packing of the tobacco and the geometry of the cigarettes. Smokers usually compensate for a lower dose of nicotine by increasing puff volume and frequency, and by deeper inhalation. Data obtained in animal studies suggest that cigarettes with high ventilation (often described as "light" or "low tar") may favour addiction to nicotine in the smokers of these products, because of an increased smoking frequency.

The particle size of smoke aerosol of commercial cigarettes is around 0.4 to 2 µm. A large fraction of ultrafine particles (<0.1 µm) probably adheres to the surface of the paper or the filter, or coagulates into larger particles, and will thus not be present in the smoke as such. The small smoke particles (submicron meter range) will enter the lower airways and alveoli, while larger particles (micron meter range) will be deposited increasingly in the upper airways.

Considering the manufacturing of cigarettes, the change of the technical characteristics of cigarettes may affect the mean particle size and, therefore, the distribution of the smoke aerosol. However, based on the limited publicly available information, it seems that exposure to nicotine cannot be substantially increased by altering the particle size of the smoke aerosol.

3.6. Nicotine

3.6.1. Pharmacological effects (incl. metabolism of nicotine)

3.6.1.1. Brief historical overview

Nicotine is the principal component alkaloid of tobacco, occurring throughout the plant (*Nicotiana tabacum*), especially in the leaves. The plant and the compound are named after Jean Nicot, a French ambassador to Portugal, who sent tobacco seeds to Paris in 1550. Crude nicotine was known by 1571, and the compound was obtained in purified form in 1828; the correct molecular formula was established in 1843, and the first laboratory synthesis was reported in 1904. It is one of the few liquid alkaloids; colourless and extremely toxic. Nicotine is commercially obtained from tobacco scraps; it has been used as an insecticide and as a veterinary vermifuge.

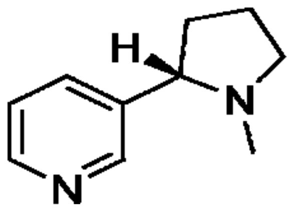

Figure 2 Structure of nicotine (CAS number 54-11-5)

3.6.1.2. General pharmacodynamic (physiological) effects

Nicotine administration induces a series of multifaceted effects which show great interindividual variability, i.e. the effects vary greatly from person to person. This is reflected in a non-linear and complex dose-response relationship ensuing from a summation of stimulatory and inhibitory actions in the central and peripheral nervous systems.

Low doses of nicotine, including those in the range of inhaled cigarette smoke (1-2 mg), produce stimulation of ganglionic neurotransmission (vegetative ganglia). This generates a complex response which results from a mix of sympathetic and parasympathetic actions. Thus, tachycardia and rise of blood pressure are to a large extent the consequence of sympathetic ganglia activation that induces an increased adrenaline release in the adrenal medulla (via splanchnic nerve stimulation). At the same time, the nicotine action on the carotid and aortic chemoreceptors and on the brain regulating centres modifies the cardiovascular effects determining the great variability observed in the final response. Therefore, the direct nicotine effects on heart rate and blood pressure are rapidly counterbalanced by the peripheral and central cardiovascular compensatory reflexes. Similarly, nicotine–induced activation of parasympathetic ganglia and cholinergic terminals causes an increase of the gastrointestinal peristalsis. In susceptible subjects, first doses may cause nausea, vomiting and related effects of hypercholinergic activation. Nicotine also increases blood glucose levels and the activity of exocrine glands. In the brain, nicotine is clearly a stimulant at low doses. It produces a pattern of alertness in the EEG, mediates fast synaptic transmission, and positively modulates a range of cognitive functions. As a result, it improves attention, learning, arousal, motor skill, facilitates memory functions and decreases irritability and anxiety, among other CNS functions (Balfour and Fagerström 1996, Benowitz 2008, Fattinger et al. 1997, Grybko et al. 2010).

An important pharmacological characteristic of nicotine is the rapid development of tolerance to its unwanted effects. Although there is a great individual variability, in many cases tolerance to the peripheral effects appears a few days after the first exposure (Benowitz 2008).

3.6.1.3. Toxicity effects

At high doses, after the initial stimulation, nicotine rapidly produces a ganglionic blockade due to the inhibition of transmission, which is a consequence of a persistent depolarisation of all autonomic ganglia. This depression of all autonomic ganglia results in bradycardia, hypotension, impairment of adrenaline release, etc. Similarly, a biphasic nicotine-induced action is also observed in the adrenal medulla (a discharge of catecholamines is evoked by small doses whilst their release is blocked by larger doses). It should be noted that most peripheral effects are influenced by compensatory reflexes. In the CNS large doses induce a generalised mental depression, tremors, nausea, and convulsions. The acute lethal dose of nicotine in an adult human is estimated to be about 60 mg (Benowitz 2008, García-Estrada and Fischman 1977, Solarino et al. 2010). This dose (less than 1 mg/kg) is derived from old reported cases of intoxication when nicotine was widely used as an insecticide (Grusz-Harday 1967, Lockhart 1939). In rats the LD_{50} is ~50 mg/kg and in mice ~3 mg/kg (Okamoto et al. 1994). Acute nicotine poisoning has occurred in children who accidentally ingest tobacco or are occupationally exposed to wet tobacco leaves. Children have played a role, and they continue to do so in many places, in agricultural production of tobacco, where absorption of nicotine from the plant is likely to happen. This nicotine-induced acute condition is known as green tobacco sickness. Clinical features are similar to those observed in adults (Gehlbach et al. 1974, McKnight and Spiller 2005).

Ingestion of tobacco products is a major reason for infant and child toxic exposures reported to poison control centres. The large majority (90%) of such accidental poisonings in the population involve children up to 6 years of age (Connolly et al. 2010). However, ingestion of cigarettes and cigarette butts by children aged ≤ 6 years resulted in minor toxic effects (CDC 1997).

Malizia et al. (1983) described four children who ingested two cigarettes each and developed salivation, vomiting, diarrhoea, tachypnoea, tachycardia, and hypotension within 30 minutes, and depressed respiration and cardiac arrhythmias within 40 minutes. Convulsions occurred within 60 minutes of ingestion. All recovered after gastric lavage with activated charcoal, intermittent positive pressure ventilation, and 5 mg diazepam intravenously for convulsions.

A prospective review of 51 cases of tobacco ingestion and five cases of nicotine resin chewing gum exposure was conducted to evaluate the incidence and degree of toxicity caused by these products in children. A dose-response relationship was observed for cigarette exposures. Nine of 10 children ingesting more than one cigarette or three cigarette butts developed signs or symptoms (Smolinske et al. 1988).

3.6.1.4. The nicotinic acetylcholine receptor

Nicotine acts on a class of cholinergic receptors which are ligand-gated ion channels (nicotine acetylcholine receptors: nAChR). These kinds of receptors are structurally similar to the ones operated by GABA, glycine, glutamate, 5-HT_3, etc. Nicotine binding to the nAChR opens the channel and increases its ionic permeability for monovalent cations (Na^+, K^+) and divalent cations (Ca^{2+}, Mg^{2+}), although with difficulty for the latter and depending on the subtype of nAChR. Neuronal nAChR embrace a conjunct of at least 20 homologous subtypes that mediate fast synaptic transmission throughout the central and peripheral nervous systems (Xiu et al. 2009).

Neuronal nAChR are pentamers of homomeric or heteromeric combinations of α (α_2 to α_{10}) and β (β_2 to β_4) subunits, which possess different pharmacological and biophysical properties and locations in the brain (Gotti et al. 2006).

The nAChRs in the CNS are localised both in postsynaptic and presynaptic neural membranes. Studies in recent years have shown that the primary site of nicotine action is presynaptic, and that nAChRs facilitate the release of neurotransmitters when localized in non-cholinergic terminals. In fact, nAChRs are present in the terminals of most of the neurotransmitter systems (GABAergic, glycinergic glutamatergic, dopaminergic, serotonergic, etc.). Likewise, nAChRs have been identified, in different densities, in most of the brain areas.

Nine individual subunits of nAChRs in the human brain have been identified and cloned, and they combine in various conformations to form individual receptor subunits. The structure of individual receptors and the subtype composition are not completely understood. Only a finite number of naturally occurring functional nAChR constructs have been identified (Luetje 2004).

The pentameric structure of the neuronal nAChR and the considerable molecular diversity of its subunits offer the possibility of a large number of nAChRs with different physiological properties. The stoichiometry of most nAChRs in the brain is still uncertain (Kuryatov et al. 2000).

For example, the neuronal nAChR subunits on presynaptic terminals of dopamine neurons projecting to the striatum have been fully defined (Luetje 2004), as has the complete subunit composition of four major presynaptic nAChR subtypes in the striatum (Salminen et al. 2004).

It should also be noted that chronic exposure to nicotine induces a marked increase in the density of nAChRs in most neurotransmitter systems and brain areas (Walsh et al. 2008).

3.6.1.5. Nicotine pharmacokinetics and metabolism

Nicotine as a weak base (pKa = 8.0) is rapidly absorbed across biological membranes with an environment at physiological pH (7.4) or slightly alkaline. This is the case for nicotine in cigarette smoke when it reaches the lung alveoli (Pankow et al. 2003). The average nicotine content of a cigarette (6-10 mg) delivers about 1 mg of nicotine (0.5-2 mg) systematically through the smoker's lungs (Henningfield et al. 1993). The pulmonary bioavailability (the amount absorbed from smoke) of inhaled nicotine is 80-90%. After inhalation it reaches high levels in the brain within 10-20 seconds, thus being equivalent to, or even faster than, an intravenous administration (Gourlay and Benowitz 1997, Hukkanen et al. 2005). In both cases the hepatic first-pass effect (metabolism) is avoided allowing higher levels of unmetabolised nicotine to be delivered to the brain. In addition, nicotine easily crosses the blood-brain barrier.

In contrast, the buccal and gastric bioavailability of nicotine is low (20-40%) due to the acidic environment at which nicotine is protonated and therefore poorly absorbed through local membranes. Better absorption is obtained in the intestinal mucosa because of its alkaline pH. Nonetheless, the liver first-pass metabolism contributes to the impairment of the oral bioavailability to a greater extent. The time of nicotine blood maximal concentration for oral administrations is about 60-90 min. Nonetheless, nicotine bioavailability through the skin is high (75-100%).

Nicotine is widely distributed in the body (liver, kidney, lungs, etc.; with adipose tissue showing the lowest affinity). Brain tissue exhibits a high affinity for nicotine. It has been reported that nAChR binding capacity for nicotine is increased in smokers compared to non smokers (Breese et al. 1997, Perry et al. 1999). This reflects the higher density of nAChRs in the brain of smokers (nicotine-induced up-regulation of nAChRs). However, the quantity of nicotine delivered from the tobacco product which reaches the brain is higher in non dependent smokers than in heavy smokers (Rose et al. 2010a).

The blood half-life ($t_{½}$) of nicotine after cigarette smoking or intravenous administration is about 2 hours ($t_{½}$ = 100-150 min). The disposition of nicotine shows a multiexponential elimination (Hukkanen et al. 2005). However cotinine, the main metabolite of nicotine, has a $t_{½} \approx 19$ hours. It was found recently that every puff of a cigarette induces a peak of nicotine in the arterial blood (Berridge et al. 2010) with a $t_{½}$ of 45 seconds, but that these peaks do not occur in the brain (Rose et al. 2010a). This finding rules out that the lack of efficacy of NRT (gums or patches) is due to a continuous delivery of nicotine. In the liver nicotine is mostly metabolized in the endoplasmic reticulum by the cytochrome P450 (CYP) system, mainly by CYP2A6 and CYP2B6. The major metabolite produced by CYP through nicotine oxidation is cotinine, which is further converted to cotinine glucuronide and other metabolites. It should be noted that CYP oxidative metabolism of nicotine to cotinine and its glucuronide conjugation are inhibited by menthol, a commonly used cigarette additive. The pathway of nicotine to cotinine represents around 70-80% of nicotine biotransformation in humans and, therefore, is commonly used as a quantitative biomarker of nicotine exposure as well as of CYP2A6 metabolic activity, which exhibits an important variation in function in humans (Benowitz 2008, Dempsey et al. 2004, Hukkanen et al. 2005, Hukkanen et al. 2010). Many other minor metabolites of nicotine are produced by CYP, glucuronidation, demethylation and other enzymatic pathways. These metabolites have no nicotinic activity, with the exception of nornicotine which is produced by N-demethylation of nicotine in humans and other mammals (besides being a major tobacco leaf alkaloid). Although nornicotine is a minor metabolite, it has been shown that after repeated nicotine administration it accumulates in the brain at pharmacologically relevant concentrations acting as agonist on nAChRs but with about 10-fold lower potency (Dwoskin et al. 2001, Hukkanen et al. 2005).

Renal excretion is the major route of elimination of nicotine and its metabolites (>90% of a dose). Unchanged nicotine accounts for about 10%, and nicotine glucuronide and nicotine N'-oxide for about 5% each, of the total nicotine-derived amount present in urine. Trans-3'-hydroxycotinine (35-40%) and its glucuronide (~10%) are the principal nicotine metabolites determined in urine, both after a single dose and in smokers; unchanged cotinine (10-15%), cotinine glucuronide (~15%) and cotinine N'-oxide (~4%) represent the rest of the cotinine metabolic pathway excreted. Small amounts of a large array of nicotine metabolites produced in the minor biotransformation pathways are also detected in urine. Nevertheless, the pattern of nicotine metabolites and their amounts are highly variable in humans due to the important polymorphism of CYPs and the other enzymatic pathways involved in the metabolic disposition of xenobiotics (Benowitz et al. 2006, Benowitz 2008, Hukkanen et al. 2005). It has been suggested that this genetic variation in xenobiotic metabolism, especially that of CYP2A6, has a role in smoking behaviour and nicotine dependence (Malaiyandi et al. 2005).

3.6.1.6. Conclusions on nicotine pharmacology

The main effect of nicotine (besides its action on the cholinergic system) is the presynaptic release in the brain of neurotransmitters such as acetylcholine, noradrenaline, dopamine, serotonin, glutamate, GABA and opioid peptides. This allows the possibility that many compounds may modify the action of nicotine on the presynaptic nicotine receptors, and consequently modify the activity of nicotine in the brain. There is substantial interindividual variability in the action and metabolism of nicotine and many aspects of its pharmacology are still not fully understood.

Nicotine metabolism may be modified by compounds inducing or inhibiting the activity of the cytochrome P450 system and other metabolic pathways, thus determining pharmacokinetic changes. While the half-life of nicotine in the arterial blood is short, nicotine levels in the brain remain at high levels much longer.

3.6.2. Addictive properties of nicotine

Nicotine exposure produces adaptive changes in the central nervous system (CNS) leading to an addictive process characterised by compulsive tobacco use, loss of control over tobacco consumption despite the harmful effects, the appearance of withdrawal symptoms upon the cessation of tobacco smoking, and relapse after periods of abstinence (McLellan et al. 2000). As in other addictive processes, the initiation of nicotine addiction has been related to its capacity to induce rewarding/reinforcing effects. However, the negative consequences of nicotine abstinence have a crucial motivational significance for maintenance and relapse of this addictive behaviour (Koob and Le Moal, 2008). The terms “reward” and “reinforcement” are often misused and confused. Reward describes stimuli that have appetitive (desirable) consequences and/or produce a hypothetical pleasurable internal state (hedonia). Reinforcement refers to the ability of a stimulus to promote behavioural responses in order to obtain (positive reinforcement) or to avoid (negative reinforcement) such a stimulus. A drug like nicotine that produces rewarding effects will also promote behavioural responses to obtain the drug, i.e. positive reinforcing effects. On the other hand, the effects induced by a drug can be associated with some particular neutral stimuli. After learning the association, this neutral stimulus becomes a conditioned stimulus associated with the drug that can also promote behavioural responses by itself. Several animal models of drug reward/reinforcement are based on these conditioning processes.

The neurobiology of nicotine addiction is a complex phenomenon in which various transmitter systems are involved (Berrendero et al. 2010). The experimental animal models that have been used to investigate nicotine addiction are mainly models of nicotine reward/reinforcement and have been useful to define the neurobiological substrate involved in this behavioural response that is crucial for the nicotine addictive process. New complex behavioural models that resemble the main diagnosis for drug addiction in humans have been developed more recently (Belin et al. 2008, Deroche-Gamonet et al. 2004, Vanderschuren and Everitt 2004). These models of addiction are extremely complex and have been validated only for cocaine addiction. Due to their complexity, these models have still not been used to investigate the neurobiology of drug addiction. Therefore, all the valuable information currently available about drug addiction, including nicotine addiction, is based on the results obtained in experimental models that evaluate drug rewarding/reinforcing effects (see section 3.9 for details about significance of the models).

3.6.2.1. Nicotinic acetylcholine receptors subunits and nicotine rewarding/reinforcing effects

The mesocorticolimbic system plays a crucial role in the rewarding/reinforcing properties of nicotine (Koob and Le Moal 2008). An important component of this system is the dopamine (DA) projection from the ventral tegmental area (VTA) to the frontal cortex and limbic structures, such as the nucleus accumbens (NAc). Nicotine administration increases DA activity in the NAc and other limbic structures (Di Chiara and Imperato 1988) by direct stimulation of nicotinic acetylcholine receptors subunits (nAChRs) within the VTA (Nisell et al. 1994). $\alpha_4\beta_2$ containing nAChRs located on DA cell bodies contribute decisively to the final activation of VTA DA neurons (Mansvelder and McGehee 2003). Indeed, the administration of selective $\alpha_4\beta_2$ antagonists block nicotine-self-administration in rodents (Grottick et al. 2000). In agreement, mice with the β_2 subunit knocked out do not self-administer nicotine (Picciotto et al. 1998). The specific location of nAChRs containing the β_2 subunit in the VTA plays a crucial role in the mediation of nicotine reinforcement as demonstrated by genetic studies in mice (Maskos et al. 2005). In addition, α_4 knockout mice fail to show nicotine-dependent enhancement of DA release in the NAc (Marubio et al. 2003), whereas a single nucleotide mutation rendering α_4 containing nAChRs hypersensitive to nicotine (Tapper et al. 2004) demonstrates that this subunit is sufficient to induce nicotine reward (Tapper et al. 2004). The precise role of the α_7 homomeric nAChRs in nicotine reinforcing effects remains unclear since conflicting results have been obtained in mutant mice lacking this subunit and in rodents injected with selective α_7 nAChR antagonists (Markou and Paterson 2001, Walters et al. 2006). On the other hand, repeated exposure to nicotine leads to up-regulation and desensitisation of nAChRs (Quick and Lester 2002), which are involved in the development of nicotine tolerance and the appearance of a withdrawal syndrome following smoking cessation. The brain regions underlying nicotine physical dependence have not yet been fully clarified, although an involvement of nAChRs located in the medial habenula and the interpeduncular nucleus has been recently reported (Salas et al. 2009).

Recent genome-wide association studies in humans have revealed a clear linkage between genetic variations in the nAChRs and the risk for nicotine dependence (Bierut 2009). Thus, the region on chromosome 15 that includes the family of α_5-α_3-β_4 nAChR genes has been associated with the development of nicotine dependence (Berrettini et al. 2008, Thorgeirsson et al. 2008) and lung cancer (Amos et al. 2008, Hung et al. 2008, Thorgeirsson et al. 2008). These studies differ on whether the connection between the genetic variant at chromosome 15 and lung cancer is direct (Amos et al. 2008, Hung et al. 2008) or mediated through a modification of smoking behaviour (Thorgeirsson et al. 2008).

3.6.2.2. Involvement of glutamatergic receptors in nicotine rewarding/reinforcing effects

Nicotine stimulates nAChRs on glutamatergic terminals that release glutamate in several brain regions including the VTA (Fu et al. 2000). Glutamate receptors located on postsynaptic DA neurons are critically involved in nicotine reinforcing effects (Liechti and Markou 2008). Thus, nicotine-induced DA release in the NAc is blocked by the administration of NMDA and AMPA ionotropic receptor antagonists (Kosowski et al. 2004). In addition, the blockade of NMDA receptor decreases intravenous nicotine self-administration in rats (Kenny et al. 2009). Several studies have also involved postsynaptic mGlu5 and presynaptic mGlu2/3 metabotropic receptors in nicotine reinforcing effects. Thus, mGlu5 receptor antagonists decrease nicotine self-administration (Paterson et al. 2003) and the incentive motivation for nicotine in rodents (Paterson and Markou 2005). The administration of a mGlu2/3 agonist also decreases nicotine self-administration in rats (Liechti et al. 2007). This last result is in accordance with previous studies showing that presynaptic mGlu2/3 receptors modulate glutamate release in a negative manner (Schoepp et al. 2003). The administration of mGlu5 receptor antagonists (Bespalov et al. 2005) or mGlu2/3 receptor agonists (Liechti et al. 2007) also decreases cue-induced reinstatement of nicotine-seeking in rats. Cholinergic and glutamatergic inputs from the pedunculopontine tegmental nucleus (PPTg) to the VTA seem to play a crucial role in nicotine reinforcement since complete lesion of the PPTg reduces nicotine self-administration (Lança et al. 2000, Picciotto and Corrigall 2002. On the other hand, the negative affective changes of nicotine withdrawal are related to a hyperactivity of corticotropin-releasing-factor neurons in the central nucleus of the amygdala (Bruijnzeel et al. 2007, Panagis et al. 2000) and a decrease of DA activity in the NAc (Hildebrand et al. 1999) that seems to be modulated by the glutamatergic system. Thus, mGlu2/3 receptor antagonists, which increase extracellular glutamate in the NAc, attenuate reward deficits associated with nicotine withdrawal in rodents and could also alleviate the depression-like symptoms related to nicotine abstinence in humans (Kenny et al. 2003, Liechti and Markou 2008).

3.6.2.3. Involvement of GABA receptors in nicotine rewarding/reinforcing effects

DA neurons in the VTA are under the inhibitory control of GABAergic inputs that also participate in nicotine rewarding/reinforcing effects. Hence, the administration of the GABA-B receptor agonists such as baclofen, as well as several GABA-B receptor positive allosteric modulators, decrease nicotine self-administration in rats (Paterson et al. 2004, Paterson et al. 2008). Baclofen also inhibits nicotine-induced conditioned place preference in rats (Le Foll et al. 2008). Although GABA neurons are also activated by nicotine, $\alpha_4\beta_2$ nAChRs located on GABA cells tend to desensitise rapidly during repeated nicotine exposure (Mansvelder et al. 2002). Desensitisation of these receptors following repeated nicotine exposure contributes to the final activation of mesolimbic DA neurons induced by the chronic administration of this drug of abuse. Recent studies have reported that the GABA system also participates in nicotine relapse. Thus, the administration of GABA-B receptor agonists decreases cue-induced reinstatement of nicotine-seeking behaviour in rodents (Fattore et al. 2009, Paterson and Markou 2005). In agreement, baclofen also prevents the reinstatement of nicotine conditioned place-preference triggered by nicotine priming in rats (Fattore et al. 2009).

3.6.2.4. Endogenous opioid system in nicotine rewarding/reinforcing effects

Nicotine administration has been reported to enhance the release of endogenous opioids in the CNS. Thus, an increased concentration of β-endorphin has been found in the hypothalamus after acute nicotine administration in rodents (Marty et al. 1985). In addition, chronic nicotine has been found to increase mRNA expression of prodynorphin and μ-opioid receptors (Wewers et al. 1999) in the striatum (Isola et al. 2008). An enhancement of proenkephalin expression has also been observed in the striatum of mice following acute or chronic nicotine administration (Dhatt et al. 1995).

Nicotine induces opposite responses on anxiety-like behaviour related to the development of nicotine addiction that are modulated by the endogenous opioid system. Thus, nicotine anxiolytic-like effects were blocked by a μ-opioid antagonist, and its anxiogenic-like effects were enhanced by a δ-opioid antagonist (Balerio et al. 2005). In addition, a reduction of nicotine anxiogenic-like effects was reported in knockout mice lacking β-endorphin (Trigo et al. 2009). The opioid system also plays an important role in nicotine rewarding effects. The efficacy of naltrexone on smoking cessation in humans supports the involvement of opioid receptors in nicotine reward (Rukstalis et al. 2005). In rodents, nicotine-induced elevations of extracellular DA levels in the NAc were modulated by the activation of μ-opioid receptors localized in the VTA (Tanda and Di Chiara 1998). In agreement, nicotine rewarding properties were blocked in knockout mice lacking μ-opioid receptors (Berrendero et al. 2002) or proenkephalin gene (Berrendero et al. 2005), revealing an involvement of endogenous enkephalins through the activation of μ-opioid receptors. In addition, proenkephalin knockout mice showed a reduction of nicotine-enhanced DA extracellular levels in the NAc (Berrendero et al. 2005). Mice lacking β-endorphin also showed a reduction of nicotine rewarding effects (Trigo et al. 2009). κ-Opioid receptors and their endogenous ligands modulate nicotine reward in the opposite way to enkephalins and β-endorphins. Hence, knockout mice deficient in the prodynorphin gene showed an enhanced sensitivity to nicotine self-administration, probably due to the modulation of its aversive effects (Galeote et al. 2009).

The opioid system is also involved in the development of nicotine tolerance. Thus, chronic nicotine exposure produces cross-tolerance with morphine (Biala and Weglinska 2006, Zarrindast et al. 1999), and increases the functional activity of μ-opioid receptors in the spinal cord (Galeote et al. 2006). In addition, μ-opioid receptor knockout mice developed faster nicotine tolerance than wild-type mice, suggesting that increased activation of μ-opioid receptors could be an adaptive mechanism to counteract the establishment of nicotine tolerance (Galeote et al. 2006). The involvement of the opioid system in nicotine withdrawal has also been demonstrated. In humans, the opioid antagonist, naloxone induces somatic signs of withdrawal in heavy chronic smokers (Krishnan-Sarin et al. 1999). In rodents, opioid antagonists precipitate somatic manifestations of withdrawal in nicotine-dependent animals (Balerio et al. 2004). In addition, somatic manifestations of nicotine withdrawal were reduced in mice lacking μ-opioid receptors (Berrendero et al. 2002) or the proenkephalin gene (Berrendero et al. 2005). Different studies also indicate that the opioid system participates in the negative emotional states associated with nicotine withdrawal. Thus, naloxone induced aversive effects in nicotine-dependent rodents, which reflects the motivational manifestations of nicotine withdrawal (Balerio et al. 2004, Watkins et al. 2000).

3.6.2.5. Involvement of cannabinoid receptors in nicotine rewarding/reinforcing effects

Several studies demonstrate that the endocannabinoid system plays an important role in the rewarding/reinforcing effects of nicotine (Maldonado et al. 2006). Indeed, the selective CB_1 receptor antagonist rimonabant reduces nicotine self-administration in rats (Cohen et al. 2002) and nicotine-induced conditioned place preference in rats and mice (Le Foll and Goldberg 2004, Merritt et al. 2008). In addition, rimonabant pre-treatment blocks nicotine-enhanced DA extracellular levels in the NAc (Cheer et al. 2007, Cohen et al. 2002) and in the bed nucleus of the stria terminalis (Cheer et al. 2007). Nicotine conditioned place preference was also absent in knockout mice lacking CB_1 receptors (Castañé et al. 2002, Merrit et al. 2008). The endocannabinoid system has also been involved in the relapse to nicotine-seeking behaviour (De Vries and Schoffelmeer 2005b). Thus, rimonabant attenuates the reinstatement of nicotine seeking-behaviour induced by nicotine-associated cues (Cohen et al. 2005, De Vries et al. 2005a), and reinstatement of nicotine-induced conditioned place-preference provoked by nicotine priming (Biala et al. 2009). The cannabinoid antagonist AM251 also reduced the reinstatement produced by the combination of nicotine-associated cues and a nicotine priming dose (Shoaib 2008). Based on the behavioural and biochemical results obtained in rodents, several clinical trials were developed to evaluate the efficacy of rimonabant for smoking cessation (STRATUS, studies with rimonabant and tobacco use) (Cahill and Ussher 2007). Rimonabant was effective in obtaining a significant smoking cessation in two clinical trials (STRATUS-NORTH AMERICA and STRATUS-WORLD WIDE), although this effect was not significant in the STRATUS-EUROPE trial. The different clinical trials performed with rimonabant have reported several gastrointestinal and psychiatric side effects including nausea, anxiety and depression. Due to these psychiatric side effects, the European Medicines Agency (EMA) recommended the suspension of the marketing authorisation for rimonabant on 23 October 2008. In spite of the withdrawal of rimonabant, the CB_1 receptor remains a promising target to develop new compounds to treat drug addiction.

3.6.2.6. Other neurotransmitters involved in nicotine rewarding/reinforcing effects

The serotonergic (5-HT) system, mainly through the activation of the $5\text{-}HT_{2c}$ receptor subtype, seems to be involved in nicotine reward/reinforcing by exerting an inhibitory influence on DA activity in the VTA (Di Matteo et al. 1999). Thus, $5\text{-}HT_{2c}$ agonists reduce nicotine-self-administration (Grottick et al. 2001), although responding for food was also attenuated by these antagonists. In contrast, no modification on nicotine-induced conditioned place preference was observed by a $5\text{-}HT_{2c}$ agonist in a recent report (Hayes et al. 2009). On the other hand, tobacco smoke contains monoamine oxidase (MAO) inhibitors which are thought to enhance the reinforcing effects of nicotine. Behavioural studies have confirmed this statement since nicotine self-administration was facilitated in rats pre-treated with MAO inhibitors (Villégier et al. 2006a, Villégier et al. 2007). Recently, the hypothalamic neuropeptides hypocretins acting in the insula have also been involved in nicotine reward (Hollander et al. 2008).

3.6.2.7. Conclusions on addictive properties of nicotine

Animal models of nicotine reward/reinforcement have enabled the neurobiological substrate involved in this behavioural response that is crucial for nicotine addictive processes. Similar animal models have been widely used to define the neurobiological substrate of the addictive properties of all drugs of abuse. Results obtained in these models suggest that the neurobiology of nicotine addiction is complex involving various transmitter systems in the CNS. Multiple neurotransmitter pathways are activated by nicotine, including dopaminergic, GABAergic and opioidergic pathways. The complexity of the mechanisms of addiction is further underlined by the involvement of the endocannabinoid system, and the serotonergic system also seems to be involved. Dose-dependency appears to have been shown in animal studies. In general, an inverted U-shaped dose-response has been revealed, which suggests that, such as for other drugs of abuse, the addictiveness of nicotine is not directly linear with the dose. The experimental animal models used for evaluating addiction are described in section 3.9.

3.6.3. Conclusions on nicotine

The action of nicotine on the CNS is multifaceted and the mechanisms of addiction are still poorly understood. There are substantial inter-individual differences in the action of nicotine and in its metabolism, which are in part genetically determined. A number of different compounds may in principle interfere with the binding of nicotine with its receptors, while others may interfere with the metabolism of nicotine via the cytochrome P450 system or other pathways. Addiction to nicotine is difficult to measure directly and is usually assessed experimentally with reference to reinforcement assessed in self-administration paradigms.

3.7. Possibilities to make tobacco more addictive or attractive

3.7.1. Introduction

Tobacco products are manipulated by tobacco companies by the addition of chemical compounds, most of which are flavours. Obviously, the flavours are added to the natural tobacco to give the product a better taste thereby increasing the attractiveness of these products. This includes the addition of humectants which keep the humidity of the tobacco product at a desired level; dry tobacco generates an unpleasant harsh smoke.

“Light” cigarettes were introduced on the market in the 1970s. Typical for light cigarettes is their high grade of ventilation. Due to the delivery of less tar, the impact and taste of the “diluted” smoke is also decreased. It is therefore probable that the light cigarettes were “enriched” by adding more substances, and in higher amounts, to compensate for reduced taste and impact. For details see sections 3.5.5 and the different sections reviewing specific tobacco additives such as section 3.8.

An important reason for using additives is to give the product a specific and standardised taste. A specific taste is important for the company to be competitive on the consumer market in view of the large variety of brands available. A unique product binds the customer/consumer to this specific product. The specific taste of a certain product must be preserved (standardised) to compensate for the yearly variation of the natural tobacco, because consumers do not like to smoke a product that changes from year to year. To circumvent this, some 40 or more substances per product are added to the majority of the brands in order to mask the variation.

3.7.2. Additives with direct or indirect addictive potency

In the following two sections, various approaches to increase the addictive and attractive potency of tobacco products have been briefly described. Details of these additives and further information about their effectiveness can be found in later sections (see section 3.8.1).

The addictive potency of tobacco products may in theory be increased by:

1. Direct enhancement of the nicotine content;
2. Addition of substances which increase the bioavailability of nicotine;
3. Addition of substances which facilitate the inhalation of tobacco smoke;
4. Addition of substances which generate compounds in the mainstream smoke which increase the addictiveness of nicotine;
5. Changing the physical properties of tobacco smoke, e.g. particle size.

The five approaches are briefly described below.

1. Direct enhancement of the nicotine content

No examples of increasing the content of nicotine in tobacco are known. Moreover, in cigarettes sold (or produced) in the EU nicotine yield has to remain below a maximal level of 1 mg per cigarette. Some Member States also have upper limits for roll your own (RYO) tobacco. Genetic techniques or classical selection of variants are available to produce tobacco with relatively high nicotine content. From public sources it cannot be deduced or concluded that such approaches are indeed used by tobacco growers or tobacco companies.

2. Addition of substances which increase the bioavailability of nicotine

a) Increase the bioavailability of nicotine by adding alkalising ingredients which increase the pH of tobacco (such as ammonium compounds). At higher pH (pH>8.0) more nicotine is in its free uncharged form, which would therefore more easily pass the (lung) membrane i.e. higher absorption leading to higher blood and brain nicotine levels. For details see section 3.8.3.2 on ammonia and other compounds affecting smoke pH.

b) Increase the bioavailability of nicotine by adding ingredients which serve as a carrier for nicotine.

c) Increase the effect of nicotine by inhibiting its metabolism.

3. Addition of substances which facilitate the inhalation of tobacco smoke

a) Certain ingredients have local anaesthetic effects. As a result coughing due to inhalation of irritating smoke is dampened and the smoker can inhale the smoke deeper (and more frequently). Examples are etheric oils, such as menthol and thymol. For details see later sections e.g. section 3.8.1.

b) Compounds which have bronchodilating properties (opening/broadening the airways) would enable the smoker to inhale deeper (a larger volume of) tobacco smoke implying an increase in the bioavailability of nicotine. It has been proposed that theobromine, generated from cocoa, caffeine and glycyrrhizine, serves such a function.

4. Addition of substances which generate compounds in the mainstream smoke which increase the addictiveness of nicotine

a) Certain natural components in tobacco have been suggested to promote the addictiveness of nicotine. Examples are components like sugars, which when pyrolysed generate acetaldehyde. The combination of acetaldehyde and nicotine appears to be more addictive than nicotine alone. The addition of sugars may thus increase the addictive nature of tobacco products. In tobacco smoke or *in vivo*, tryptophan may react with aldehydes to form beta-carbolines, like harman and norharman. Both beta-carbolines are inhibitors of monoamine oxidases (MAO). Monoamine oxidases are enzymes that degrade neurotransmitters involved in addiction such as dopamine, serotonin and noradrenaline. As such, tryptophan as an ingredient may potentiate nicotine addiction.

b) Acetaldehyde can react *in vivo* with biogenic amines to yield carbolines or isoquinolines, which have affinity for the opiate receptor. These ligands are, however, formed in very low amounts.

5. Changing the physical properties of tobacco smoke, e.g. particle size

Changing the particle size of the tobacco smoke aerosol. Considering the entry of particles to deeper lung levels, there is probably an optimum in size. Cigarette paper and/or filters can be modified in a technological way to attain an optimal particle size (see section 3.5).

The size and its distribution of smoke particles can be changed to obtain an optimum so that particles enter deeper levels of the lungs. As a result, a more efficient absorption of nicotine from the particles and higher blood nicotine levels can be attained. Examples of such applications are the use of cigarette paper with a higher porosity and filters with higher ventilation (see section 3.5).

3.7.3. Additives with attractive properties

A large number of tobacco additives are flavours, which are mostly aromatic compounds or generate aromatic compounds found in the smoke. Flavours are mainly applied for two reasons: firstly, to enhance the attractiveness of a product (appeal to consumers); and secondly, to produce a unique product, typical in “taste” and markedly different from competitor products. The aim here is to get and maintain a certain and stable market share. Note that each of the many flavours is added to tobacco in minute amounts (nano to microgram range per unit). As reported by the tobacco industry to several national competent authorities and as described on tobacco industry websites, cigarettes contain up to 40 (sometimes even more) different additives.

Sugars are natural components of tobacco, but they are also added to tobacco products during manufacturing. The heating of sugars in the tobacco product initiates a caramalisation, generating secondary products which have an attractive smell and taste.

Other additives which may increase the attractiveness of tobacco products, e.g. menthol, are mentioned later (see section 3.8.).

A number of additives have an effect on colour, smell, visibility, taste, and harshness of the smoke.

Note that some additives may fall into several of the above mentioned groups.

3.7.4. Conclusions on addictive and attractive additives

Section 3.7 has provided a preview of the additives used in tobacco which may have addictive or attractive properties. Conclusions about their efficacy are found at the end of the individual sections, which describe their effects in full detail. The addictiveness of tobacco products can theoretically be increased by additives in a number of ways including enhancing the bioavailability of nicotine, promoting smoke inhalation, and influencing particle size. Attractiveness can similarly be improved in a number of ways, such as by adding flavours. Importantly, some additives may at the same time have addictive and attractive properties, or may influence addictiveness indirectly, for example by promoting smoke inhalation.

3.8. Classification of additives

According to the EU Tobacco Products Directive (2001/37/EC) tobacco companies are obliged to provide information about the ingredients added to tobacco products, and their function, to the local authorities. In Germany, this information is published on the website of the Federal Ministry of Nutrition, Agriculture, and Consumer Protection[7]. Consumers can search for brands and ingredients. The reports from 2008 showed the amount of each ingredient listed. However, only the amounts of major ingredients such as sucrose, propylene glycol or cocoa are disclosed to the public. Furthermore, only 22 of the 50 most-used ingredients have been specified by name. In the reports for the general public the tobacco industry does not reveal the nature of all flavourings, colours, or adhesives used. Quantitatively, sugars and humectants (e.g. glycerol, propylene glycol) are the dominant additives in cigarettes. Furthermore, compounds which influence the taste of the cigarette are used in many brands; relevant substances are cocoa (incl. cocoa powder, cocoa extracts, shells of cocoa bean etc.) and liquorice (incl. liquorice extract). Other ingredients are part of the cigarette paper, the filter or are used as glue. Even if the tobacco companies are secretive about the exact amount of flavours used in each brand, some information is available on the websites of the tobacco companies (e.g. BAT[8]). Most of the tobacco companies disclose only the highest amount of ingredients used in their brands (i.e. Quantity Not Exceeded (QNE)). Therefore, it is not possible to draw conclusions about the average amount added or about the percentage of brands that contain a particular ingredient. As an example the information on the Philip Morris website[9] for German cigarettes has been evaluated. In the compilation the maximum use levels are given, i.e. Philip Morris only discloses the highest amount used in its brands. Most of the flavours are added in very small amounts. On the other hand, menthol and lactic acid are flavours used in milligram amounts per cigarette (see table 2). For the calculation it was assumed that each cigarette contains about 700 mg of tobacco.

[7] http://service.ble.de/tabakerzeugnisse/index2.php?site_key=153&site_key=153

[8] http://www.bat-ingredients.com/

[9] http://www.pmintl-technical-product-information.com/aspx/IngredientsInformation.aspx

Table 2 **Ingredients added to the tobacco based on a table presented by Philip Morris International (PMI) on cigarettes manufactured for sale in Germany**[9]

Ingredient	maximal use level (w/w%)	maximal use level (mg/cigarette (700 mg))
sucrose	4.2	29.4
propylene glycol	3.9	27.3
glycerol	2.2	15.4
invert sugar	2.1	14.7
l-menthol	1.1	7.7
d-sorbitol	1.1	7.7
liquorice extract	0.9	6.3
lactic acid	0.7	4.9
guar gum	0.6	4.2
benzoic acid	0.3	2.1
benzoic acid sodium salt	0.3	2.1
carob bean and/or extract	0.2	1.4
cocoa and cocoa products	0.2	1.4
acetic acid	0.01	0.07
lovage extract	0.01	0.07
peppermint oil	0.01	0.07
vanillin	0.01	0.07
benzoin, resinoid	0.005	0.035
phenylcarbinol	0.005	0.035
coffee extract	0.005	0.035
ethyl acetate	0.005	0.035
ethyl hexanoate	0.005	0.035
ethyl vanillin	0.005	0.035
fenugreek extract	0.005	0.035
maltol	0.005	0.035
methyl-cyclopentenolone	0.005	0.035
3-methyl-butyraldehyde	0.005	0.035
orange oil, sweet	0.005	0.035
piperonal	0.005	0.035
spearmint oil	0.005	0.035
veratraldehyde	0.005	0.035
bergamot oil	0.001	0.007
ethyl heptanoate	0.001	0.007
ethyl maltol	0.001	0.007
isoamyl acetate	0.001	0.007
isoamyl formate	0.001	0.007
orris root extract	0.001	0.007
2,3,5,6-tetramethylpyrazine	0.001	0.007
valerian root extract	0.001	0.007

3.8.1. Addictiveness

3.8.1.1. Introduction

Only few scientific articles have addressed the possibility that individual additives may cause addiction. It is probable that many additives have not been examined/analysed or the results (either positive or negative) have simply not been described in publicly available literature.

The available documentation on additives in respect to a direct addictive effect is reviewed in section 3.8.1.2. Examples of additives causing addictiveness indirectly are provided in section 3.8.1.3. Finally, an assessment of how different forms of sugar may have an indirect addictive effect due to combustion products such as acetaldehyde is presented in section 3.8.1.4.

3.8.1.2. Additives with addictive properties (direct effect)

In the peer-reviewed scientific articles assessed there is no documentation for certain individual additives to cause addiction directly.

The following compounds, used as tobacco additives, may have an effect on the central nervous system: acetophenone, isoamyl alcohol, valerian oil, theobromine, and valerenic acid (Lington and Bevan 1994, Moreno 1978a, Moreno 1978b, Moreno 1978c, Oliva et al. 2004, Ortiz et al. 1999, Reynolds 1983a, Reynolds 1983b, Reynolds 1998, Simons et al. 1985, Yuan et al. 2004). However, the fact that these additives may have an effect on the central nervous system (CNS) does not imply that they are addictive. Moreover, they are present in the products in very low amounts.

Although several articles point out that some of the above mentioned additives may create dependence, it is probably more likely that they are acting by attractiveness, as they induce a more pleasant experience of smoking and therefore reduce the barrier in relation to smoking initiation.

3.8.1.3. Additives enhancing addictiveness indirectly

Additives which increase the absorption of nicotine or potentiate in whatever way the effect of nicotine on the nervous system implicitly increase the addictiveness of tobacco products.

Examples of additives

<u>Ammonium salts</u>

It has been proposed that the free nicotine content of smoke increases with increasing pH, which would lead to a higher uptake of nicotine in the bloodstream. A higher pH also increases the nicotine/tar ratio (Wayne and Carpenter 2009) as well as the harshness of the smoke (Hurt and Robertson 1998). The increased harshness will be disguised by using different additives that remove the smoker’s sensation of harshness. Ammonium salts are used as additives to increase the pH of tobacco. See Section 3.8.3.2 for full description of ammonia technology.

<u>Menthol</u>

Because of its local anaesthetic properties, menthol allows a deeper inhalation of the irritating tobacco smoke. As such, more smoke could be inhaled and deeper puffs could be attained, resulting in a higher nicotine dose. See section 3.8.3.1 for detailed description of the action of menthol.

<u>Theobromine</u>

Theobromine is found in cocoa beans; therefore this substance is present in cocoa and chocolate, both of which are used as additives in tobacco. Theobromine is a bronchodilator and has been used in the treatment of asthma (Simons et al. 1985). It has been proposed that the bronchodilating effect of the substance may contribute to the absorption of nicotine in connection with smoking (Bates et al. 1999, Fowles 2001). In a document from the New Zealand Ministry of Health (Fowles 2001) it is reported that up to 3% of the weight of cigarettes is cocoa extract and another 0.2% is chocolate. There is typically 0.2% theobromine in cocoa (Rambali et al. 2002). In most of the types of cigarettes containing cocoa and chocolate, which were reported to the Danish competent authorities[10] in 2006, the contents of cocoa and chocolate are 0.3-0.5% and 0.2%, respectively. Based on the information available on the PMI and BAT websites the percentage of cocoa used in cigarettes ranges from 0.2% to 0.66%. Taking this information into account, the content of theobromine per cigarette will be too low to have a bronchodilating effect on the lungs and thereby increase the absorption of nicotine.

Eucalyptol

Like theobromine, eucalyptol has an effect on the lungs as a bronchodilator (Hasani et al. 2003, Juergens et al. 2003). For eucalyptol it is also clear that the contents per cigarette are not large enough to exert this effect. However, even though the doses of theobromine and eucalyptol are so low in cigarettes that they probably do not have a bronchodilating effect, it cannot be excluded that there are other additives with a similar effect.

Lactones

The addictive effect of nicotine may be increased if the metabolism rate of nicotine is reduced. Reduction of the metabolic rate of nicotine, e.g. by inhibition of the metabolic enzymes involved in nicotine degradation, implicates a higher bioavailability of nicotine (nicotine is present in the body for a longer time or at a higher blood level). The additives gamma-heptalactone, gamma-valerolactone, gamma-decalactone, delta-decalactone, gamma-dodecalactone, delta-undecalactone and gamma-hexalactone are mild to weak inhibitors of CYP2A6, an enzyme within the P450 enzyme system, involved in the metabolism of nicotine (Juvonen et al. 2000). However, with IC_{50}-values in the range 560-12,000 µM it seems unlikely that these compounds will inhibit nicotine metabolism at the amounts used in cigarettes.

3.8.1.4. Additives enhancing addictiveness indirectly by combustion of sugar

Sugar is already present naturally in considerable amounts in the tobacco leaf (up to 20%) and the quantities remaining in the final product depend on the curing methods. Sugar in different forms is also one of the most common additives in tobacco (see table 2 in section 3.8). When the sugars, including complex polysaccharides like cellulose (Seeman et al. 2002) in the tobacco product are combusted, various aldehydes are generated. Acetaldehyde is claimed to increase the addictiveness of nicotine in a synergistic way (Belluzzi et al. 2005, Charles et al. 1983, Philip Morris 1992). The mechanism of action may be that acetaldehyde forms secondary condensation products which inhibit monoamine oxidase (MAO).

However, one study showed that even during heavy smoking, acetaldehyde in breath rose six-fold in smokers although only minor amounts of the acetaldehyde in the smoke is absorbed into the blood stream (McLaughlin et al. 1990), suggesting no (indirect) addictive effect of sugars when used as a tobacco additive. Alcohol consumption leads, in contrast to smoking, to a significant increase in the acetaldehyde blood level by its

[10] http://www.sst.dk/Sundhed%20og%20forebyggelse/Tobak/Indberetning/Indberetninger.aspx

metabolism. Acetaldehyde is very reactive and forms adducts with proteins and DNA. Chen et al. (2007b) found only a small contribution of chronic smoking to the formation of acetaldehyde DNA adducts, whereas alcohol consumption had a much higher effect, suggesting again that in chronic smokers lower amounts of acetaldehyde enter the circulation than in alcohol consumers.

Finally, the addition of sugars to tobacco increases the content of acids in the smoke, which results in a lower pH value of the tobacco smoke. This may be one of the reasons why ammonia compounds are added to neutralise these acids.

Examples of sugar additives

The sugars added to tobacco are mainly inverted sugar (fructose and glucose), and sucrose (Philip Morris 2002, Seeman et al. 2003), and are often added in the form of syrups (Covington & Burling 1992, Reynolds 1985). The main part of sugar substances in tobacco is non-volatile and only a small part is transferred unmodified into the mainstream smoke. The sugar substances are not hazardous to health by oral consumption, but are transformed to a number of toxic compounds under pyrolysis. These mainly include formaldehyde, acetaldehyde, acetone, acrolein and furans (Burton 1976). The pyrolysis products have a hazardous effect on health; formaldehyde is classified as a carcinogen to humans (IARC 2006, IARC 2009), whereas acetaldehyde and acrolein are highly irritating to the respiratory tract.

<u>Mono- and disaccharides (natural sugars like glucose, fructose, sucrose)</u>

Mono- and disaccharides are derived from a number of sources including brown sugar, honey, corn syrup, molasses, sugar cane, fig juice and prune juice. Sugars are flavourings that constitute the largest part of additives in cigarettes (Bates et al. 1999). According to table 2 in section 3.8 the levels of sugars applied to the cigarette tobacco blends constitute more than 10% of the total amount of additives. They are added to the tobacco in order to contribute to the taste and flavour (Philip Morris 2002, Reynolds 1985, Reynolds 1994) and increase the content of acids in the smoke, which results in a lower pH value of the tobacco smoke. This reduces irritation and makes the taste milder (Covington & Burling 1986, Covington & Burling 1987a, Seeman et al. 2002).

Inverted sugar is responsible for a large part of the contents of formaldehyde in smoke and also contributes to the formation of furfural, furan, levoglucosan, and acetaldehyde (Baker et al. 2004b, Philip Morris 2002).

<u>Polysaccharides (e.g. cellulose, pectin, starch)</u>

Apart from the sugar substances mentioned, cellulose fibres are a natural part of the tobacco, and are also added as a binding agent (Baker et al. 2004b, Baker 2006, Fox 1993). Pyrolysis of cellulose fibres results in the formation of volatile aldehydes and levoglucosan (Seeman et al. 2002). The amount of pyrolysis products varies depending on the sugar contents and the temperature within the cigarette. It is difficult to estimate the relative contribution of pyrolysis products of simple sugars in relation to polysaccharides (Covington & Burling 1986). The pyrolysis products of polysaccharides and simple sugars are similar, but their yields differ (Fox 1993, Rodgman 2002, Sanders et al. 2003, Seeman et al. 2002). It is estimated that more formaldehyde and less acetaldehyde and acetone are generated from the pyrolysis of simple sugars compared to polysaccharides (Burton 1976).

Addictive potential of acetaldehyde

Animal studies have shown that acetaldehyde can maintain self-administration behaviour equal to, or probably more effectively than, nicotine (Charles et al. 1983, Philip Morris 1992). Belluzzi et al. (2005) found that acetaldehyde has reinforcing properties (Belluzzi et al. 2005).

A number of studies have elaborated on the interaction between nicotine and acetaldehyde (Belluzzi et al. 2005, Cao et al. 2007, Charles et al. 1983, Philip Morris 1992). The combination of nicotine and acetaldehyde increases the degree of self-administration in young rats (Belluzzi et al. 2005). It is possible that norepinephrine contributes to the age-dependent difference in acetaldehyde uptake in rats (Sershen et al. 2009). A study by Cao et al. (2007) shows that acetaldehyde potentiates hyperlocomotive effects of nicotine in young as well as adult rats, but that these effects are more pronounced in adult rats. No effect of acetaldehyde on the nicotine level in the brain was observed (Cao et al. 2007). In Philip Morris publications, the interaction between nicotine and acetaldehyde is examined with the purpose of increasing the reinforcing effect of tobacco (Charles et al. 1983, Philip Morris 1992). The synergistic interaction between nicotine and acetaldehyde is substantiated by experiments where the combination of nicotine and acetaldehyde results in a rewarding effect that exceeds the additive effects of each substance in rats (Philip Morris 1992). It is likely that the combination of nicotine plus acetaldehyde is more reinforcing than nicotine alone, as a long-lasting instrumental conditioned response in young rats was observed (maintains lever pressing at a higher rate than nicotine alone) (Charles et al. 1983, Philip Morris 1992). However, the effect of acetaldehyde seems not to be mediated by opioid receptors in the CNS and the substance does not cause physiological addictiveness (Charles et al. 1983). It is discussed whether acetaldehyde may pass the blood-brain barrier and directly affect the CNS (Cao et al. 2007). It is proposed that acetaldehyde has to be present in high concentrations (>100 µM) in the blood to overcome aldehyde dehydrogenase in the blood brain barrier (Tabakoff et al. 1976). It should be noted that the experiments in animals used intravenous infusion of acetaldehyde, and as mentioned before, it is uncertain whether the acetaldehyde in smoke contributes significantly to the blood level of this substance (Chen et al. 2007b, McLaughlin et al. 1990).

Proposed mechanisms of action

The reinforcing effect of acetaldehyde may be due to the reaction between acetaldehyde and catecholamines, which results in the formation of tetraquinolines (beta-carboline and tetrahydroquinoline) (DeNoble 1994, Philip Morris 1992, Rahwan 1975). Tetraquinoline derivatives may act as false neurotransmitters and therefore promote addictiveness of the product (DeNoble 1994, Rahwan 1975).

Others argue that acetaldehyde has an addictive effect because of the formation of the condensation products harman and norharman, which inhibit the enzyme monoamine oxidase (MAO). Inhibition of MAO results in a slower metabolism of the biogenic amines, like dopamine, noradrenaline and serotonine in the brain, so that the brain levels are increased by MAO-inhibition. However, it is only proven that harman could have significance for tobacco addiction by virtue of its inhibitory effect on MAO-A (Guillem et al. 2006). Indeed, harman is formed in the smoke (0.1 to 5.8 microgram per cigarette). At this level, harman, following its absorption, may be responsible for 3 to 11% of the inhibition of MAO-A (note that drinking a cup of coffee delivers 1 to 8 microgram orally). Nevertheless, whatever the active product, one smoked cigarette decreases MAO in the monkey heart by 25% (Valette et al. 2005). Smokers have decreased MAO-A and MAO-B activities in brain (Fowler et al. 1996), which recovers following smoking cessation. The relevance of this observation in the addiction of tobacco smoking is not clear.

Open issues, acetaldehyde

The levels of isoquinolines generated in the body (by reaction of acetaldehyde with biogenic amines) are too low to be biologically significant. Formation of harman and norharman in the tobacco/cigarette smoke (reaction product of acetaldehyde with tryptophan/tryptamine) is, however, relevant considering their concentration, absorption and inhibitory potency on MAO-A (i.e. IC_{50} value).

There are, however, many conflicting data regarding the presumed pro-addictive effect of acetaldehyde.

1. Following i.v. administration acetaldehyde has an addictive effect in rodents.
2. Acetaldehyde seems not to be absorbed (or is degraded very rapidly in the circulation).
3. The mechanism of action of harman is not well established. For instance, does coffee drinking also lead to inhibition of MAO?
4. Assuming it is not harman which is the active compound, which compounds (acetaldehyde products) are formed which may be responsible for an addictive effect?

3.8.1.5. Denicotinised cigarettes

Nicotine plasma levels are associated with cigarette smoking behaviour and nicotine is considered the main factor driving cigarette addiction. In apparent contradiction to this observation, nicotine replacement therapy, as a smoking cessation treatment, does not show the expected effectiveness. Therefore, it has been assumed that non-nicotine components are important in smoking reinforcement. The exact nature of these factors (chemical composition) is largely unknown, but constituents which provide reinforcing sensory stimulation and/or minimize excessive irritation from inhaled nicotine are considered to play an important role in non-nicotine effects in cigarette smoke (Rose 2006).

In this chapter several studies with denicotinised cigarettes are briefly described to highlight the importance of the non-nicotine components in tobacco.

Denicotinised cigarettes have the appearance, draw and taste of standard cigarettes but contain (and deliver) virtually no nicotine (<0.06 mg), but deliver tar and carbon monoxide (CO) in a comparable way to traditional cigarettes (Pickworth et al. 1999).

In short term (for a few hours; maximum up to 24 hours) experiments, smoking volunteers were placed under tobacco (nicotine) abstinence and were allowed to smoke denicotinised or conventional cigarettes.

- In 1999, Pickworth et al. reported that the denicotinised cigarettes did not increase heart rate or activate the EEG, but subjects reported that both conventional and denicotinised cigarettes reduced (subjective) measures of tobacco craving and withdrawal (Pickworth et al. 1999).
- In a study by Eid et al. (2005) a stimulating effect on heart rate of denicotinised cigarettes was reported. Smoking of either denicotinised or conventional cigarettes caused a significant reduction in the craving score. The authors could not find a correlation between the nicotine yield and behavioural effects.
- Perkins et al. (2010) simulated different stressful situations (negative affects) during smoking abstinence and studied how relief was perceived after smoking. The authors did not find an association between the relief of several negative affects and smoking (also not from denicotinised cigarettes) but the relief was not dependent on nicotine intake, therefore, challenging the assumption that nicotine in smoking alleviates negative affects.
- Brody et al. (2009) found that, compared to conventional cigarettes, smoking denicotinised cigarettes (0.05 mg nicotine) resulted in a decrease in occupancy of the brain nicotine acetylcholine receptor (nAChR), as predicted on the basis of nicotine concentration. They did not observe occupancy of the nAChR with other factors, suggesting that only nicotine in cigarette smoke is capable of binding this receptor (Brody et al. 2009).

These acute studies show that denicotinised cigarettes, compared to conventional cigarettes, do not exert the same pharmacological effects, but cravings and symptoms of withdrawal can be diminished and this phenomenon is, in many cases, independent of the delivered nicotine. Some components of tobacco smoke, other than nicotine, may be biologically active; thus it has been suggested that non-nicotine components of tobacco smoke decrease brain levels of monoamine oxidase A and B which possibly change sensitivity to the actions of nicotine and/or exert independent behavioural effects (Eid et al. 2005).

Recently, Rose et al. (2010b) found that denicotinised smoke was self-administered more than any other alternative (i.v. nicotine self-administration or sham puffs) in established smokers, even after a few days of nicotine abstinence. This preference for denicotinised smoke compared to i.v. nicotine was inversely correlated with subjective ratings of "comfort" (normally) associated with nicotine; therefore non-nicotine aspects of cigarette smoking have potent reinforcing effects in established smokers. These authors, therefore suggested that in contrast to current smoking cessation pharmaco-therapies, which address only the nicotine component of nicotine (tobacco) addiction, future cessation strategies should also be designed to target non-nicotine factors such as added flavour constituents (e.g. menthol).

In conclusion, besides nicotine, a mixture of other factors in cigarette smoke probably plays an important role in craving and reinforcement. Although these unknown factors do not have pharmacological effects similar to nicotine and are probably not addictive, they definitely play a role in smoking behaviour.

3.8.1.6. Conclusions on how additives can increase the addictiveness of tobacco products

Certain tobacco additives may affect the central nervous system in smokers directly, but their concentration in tobacco products is probably too low to have a physiological effect. However, an indirect addictive effect of certain substances cannot be excluded.

Some additives increase the pH of the smoke, thereby increasing the quantity of nicotine delivered to the smoker.

Sugars generate acetaldehyde during combustion. When given intravenously to animals, acetaldehyde potentiates the addictive effect of nicotine. The mechanism of action of the reinforcing effect of acetaldehyde in animals is not clear, although an inhibition of MAO is the most likely reason. Inhibition of MAO has also been observed in human smokers. However, the acetaldehyde, generated from the sugars during combustion, is presumably not absorbed into the blood stream, and this sheds some doubt on the role of sugars in the addictiveness of tobacco products.

Natural tobacco already contains considerable amounts of sugars, especially Virginia tobacco. In addition, polysaccharides and cellulose fibres in the tobacco leaves generate acetaldehyde upon combustion. In this respect it is not clear whether the addition of sugars to tobacco leads to a significant increase in the addictiveness of the product.

The data in the literature on the presumed indirect addictive effect of sugars (exerted via the generation of acetaldehyde) are inconclusive.

3.8.2. Attractiveness

3.8.2.1. Introduction

A number of additives increase the attractiveness of tobacco products. This may be attained by creating a better experience of the product (e.g. appearance of the product, white and full smoke) or by making it easier to start smoking (e.g. by means of a cool, sweet and mild smoke, as well as causing less irritation in the lungs).

For many additives, attractiveness depends on multiple functions which may be difficult to distinguish clearly. One of the reasons to use additives is to attract the smoker to a specific product and to promote/encourage (young) people to start using the product.

Other reasons for using additives are to produce a unique product, typical in taste and markedly different from competitor products, and to maintain the stability of the taste of the product.

3.8.2.2. Better experience of the product

Preservation of humidity of the tobacco product

Humectants are added to tobacco products to retain the water, i.e. to prevent them from drying out, and consequently increase the shelf life of the products.

Examples of additives

Glycerol, propylene glycol and sorbitol.

Appearance, smell and irritation of tobacco smoke

In order to make the smoke more attractive to the smoker, but also to other people in the proximity of the smoker, it is important that the smoke is appealing and not annoying. This may be attained with additives which make the smoke whiter and more attractive to people seeing the smoke. The smell of the smoke may be also changed so that it is also more attractive and less irritating (Connolly et al. 2000, Ling and Glantz 2005).

Connolly et al. (2000) examined tobacco industry patents covering the function of environmental tobacco smoke masking. These strategies include reducing smoke odour, and reducing side-stream smoke visibility and emissions.

Methods to neutralize or reduce lingering smoke odour include addition of acetylpyrazine, anethole and limonene to modify the side-stream odour. These compounds have rather low odour thresholds, and are subsequently easily picked up, while they elicit no trigeminal nerve response. Aroma precursors, e.g. polyanethole provided a noticeable fresher, cleaner and less irritating cigarette side-stream aroma, while others (e.g. cinnamic aldehyde, pinanediol acetal) produce slightly sweet, spicy, clean, fresh, and less cigarette-like aroma. Also, more “classic” additives (e.g. vanillin, benzaldehyde, bergamot oil, cinnamon/cinnamon extract, coffee extract and nutmeg oil) modify side-stream odour.

Reduced visibility of side-stream is accomplished by the addition of magnesium oxide, magnesium carbonate, sodium acetate, sodium citrate and calcium carbonate to the wrapper (cigarette paper). This has an effect on particle size; particles become smaller and therefore do not easily scatter light and become less visible.

Reducing side-stream emissions is based on encapsulating the smoke in an impermeable cone using different types of additives such as potassium succinate, potassium citrate and magnesium carbonate.

By combining the use of additives and the look of the tobacco product, greater acceptance of the smoke may be created. Less resistance may be encountered from persons that do not smoke, and at the same time greater pleasure for the smoker may be created. The same agents may also be used to target the individual product at certain target groups (Carpenter et al. 2005a, Connolly 2004).

Taste and experience of the smoke

Cis-3-hexenol is added to increase the organoleptic characteristics of tobacco and it has a characteristic smell of new-mown grass (Alford and Johnson 1970). *Cis*-3-hexenol adds a green, foliaceous taste and a smell of chlorophyll to the tobacco smoke (Leffingwell et al. 1972). Apart from adding a taste and flavour of fresh tobacco to the tobacco smoke, the substance has another important characteristic: *cis*-3-hexenol reduces irritation (Alford and Johnson 1969).

The American tobacco company Brown & Williamson has tested the effect on the characteristics of the smoke when adding *cis*-3-hexenol to cigarettes (Alford and Johnson 1969, Alford and Johnson 1970). Cigarettes with added *cis*-3-hexenol in concentrations of 0.05, 0.10 and 0.15 mg per cigarette were tested against control cigarettes without added *cis*-3-hexenol by having an expert panel smoke the various cigarettes. All cigarettes with *cis*-3-hexenol were preferred to the control cigarettes (Alford and Johnson 1969, Alford and Johnson 1970). The effect of *cis*-3-hexenol was *"A dramatic increase in smoke freshness and acceptability. Irritation is also markedly reduced."*

Harshness

According to the tobacco industry definition, harshness is a chemically induced physical effect associated with a roughness, rawness experience generally localized in the mouth and to a lesser degree in the upper reaches of the throat and the trachea due to inhalation of tobacco smoke. Harshness can also cause a drying, rasping, coarse, astringent sensation usually associated with the smoke flavour of Virginia or air-cured type tobaccos.

Harshness is classically measured in four degrees: (i) Free – an absence of harshness; (ii) Touching – a slight awareness of a sensation; (iii) Scratchy – some discomfort, a stinging effect; and (iv) Harsh – rough, raw, raspy, coarse, astringent, painful inhalation.

Reducing the harshness of the smoke makes it possible to inhale deeper and increase the number of puffs, as more physical barriers will be reduced (Wayne and Henningfield 2008b).

The ratio between nicotine and tar is an important parameter in relation to the smoker's experience of the cigarette. If the concentration of nicotine in relation to tar is too high, the harshness of the smoke will be much higher (Hurt and Robertson 1998). Nicotine is irritating in high doses compared to other substances in the smoke (Baker 1990).

The irritating effect of nicotine on the lungs and the bad experience at too large amounts of nicotine in relation to the amount of tar may be remedied by additives that may drown or reduce the harshness of the smoke. This may also be achieved by adding nicotine salts that do not cause the same irritation, but are still delivering nicotine or keeping the nicotine effect by means of a quicker absorption by ensuring larger amounts of free nicotine (Bates et al. 1999, Keithly et al. 2005).

Smoothness

Tar provides a strong flavour and mouth sensation, masking the harsher, bitter taste of nicotine which may be unpalatable to new smokers and uncomfortable to established smokers. Certain highly flavoured additives may also have the same properties to "smoothen" or reduce the harsh irritation of nicotine in tobacco smoke.

A central feature of tobacco marketing strategy has been to promote the perception that some cigarettes are less hazardous than others, so that smokers worried about their health are encouraged to switch brands rather than quit. Products bearing the word "smooth" or using lighter coloured branding mislead people into thinking that these products are less harmful to their health. Adults and children are significantly more likely to rate packs with the terms "light", "smooth", "silver" and "gold" as lower tar, lower health risk and either easier to quit (adults) or their choice of pack if trying smoking (children). For example, more than 50% of adults and youth reported that brands labelled as "smooth" were less harmful than the "regular" variety. The colour of packs was also associated with perceptions or risk and brand appeal. For example, compared to Marlboro packs with a red logo, cigarettes in packs with a gold logo were rated as lower health risk by 53% and easier to quit by 31% of adult smokers.

Plain packs significantly reduced false beliefs about health risk and ease of quitting and were rated by the children as less attractive and appealing (Hammond et al. 2009a).

Examples:

Propylene glycol

The addition of propylene glycol (1,2-dihydroxypropane) to tobacco results in a milder smoke (Danker 1958). It was found that propylene glycol reduces the delivery of nicotine, while the formation of tar is increased (Shepperd and Bevan 1994b). In another study, also by the Brown & Williamson Tobacco Company, a reduction of nose irritation was observed and a reduced delivery of nicotine was confirmed (Shepperd 1994a). It was suggested that the sensation of reduced effect and irritation in cigarettes with added propylene glycol is caused by reduced liberation of nicotine, since the tar/nicotine ratio is of importance to the sharpness of the smoke (Danker 1958, Shepperd and Bevan 1994b).

Levulinic acid and levulinates

Based on the information submitted by the tobacco industry to the competent authorities of the EU Member States, these two substances have in many cases not been included in the reports, but have been used and mentioned several times in the internal documents of the tobacco industry.

These organic salts would also be able to reduce the harshness of nicotine, as the salts do not cause the harshness that otherwise characterise high levels of nicotine (Bates et al. 1999). In a study of the published literature up until 2004, Keithly has also shown that the primary purpose of levulinic acid as an additive in tobacco is to make the smoke sweeter and softer and at the same time increase the nicotine absorption and the effect of nicotine in the brain. Keithly also describes the use of nicotine levulinate and levulinic acid to cause less harshness (Keithly et al. 2005).

3.8.2.3. Easier to start smoking

Tobacco products may also be designed in such a way that they are easier to start smoking with. This may be attained by making it easier to inhale the smoke in the lungs and by creating a sweeter, milder or “colder” smoke. By reducing and changing the harshness of the smoke, special target groups may be reached (Carpenter et al. 2005a, Carpenter et al. 2005b, Cummings et al. 2002, Klein et al. 2008, Wayne and Connolly 2002).

In a number of countries, sweet and tasteful tobacco products are the most preferred tobacco products among children and adolescents as well as experimenting smokers (Ashare et al. 2007, Giovino et al. 2005, Klein et al. 2008).

How to make inhalation of smoke less aversive

Liquorice

Glycyrrhizin is the active substance of liquorice i.e. the root extract of Glycyrrhiza glabra and has a sweet taste (Hodge and Shelar 1979). Apart from glycyrrhizin, liquorice also contains sugar substances, cellulose fibres and essential oils (Covington & Burling 1987b).

The taste and flavour of tobacco with liquorice/liquorice root added are described as sweet, woody and round (Leffingwell et al. 1972), but adding liquorice/liquorice root also has the objective of camouflaging the unpleasant taste of tobacco (Covington & Burling 1987b).

The use of adding liquorice/liquorice root to tobacco has the following advantages (Vora 1983); it reduces the harshness of tobacco smoke, the dryness in the mouth and throat, and it provides a pleasant sweet undertone to the smoke.

Menthol

The additive menthol is relevant for how a smoker experiences the smoke in the lungs and the concentration of menthol may be an important issue for the group that the cigarette brand is targeted at. This is described further in section 3.8.3.1, which broadly outlines the potency of menthol to inhale smoke more easily and deeply.

Cooler and milder smoke

Certain substances make the smoke milder and cooler, e.g. menthol (see section 3.8.3.1), liquorice and propylene glycol. However, many more additives probably have these effects on the smoker's lungs, but they have not yet been evaluated, or have not been described in the literature.

Sweeter taste

The presence of sugars in cigarettes is associated with a more favourable taste. The experience of the smoke is less negative and the irritability is somewhat masked.

The tobacco producers have used additives that create sweetness and taste in the smoke to make it easier for new smokers to start smoking, since these tobacco products do not have the same harshness and bad experience at the first inhalations (Cummings et al. 2002, Wayne and Connolly 2002).

3.8.2.4. Conclusions on how certain additives can increase the attractiveness of tobacco products

The attractiveness of tobacco products may be increased by a number of additives. An attractive effect may be obtained in a number of ways, such as changing the appearance of the product and the smoke, decreasing the harshness of the smoke, and inducing a pleasant experience of smoking. The harshness depends partly on the tar/nicotine ratio, but may also be decreased by certain additives such as propylene glycol or levulinates. Various sugars constitute a large proportion of additives, and the sweetness of the smoke is an important characteristic.

Many different additives are used to create a specific taste/flavour in order to attract certain target groups. In order to make the smoke less aversive and permit deeper inhalation, additives such as liquorice and menthol are used. Finally, in order to make smoking more acceptable to people around, some additives have the function of reducing lingering odour or side-stream smoke visibility.

3.8.3. Most prominent additives in tobacco products

3.8.3.1. Menthol

Menthol is an important tobacco additive and it is the only additive explicitly declared to the consumer. For more than 40 years, scientific discussions have covered the health effects of the addition of menthol to tobacco. Menthol is a monocyclic terpene alcohol. It is a naturally occurring compound of plant origin which gives plants of the *Mentha* species the typical minty smell and flavour (Eccles 1994). Mentholated cigarettes have a major share of the market in the USA. However, in most European countries, the market shares for mentholated cigarettes range between 1 and 5% (Giovino et al. 2004). The menthol content has been investigated in the USA in 48 commercially available mentholated cigarette sub brands. Menthol content per g tobacco was reported to range between 2.88 and 5.75 mg menthol (Celebucki et al. 2005). In Germany, the menthol content was analyzed in non-mentholated cigarettes as well as in raw tobacco. Menthol content in raw tobacco and home grown tobacco was in the range 0.02-0.18 µg menthol/g tobacco. Menthol content per g tobacco in non-mentholated cigarettes ranged between 0.019 and 13.3 µg menthol (Merckel et al. 2006). These data clearly prove three points: firstly, menthol occurs naturally in very small amounts in tobacco; secondly, some brands contain no added menthol at all and in some brands, microgram amounts of menthol have been added; and finally, mentholated brands contain milligram amounts of menthol per g tobacco.

The tobacco industry advertises menthol as a substance which alleviates harshness and enhances taste and smoothness, but menthol may also facilitate nicotine delivery and increase the sensory impact of cigarettes.

Menthol can be applied to cigarettes in a number of ways; it can be applied directly to the tobacco or introduced into the cigarette filter, or it can be applied to the cigarette packaging (see section 3.4.).

The fate of menthol in the cigarette has only been investigated by the tobacco industry. Philip Morris showed with ^{14}C-labelled menthol that 29% of menthol went into the mainstream smoke (Jenkins et al. 1970). The transfer of menthol from tobacco into smoke was investigated by another company in 11 cigarette brands; the values ranged from 19 to 31% (Brozinski et al. 1972).

A report by Schmeltz and Schlotzhauer raised concerns about the pyrolysis of menthol. The authors pyrolysed menthol under nitrogen at 860°C and analysed the pyrolysate by paper-chromatography and thin-layer chromatography. They found approximately 400 µg benzo[a]pyrene per g menthol (Schmeltz and Schlotzhauer 1968). In the following 40 years only one study conducted by the tobacco industry addressed this question again: Baker and Bishop heated menthol at 30°C per second from 300 to 900°C under a flow of 9% oxygen in nitrogen. The products were analysed by gas chromatography and mass spectrometry. The authors found 99% of menthol was unchanged in the gas phase; additional products were menthon (0.9%) and menthen (0.1%) (Baker and Bishop 2004a). No further data have been found on this topic.

Some companies have investigated the influence of tobacco additives on the composition of smoke constituents. For example, Philip Morris studied experimental cigarettes with many additives. They prepared two sets of cigarettes containing, among other additives, 18.000 ppm menthol, yielding 13 mg menthol per cigarette (Carmines 2002). The cigarettes were machine-smoked and compared to control cigarettes without ingredients added. The benzo[a]pyrene content in the smoke of menthol cigarettes was significantly higher compared to the smoke of the control cigarettes. The smoke of the control cigarettes contained 5.1 ng benzo[a]pyrene per cigarette in comparison to 5.63 and 5.51 ng benzo[a]pyrene per cigarette in menthol cigarettes (Rustemaier et al. 2002).

The hypothesis that smoking mentholated cigarettes increases lung cancer risk compared with smoking non-mentholated cigarettes was tested in several epidemiological studies. Sidney and colleagues found a 1.45-fold increase of the relative risk for men smoking mentholated cigarettes for 20 years and more (Sidney et al. 1995), whereas three other studies (Brooks et al. 2003, Carpenter et al. 1999, Stellman et al. 2003) did not find a difference between menthol smokers and non-menthol smokers.

Menthol has a cooling effect on the skin or mucosal surfaces. The perceived temperature effect is not caused by evaporation of menthol. Furthermore it is not due to vasodilatation, but is due to a specific action on sensory nerve endings (Eccles 1994). Menthol activates a transient receptor potential channel (TRPM8). This channel is expressed in small-diameter primary sensory neurons (Clapham et al. 2005). The use of menthol causes a subjective sensation of improved airflow without any change in nasal airway resistance, breathing pattern or ventilation (Eccles 1994, Nishino et al. 1997). Furthermore, menthol has a local anaesthetic activity (Galeotti et al. 2001).

It is important to take into account that this cooling and anaesthetic effect may mask early symptoms of tobacco induced respiratory disease (Garten and Falkner 2003). In a follow-up paper, it was postulated, that there is a greater opportunity for exposure and transfer of the contents of the lungs to the pulmonary circulation. For the smoker of mentholated cigarettes this could result in a greater exposure to nicotine and the particulate matter of the smoked cigarette (Garten and Falkner 2004). Additionally, it was postulated that menthol increases the absorption with other chemicals through permeability and increased salivation. This would mean that menthol facilitates the absorption of other substances from the smoke (Ahijevych and Garrett 2004, Eccles 1994). Two recent biomarker studies addressed the question if the use of mentholated cigarettes would lead to higher exposure to toxic compounds from smoke (Heck 2009, Muscat et al. 2009). Muscat and colleagues investigated a group of 525 smokers and stratified them for sex and race. In the United States, most African Americans smoked mentholated cigarettes (90% and 82%, respectively); whereas European Americans smoked predominantly non-mentholated cigarettes (percentage of menthol cigarettes smoked was 25% and 31%, respectively). European Americans smoked significantly more cigarettes per day than African Americans. There were no significant differences in the mean concentrations of all cigarette smoke metabolites (plasma cotinine, urinary cotinine, plasma thiocyanate and urinary 4-N-nitrosomethylamino)-1-(3-pyridyl)-1-butanol (NNAL)) between menthol and non-menthol cigarette smokers in African Americans and European Americans, after adjustment for sex and other factors (Muscat et al. 2009). However, the ratio of NNAL-glucuronide to NNAL, a possible indicator of lung cancer risk, was significantly lower in menthol versus non-menthol cigarette smokers. The NNAL-Gluc/NNAL ratio was 34% lower in European Americans ($P<0.01$) and 22% lower in African Americans (Muscat et al. 2009). In subsequent human liver microsome studies, menthol inhibited the rate of NNAL-*O*-glucuronidation and NNAL-*N*-glucuronidation. These results suggest that menthol may modify the detoxification of the potent lung carcinogen NNAL (Muscat et al. 2009).

A similar study has been performed and published by the tobacco industry (Heck 2009). They investigated 112 smokers (28 African Americans and 84 European Americans; 54 menthol cigarette smokers and 58 non-menthol cigarette smokers). Smokers continued smoking *ad libitum* throughout the one week study interval. The participants were provided with a commercially available menthol cigarette brand and several non-mentholated brands of similar smoke yield. Menthol content in smoke was determined as 0.34 mg/cigarette. Content of 4-(N-nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) was determined as 63 ng/cigarette in the mentholated brand and with a range from 45 to 80 ng NNK/cigarette in five non-mentholated brands (Heck 2009). Neither total urinary NNAL nor urinary nicotine equivalents exhibited statistically significant differences between the menthol and non-menthol cigarette smokers (Heck 2009).

The possible influence of menthol on the metabolism of nicotine was investigated in a cross-over study in 14 healthy smokers (Benowitz et al. 2004). Subjects were randomly assigned to smoke mentholated or non-mentholated cigarettes for one week, then to cross over to the other type of cigarettes for another week. The blood levels of deuterium-labelled nicotine and cotinine were measured after intravenous infusion of these compounds. It was demonstrated that, when smoking similar numbers of mentholated and non-mentholated cigarettes of similar machine-determined yield and nicotine content, the systemic intake of nicotine and carbon monoxide during non-menthol cigarette smoking is on average not affected by mentholation. Furthermore, it was shown that mentholated cigarette smoking inhibits the metabolism of nicotine. Inhibition of nicotine metabolism by menthol most likely involves inhibition of both oxidative metabolism to cotinine, and glucuronide conjugation (Benowitz et al. 2004). *In vitro* studies using human liver microsomes showed that menthol inhibits nicotine metabolism (MacDougall et al. 2003) However, mentholated cigarette smoking did not substantially affect cotinine metabolism. Finally, the systemic intake of menthol was determined as 12.5 mg menthol from 20 cigarettes. Thus, on average 20% of menthol contained in each cigarette is absorbed systemically by the smoker (Benowitz et al. 2004).

Studies on the influence of menthol on puff numbers and puff volume gave conflicting results. Puff numbers have been investigated in seven studies, three showing a reduced number of puffs in smokers of mentholated cigarettes (Jarvik et al. 1994, McCarthy et al.

1995, Nil and Bättig 1989). Four other studies did not show any influence of mentholation on the number of puffs (Ahijevych et al. 1996, Caskey et al. 1993, Miller et al. 1994, Pickworth et al. 2002). Puff volume was investigated in six studies, three of them showing a decrease in puff volume when smoking mentholated cigarettes (Jarvik et al. 1994, McCarthy et al. 1995, Nil and Bättig 1989). Two studies did not find any effect of mentholation on puff volume (Ahijevych et al. 1996, Miller et al. 1994) and one study even showed an increase in puff volume (Ahijevych and Parsley 1999).

The results of studies on the CO exhalation in smokers of mentholated and non-mentholated cigarettes are contradictory. In a study with experimental cigarettes smokers inhaled defined volumes of cigarette smoke. The experimental cigarettes had been injected with 0 mg, 4 mg or 8 mg of menthol. The CO content in exhaled air increased from 5.6 ppm to 6.1 ppm and reached 8.1 ppm CO after use of 8 mg menthol cigarettes (Miller et al. 1994). Clark and colleagues did find a non-significant difference of 40.3 ppm CO (mentholated cigarettes) against 35.8 ppm CO (non-mentholated cigarettes) (Clark et al. 1996). In a study in women, smokers of non-mentholated cigarettes showed a higher CO exhalation (10.6 ppm) than smokers of mentholated cigarettes (6.5 ppm) (Ahijevych et al. 1996). In a cross-over study, Benowitz and colleagues did not find any significant difference in the blood carboxyhaemoglobin content in smokers of mentholated and non-mentholated cigarettes (Benowitz et al. 2004). Six other studies also did not show significant differences between CO uptake or CO exhalation in smokers of mentholated or non-mentholated cigarettes (Caskey et al. 1993, Heck 2009, Jarvik et al. 1994, McCarthy et al. 1995, Nil and Bättig 1989, Pickworth et al. 2002).

Menthol may increase the degree of dependence, or promote maintenance of smoking behaviour. Several findings suggest that menthol is involved in tobacco addiction. Some investigators have found that menthol cigarette use increases cotinine levels, and a significant correlation between cotinine and nicotine dependence has been reported, as well as a reduction in time to first cigarette of the day (Pomerleau et al. 1990).

Greater smoking urgency among menthol compared to non-menthol adolescent cessation-treatment seekers has been reported (Collins and Moolchan 2006).

Evaluating the tobacco industry documents, it was shown that cigarettes with low contents of menthol appeal to young smokers, new smokers, and smokers that do not like the harshness of the smoke. This can be due to the fact that lower contents of menthol in the smoke cover the harshness of the smoke, whereas a large dose of menthol causes harshness. On the other hand, cigarettes with a higher concentration of menthol appeal to smokers who are used to the harshness of the smoke (Kreslake et al. 2008b).

3.8.3.2. Ammonia and other additives affecting smoke pH

Armitage et al. (2004) described a study in which 10 volunteers smoked either control cigarettes, cigarettes with diammonium hydrogen phosphate (DAP) or cigarettes with urea added. The venous blood levels of nicotine were independent of the amount of DAP or urea added to the tobacco. Preliminary data of a human study performed by van Amsterdam et al. (to be published), comparing two commercial brands (one with low and one with high ammonia content) with respect to nicotine absorption, showed no difference in venous blood nicotine levels (no difference in total absorption and peak plasma of nicotine) when smoking the two brands.

The bioavailability of nicotine is dependent upon the pH as only uncharged nicotine is volatile and can be absorbed readily across cell membranes. The different ways of manipulating cigarettes so that more free nicotine is delivered have recently been reviewed (Wayne and Carpenter 2009). At lower pH the nicotine molecule will be positively charged and an equilibrium between the three forms of nicotine is created in relation to the pH (see figure 3).

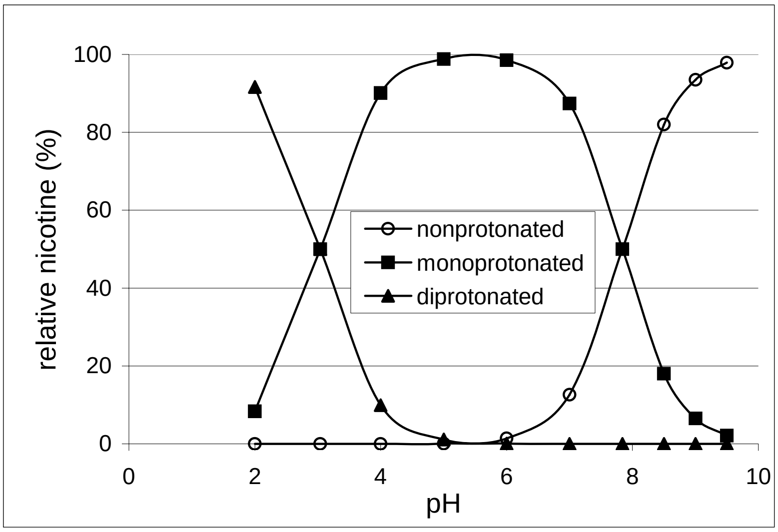

Figure 3: Chemical form of nicotine (charged or free base) and their percentages as function of pH, ranging from 2 to 9.5 (adapted from Hoffmann and Hoffmann (1997)).

Initially, cigarette smoke is lightly acidic and the nicotine is therefore poorly absorbed. However, the pH value is higher in the lungs (7.4) and some of the nicotine is found in uncharged form. Internal documents from the tobacco industry show that manufacturers started to use ammonia to increase smoke pH levels in the early 1970s (Willems et al. 2006). Particular focus has been on ammonia and related compounds, but any compound that contributes to increasing the pH value will have a potential effect in increasing the impact of nicotine and the rate at which inhaled nicotine is absorbed into the bloodstream.

While it has been shown that the absorption of nicotine in smokeless tobacco by the oral mucosa is dependent on the pH of the product (Fant et al. 1999), it is uncertain if the pH in cigarette smoke has a significant impact on the nicotine absorption in the lungs. This is due to the high local buffering capacity of the lung lining fluid which will cause free nicotine to be charged (protonated) again in the deeper airways (Willems et al. 2006). The high buffering capacity of mucus has been shown experimentally in human volunteers (Holma and Hegg 1989).

It is widely accepted that smoke from different pyrolysed tobacco delivery devices (e.g. cigarettes, cigars, waterpipes, etc.) is inhaled differently. For example, cigarette and waterpipe smoke tends to be inhaled into the lungs, while cigar smoke is typically only inhaled into the mouth (except among former cigarette smokers who have switched to cigar smoking, in which case they often smoke cigars like cigarettes). It has been argued that this may be due to the characteristics of both the delivery device (for example, waterpipes cool the tobacco smoke, thereby allowing easier, deeper inhalation) and the tobacco itself. Waterpipe smoking is associated with greater smoke exposure (a larger volume of smoke is inhaled) than cigarette smoking (Maziak et al. 2009).

This difference in inhalation may be due in part to the more acidic pH of cigarette smoke. The smoke of most cigars has an alkaline pH; as a result, nicotine contained in the smoke can be readily absorbed across the oral mucosa without inhalation into the lung. The more acidic pH cigarette smoke produces a protonated form of nicotine which is much less readily absorbed by the oral mucosa, and the larger absorptive surface of the lung is required for the smoker to receive the desired dose of nicotine. According to the

National Cancer Institute (NCI), cigarette smokers must inhale to ingest substantial quantities of nicotine (the active agent in smoke), whereas cigar smokers can ingest substantial quantities of nicotine without inhaling (NCI 1998). The difference may, however, also be explained by the fact that cigar smoke is more concentrated and contains much more nicotine than cigarette smoke.

While there has been considerable research into the effects of product characteristics on cigarette smoking behaviour (such as ventilation holes in “light” cigarettes resulting in compensatory smoking whereby smoke is inhaled more deeply to extract the required dose of nicotine), there is relatively little research into the effects of other delivery devices such as waterpipes. This is despite the rapid growth in the popularity of waterpipe smoking in European countries in recent years.

3.8.3.3. Conclusions on most prominent additives

Menthol is one of the most prominent additives in tobacco. If it is added in milligram amounts to cigarettes it dominates the taste of the smoke and the application is usually mentioned in the brand name. Menthol has a cooling effect on mucosal surfaces and a local anaesthetic activity. The use of menthol causes a subjective sensation of improved airflow without any change in nasal airway resistance, breathing pattern or ventilation. It has been proposed, that the cooling and local anaesthetic effects could lead to deeper inhalation of the smoke and higher exposure to other smoke constituents, but current data are inconclusive. However, menthol has been shown to inhibit the metabolism of nicotine. Furthermore, the taste of menthol could be an important reason for some smokers to consume mentholated cigarettes.

It has been proposed that the addition of ammonia compounds increases the absorption of nicotine in the lungs by raising the pH in smoke, but this seems unlikely because of the high buffering capacity of the lung lining fluid.

3.8.4. Additives in tobacco products other than cigarettes

3.8.4.1. Cigars

Very few additives are used in the classical manufacture of cigars; recently marketed cigarillos being an exception. In general, cigar brands contain only glue as an additive; several compounds are used as glue (e.g. ethyl-2-hydroxy ethyl cellulose, sodium carboxy methyl cellulose, gummi arabicum, methyl hydroxy ethyl cellulose). Several brands contain humectants such as propylene glycol or glycerol. Citric acid is added to influence the burning properties of the cigars. Some companies sum up their flavouring ingredients as “flavouring”, whilst others mention all compounds, including the amounts used.

As written earlier, in Germany, the information about ingredients of cigars can be found on the website of the Federal Ministry of Nutrition, Agriculture and Consumer Protection[7]. Consumers can search for brands and ingredients.

Data from 2008, published on this website, showed that many of the flavourings were added in tiny amounts of 1 ppm. However, other flavourings such as 2-methylburic acid were added at a level of 60 ppm and ethyl vanillin was added at levels up to <0.5%. Some cigar manufacturers disclosed probably most, if not all of the additives, for example 211 additives are listed for the brand “7B Bonajuto” starting with 34 mg dextrose down to 8 µg clary sage oil.

3.8.4.2. Pipe tobacco

Pipe tobaccos contain humectants (e.g. glycerol and propylene glycol), preservatives (e.g. sodium benzoate, potassium sorbate), sweetening agents (e.g. dextrose, fructose, invert syrup, honey) and many flavours (e.g. cocoa, prune flavour, apple treacle concentrate, tamarind extract).

The ingredients reported in 2009 in Germany can also be found at the website of the Federal Ministry of Nutrition, Agriculture and Consumer Protection[7].

3.8.4.3. Water pipes

The use of waterpipes has increased in the eastern Mediterranean region since the 1990s with the introduction of maassel, a sweetened and flavoured tobacco (Maziak et al. 2004a). During recent years, the smoking of waterpipes has become a habit among teenagers in Germany and other European countries, and in the USA (BZgA 2008, Jackson and Aveyard 2008a, Primack et al. 2008). The mild, sweet and flavoured tobacco appeals to many waterpipe smokers, especially young smokers. No information is available about the flavours used in waterpipe tobacco. The nicotine content in flavoured waterpipe tobacco ranged from 1.8 to 6.3 mg nicotine/g tobacco; the average was 3.35 mg nicotine/g tobacco. In contrast, the traditional waterpipe tobacco without flavour contained 30 to 41 mg nicotine/g tobacco (Hadidi and Mohammed 2004).

There are major differences in the consumption of waterpipes compared to other tobacco products. In contrast to cigarettes and cigars, the tobacco in waterpipes is not burned. The waterpipe tobacco is placed in the tobacco head, which is covered by a perforated aluminium foil on which the glowing charcoal is placed. In a study in Lebanon, Shihadeh measured the temperature during a waterpipe session. Within 15 minutes the foil reached a temperature of 400 to 450°C, whereas the waterpipe tobacco reached temperatures ranging from 60°C (after 10 minutes) to 120°C (after 50 minutes) (Shihadeh 2003). To prevent the tobacco from burning, high amounts of humectants are added to waterpipe tobacco. Besides glycerol and propylene glycol, the companies use honey and molasses. The resulting smoke is very mild and it is easy to inhale, even for inexperienced smokers. Since the smoke has almost no harshness the smoker can inhale huge volumes. Some waterpipe smokers refuse to smoke cigarettes. Waterpipe smokers inhale between 0.3 and 1.0 l per puff (Eissenberg and Shihadeh 2009, Monn et al. 2007, Shihadeh 2003, Shihadeh et al. 2004) compared to approximately 0.050 l per puff in cigarette smokers (Kozlowski and O'Connor 2002).

In Germany, the addition of humectants to water pipe tobacco is restricted to an upper limit of 5%. The Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung, BfR) argued that it is possible that higher concentrations of glycerine in the waterpipe tobacco could lead to higher contents of acrolein in waterpipe smoke. Acrolein is present in waterpipe smoke as shown in a recent investigation from Lebanon. The authors not only found acrolein, but also high amounts of acetaldehyde. In one waterpipe session, 2520 µg acetaldehyde was measured in the smoke (Al Rashidi et al. 2008).

In 2008, few companies reported added ingredients in waterpipe tobacco to the German authorities. However, the values reported were interesting: in some brands the total tobacco content was small, for example the label "Al-Waha" contained per kg 200 g tobacco, 710 g fructose, 50 g glycerine and 40 g flavouring. Another label ("Sindbad") contained per kg 398 g invert syrup, 210 g water, 42 g propylene glycol, 28.6 g flavouring, 6 g ethyl alcohol and 1.92 potassium sorbate, leaving 313 g of tobacco. The tobacco content of waterpipe tobacco is thus not very high (20 to 31%).

Studies from Syria show that waterpipe use can be addictive. The frequency of waterpipe use was strongly correlated with the participants' subjective judgement of how hooked they are on waterpipes (Maziak et al. 2004b).

3.8.4.4. Smokeless tobacco

There are many different types of smokeless tobacco in use around the world, some being more toxic than others.

In Europe, smokeless tobacco is widely used in Sweden (24% of men, 3% of women), in particular in the form of moist snuff called “snus”. Snus is sold in loose weight in boxes or in small “tea-bag”-like sachets. The sale of snus is banned in all other EU countries. As described in the SCENIHR opinion on smokeless tobacco products (SCENIHR 2008), the frequency of smokers in Sweden is lower than in other European countries and the morbidity due to tobacco related diseases is also lower. The use of smokeless tobacco itself is less pronounced in the neighbour countries Norway and Finland than in Sweden.

Due to immigration, many different smokeless tobacco products have found their way into EU countries, and their use is typically clustered in local communities. A similar clustering of use may be seen with now increasingly rare traditional European products such as nasal snuff.

The Swedish “snus” is, according to the manufacturers (Swedish Match[11], Fiedler & Lundgreen[12]), a standardised product using mainly air cured tobacco. Sodium carbonate is added in order to raise the pH to around 8, thus facilitating the uptake of uncharged nicotine in the mouth (Fant et al. 1999). A number of artificial or natural flavours are added according to the brand; the flavours all comply with food regulations. Two sorts of humectants are used, glycerol and propylene glycol. Snus is pasteurised and the fermentation that takes part in other tobacco products is thus inhibited, leading to a lower content of tobacco specific nitrosamines. More than 250 additives are found in snus, most of them are flavours which are used in small amounts. Table 3 shows the 50 substances that are added in greatest amount.

Gutkha is another smokeless tobacco product that is popular among Indian communities in the UK. This is a chewing tobacco that in addition to tobacco contains areca nut, catechu, lime, saffron, saccharine, mint and various flavourings. A table describing the many different smokeless products that are rarer in Europe is found in the SCENIHR report from 2008 (SCENIHR 2008).

[11] www.swedishmatch.com/

[12] www.flsnus.se

Table 3 The 50 additives present in greatest amount in snus[13]

Ingredient	Maximum percentage found in different brands
Sodium chloride	6.7
Ethanol	5.1
Propylene glycol	4.2
Coffee extract	3.7
Plant fibre	3.7
Glycerol	3.6
Sodium carbonate	2.9
Benzyl alcohol	2.1
Anethole (trans-)	1.5
Peppermint oil	1.5
Maltodextrin	1.4
Calcium carbonate	1.2
Licorice and liquorice extract	1.1
Gum Arabic	0.9
Lemon oil	0.7
Ammonium chloride	0.6
Vanillin	0.6
Lime oil	0.4
Ginger extract	0.3
Linalyl acetate	0.3
Menthol	0.3
Ethyl butyrate	0.2
Eucalyptus oil	0.2
Hydroxyphenyl-2-butanone (4-(para-))	0.2
Potassium sorbate	0.2
Sugar, invert	0.2
Acesulfame K	0.1
Acetic acid	0.1
Benzaldehyde	0.1
Buchu leaf oil	0.1
Butyric acid	0.1
Citronellol	0.1
Clary sage oil	0.1
Damascenone	0.1
Damascone (beta-)	0.1
Diacetyl	0.1

[13] Data extracted from www.swedishmatch.se

Ingredient	Maximum percentage found in different brands
Dimethyl-1,2-cyclopentadione (3,4-)	0.1
Ethyl 2-methylbutyrate	0.1
Ethyl acetate	0.1
Geraniol	0.1
Geranium rose oil	0.1
Hexen-1-ol (cis-3-)	0.1
Hexen-1-yl acetate (cis-3-)	0.1
Hexenyl butyrate	0.1
Hexenyl formate (cis-3-)	0.1
Hexyl alcohol	0.1
Hydroxy-2,5-dimethyl-3(2H)-furanone (4-)	0.1
Ionone (alpha-)	0.1
Ionone (beta-)	0.1
Jasmone	0.1
Lactic acid	0.1

3.8.4.5. Conclusions on tobacco products other than cigarettes

Compared with the widespread use of cigarettes, other tobacco products are consumed much less commonly. There is a great variety of additives which either have a specific function as humectants, glues, acidity regulators etc., or determine the specific flavour of the product or brand. Apart from sugar, most flavours are added in small amounts. There is no proof that any of the additives are by themselves contributing to addictive potential, either directly or indirectly. The additives and the design characteristics of tobacco products are likely to attract specific groups of consumers and perhaps facilitate initiation of tobacco use. The aspects of target groups will be addressed in later sections (3.10.2).

3.8.5. Overall conclusions concerning additives which can increase the addictiveness and/or attractiveness of tobacco products

For most tobacco additives, information about possible effects on addictiveness and attractiveness does not exist. A number of studies have been conducted by the tobacco industry, and there are indications that some additives have effects in relation to addictiveness and attractiveness.

The pyrolysis of sugar substances to acetaldehyde may increase nicotine addictiveness, but the data are inconclusive. Additives that reduce the acidity, and thereby the formation of free nicotine, may contribute to addictiveness, but the efficacy of these compounds has not been shown. In view of the buffer capacity of the body fluids involved (saliva, lung lining fluid), the presence of such an effect is doubtful.

A large number of additives are used to increase attractiveness. Among these, various sugars constitute an important part. Menthol is widely used in certain brands in considerable amounts while most other additives are used in small amounts, and the mixture of additives is characteristic for each brand. This is an important aspect for maintaining consistency of the tobacco products and in targeting special groups.

3.9. Experimental animal models

Several animal models are available to study particular responses that are related to nicotine addiction. Thus, predictive models are available in animals to evaluate the development of nicotine tolerance and physical dependence as well as the rewarding/reinforcing effects produced by nicotine. The animal methods currently used to evaluate nicotine addictiveness are mainly based on the evaluation of its rewarding/reinforcing properties. New complex behavioural models that resemble the main diagnosis for drug addiction in humans have been developed very recently. However, these new models can only be applied for some particular drugs and are not yet available for nicotine addiction.

3.9.1. Experimental models to evaluate the development of nicotine tolerance and physical dependence

Long-term consumption of nicotine produces adaptive changes in the central nervous system leading to the development of tolerance and physical dependence that can be easily evaluated in animal models. Thus, chronic nicotine administration produces tolerance to most of its pharmacological effects (Benowitz 2008). Tolerance to several nicotine responses such as hypolocomotion, convulsive effects, hypothermia or antinociception has been widely described in animal models, whereas an absence of tolerance to the effects on cognitive processes has been currently reported in these studies (Benowitz 2008, Collins et al. 1988, Damaj and Martin 1996, Marks et al. 1986, Miner and Collins 1988).

In humans, cessation of tobacco intake precipitates both somatic and affective symptoms of withdrawal which may include severe craving for nicotine, irritability, anxiety, loss of concentration, restlessness, decreased heart rate, depressed mood, impatience, insomnia, increased appetite and weight gain (Hughes and Hatsukami 1986, Hughes 2007). In rodents, nicotine withdrawal is also characterised by the manifestation of both somatic signs and affective changes similar to those observed in humans. The somatic signs include teeth chattering, palpebral ptosis, tremors, wet dog shakes, and changes in locomotor activity and other behavioural manifestations (Malin et al. 1992). Although the development of nicotine tolerance and physical dependence is concurrent to the development of addiction, they are not aetiologically related to nicotine addiction (Volkow and Li 2005). However, the affective manifestations of nicotine withdrawal seem to play an important role in the maintenance of the nicotine addictive process. These manifestations can be evaluated in rodents by measuring several emotional symptoms such as increased anxiety, aversive effects and reward deficits (Jackson et al. 2008b, Johnson et al. 2008). The aversive manifestations of withdrawal are mainly evaluated in rodents by using the place conditioning paradigm, whereas the associated reward deficits are currently evaluated using intracranial self-stimulation techniques. Both behavioural paradigms have also been extensively used to evaluate nicotine rewarding effects and will be described in the next section.

3.9.2. Experimental models to evaluate nicotine rewarding effects

Drug consumption is promoted and maintained by the rewarding properties of the drug. However, it is important to underline that drug consumption is a requirement for the development of addiction, although addiction is not a necessary consequence of drug intake.

3.9.2.1. Self-administration paradigms

Self-administration methods are widely used to directly evaluate the reinforcing properties of a drug. The procedures are considered by most researchers to be valid and reliable models of drug consumption in humans, and to have a high predictive value. It is assumed that the neurobiological mechanisms involved in drug self-administration in animals are similar to those underlying drug-intake in humans (Sanchis-Segura and Spanagel 2006). Self-administration methods can be classified considering the route of administration and the behavioural paradigm. From a behavioural perspective, these methods can be classified as operant and non-operant procedures. Non-operant paradigms are centred on the amount of drug consumed whereas the operant procedures require a conditioned response in order to obtain the drug, and the analysis of this response provides valuable information about different behavioural aspects of drug consumption. Non-operant paradigms in animals are mainly restricted to oral self-administration and they are very useful for alcohol research considering the similarities with the route of alcohol consumption by humans. The use of the appropriate route of self-administration for each drug of abuse provides an additional source of validity to these animal models, and these non-operant paradigms are therefore not useful in evaluating nicotine rewarding effects.

The use of operant models is based on the learning contingency defined as “positive reinforcement”. In these models, the drug constitutes a positive reinforcer that is delivered contingently to the completion of the schedule requirements (Sanchis-Segura and Spanagel 2006). The operant chambers are equipped with one or more manipulandi, transmitting the operant response and devices to deliver the drug (reinforcer). Usually, there is an active manipulandum that is linked to the delivery of the drug and an inactive one, which results in the delivery of the drug vehicle or lacks any programmed consequence. The programmes of reinforcement commonly used are the fixed ratio and the progressive ratio schedule and the animal species currently used for nicotine self-administration is the rat. It is suggested that fixed ratio schedules measure the pleasurable or hedonic effects of a drug (McGregor and Roberts 1995, Mendrek et al. 1998), whereas progressive ratio schedules are more related to motivation and provide a better measure of incentive salience or craving (Arnold and Roberts 1997). Under a fixed ratio schedule, the drug is delivered every time that a pre-selected number of responses are completed. For nicotine self-administration, the number of responses required to obtain the drug is generally kept low, and the most used is the fixed ratio 1 (a nicotine delivery after each response in the active manipulandum), although fixed ratio 3 and 5 schedule of reinforcement have also been used (for instance, Shram et al. 2008). Multiple studies have demonstrated that rats easily maintain an operant behaviour to self-administer nicotine under these fixed ratio experimental conditions (Maldonado and Berrendero 2009). In contrast with other drugs of abuse, when dose-response curves have been constructed for nicotine self-administration in rats, they have been relatively flat or inverted U-shaped, which may be because of the aversive effects and toxicity associated with high doses of nicotine (Corrigall and Coen 1989, Shoaib et al. 1997). In a large number of studies the dose of 0.03 mg/kg (free base) per infusion showed very robust self-administration behaviour in rats (Corrigall and Coen 1989, Donny et al. 1999, Shoaib et al. 1997).

Under the progressive ratio schedule, the response requirement to deliver the drug escalates according to an arithmetic progression. The common index of performance evaluated in this schedule is the break point defined as the highest number of responses that the animal accomplished to obtain a single delivery of drug. In rats, several studies have also revealed that nicotine can maintain self-administration on a progressive ratio schedule of reinforcement. The break point achieved for nicotine self-administration has been compared by the authors with other drugs of abuse. They found that it was lower than the final ratio obtained for cocaine under an identical schedule of reinforcement, higher than that reported for heroin under similar progressive ratio schedule, and slightly lower than heroin when a slowly accelerating schedule was used (Donny et al. 1999). However, comparison across studies and drugs is difficult due to procedural differences in training parameters, sequence of progressive reinforcement or degree of drug dependence (Stafford et al. 1998). Increasing doses of nicotine usually resulted in a more linear increase in the performance in the progressive ratio schedule than in the fixed ratio schedule (Donny et al. 1999). The maximum break points usually reached by the adult rats when using the progressive ratio schedule are around 50 responses to obtain a single nicotine injection (Shram et al. 2008). Interestingly, higher break point values were obtained in adolescent rats (around 95) than in adult rats (Shram et al. 2008).

Operant nicotine self-administration has been difficult to establish in mice. A recent study has reported the validation of a new reliable operant model of nicotine self-administration, extinction and relapse in mice. This model was developed in C57BL/6 mice which are particularly sensitive to the behavioural effects of nicotine (Martín-García et al. 2009). Mice were successfully trained to self-administer a dose of nicotine similar to that previously used in rats (0.03 mg/kg, free base) under a fixed ratio 1 schedule of reinforcement. An inverted U-shaped dose-response function was also obtained using mice to self-administer different doses of nicotine (Galeote et al. 2009). Similar to other drugs of abuse, the break point achieved for nicotine self-administration in mice was lower than in rats. Indeed, the maximum break point (27 responses to obtain a single nicotine injection) was reached by the mice when using the dose of nicotine of 0.042 mg/kg (free base) (Galeote et al. 2009).

3.9.2.2. Conditioned preference paradigms

In the conditioned preference paradigms, the subjective effects of the drug are repeatedly paired to a previously neutral stimulus. Through this repeated conditioning process, this stimulus acquires the ability to act as a conditioned stimulus, and the animal will prefer or avoid this conditioned stimulus depending on the rewarding or aversive effects produced by the drug. The most commonly used paradigms apply a spatial environmental stimulus as conditioned stimulus and the animal will show a conditioned place preference or a conditioned place aversion for the environment associated to the effects of the drug or its withdrawal. Although a conditioned approach/avoidance towards specific stimuli can also occur in humans as a result of drug consumption (Bardo and Bevins 2000), the place conditioning paradigms are not primarily intended to model any particular feature of human behaviour. These paradigms mainly represent an indirect assessment of the rewarding or aversive effects of a drug or its withdrawal, by measuring the response of the animal towards the conditioned stimulus. Drugs of abuse display a differential ability to produce conditioned place preference. Opioids and psychostimulants easily produce robust place preference over a wide rang of experimental conditions, whereas other drugs such as ethanol, cannabinoids or nicotine produce more inconsistent results (Sanchis-Segura and Spanagel 2006). Thus, nicotine has been shown to induce in rodents conditioned place preference across a wide range of doses in some experiments, although inverted U-shaped dose-response curves have been often reported, and the magnitude of the effect is generally small and affected by environmental stimuli or previous handling history (Castañé et al. 2006, Forget et al. 2005, Grabus et al. 2006, Le Foll and Goldberg 2004). Nicotine also produced aversive effects when used at high doses in some, but not all, studies (Grabus et al. 2006, Le Foll and Goldberg 2004). These results suggest that the rewarding effects of nicotine may be weaker than other drugs of abuse in this particular experimental paradigm (LeFoll and Goldberg 2004). Interestingly, sex differences were clearly revealed in mice exposed to nicotine in the conditioned place preference paradigm. Thus, female mice responded more to the conditioned rewarding effects of nicotine compared with males (Isiegas et al. 2009).

3.9.2.3. Intracranial self-stimulation paradigms

Intracranial electric self-stimulation procedures were essential in the discovery of the brain reward circuits (Olds and Milner 1954) and are now widely used to study the effects of drugs of abuse in the activity of the reward circuits (Sanchis-Segura and Spanagel 2006). In this paradigm, animals are trained to maintain an operant behaviour in order to obtain an electric pulse through an electrode that has been previously implanted in a reward-related brain site, most frequently the lateral hypothalamic area. The threshold of the minimal current needed to promote intracranial electric self-stimulation is estimated. A drug that stimulates the reward circuit will decrease this threshold, which would be related to its rewarding properties, whereas a drug having aversive effects will enhance the minimal current required to maintain the self-stimulation (Markou and Koob 1993). Nicotine as well as other drugs of abuse such as psychostimulants, opioids or ethanol, reduces the threshold to promote intracranial electric self-stimulation in some reward brain areas (Huston-Lyons and Kornetsy 1992, Kornetsky and Bain 1992, Wise 1996). Therefore, this behavioural paradigm clearly demonstrates the capability of nicotine to activate the brain reward circuits.

3.9.3. Experimental models to evaluate nicotine addiction

The behavioural models available to evaluate drug rewarding effects have been very useful in clarifying the neurobiological basis of drug taking. However, addiction is not just the taking of drugs, but represents a relapsing disorder characterised by compulsive drug use maintained despite adverse consequences for the user (APA 1994). Behavioural models that resemble the main diagnosis criteria for addiction are difficult to validate in animals. Recently, two independent research groups have validated behavioural models of compulsive drug seeking in rodents that resemble addictive behaviour in humans (Belin et al. 2008, Deroche-Gamonet et al. 2004, Vanderschuren and Everitt 2004). In these models the authors have evaluated the difficulties in stopping drug use by measuring the persistence of drug seeking during a period of signalled non-availability. The extremely high motivation of the addicts to take the drug has been evaluated by using a progressive ratio schedule where the number of operant responses to obtain a single drug injection was increased progressively within the same session. The maximal amount of work that the animal performs before cessation of responding (referred to as the break point) is considered a reliable index of the motivation for the drug. These new animal models of addiction report a break point over 500 to obtain a single cocaine injection in "addict rats" (Deroche-Gamonet et al. 2004). In these new animal models of addiction, the continued use of the drug despite its harmful consequences has been resembled by the persistence of the animal's responding for the drug when drug delivery was associated with a punishment.

However, these models validated for cocaine consumption are still not available for other drugs, such as nicotine. Indeed, nicotine self-administration has not been reported to be maintained when drug delivery was associated with a punishment. In addition, only moderate break point values were obtained when a progressive schedule of reinforcement was used for nicotine self-administration. Thus, the maximum break points usually reached to obtain nicotine, i.e. around 50 responses in adult rats (see for instance, Shram et al. 2008) and around 95 in adolescent rats (Shram et al. 2008), are far away from the break point values reached to obtain cocaine by the "addicted rats" (over 500, Deroche-Gamonet et al. 2004).

In contrast, recent advances using animal models of relapse have shown that nicotine seeking after extinction of the operant behaviour can be triggered in rats and mice by nicotine-associated (conditioned) cues (Caggiula et al. 2002, Liu et al. 2007, Martín-García et al. 2009), stressors (Bilkei-Gorzo et al. 2008, Buczek et al. 1999) (e.g. mild footshocks) and re-exposure to the previously experienced drug (Chiamulera et al. 1996, Dravolina et al. 2007, Shaham et al. 1997), which are the same events that trigger nicotine craving and relapse in humans. Nicotine-paired cues have a critical role in sustaining nicotine self-administration after prolonged periods of abstinence and in maintaining smoking behaviour in humans. Indeed, a critical role of the environmental stimuli previously associated with drug consumption has been attributed when explaining the high rate of nicotine relapse (Caggiula et al. 2001, Caggiula et al. 2002, Liu et al. 2007). In agreement, the exposure to the associated cues was the most effective stimulus reinstating nicotine-seeking in mice, whereas stress exposure reinstated nicotine-seeking behaviour in half of the mice, and a priming injection of nicotine only reinstates seeking behaviour in a low percentage of mice (Martín-García et al. 2009). The neurobiological mechanisms involved in the processes underlying relapse to nicotine seeking are poorly understood. Further studies will be required to clarify the mechanisms involved in nicotine relapse using these animal models now available.

3.9.4. Conclusions on experimental animals

Animal models to evaluate the rewarding and the reinforcing properties of nicotine, and the development of nicotine tolerance and dependence, are available. The models most currently used to evaluate nicotine addictiveness are based on its rewarding/reinforcing properties, are well established and have been widely used for other drugs of abuse to determine their addictive potential. Among these models, the operant self-administration paradigm is particularly useful considering its high predictive value for the abuse liability of a drug and therefore also possibly for its addictive potential in humans. A response easy to evaluate in the self-administration paradigm that has been related to the addictive potential is the break point (highest number of responses that the animal accomplishes to obtain a single delivery of a drug). A higher break point represents a direct measure of the motivation of the animal to obtain the drug and is often taken to imply an increase in the addictive potency of the drug. New complex behavioural models that resemble the main diagnosis for drug addiction in humans have been developed very recently, although these new models can only be applied for some particular drugs and experimental conditions at the present moment.

3.10. Human studies of role of additives in addictiveness and attractiveness of tobacco products

Tobacco addiction is maintained by nicotine, and tobacco products that do not deliver nicotine do not sustain addiction. However, it is important to distinguish between the stages of tobacco use, from early experimentation and initiation (prior to the development of dependence), through to regular use (and possible dependence) and possibly eventual cessation. Therefore, nicotine and additives may play different roles, or may differ in their relative importance during experimentation and initiation compared with the progression to regular use. In addition, the role of additives will differ according to whether the tobacco is delivered as a smoked or smokeless product.

Smoking and inhalation into the lungs, in particular, is a highly efficient form of nicotine administration, as the drug enters the circulation rapidly through the lungs and moves into the brain within seconds. This also allows precise dose titration, so a smoker may obtain the desired effects (Benowitz 2008). Therefore, additives and design characteristics which require the inhalation of tobacco smoke will be associated with increased dependence potential, and this will be particularly true when inhalation into the lungs (as opposed to the oral cavity only) is encouraged. In addition, various tobacco additives and flavourings can modulate the impact of nicotine, including via administration and inhalation behaviour. The impact of these additives on the attractiveness and palatability of tobacco products, in particular in naive users, may influence initiation of use and progression to regular use, before dependence is established.

Tobacco dependence is operationalised in multiple ways, but all definitions share core features of tolerance and withdrawal symptoms in relation to tobacco use. Most studies use either the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for tobacco dependence, or a proxy measure such as the Fagerström Test for Nicotine Dependence (FTND), or the number of cigarettes smoked per day. However, the number of cigarettes smoked per day is often a poor measure of dependence, given the substantial inter-individual variability in the amount of nicotine extracted from a cigarette. The majority of the variance in scores on the FTND is accounted for by the first item (“How soon after you wake do you have your first cigarette?”), and it is likely that many dependent cigarette users can be identified by how soon after waking they smoke their first cigarette. This is most likely due to the short half-life of nicotine, which means that after a period of sleep most tobacco users have very low levels of circulating nicotine, resulting in withdrawal symptoms which are rectified by tobacco use.

Human behavioural studies require either subjective or objective measures of the effects of tobacco, and this allows a comparison of these effects between tobacco products which do and do not contain specific additives. Subjective measures include self-report measures of mood and craving, which may be as simple as single visual analogue scale measures of liking (e.g. “How much do you like the taste of this cigarette”), or include validated questionnaire measures (e.g. the Positive and Negative Affect Schedule). The latter refers to a range of laboratory assessments, including actual smoking behaviour through smoking topography measurement, which allows the detailed measurement of number of puffs taken per cigarette, depth of inhalation, inter-puff interval, and so on. This may also include self-administration or cigarette choice paradigms (e.g. presenting participants with two cigarettes, only one of which contains an additive of interest, to determine which is preferentially smoked), which are more closely comparable with paradigms used in animal studies.

These measures are generally impossible or impractical to collect in survey studies, although the rates of use of different tobacco products, containing different additives, may allow their attractiveness to certain sub-groups (e.g. defined by age or ethnicity) to be inferred. A further complication is the possibility that what constitutes an attractive or palatable product may be culturally or ethnically specific.

3.10.1. Experimental and observational studies

Cigarette smoking topography describes the pattern of smoking behaviour for an individual cigarette smoker, and includes measures of puff volume, puff duration, puff flow, interpuff interval, and number of puffs per cigarette. This technology can be used to assess the effects of product design characteristics and additives on smoking behaviour. There is good evidence, for example, that cigarette smokers partially compensate for the low nicotine delivery by low tar cigarettes, possibly by inhaling more deeply, taking more puffs per cigarette, and so on (Frost et al. 1995), so that the addictive potential of low tar cigarettes may not be substantially different than high tar cigarettes (see also section 3.5.5). Similar effects have been observed when comparing nicotinised and denicotinised cigarettes (Strasser et al. 2007).

Neurological techniques have also been used (e.g. by Philip Morris) to assess the effects of additives on smokers’ central nervous system functioning. Electroencephalography (EEG), pattern reversal evoked potential (PREP), and chemosensory event-related potential (CSERP) were used to measure physiological, sensory, and cognitive changes related to nicotine, flavourings and other additives (Gullotta 1994).

Other chemicals (e.g. pyrazine, vanillin, and propylene glycol) appear to increase P1-N2 amplitudes (the first positive and second negative peaks in the EEG waveform elicited by a novel stimulus, corresponding to early sensory processing) (Philip Morris 1995), and different tobacco flavourings affect CSERPs (EEG waveforms elicited by olfactory or gustatory stimuli) differently, even when smokers were unable to discriminate these subjectively (Gullotta 1994). This indicates that objective measures may be more sensitive to the modulation of smoking behaviour by specific additives than subjective measures (see also section 3.8.1 and 3.8.2).

The sensory effects of tobacco smoke may themselves acquire reinforcing properties through their repeated association with the rewarding properties of tobacco. This has been shown in various studies where, for example, denicotinised cigarettes continue to be smoked in the absence of nicotine reward but are not smoked as frequently when the upper airway is anaesthetised to block the sensory effects of the tobacco smoke (Rose et al. 1985). This may explain in part the loyalty to specific brands shown by tobacco users, since the exact sensory properties of individual brands will differ. It is also possible that extended product characteristics (e.g. pack designs) may acquire reinforcing properties through similar processes, although this has not yet been investigated systematically.

A variety of product design strategies (e.g. ventilation holes – see section 3.5) and application of additives (e.g. ammonia or ammonia-derivatives, see section 3.8.1 and 3.8.3.2) may play important roles either via smoking behaviour such as puffing characteristics (see section 3.5.5), or via more direct biological effects such as nicotine bioavailability. These may in turn influence addictive effects and appeal to the user (Baker et al. 2004c, Djordjevic and Doran 2009). As reported by the tobacco industry, approximately 600 substances are used as cigarette additives, but among the most commonly used products only one additive (menthol) is widely advertised by the industry (Ahijevych and Garrett 2004).

3.10.2. Target groups (age, ethnicity, gender, socioeconomic position)

Internal tobacco industry documents illustrate that additives and technical characteristics have been extensively evaluated in relation to their appeal to specific target groups and markets (Carpenter et al. 2007). Some of this evidence relates to the US experience, in particular with respect to ethnicity, and it is not clear whether these results will generalise, in full or in part, to the European situation. However, some findings, such as those relating to younger age groups and gender, are more likely to generalise.

3.10.2.1. Age groups

There is evidence from tobacco industry documents that flavourings have been used to target younger smokers: "[U]se the FLITE technology to inject various flavours into the blend. These flavours would be new and unconventional. Two flavours which were discussed as options were Root Beer and Brazilian Fruit Juice, both of which *tend to appeal to the younger generation* while being rejected by their parents" (emphasis added) (BAT 1997). This may act as a gateway to subsequent tobacco use in adulthood.

A survey in the US showed that 17 year old smokers are three times as likely to use flavoured cigarettes as are smokers over the age of 25 (Klein et al. 2008). Therefore, the addition of exotic flavours may be used to increase the appeal of tobacco products (including smokeless products), and in particular their appeal to naive users and younger age groups. Dutch survey data indicate that taste and smell are important determinants of brand preference among young smokers aged 10-18 years, with brands with light or mild taste regarded as less unhealthy (Talhout et al. 2009).

3.10.2.2. Ethnicity

In the USA, there is a striking difference in the use of mentholated cigarettes among African Americans and European Americans, with the prevalence of mentholated cigarette smoking much higher in the former group. Menthol is the most widely-studied additive, and therefore provides a case-study for some of the behavioural consequences of tobacco additives. This suggests that specific additives may be used to improve the attractiveness of tobacco products to specific populations or target groups.

Internal tobacco industry documents, available under the Freedom of Information Act in the USA, describe the relationships between sensory perception and the attitudes, preferences, and patterns of cigarette use among menthol smokers. Two unique types of menthol smoker are described: those who cannot tolerate the harshness and irritation associated with smoking non-menthol cigarettes, and those who seek out the specific menthol flavour and associated physical sensation (Kreslake et al. 2008b).

Additives also contribute to the effects of other tobacco products with either marginal or region-specific use. For example, clove cigarettes, used predominantly by East Asian populations, are composed of a mixture of tobacco (60–80%) and ground clove buds (20–40%), available with or without filters. Eugenol, an analgesic, is naturally occurring in cloves, and is present in milligram quantities in the clove cigarette filler. Like menthol, eugenol diminishes the harshness of the tobacco smoke (Djordjevic and Doran 2009).

3.10.2.3. Gender

While the targeting of specific groups and populations (e.g. young people, women, ethnic groups) is primarily through advertising campaigns for tobacco products, this targeting can also include the development of specific tobacco products, and the use of specific additives in these products. For example, cigarettes with perfumed scents and labelled as "slim" or "light" brands have been marketed to women. This is reflected in evidence that more women than men smoke light and ultra-light cigarettes (ONS 2007).

3.10.2.4. Socioeconomic position

Tobacco use is heavily socially patterned in developed countries, with prevalence of use being higher in lower income groups compared to higher income groups (Eek et al. 2010, Main et al. 2008). While tobacco use in general, and cigarette use in particular, has declined dramatically in wealthier socioeconomic groups over the last few decades, the decline in less wealthy socioeconomic groups has been much less pronounced. In particular, in the most economically disadvantaged groups, tobacco use prevalence has remained almost unchanged over this period. As a result, tobacco use is one of the largest causes of health disparities between socioeconomic groups in European countries. However, there is no evidence suggesting that changing patterns of use in Europe are a result of tobacco industry's targeting certain socioeconomic groups.

3.10.3. Emotional/subjective effects

Flavours impart a specific taste or aroma to a product, while other additives may be used for a specific technological purpose in the manufacture of tobacco products (Baker et al. 2004b). Both flavours and other additives can confer emotional and subjective effects. The term "impact" is widely used in tobacco industry research and documents, and is a tobacco industry term for smokers' subjective awareness of the drug effects of nicotine.

Organic acids have been used since the 1950s to improve "smoothness" of cigarettes. For example, Philip Morris found that lactic acid decreased subjective ratings of harshness and bitterness, and produced a sweeter flavour. Citric additives have been used not only for reduced harshness and flavour modification, but also to modify smoke pH, to neutralize nicotine "impact" (an industry term denoting the organoleptic sensation caused by nicotine; smokers often describe this as "throat catch" or "throat hit"). Tartaric and lactic acids likewise modify the pH of smoke. All of these organic acids increased smoothness and are associated with a decrease in nicotine "impact" (Philip Morris 1989, see also section 3.8.2.2.) However, it is unclear whether these effects are due directly to pH modification.

Unregulated botanical and chemical additives might have "multiple-use" purposes, such as enhancing flavour and producing "smoother" cigarette smoke, as well as potentially preventing or masking symptoms associated with smoking-related illnesses (Rabinoff et al. 2007).

3.10.4. Conclusions

A wide range of subjective and behavioural effects of tobacco additives have been reported in humans, but there are relatively few studies published in the scientific literature, with much information having been obtained from tobacco industry documents under freedom of information legislation. In principle, similar methods to many of those used in experimental animal models may also be used in humans. However, there is greater variability in the specific methods employed, which include subjective reports of liking, behavioural measures of drug choice, neurobiological measures of drug effects (such as neuroimaging techniques), and direct measures of drug administration (such as cigarette smoking topography). The majority of additives used appear to be flavourings, and these may be used to target specific markets, such as young people, women, or ethnic groups. There is some evidence that these additives modify objective measures of cigarette smoking behaviour (i.e. smoking topography), but this is somewhat inconsistent.

3.11. Effects of additives on nicotine-addictive properties

3.11.1. Modification of the pharmacology and reinforcement properties of nicotine

3.11.1.1. Comparison of addictive properties of nicotine vs. whole tobacco and modification of reinforcing properties of nicotine

Acetaldehyde is formed in high concentrations when cigarette constituents, including sugars, are burned. Animal research conducted by Philip Morris demonstrated a synergistic interaction between nicotine and acetaldehyde, using a lever-pressing model of self-administration in rodents (Charles et al. 1983, DeNoble et al. 1997). Rats pressed a bar more for the combination of nicotine and acetaldehyde than for either substance alone. If these results apply to humans, smokers would puff more with the combination of nicotine and acetaldehyde. As described below, an inhibitory effect of acetaldehyde on MAO-A and B is one of the possible mechanisms that reinforce the properties of nicotine. It should be noted that the contribution of acetaldehyde in smoke to the level in blood is minimal compared to, for example, the effect of ethanol consumption (Chen et al. 2007b, McLaughlin et al. 1990). There are indications that users of smokeless tobacco do not have a reduced MAO activity, suggesting that constituents of the smoke (acetaldehyde?) are needed to inhibit MAO activity (Berggren et al. 2007). In section 3.8.1.4 the action of acetaldehyde is described in more detail.

Tobacco is a potent reinforcing agent in humans, and nicotine is generally considered to be the major compound responsible for its addictive properties (Balfour et al. 2000, Dani et al. 1996, Di Chiara 2000). However, animal experiments indicate some discrepancies between the effects of nicotine and those of other drugs of abuse. For example, the capacity of repeated nicotine to elevate dopamine levels in the nucleus accumbens is controversial (Balfour et al. 1998, Di Chiara 2000, Vezina et al. 1992) and repeated nicotine treatments in rats induce a behavioral sensitisation which vanishes more quickly than that for other drugs of abuse (Ksir et al. 1985, Villégier et al. 2003). Furthermore, with the exception of ethanol which possesses potent sedative effects, most drugs of abuse, such as psychostimulants and opiates, induce a substantial locomotor hyperactivity both in rats and mice. Nicotine, however, is a weak locomotor stimulant in rats and generally fails to induce locomotor hyperactivity in mice at any dose (Marks et al. 1983, Sparks and Pauly 1999). Nevertheless, when animals are pretreated with an inhibitor of monoamine oxidases, nicotine is able to induce a potent locomotor hyperactivity, even in mice (Villégier et al. 2006a). These differences could suggest that the addictive effects of tobacco are not only due to nicotine and that monoamine oxidase inhibitors have a critical effect.

In fact, tobacco and tobacco smoke are known to contain a number of compounds, among which monoamine oxidase (MAO) inhibitors, such as harman, norharman or acetaldehyde, have been the focus of special interest (Breyer-Pfaff et al. 1996, Gaddnas et al. 2000, Rommelspacher et al. 2002). Monoamine oxidases exist under two forms; MAO-A and MAO-B. They are enzymes that degrade dopamine, serotonin and noradrenaline - three neurotransmitters involved in addiction. The inhibition of MAO increases brain monoamines levels which decrease the sensitivity of their respective receptors. Human MAO-A and MAO-B genes isolated from X chromosome-specific libraries span at least 60 kilobases, consist of 15 exons, and exhibit identical exon-intron organisation (Grimsby et al. 1991). Inhibition of monoamine oxidases by tobacco smoke does not result from the actions of nicotine (Carr and Basham 1991), but from that of other compounds also present in other psychotropic plants (Uelbelack et al. 1998). It was shown that MAO inhibitor pre-treatment allows the maintenance of behavioural sensitisation to nicotine in rats (Villégier et al. 2003), thus suggesting a role of MAO inhibitors in the addictive properties of tobacco. More recently, tranylcypromine, a cyclized amphetamine five thousand times as potent an MAO inhibitor as amphetamine (Zirkle and Kaiser 1964), was found to be able to trigger a locomotor response to nicotine in mice (Villégier et al. 2006a) and nicotine self-administration in rats (Guillem et al. 2005, Villégier et al. 2006a). Moreover, increases in extracellular 5-HT levels induced by monoamine oxidase inhibitors appeared to be crucial for these effects (Villégier et al. 2006b).

Nicotine is commonly considered as a monoamine releaser (Summers and Giacobini 1995, Summers et al. 1996) that increases serotonergic neurons firing (Li et al. 1998; Marubio et al. 1999, Olausson et al. 2001a, Olausson et al. 2001b, Olausson et al. 2002). This increased release of 5-HT, in absence of MAO inhibitors, is however transient. Indeed, an immediate inhibitory retro-control blocking the firing of serotonergic raphe neurons through the stimulation of somato-dendritic 5-HT1A receptors has been described (Engberg et al. 2000, Li et al. 1998, Mihailescu et al. 1998). It has therefore been proposed that MAO inhibitors, because of their enhancing effects on extracellular 5-HT levels, compensate the consequences of the indirect inhibition of serotonergic cells by nicotine, thus suggesting a mechanism by which MAO inhibitors contained in tobacco smoke could act in synergy with nicotine to induce addiction (Tassin 2008). Very recent experiments using 5-HT1A agonists and antagonists have indicated that MAO inhibitors contained in tobacco desensitize 5-HT1A autoreceptors to trigger the strong addictive properties of tobacco (Lanteri et al. 2009).

In humans, nicotine replacement therapies are the most widely used form of pharmacological intervention, but have proven to be remarkably unsuccessful (Medioni et al. 2005, Silagy et al. 2004). Interestingly, most tobacco smokers (> 80%) relapse after a few weeks withdrawal, i.e. when inhibition of MAO activity by tobacco and tobacco smoke is likely to have disappeared. It has also been argued that the lack of efficacy of nicotine replacement therapies was due to the continuous delivery of nicotine by gums or patches. It was indeed believed that peaks of nicotine occur in the brain after each puff of tobacco smoke. Very recent experiments, performed with PET and ^{11}C-nicotine, indicate that these peaks exist only in the arterial blood of smokers and do not appear in the brain (Rose et al. 2010a). The half-life of nicotine in the human brain is 13 minutes, which is much longer than the ~45 seconds which separates two successive puffs. Indeed, brain nicotine levels increase regularly along with the cigarette consumption (Rose et al. 2010a).

The role of tobacco smoke on MAO is even more important than originally thought. A substantial inhibition of MAO-A has been found by neuroimaging in chronic smokers (Leroy et al. 2009). Another study has shown that smokers have the methylation frequency of their MAO-B gene promoter markedly lower (P<0.0001) than non-smokers, thus inducing a higher quantity of MAO-B in smokers (Launay et al. 2009). Interestingly, this is also true for smokers who have quit for about 10 years. This was explained by showing that cigarette smoke induces an increase of nucleic acid demethylase activity and an epigenetic regulation of MAO-B. Altogether, these authors have shown that metabolism of 5-HT is modified in smokers but that it is also true for those who have stopped smoking for a long time (over 10 years) (Launay et al. 2009).

It seems therefore that MAO inhibitors, or any compound able to modify 5-HT metabolism and desensitize 5-HT1A autoreceptors, may provide a more complete scheme of the addictive properties of tobacco in experimental models of reward.

3.11.2. Conclusions on effects of additives on nicotine addictive properties

There is evidence that nicotine cannot, by itself, explain the high addictive potential of tobacco and tobacco smoke. The increase of nicotine in the brain resulting from smoking a single cigarette is extremely rapid due to the absorption of smoke inhaled into the lungs but the peak observed in arterial blood after a puff is not reflected in the brain where the half-life of nicotine is much higher than in blood. Converging data indicate that MAO (monoamine oxidase) inhibitors contained in tobacco and tobacco smoke act synergistically with nicotine to enhance addiction potential. Smokers have reduced levels of MAO in the brain. Among MAO inhibitors, compounds resulting from sugar combustion, such as acetaldehyde, may play a crucial role in tobacco addiction. MAO inhibitors increase serotonin extracellular levels and desensitize 5-HT1A autoreceptors, thereby allowing nicotine to activate serotonergic neurons and become addictive. As yet, data about the role of acetaldehyde are inconclusive and need further investigation before a role for sugars as indirectly addictive compounds can be established/confirmed.

3.12. Methods to assess attractiveness

3.12.1. Introduction

According to the World Health Organisation (WHO), the terms “attractiveness” or “consumer appeal” refer to factors such as taste, smell and other sensory attributes, ease of use, flexibility of the dosing system, cost, reputation or image, assumed risks and benefits, and other characteristics of a product designed to stimulate use (WHO 2007b).

Overall, attractiveness is likely to be influenced by a subtle array and interaction of any number of these factors, although at certain times individual factors may take precedence (e.g. price, particularly during a recession). In addition, certain factors might be essential for enduring attractiveness (e.g. the presence and ease of delivery of nicotine).

The factors influencing attractiveness can be broadly divided into: extrinsic factors (e.g. marketing, packaging, pricing); and intrinsic factors (e.g. taste, smell, sensory attributes, and pharmacological factors). Additives play a role mainly in the intrinsic factor category, but marketing and packaging can also reflect the presence of additives in a way to attract and maintain customers (e.g. by signalling that the tobacco product contains menthol). Given the subtle interactions between different factors however, identifying and measuring the influence of individual addictives on attractiveness of products is difficult. Separating the role of additives in enhancing addictiveness, from their role in enhancing other attractive attributes of a tobacco product is also complex.

3.12.2. Measuring attractiveness

There are two main ways of examining the influence of additives on the attractiveness of a product. Firstly, one can assess individual tobacco products, and compare their attractiveness on a number of scales/dimensions, against other tobacco products. By then examining what is known about the additive content of these products, indirect inferences can be made as to the role of individual additives in the overall attractiveness of the product, although there are important limitations to studies of this kind. Secondly, one can examine the influence of individual additives on attractiveness of a tobacco product, along a number of scales, by experimentally adjusting tobacco products to include or exclude individual additives and testing responses to them. In addition, the quantity of the additive can be varied to assess dose response and whether there is a threshold below which any impact is not observed. However, in practice this may be difficult to achieve by research groups outside of the tobacco industry, who are likely to lack the resources to manipulate additive content in this way.

Tobacco industry documents show that the tobacco companies frequently tested human smokers on their reaction to different cigarettes using focus groups, market testing, human smoking behaviour studies or consumer panels. For example, one study carried out by British American Tobacco in 1980 exposed a panel of smokers, trained to be objective in their evaluation of cigarettes, to different conditions wherein brand identification was either masked or visible, in order to understand how brand identification and imagery affected subjective evaluation of cigarettes (Ferris 1980).

The difficulties with this type of research are that ethical restrictions will usually preclude human testing of different tobacco products, particularly among non-users or children. In addition, there are technical constraints on the ability to manipulate the presence or absence of specific additives in tobacco products. While the tobacco industry may be able to achieve this, such manipulations may be beyond the resources of independent academic research groups.

Both the main methods have advantages and disadvantages and should be seen as complementary. Ideally, a variety of methods and tests would be utilised and assessors would be looking for overall consistency in the findings, in order to conclude that an additive affected attractiveness.

3.12.2.1. Measuring attractiveness of different brands

Actual brand choices

Assessing actual brand use gives an overall indicator of attractiveness of products which reflects all the factors listed at the outset of this section covering both extrinsic and intrinsic variables, of which additive content is only one factor. A major difficulty of this approach will therefore be separating the influence of these factors. The largest influence is likely to be the marketing budget. For example, the popularity of Marlboro worldwide is likely due to the substantial funding spent on its advertising and promotion. A further complication with interpretation of brand preference data over time is that the tobacco industry has been expanding the number of variants of existing brands; since 1998 brand families have increased by more than 50%. For example, Benson & Hedges increased the number of brands from four in 1998 to 12 by 2008 (ASH 2010).

Brand choices can be examined cross-sectionally in populations (nationally and globally) but longitudinal data enable trends in brand preferences to be examined over time and in relation to changing product make up (content and design) as well as tobacco control policies and other factors. Brand preferences should be examined in subpopulations such as by gender, age, and sociodemographic factors, which might reflect targeting by tobacco companies. Brand preferences in younger age groups (e.g. 11-16 year olds) are especially important to identify as these can enable an assessment of attractiveness and appeal to children. In particular, it is important to assess which brands are used initially by children, followed by those that they progress onto over time. Products that attract children to smoking have been referred to in the literature as “starter products”. This refers to two main types of products: confectionary products which are made and packaged to look like cigarettes, thereby enabling children to imitate smoking (e.g. candy cigarettes, not discussed further here), and tobacco products which are made to look like confectionary (e.g. candy-flavoured cigarettes), thought particularly to appeal to children and ethnic minorities (Connolly 2004).

Comprehensive sources of data on brand preferences at country level broken down by socio-demographics are not readily accessible. As an example, we have selected data from the UK which suggest that brand preferences of children and adults can be quite similar. The top five brands in 2009 were identified as: Lambert & Butler King Size, Mayfair King Size, Marlboro King Size Gold, Benson & Hedges King Size Gold and Richmond King Size (Hegarty 2010). Comparable data are not available for youth from 2009 but in 2006, the most popular brands with 11-16 year olds were: Mayfair (58%), Lambert & Butler (56%), Richmond (45%), Benson & Hedges (28%) and Sovereign (23%) (Amos and Hastings 2009). Four of the brands were common to both adults and youth, and for each age group there was a dominance of economy brands. Trends over time indicate increasing popularity of economy over premium brands suggesting price may be playing a key role in current brand choices. As indicated in section 3.13.2., there may be a trend in the UK for preferring brands marketed as containing no additives, but this observation needs confirmation.

Careful monitoring of brand preferences over time will be important for future research, as will disclosure by the tobacco industry of detailed product content information for all brands on the market.

Perceived brand preferences

By showing different brands to consumers, assessments can be made about how attractive the products are perceived to be. For non-tobacco users, responses will largely reflect extrinsic factors such as the packaging, but will also reflect their knowledge of experiences of others with the products. For users, such assessments also reflect knowledge and experience of using the products in addition. The role of additives therefore will need to be assessed and inferred alongside these other factors, assuming that differences in additives between the different brands are known. As stated above, this research involves examining the look of a pack, and its design and packaging.

Packages can be digitally altered experimentally to test the responses of the presence or absence of attributes (e.g. whether listing an additive such as menthol alters how people respond to the product). However, studies have shown that colours of packs quickly become associated with certain attributes; for example, one study in New Zealand found that green colouring indicated the presence of menthol (Peace et al. 2007). In these types of studies, different population groups should be compared to test if some products are more appealing than others. For example, one experimental study indicated that some adolescents had more favourable impressions of tobacco brands that featured cherry flavouring in the packaging (Manning et al. 2009).

This type of research has now been carried out in a variety of settings (e.g. internet, supermarket, and mall intercept studies) and using a variety of qualitative and quantitative research techniques (Hammond et al. 2009a, Hammond and Parkinson 2009b, Manning et al. 2009). The products have been assessed along several attributes including their perceived attractiveness, harmfulness, ease of initiation or cessation. Standardised designs, methodologies and questions therefore exist which can be utilised to facilitate comparative analysis.

Sensory attributes to users and others

Consumer perceptions of sensory attributes such as taste or palatability, smoke irritation and odour, can also be useful for indicating differences in brands. Although there is likely to be some impact of packaging and design on expectations of sensory effects, this area of testing will be more focused on attributes of the content and emissions of the product itself. This research can be done in two main ways:

a) Through surveys of smokers in which questions cover reasons for selecting the brands they smoke and the role of sensory attributes.

b) Experimentally, using panels of test subjects trying products and expressing preferences using, for example, visual analogue scales (see section 3.10). However, whilst perceived responses to these attributes are important, it is also useful to see how sensory differences translate into topography measurements and the presence of biomarkers, such as cotinine (see below).

These factors could be attractive to a smoker as they make it less troublesome for others in their presence, who are then less likely to complain about their smoking. The sensory attributes to be measured here would include smoke irritation, smoke odour, and visibility of sidestream and mainstream smoke. These assessments can be made as described above, but of non-smokers who live, work or are in the presence of smokers.

3.12.3. Conclusions on methods to assess attractiveness

Attractiveness depends on multiple factors that combine to stimulate use. These include extrinsic factors such as marketing, packaging and price, and intrinsic factors such as taste and smell. It is very difficult to identify the role of individual additives in enhancing addictiveness or enhancing other attractive attributes of tobacco products. The attractiveness of a product may be assessed by the direct comparison of different products by surveys, experimental measures or human testing.

Another way to examine the attractiveness of individual additives is to test a certain tobacco product by introducing the additive in different doses. When additives are thought to act in synergy, they may be tested together. In practice, however, overall attractiveness is assessed by comparison of brand choice in subpopulations according to gender, age and sociodemographic factors. By showing different brands to consumers, assessments can be made about their perceived attractiveness.

Sensory attributes such as taste, irritation etc. may be tested by surveys of users or experimentally on panels of test subjects. In general, methods similar to those described in section 3.10 may be used.

The main disadvantage of using any of the data described above is the lack of detailed information available on additive content of different brands and the extent to which additives contribute to any differences observed, over and above other factors intrinsic to the brand, and the price and marketing of the brands.

3.13. Tobacco use in the European Union

Manufactured cigarettes are by far the most preferred tobacco products in the 27 Member States of the European Union. Cigarettes constitute well over 90% of the tobacco sold whereas tobacco used in pipes and for RYO cigarettes (roll-your-own) amounts to about 5%. In most Western EU countries, smoking prevalence among men and women has in general stabilized or is decreasing. The number of smokers has also started to decrease in some countries in the eastern part of EU, although generally it is only stabilizing among men, with no clear overall trends, and in some cases a slight rise in prevalence among women is being recorded. In the EU as a whole the situation has been stable in the last decade (WHO 2007a).

The use of smokeless tobacco (snus) is common among males in Sweden. The sale of snus is banned in all other countries in the EU but other oral tobacco products may be sold. In the United Kingdom, both male and female migrants from the Indian subcontinent use a wide variety of smokeless tobacco products. Elsewhere, smokeless tobacco use is rare but a wide variety of tobacco products do find their way to Europe through migration (SCENIHR 2008). Similarly, waterpipe smoking is spreading through cultural influence, mainly by migrants from the Middle East. However, during recent years, waterpipe use has become increasingly popular among teenagers in the general population.

The latest comprehensive data from the 27 Member States were collected for 2002 and 2005, respectively (WHO 2007a). Where data were missing other sources have been used in an effort to get the full picture. The information for some countries may not have been collected during the 2005 survey and the figures may therefore not be entirely correct.

3.13.1. EU adult smoking rates 2005

The overall adult daily estimated smoking prevalence (population-weighted) has stabilized at around 28.5% in the EU. The estimated average smoking prevalence among males is 34.2% in 10 (mostly Eastern European) countries and there is a higher prevalence rate of male smoking, while in eight (mostly Western European) countries the male smoking prevalence is below 30% (see figure 4). The estimated average female smoking prevalence in the EU is 22.6% in 14 (mostly Western European) countries and the prevalence rate is higher, while in only three countries is it below 15% (see figure 5).

3.13.1.1. Gender differences

In all but one country (Sweden), smoking prevalence is higher among men than among women. Data from Latvia show the widest gender gap of 29%. A small difference between male and female smoking prevalence of less than 10% can be found in 11 (mostly Western European) countries.

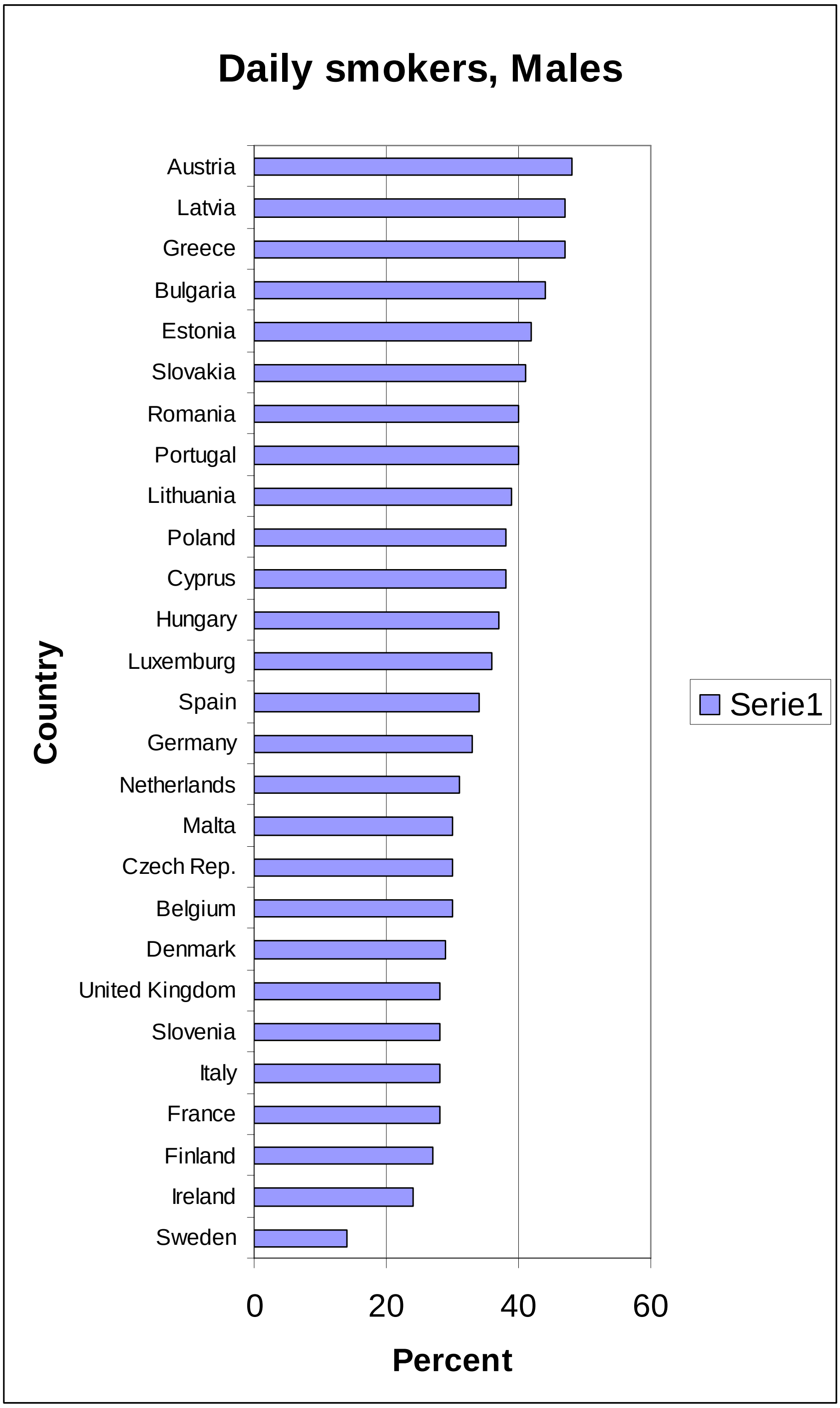

Figure 4: Rates of daily smokers among males in EU countries (WHO 2007a)

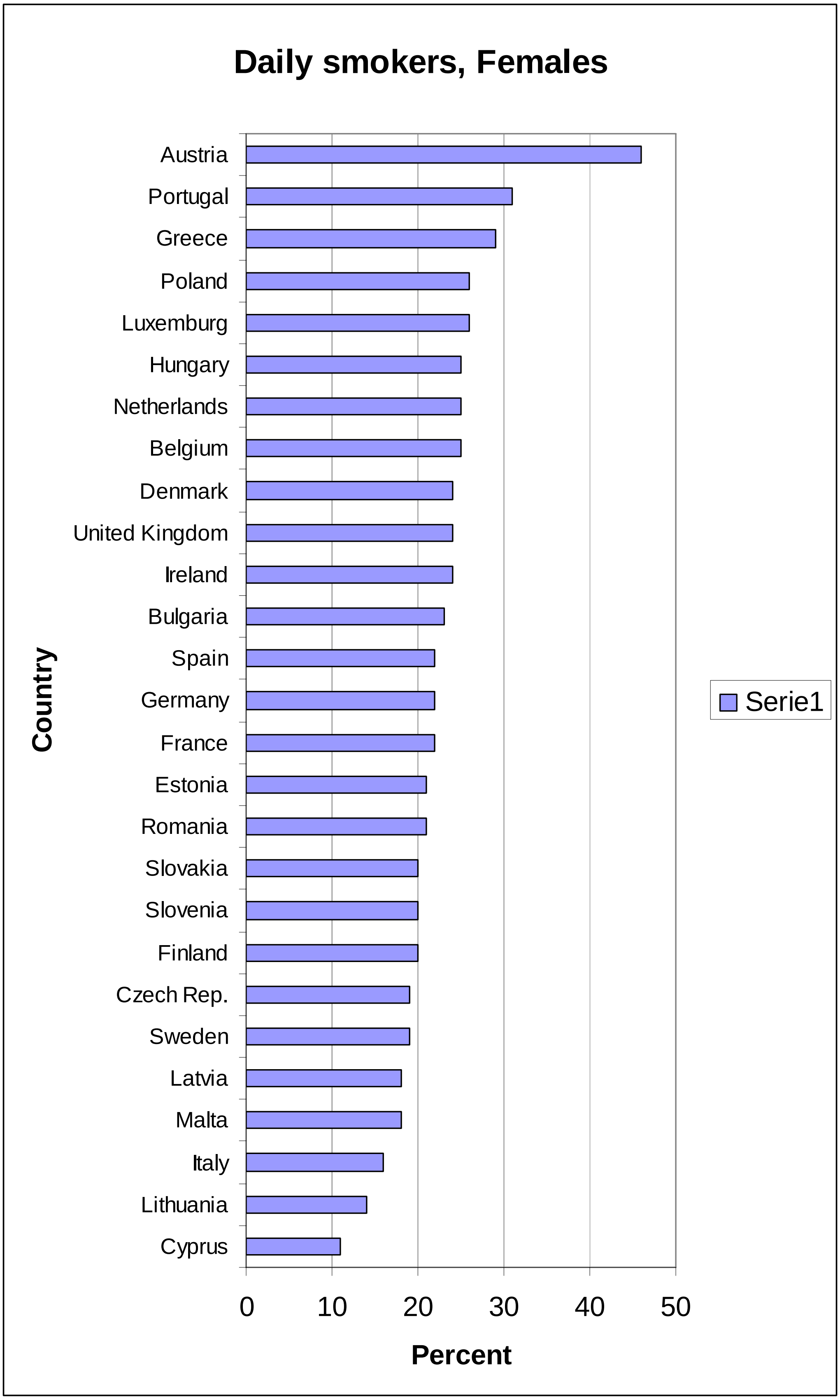

Figure 5: Rates of daily smokers among females in EU countries (WHO 2007a)

3.13.1.2. Changes in smoking prevalence

Estimates for male and female smoking prevalence for 2002 and 2005 are available for 24 of the 27 EU countries. Only relative differences of more than +/-10% have been taken into account as noteworthy changes when comparing data for these two years.

Since the 2002 European report on tobacco control policy, smoking prevalence among the male population has in general stabilized across the EU. A notable decrease has been reported for Sweden (16.3% to 14.4%), but in most countries in the EU male smoking prevalence did not show a significant change between 2002 and 2005. There was no significant change in female smoking prevalence although slight increases were observed in many countries.

In May 2010, near completion of the present report, the Special Eurobarometer 332/72.3 was published (EC 2010). This Eurobarometer, performed upon request of Directorate General Health and Consumers (SANCO) of the European Commission, reports on the results of an EU-wide telephone survey on tobacco conducted in late 2009. The survey method is standardised but the results are not directly comparable to the WHO reports quoted above. Furthermore, they are not comparable to an earlier Eurobarometer published in 2006 (EC 2006) due to changes of design (EC 2006, EC 2007a). Still, some additional information can be extracted. The Eurobarometer (EC 2010) reports the proportion of smokers as 29% (males 35%, females 25%) but does not distinguish between daily and non-daily smokers. It is not possible to ascertain whether this represents a further drop in adult daily smoking rates compared to the WHO report from 2007 mentioned above.

However, Eurobarometer (EC 2010) provides other data of interest. The average number of cigarettes consumed is 14.4/day, ranging from 22 in Cyprus to 10 in Sweden. Men smoke, on average, three cigarettes/day more than women. When asked to single out the most important reason for choice of brand, taste is most important for 22% of smokers in the EU 27 while price is most important for 6%. The package scored 0%. One out of 10 smokers in the EU believes that a less harmful cigarette can be identified by taste (ranging from 27% in Hungary to 3% in Denmark). Unique for the Eurobarometer (EC 2010) is the data on waterpipe smoking. On average, 11% of EU adults have tested or use a waterpipe occasionally, whereas 1% smoke it daily. Differences of use vary between countries but being a young adult appears to increase the probability of use.

3.13.1.3. Conclusions on tobacco use in different EU countries

Manufactured cigarettes are by far the most preferred tobacco products in the 27 countries of the European Union and constitute well over 90% of smoked tobacco. The overall adult daily estimated smoking prevalence (population-weighted) has stabilized at around 28.5% in 2005 (males 34.2%, females 22.6%) but higher rates are found mainly in Eastern European countries. Smoking rates have not changed significantly between 2002 and 2005. Smokeless tobacco is used by over 10% of the population in Sweden but its use is rare in other EU countries.

3.13.2. Brand preference in selected countries

United Kingdom

The cigarette market in the UK (and Ireland and Malta) is quite divergent from the continental European countries. This is mainly because in the UK some typical “English” brands are popular and have a large market share. Some quite surprising observations can be made when looking at the top-10 brands marketed in the UK (Hegarty 2010):

1. Of the top-10 brands (according to market share), three brands (Lambert & Butler King Size, Richmond King Size and Richmond Superkings) contain no additives (water is not considered as an additive).
2. Five brands contain up to 10 additives.

3. Two brands (Marlboro King Size Gold of PMI and Royals King Size Red of JTI) both contain over a dozen additives.
4. Lambert & Butler King Size is by far the most sold cigarette brand. Brands without additives have a market share of 42%, whereas those with 1 to 10 additives have a market share of 48%. Brands containing over a dozen additives have a market share of only 10%.

The "taste" of a tobacco product is not only defined by additives but also by blend-selection. English brands i.e. the typical UK brands are made predominantly from flue-cured Virginia tobacco, which contains relatively high amounts of sugars. Marlboro for instance uses the "American blend" (a mixture of Virginia, Burley and Oriental tobaccos) as a base to which many compounds are added during the manufacture.

By blending, it is possible to manufacture cigarettes with a characteristic taste, without using additives. Imperial Tobacco has thus succeeded in producing a typical brand (Lambert & Butler King Size) via the blending approach. In addition, cigarettes marketed as "additive free", may appeal to smokers that prefer "natural products".

Tobacco products in Central and Eastern European countries before and after 1990

Before 1990, the tobacco used for making cigarettes was usually domestic black shag, and most cigarettes were made with low amounts of additives. Cigarettes were sold without filters and tar levels of 20 to 30 mg per cigarette have been reported. The average nicotine content in Poland in the 1980s was 2 mg per cigarette implying that levels were 1.5 to 2 times the level in Western Europe. After 1990, the large international tobacco companies quickly took over and cigarettes were manufactured in Central and Eastern Europe according to international standards. Most cigarettes are manufactured from light tobacco and the proportion of filter cigarettes rose to 90%. The properties of cigarettes, additives and taste enhancers are now similar to those used in Western Europe and follow the European Union requirements (Zatonski 2008). Availability, marketing, trends, taste, and attractiveness are all factors that may have contributed to the rapid market change.

3.13.3. Smoking prevalence among young people / Target Groups

The analysis of smoking prevalence among young people is from the European Tobacco Control Report 2007 based on the WHO Health Behaviour in School-aged Children (HBSC) study, a cross-national research study conducted every four years: 1993/1994, 1997/1998 and 2001/2002 (WHO 2007a). The 2005/2006 survey was launched in 41 countries and regions and no comparable data are yet available. Information based on a second survey instrument, the Global Youth Tobacco Survey (GYTS) was also used (GYTS Collaborative Group 2002). The GYTS was developed by the United States Centers for Disease Prevention and Control (CDC) and WHO and has been carried out in a large number of countries in the European Region (see table 4). With more and more countries carrying out and repeating the GYTS, comparisons should be possible in the coming years.

3.13.3.1. Current status

According to the HBSC study, weekly smoking prevalence rates were on average 2% among 11-year-olds, 8% among 13-year-olds, and 24% among 15-year-olds. In general, smoking prevalence rates increased more steeply between the ages of 11 and 13 years than between 13 and 15 years. The results of the HBSC and GYTS studies show that weekly smoking prevalence rates in 15-year-old boys were especially high (>30%) in some Eastern European countries (Estonia, Latvia and Slovakia). The highest smoking prevalence rates (>30%) among 15-year-old girls were found mostly in Western European countries such as Austria, the Czech Republic, Finland and Spain. The lowest smoking prevalence rates among 15-year-old boys (<15%) were in Greece and Sweden. Smoking prevalence rates among girls were below 10% only in Greece. An overview of smoking prevalence rates among young people in the EU obtained by the HBSC and GYTS is provided in table 4.

Table 4 Weekly smoking rates among boys and girls in EU countries (WHO 2007a)

	HBSC				GYTS		
Country	**1997-1998**		**2001-2002**		**2001/2004**		
	Boys	**Girls**	**Boys**	**Girls**	**Year**	**Boys**	**Girls**
Austria	30	36	26.1	37.1			
Belgium	28	28	21.3	23.5			
Bulgaria					2002	28.7	26.4
Czech Rep.	22	18	28.7	30.6	2002	29.9	32.8
Denmark	20	28	16.7	21			
Estonia	24	12	30.4	18.2	2002-3	31.8	23.0
Finland	25	29	28.3	32.2			
France	28	31	26.0	26.7			
Greece	18	19	13.5	14.1	2003	16.3	9.5
Hungary	36	28	28.2	25.8	2003	24.1	27.4
Ireland	25	25	19.5	20.5			
Italy			21.8	24.9			
Latvia	37	19	28.9	21.1	2002	30.2	22.1
Lithuania	24	10	34.9	17.9	2001	29.0	20.5
Malta			16.9	17.4			
Netherlands			22.5	24.3			
Poland	27	20	26.3	17.0	2003	20.8	14.3
Portugal	19	14	17.6	26.2			
Romania					2004	16.8	12.8
Slovakia	28	18			2003	31.3	28.8
Slovenia			29.5	29.7	2003	24.2	28.8
Spain			23.6	32.3			
Sweden	18	24	11.1	19.0			
United Kingdom	25	33	21.1	27.9			

3.13.3.2. Gender differences

The prevalence of weekly smoking among 15-year-old girls was higher than that of 15-year-old boys in 16 mainly Western European countries of those that implemented the HBSC study in 2001/2002 (Austria, Belgium, the Czech Republic, Denmark, Finland, France, Greece, Ireland, Italy, Malta, the Netherlands, Portugal, Slovenia, Spain, Sweden and the United Kingdom). In Austria, Belgium, Sweden and the United Kingdom, this difference was even greater than in the late 1990s. In the remaining (mainly Eastern European) countries (Estonia, Hungary, Latvia, Lithuania, Poland), smoking prevalence in girls was lower, but in many of these 10 countries, it was catching up and, in two countries (Czech Republic and Hungary), even overtaking smoking prevalence in boys. The GYTS data in general confirmed the pattern of higher rates of smoking prevalence among boys than girls in Eastern Europe.

3.13.3.3. Changes in smoking prevalence

Sixteen countries implemented the HBSC survey both in 1997/1998 and 2001/2002.

A comparison of the results from these two surveys shows that weekly smoking prevalence rates in 15-year-old boys decreased in 11 (mostly western European) countries of the 16 countries, increased in four countries and remained stable in one. The picture among 15-year-old girls is quite similar: weekly smoking prevalence rates decreased in nine out of the 16 countries, and increased in seven.

A calculation of the averages from these two HBSC surveys shows that the average weekly smoking prevalence among 15-year-old boys and girls did not change significantly between the two periods, although a slight downward trend in boys and a slight upward trend in girls can be observed.

3.13.3.4. Conclusions on smoking according to different groups of young people

Weekly smoking rates among children and adolescents living in the European Union increase four-fold from about 2% at age 11 to 8% at age 13, and another 3-fold increase to 24% at age 15. The highest rates among boys are found in some Eastern EU countries whereas the highest rates among girls are seen in some Western EU countries. From the year 2000, non-significant trends towards decreased smoking among boys and increased smoking among girls have been observed. Smokeless tobacco use is common among adolescent boys in the Nordic countries but rare elsewhere.

Referring to section 3.12 it is clear that the tobacco industry not only has aimed to target different groups of users through advertising and promotion. They have also manipulated the cigarettes themselves. We have very limited data on market share by brand. Top ten lists have only been found from the UK (2009) and Germany (2007). Detailed information on annual cigarette sales in individual EU countries can be purchased dearly from commercial sources[14].

However, even in those publications no data on brand preferences according to gender, age, ethnicity or culture/region are presented. Again, referring to section 3.12 it is conceivable that such information is collected by the manufacturers but treated as secrets of trade.

Information about top selling individual brands in EU countries is available from commercial sources. In the public domain, only limited data are available. Data on brand preferences according to gender, age, ethnicity or culture/region are almost non-existent

[14] http://www.euromonitor.com

with a couple of limited reports from the UK being the exception. Referring to section 3.12 it is conceivable that such information is collected by the tobacco companies but treated as trade secrets.

3.13.4. Conclusions on EU

European Union tobacco smokers prefer manufactured cigarettes. The overall adult daily estimated smoking prevalence (population-weighted) had stabilized at around 28.5% in 2005 (males 34.2%, females 22.6%) but higher rates were found mainly in Eastern European countries. Smoking rates had not changed significantly between 2002 and 2005. The prevalence of weekly smoking among 15-year-old girls was higher than that of 15-year-old boys in 16 mainly Western European countries whereas the opposite was found in most Eastern European countries. In some countries (e.g. the UK) a large proportion of smokers preferred cigarettes marketed as “additive free”. Significant use of oral tobacco was seen only in Sweden and the UK.

3.14. Gaps of knowledge

In a number of areas, it was felt that insufficient information was available concerning tobacco additives:

- Smoke composition of tobacco products other than cigarettes (cigars, cigarillos, waterpipes).
- Importance of different sugars for the addictive potency of nicotine and tobacco products.
- Objective measures for attractiveness of tobacco products and additives.
- Information about which brands are preferred by new smokers and the reasons for brand choice.

3.15. Research Recommendations

It is evident that advanced studies on the action of nicotine and tobacco additives need considerable financial resources that are generally not available in public laboratories. Technological advances have been made in recent years that permit new information to be obtained, for instance on smoke composition and neural networks (functional neuroimaging). We propose either calls for European collaborative projects addressing questions about nicotine and additives or the creation of a European Institute for testing and research on drugs of abuse. A better knowledge in these areas would allow evidence based regulation of the manufacture and marketing of tobacco products to be established. Among the potential research areas we would like to mention:

- Investigate the effect of different sugars with respect to their presumed pro-addictive potency: (1) mode of action, (2) relative efficacy of various sugars, (3) generation of relevant biologically active compounds in the smoke or following entry of acetaldehyde into the blood stream, (4) the capacity of different tobaccos (i.e. Burley vs. Virginia) to form acetaldehyde and inhibit MAO in situ.
- Investigate the reasons why certain brands (e.g. certain typical UK brands) are popular in some countries although no additives have been used in their manufacture and study whether cigarettes without additives are less addictive than those with additives.

- Perform innovative neuroimaging techniques to assess the attractivity of tobacco additives objectively. The methods should be sufficiently sensitive to detect the contribution of a single additive added to a tobacco product.
- Determine what makes a specific brand attractive for new smokers. Is it the image, popularity, peer influence or taste?
- Determine, by neuroimaging studies, whether nicotine alone (given as pills) induces signals in the brain of dependent smokers that are different from non-smokers.
- Determine in animal studies (e.g. by neuroimaging, neurochemical, and behavioural approaches) the influence of different tobacco additives on the addictive potential of nicotine. These studies are crucial to define the exact role of the multiple tobacco additives in the final high addictive potential of tobacco (in humans).

3.16. Conclusions

In the present report we have evaluated the available scientific evidence for the role of additives in the addictiveness and attractiveness of tobacco products. The main addictive substance in tobacco leaves is nicotine, but pure nicotine is only weakly addictive in animal studies, and great variations are found between individual animals. In humans, pure nicotine products are not very efficient for cessation of tobacco use and other substances in tobacco products are likely to play a role in addiction. The vast majority of tobacco products are consumed as cigarettes, and they typically contain around 10% additives by weight; mainly sugars, humectants and various flavours. Most of the additives are used in small amounts. We have indicated various gaps of knowledge and made some recommendations for research in order to permit filling the gaps. In the following opinion chapter (section 4), we summarise the scientific evidence detailed in the previous sections in order to answer the questions concerning the contribution of additives to addictiveness and attractiveness of tobacco products.

4. OPINION

In the light of the most recent scientific information, the Scientific Committee is requested to answer the following questions:

1. Which are the criteria which will define whether an additive or a combination of additives increases the addictive potency of the final tobacco product?

In human studies there are clinical criteria for dependence (e.g. DSM, difficulty in quitting), laboratory measures of self-administration (e.g. neurobiological measures) and smoking frequency and depth of inhalation, as well as preference studies. These criteria indicate that tobacco in humans has a high addictive potential, but they have limitations when assessing the addictiveness of individual additives in the final tobacco product. There is no widely-agreed universal standard for human studies and as a result various possible endpoints exist. An addicted individual can be considered as someone who is suffering from a specific set of chronic conditions related to a modification of the regulation of their neural networks. It is the potential to induce these modifications which should be the criteria used to define the addictive potency of a product.

In animal studies the reinforcing potency of a drug is used as a criterion for addictive potential. However, some self-administration studies indicate that nicotine could have a weak addictive potential. At present it is not possible to evaluate whether additives increase the addictive potency of the final tobacco product. Drugs of abuse such as nicotine induce different types of behavioural and neurochemical dysregulations in animal studies but no consensus about which of those are directly related to the addiction process in humans has yet been attained among scientists.

In conclusion, the criteria for defining dependence indicate that tobacco is highly addictive in humans. Animal studies that use intravenous administration show that nicotine could have a weak addictive potential. An evaluation of the role of additives has not yet been done in animals.

2. What are the methods currently used for assessing the addictive potency of a substance and are they considered adequate?

Many different methods are used in humans, but there is a lack of consistency between these methods. Human studies have many limitations in design (e.g. the use of conditioned cues and the need to work with smokers). Furthermore, ethical issues may arise when testing substances in humans.

There is currently no animal model to assess the addictive potency of the final tobacco product; however, pure nicotine has been studied extensively.

The methods currently used in animals to evaluate the addictiveness of any drug of abuse, including nicotine, are mainly based on the evaluation of the re-inforcing properties of the drug. These experimental animal models are mainly based on self-administration protocols in rodents, usually rats. The model with the highest predictive validity is the operant self-administration paradigm. A response which is easy to evaluate is the break point. This is defined as the highest number of responses that the animal completes in order to obtain a single delivery of a drug. A higher break point represents a direct measure of the motivation of the animal to obtain the drug and is often taken to imply an increase in the addictive potency of the drug.

Other models have also been used, such as the intracranial self-stimulation and the conditioned place preference paradigms. New complex behavioural models that resemble the main diagnosis for drug addiction in humans have been developed very recently, although these new models can only be applied for some particular drugs and experimental conditions at the present moment. The methods have additional limitations as in animal studies pure nicotine is injected intravenously and shows only a weak addictive potential whereas in humans tobacco is used differently (e.g. inhalation, oral consumption). The operant self-administration paradigm has been widely accepted as a reliable animal model with high predictive value for the abuse liability of a drug and therefore, possibly also for its addictive potential in humans. However, a consensus between scientists has not yet been attained on whether this method, which is appropriate to define the abuse liability, would also be the most suitable method to define the addictive potential of a drug.

In conclusion, there are many methods for assessing the addictive potency of a substance in humans, but they have limitations in design and ethical issues may arise. Animal studies using self-administration protocols evaluate the reinforcing properties after intravenous injection of the drugs but there is no consensus concerning the most suitable method for defining the addictive potential. The current methods can thus not be considered adequate.

3. Is the development of nicotine addictiveness dose-dependent?

In humans, there are little data available on pure nicotine use. However, when consumed in tobacco, frequency of use (number of cigarettes smoked per day) is positively correlated with dependence. This suggests that individuals who maintain higher nicotine levels in blood are more dependent than individuals who maintain low levels.

Based on the criteria described in Question 1, dose-dependency appears to have been shown in animal studies. In general, an inverted U-shaped dose-response has been revealed in animals, suggesting that the addictiveness of nicotine is not directly linear with the dose. In addition, pure nicotine is only weakly addictive in some animal studies.

There is substantial variation in response to nicotine and addictive potential in both animals and humans, and genetic factors probably play an important role.

4. Which additives are addictive by themselves in tobacco products?

No tobacco additives, which are addictive by themselves, have so far been identified. However, sugars, added in high quantities to most tobacco products, give rise by pyrolysis to acetaldehyde which is self-administered by animals.

However, experiments using denicotinised cigarettes show that besides nicotine, a mixture of factors in cigarette smoke probably plays an important role in craving and reinforcement. Although these unknown factors do not have pharmacological effects similar to nicotine and are probably not addictive, they definitely play a role in smoking behaviour.

5. Which additives enhance the addictiveness of nicotine and how?

A large percentage of the additives found in tobacco are sugars, or their derivatives, that by pyrolysis produce numerous toxic substances, including different combinations of aldehydes, one of which is acetaldehyde. Acetaldehyde injected into experimental animals enhances the addictiveness of nicotine, probably by inhibiting monoamine oxidase (MAO) in the brain. Smokers have decreased levels of MAO in the brain. However, there is no proof that acetaldehyde in the smoke contributes significantly to blood levels of acetaldehyde. This does not exclude that there is a biological effect of acetaldehyde, possibly by generation of harman and norharman that also may inhibit MAO.

Additives that facilitate deeper inhalation (e.g. menthol) may enhance the addictiveness of nicotine indirectly. Other substances may enhance the addictiveness of nicotine by inhibiting its metabolism. Substances such as ammonia that increase the pH of the tobacco (and the smoke) result in higher amounts of uncharged nicotine, that is more easily absorbed by the cells. However, due to the high buffer capacity of the lining fluid in the lungs it is uncertain if more nicotine is absorbed with higher smoke pH. It is unlikely that additives in smoked tobacco would increase nicotine blood levels sufficiently to enhance the addictive potential of the tobacco product. For smokeless tobacco it has been shown that more nicotine is absorbed in the mouth when the pH of the product is increased.

In conclusion, apart from the possible action of combustion products of sugars (acetaldehyde and similar compounds that enhance the action of nicotine by inhibition of MAO), there is no evidence that additives enhance the addictiveness of nicotine and therefore of tobacco.

6. Which are the methods used to quantify the potency of additives in enhancing the addictiveness of nicotine and are they considered adequate?

The methods used to quantify the potency of additives to enhance the addictiveness of nicotine or tobacco, are described in the answer to question 2. The limitations of these methods arise from technical challenges in experimentally manipulating the presence or absence of an additive in the tobacco products used in these experiments. Such experiments have probably been carried out by the tobacco industry for some additives, especially sugars and their derivatives, but they require technical and financial resources that are not generally available except to the tobacco industry. In addition, there are ethical issues if testing in humans is considered.

In conclusion, the methods used to quantify the potency of additives in humans or animals have limitations, and the available methodologies are thus not considered adequate for a reliable quantification.

7. Which technical characteristics enhance the addictive potential of tobacco products?

A number of technical characteristics of cigarettes influence the content of different substances in the smoke and the size of smoke particles. The so-called TNCO values (tar, nicotine and carbon monoxide) are determined by, amongst other things, ventilation (paper, filter), the packing of the tobacco and the geometry of the cigarettes. Smokers usually compensate for a lower dose of nicotine by increasing puff volume and frequency, and by deeper inhalation. In order to achieve the desired level of nicotine impact many smokers apparently take more puffs and inhale deeper when smoking low nicotine cigarettes.

A change of the technical characteristics of cigarettes may affect the mean particle size and, therefore, the distribution of the smoke aerosol. However, based on the limited publicly available information, it seems that exposure to nicotine cannot be substantially increased by altering the particle size of the smoke aerosol.

In conclusion, it does not seem that technical characteristics can enhance the addictive potential of tobacco products.

8. Which are the criteria based on which an additive or a combination of additives can be considered (classified) attractive?

The criterion of attractiveness is the stimulation to use the product.

Attractiveness of additives refers to factors such as taste, smell and other sensory attributes. In addition, a number of external factors (e.g. ease of use, flexibility of the dosing system, cost etc.) contribute to the attractiveness of the product.

The attractiveness of tobacco products may be increased by a number of additives. Many different additives are used to create a specific taste/flavour in order to attract certain target groups. An attractive effect may be obtained by changing the appearance of the product and the smoke, decreasing the harshness of the smoke, and inducing a pleasant experience of smoking. The sweetness of the smoke is an important characteristic for certain users. Finally, in order to make smoking more acceptable to other people nearby, some additives have the function of reducing lingering odour or side-stream smoke visibility.

In conclusion, many different factors influence the attractiveness of tobacco products, not only the additives used but also a number of external factors.

9. What are the methods currently used for assessing attractiveness and are they considered adequate?

Animal models do not currently exist to allow the assessment of attractiveness.

There are two main ways of examining the influence of additives on the attractiveness of a product which have largely been conducted by tobacco industry.

The first is to assess individual tobacco products and compare their attractiveness against other tobacco products on a number of scales/dimensions. By then examining what is known about the additive content of these products, judgements can be made as to the role of individual additives in the overall attractiveness of the product. This can be done using a variety of research methods, such as panel studies and surveys, experimental measures and human testing.

The second is to examine the influence of individual additives or combination of additives on attractiveness of a tobacco product, along a number of scales, by experimentally adjusting tobacco products to include or exclude individual additives and testing responses to them. In addition, the quantity of the additive can be varied to assess dose response and whether there is a threshold below which any impact is not observed.

The difficulties with this type of research include ethical considerations that will usually preclude human testing of different tobacco products, particularly among non-users or children.

In conclusion, it is only possible to assess attractiveness in humans, and this may be done by comparison of different products used or by adjusting tobacco products experimentally. However, such studies in human subjects are difficult to carry out due to ethical considerations and the current methods are thus not considered adequate for a reliable quantification of attractiveness in humans.

10. Which additives increase attractiveness of tobacco products?

Numerous additives are used in order to increase the attractiveness of tobacco products.

Various sugars constitute a large proportion of additives, and the sweetness of the smoke is an important characteristic of the product.

Some additives are used to attract certain target groups, because they give the product a specific taste/flavour particularly appreciated by the target group. The best known example is menthol (African Americans) and the use of fruit and candy flavours in high amounts to favour smoking initiation by young people.

A number of additives decrease the harshness and increase the smoothness of the smoke. As a result the smoke inhaled is less aversive, cooler and milder, which improves the experience of smoking and promotes smoking initiation. The harshness depends partly on the tar/nicotine ratio, but may also be decreased by additives such as propylene glycol and glycyrrhizin, a substance in liquorice. Menthol, due to its local anaesthetic effect may enable a deeper inhalation of the smoke. It also acts on sensory nerve endings, resulting in a cooling effect appreciated by smokers.

For cigarettes, certain additives yield a full and white smoke (for example, magnesium oxide, magnesium carbonate, sodium acetate, sodium citrate, calcium carbonate). Other additives reduce the lingering odour of the smoke in order to favour the acceptability of smoking to people around (for example, acetylpyrazine, anethole, limonene, vanillin, benzaldehyde).

In conclusion, many different additives have been used to increase the attractiveness of tobacco products but it is very difficult to identify the role of individual additives in enhancing attractiveness. In several countries there is a growing trend of using "natural" tobacco products advertised as containing no additives.

11. What is the association between additives and tobacco consumption (independent of any addictive potential they might have)? Which additives are used to target specific groups?

Additives considered attractive may in principle lead to brand preference or a higher consumption of tobacco products, although it is difficult to disentangle the direct effects of additives from indirect effects such as the marketing of specific products at specific groups. For example, the consumption of menthol cigarettes is much higher among African Americans in the USA than among other populations, while flavourings (e.g. fruit and candy) appear to be targeted at young people.

It is notable that waterpipe smoking is becoming increasingly popular in some EU countries (and elsewhere), potentially due to the flavoured tobaccos used and the mild smoke, which facilitate the inhalation of large volumes into the lungs. Smokeless tobacco products have gained increased interest from the tobacco industry because they may be used in places where smoking is prohibited.

Additives and design characteristics may modify consumption patterns, theoretically in a way which may impact on uptake of tobacco use and/or the development of dependence. However, in spite of the many additives commonly used, tobacco products openly marketed as containing specific additives (e.g. menthol cigarettes) command a relatively small market share in EU countries and in some markets so-called natural tobacco products are becoming popular.

In conclusion, additives have been used largely by the tobacco industry to target specific groups. However, the effect of marketing is probably very important and there is currently a trend in several countries to use products labelled "without additives".

Gaps in knowledge:

- Smoke composition of tobacco products other than cigarettes (cigars, cigarillos, waterpipes).
- Importance of different sugars for the addictive potency of nicotine and tobacco products.
- Objective, quantitative measures for attractiveness of tobacco products and additives.

- Information about which brands are preferred by new smokers and the reasons for brand choice.
- Why are certain brands, apparently without additives, popular in certain countries (UK)?
- Effect of pure nicotine in smokers and non-smokers (neuroimaging).
- Effect of nicotine and additives in experimental animals (neuroimaging).
- Role of substances other than nicotine and in the absence of nicotine, on the use of tobacco.

Recommendations:

- European funding of research on nicotine/European research institute.
- Investigate effect of sugars when pyrolysed.
- Perform epidemiogical/sociological studies on trends.
- Investigate effect of nicotine and other substances, in particular by functional neuroimaging in animals and humans.
- Analyse constituents of tobacco smoke.

5. MINORITY OPINION

None

6. LIST OF ABBREVIATIONS

Ach	Acetylcholine
AM251	N-(piperidin-1-yl)-5-(4-iodophonyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide
AMPA	α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
APA	American Psychiatric Association
ASH	Action on Smoking and Health
BAT	British American Tobacco
BfR	Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment)
BN	Bates Number
BZgA	Bundeszentrale für gesundheitliche Aufklärung (Federal Centre for Health Education)
CAS	Chemical Abstracts Service
CB1	Cannabinoid receptor
CDC	Centers for Disease Prevention and Control

CLD	Cased Leaf Dryer
CMD	Count median diameter
CNRS	Centre national de la recherche scientifique (French National Center for Scientific Research)
CNS	Central nervous system
CO	Carbon monoxide
CSERP	Chemosensory event-related potential
CYP	Cytochrome P450 monooxygenase
DA	Dopamine
DAP	Diammonium hydrogen phosphate
DKFZ	Deutsches Krebsfoschungszentrum (German Cancer Research Center)
DNA	Deoxyribonucleic acid
DSM(-IV)	Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition)
EC	European Commission
ECDC	European Centre for Disease prevention and Control
ECHA	European Chemicals Agency
EEG	Electroencephalography/Electroencephalogram
EFSA	European Food Safety Authority
EMA	European Medicines Agency
EMTOC	Electronic Model Tobacco Control
EU	European Union
FCTC	Framework Convention on Tobacco Control
FDA	(United States) Food and Drug Administration
fMRI	Functional Magnetic Resonance Imaging
FTND	Fagerström Test for Nicotine Dependence
GABA	Gamma (γ)-Aminobutyric acid
Glu	Glutamate
GM	Genetically modified
GYTS	Global Youth Tobacco Survey
HBSC	Health Behviour in School-aged Children
5-HT	5-Hydroxytryptamine
IARC	International Agency for Research on Cancer
IC_{50}	The half-maximal inhibitory concentration
ICD	International Classification of Diseases
ICRP	International Commission on Radiological Protection
i.v.	Intravenous
JTI	Japan Tobacco Inc.
LD_{50}	Median lethal dose
MAO	Monoamine oxidase
mGlu5	Metabotropic glutamate 5

mGlu2/3	Metabotropic glutamate 2/3
MMD	Mass median diameter
MRI	Magnetic resonance imaging
mRNA	Messenger ribonucleic acid
MS	Member State(s)
NAc	Nucleus accumbens
nAChR	Nicotine acetylcholine receptor
NCI	National Cancer Institute
NMDA	N-Methyl-D-aspartate
NNAL	4-N-(Nitrosomethylamino)-1-(3-pyridyl)-1-butanol
NNAL-Gluc	NNAL-Glucuronide
NNK	4-N-(Nitrosomethylamino)-1-(3-pyridyl)-1-butanone
NRT	Nicotine replacement therapy
ONS	Office for National Statistics
pH	Measure of acidity or basicity of a solution
pKa	Dissociation constant – measure of the strength of an acid or a base
PMI	Philip Morris International
ppm	parts per million
PPTg	Pedunculopontine tegmental nucleus
PREP	Pattern reversal evoked potential
QNE	Quantity not exceeded
RECON	Reconstituted tobacco
RIVM	Rijksinstituut voor Volksgezondheid en Milieu (The Netherlands National Institute for Public Health and the Environment)
RYO	Roll your own
SCCS	Scientific Committee on Consumer Safety
SCENIHR	Scientific Committee n Emerging and Newly Identified Health Risks
SCHER	Scientific Committee on Health and Environmental Risks
STRATUS	Studies with Rimonabant and Tobacco Use
$T_{1/2}$	Half-life
TNCO	Tar, nicotine and carbon monoxide
TRPM8	Transient receptor potential channel
UK	United Kingdom
US(A)	United States of America
UV	Ultraviolet
VTA	Ventral tegmental area
WHO	World Health Organization

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8. GLOSSARY

Abuse liability	Abuse liability of a drug is the likelihood that its use will result in addiction (dependence) and it can be assessed in laboratories by methods referred to as abuse liability testing.
Additives	The present report uses the term additives for added ingredients or substances. Additives are defined as any substance that is added except water, during the course of manufacture of a tobacco product, including preservatives, humectants, flavours, and processing aids.
Addiction	Addiction is the commonly used term referring to what is technically known as "dependence" and is widely employed to connote severe substance dependence.
Addictiveness	Addictiveness refers to the pharmacological potential of a substance to cause addiction.
Agonist	A ligand for a receptor which induces a response, identical or partial to the response obtained with the endogenous ligand.
Attractiveness	The terms "attractiveness" or "consumer appeal" refer to factors such as taste, smell and other sensory attributes, ease of use, flexibility of the dosing system, cost, reputation or image, assumed risks and benefits, and other characteristics of a product designed to stimulate use.
Break point	Highest number of responses that the animal accomplishes to obtain a single delivery of a drug.
Bronchodilatator	A substance that dilates the bronchi and bronchioles.
Casing	Casing refers to the sauce composed of a variety of ingredients such as humectants, sugars, cocoa, liquorice and fruit extracts which is applied to tobacco during the manufacturing process.
Conditioned cue	Neutral stimulus that associates with a reward. Used in abuse liability testing.
Curing	Curing is the process for drying freshly harvested tobacco with partially or fully controlled temperature and moisture schedules.
CYP2A6	It is an abbreviation of Cytochrome P-450 2A6 (family 2, subfamily A, polypeptide 6), a constitutent of the endoplasmic reticulum P-450 mixed function oxidase system. CYP2A6 is the main enzyme system involved in the oxidative metabolism of nicotine and cotinine, as well as many other xenobiotics and pharmaceuticals. A significant interindividual variability in CYP2A6 and mRNA levels has been observed in humans and other mammals
Denicotinised	The removal or reduction in the nicotine content of tobacco, for example by means of blending genetically-modified tobacco which has been engineered to lack nicotine.
DSM	Diagnostic and Statistical Manual of Mental Disorders. Published by the American Psychiatric Association (USA) provides standard criteria for the classification of mental disorders. It is used in the United States and in varying degrees around the world. It is not exempt of scientific criticism in many countries
EEG	Electroencephalogram.

GABA receptor	An oligomeric class of neuron membrane receptors to which the γ–aminobutyric acid (GABA), the major inhibitory neurotransmitter in the brain, binds.
Harman	A beta-carboline that is formed in smoke by interaction between acetaldehyde and tryptophan. It inhibits the enzyme monoamine oxidase (MAO).
Harshness	A chemically induced physical effect associated with a roughness, rawness experience generally localized in the mouth and to a lesser degree in the upper reaches of the throat and the trachea due to inhalation of tobacco smoke. It can cause a drying, rasping, coarse, astringent sensation.
Hyperlocomotive effect	Increase in locomotor activity usually recorded in rodents.
IC50	Inhibitory concentration 50. The concentration of a compound that inhibits 50% a given maximal response (biological, biochemical, etc)
Ingredients	see Additives. The present report uses the term additives for added ingredients or substances.
LD50	Lethal dose 50. Dose of a compound that kills 50% of a group of administered animals (it represents a probabilistic concept).
Manipulandum	Device used in experimental settings in order to transmit an active response. In the present report the device is used to measure self-administration of drugs in experimental animals.
MAO	Monoamine oxidases exist in two forms, A and B. They metabolize monoamines such as noradrenaline, dopamine and serotonin.
Metabolism	The chemical processes occurring within a living cell or organism that are necessary for the maintenance of life. In metabolism some substances are broken down to yield energy while other substances are synthesized.
Narghile or shisha	Expressions for the Oriental waterpipe.
Norharman	Condensation product in smoke that inhibits the enzyme monoamine oxidase (MAO). See also harman.
pH	Measure of the acidity or alkalinity of a solution, numerically equal to 7 for neutral solutions, increasing with increasing alkalinity and decreasing with increasing acidity. The pH scale commonly in use ranges from 0 to 14.
P450 enzyme system	The cytochromes P450 are hemproteins and important constituents of the so-called monooxygenase system
Pyrolysis	Chemical decomposition of condensed substances that occurs spontaneously at high enough temperatures.
Receptor	Protein or protein complexes present in the cell membranes (plasmatic, endoplasmic or nuclear) or the cytoplasm to which physiological signaling molecules, e.g. neurotransmitters, hormones, etc., drugs and xenobiotics specifically, bind.
Reinforcement	Ability of a stimulus to promote behavioural responses in order to obtain (positive reinforcement) or to avoid (negative reinforcement) such a stimulus.
Rewarding	stimuli that have appetitive (desirable) consequences and/or produce a hypothetical pleasurable internal state (hedonia)
Self-administration	Experimental procedures that allow the animal/human to

	administer himself a drug. Self-administration methods are widely used to directly evaluate the reinforcing properties of a drug.
Smoothness	Reduction in the harsh irritation of nicotine-containing tobacco smoke.
Uncharged	Used e.g. for nicotine to describe the free base, that under acidic conditions (lower pH) may be charged (protonated) with one or two protons.

E-cigarette use as a predictor of cigarette smoking: results from a 1-year follow-up of a national sample of 12th grade students

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ABSTRACT

Objective To prospectively examine vaping as a predictor of future cigarette smoking among youth with and without previous cigarette smoking experience. A secondary aim is to investigate whether vaping may desensitise youth to the dangers of smoking.

Methods Analysis of prospective longitudinal panel data from the nationally representative Monitoring the Future study. The analysis is based on 347 12th grade students who were part of a randomly selected subsample that completed in-school surveys in 2014 and were resurveyed 1-year later.

Results Among youth who had never smoked a cigarette by 12th grade, baseline, recent vapers were more than 4 times (relative risk (RR)=4.78) more likely to report past-year cigarette smoking at follow-up, even among youth who reported the highest possible level of perceived risk for cigarette smoking at baseline. Among 12th grade students who had smoked in the past but had not recently smoked at baseline, recent vapers were twice (RR=2.15) as likely to report smoking in the past 12 months at the follow-up. Vaping did not predict cessation of smoking among recent smokers at baseline. Among never-smokers at baseline, recent vapers were more than 4 times (RR=4.73) more likely to move away from the perception of cigarettes as posing a 'great risk' of harm, a finding consistent with a desensitisation process.

Conclusions These results contribute to the growing body of evidence supporting vaping as a one-way bridge to cigarette smoking among youth. Vaping as a risk factor for future smoking is a strong, scientifically-based rationale for restricting youth access to e-cigarettes.

INTRODUCTION

Use of e-cigarettes (vaping) among US high school students has increased rapidly in recent years. Any vaping in the past 30 days as of 2015 was 16% among 12th graders, 14% among 10th graders, and 10% among 8th graders.[1] This is rapid growth from a 30-day prevalence of near 1% among secondary school students in 2011.[2] As prevalence has increased so too has concern that vaping among school-aged adolescents may be a bridge to future use of traditional combustible cigarettes.

Evidence is building to bolster this concern. Prospective observational studies provide some of the strongest possible scientific evidence to assess vaping as a risk factor for smoking. To date, five such studies based on US samples have examined the issue and all find vaping to be an independent predictor of smoking initiation. Among youth who had never smoked at baseline, the odds of incident smoking were 1.75–2.87 times higher among youth who vaped compared with those who did not among 9th and 10th grade students,[3–5] and odds were >6 among 12th grade students.[6] Among a panel of Hispanic youth at mean age 23, odds of incident smoking 1-year later were more than three times higher among vapers.[7]

This finding is robust across research designs. The studies noted above are all school-based samples that originally surveyed respondents in schools and then followed them longitudinally. An analysis that used random digit dialling to recruit participants nationally throughout the USA found odds of incident smoking to be more than eight times higher for vapers among a sample aged 16–26.[8]

Importantly, in all these studies vaping remains a significant predictor of smoking incidence after taking into account potential confounders such as baseline smoking susceptibility. In fact, a recent analysis indicates that vaping had the greatest predictive power for incident smoking among adolescents who had the *lowest* propensity to smoke at baseline.[9]

This study focuses on vaping as a risk factor for smoking among 12th grade students originally surveyed in schools in 2014 and contributes to the field in three ways. First, to the best of our knowledge we report the first results on this topic from a sample of schools selected to be nationally representative. All current school-based samples on the topic sample a specific US state or city, and replication of results from existing studies with a national, school-based sample strengthens the case for all these studies to directly inform national policy and regulation.

Second, the analysis examines perceived risk of harm from cigarette use as both a baseline confounder and also a possible intervening mechanism connecting vaping with future smoking. Perceived risk of harm predicts use of a wide variety of substances[10–12] and is substantially associated with cigarette smoking.[13] Evidence that baseline levels of perceived risk from cigarette smoking do not 'explain away' the finding of vaping as an independent predictor of future smoking would show that the finding is robust across different, major measures of smoking propensity. In addition, evidence that vaping predicts later reductions in perceived risk of smoking would be an important step towards the identification of a possible desensitisation process that would help explain how vaping is connected to later smoking. Finally, we examine vaping as a predictor of future smoking among

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youth with past cigarette smoking experience, a group that has received relatively less attention than never-smokers. This is a preliminary step to consider whether vaping leads this group of youth away from smoking or not.

METHODS

Data

Data come from the annual Monitoring the Future (MTF) study, which since 1975 has used questionnaires administered in classrooms to survey nationally representative samples of US 12th graders in the 48 contiguous states.[12 14] The project has been approved by the University of Michigan Institutional Review Board. The target sample is all schools in the contiguous USA that enrol 25 or more 12th grade students, and in 2014 the study surveyed 122 schools (105 public and 17 private). In 2014, 13 015 12th grade students completed questionnaires, for a response rate of 82%. Almost all non-response was due to school absences. This non-response did not lead to a substantial upward or downward bias of the study's prevalence estimates for smoking and vaping in comparison to other nationally representative, school-based surveys.[15 16]

The geographical areas sampled included the 28 largest metropolitan areas containing about one-third of the nation's population, as well as 136 other primary areas. In 2014, either an original school or a replacement school was obtained in 92% of the sample units.

This analysis uses information from 347 follow-up participants in 2015. Figure 1 presents information on how they were selected. Every year a random subsample of 2450 members of the 12th grade class is selected to participate in a panel that receives follow-up surveys. Questions on vaping were included on four of the six forms of the survey (the forms are randomly distributed in equal proportions). Consequently, 1643 (~2/3) of the 2450 respondents selected for follow-up were eligible for the analyses. To reduce respondent burden the panel is split into two random halves, with one half receiving questionnaires in even years and the other in odd years. In 2015 out of the 822 target panel respondents 347 provided sufficient information to be included in the analyses, for a response rate of 42% at modal age 19. Only respondents who had complete information on their 2015 cigarette smoking status were retained in the final analyses (97% of responders). Of these, the average length of the follow-up period was 13.40 months (with a 95% CI of 13.23 to 13.57). Online supplementary tables A1 and A2 in the Appendix provide more detailed information on the sample size of the analysis pool.

Statistical analysis

We developed and used attrition weights to control the potential influence of panel attrition. The attrition weight was the inverse of the predicted probability of follow-up response, based on a regression equation modelling panel retention as a function of respondents' baseline characteristics, which are defined in table 1. Final weights were calculated as this attrition weight multiplied by a weight used to control the panel's intentional oversampling of individuals with higher levels of illicit drug use at baseline.[17]

Online supplementary table A3 in the Appendix shows that with use of the attrition weights none of the baseline variables differed for the follow-up responders as compared with the target sample. The attrition weights took into account a higher likelihood of response for women and whites, as well as respondents with lower levels of substance use.

To control for missing item-level data among follow-up respondents the analysis used multiple imputation with 20 imputed data sets,[18] in conjunction with the survey weights. The imputation process had little effect on the study results because item-level missing data were uncommon (92% of the 347 respondents had complete information on all analysis variables). In a parallel analysis that used list-wise deletion instead of multiple imputations all statistically significant differences remained, in the same direction, across the two analyses. Likewise, all significant differences remained and were in the same direction when the attrition weights were not used, both in analyses with and without multiple imputation.

The main analyses consist of two main components. First, tables 2 and 3 examine vaping as a predictor of future smoking (detailed results presented in the online supplementary tables A4 and A5). The predictive power of vaping may differ by respondents' past level of smoking experience and/or perceived risk of harm from smoking cigarettes, and consequently the analyses are stratified by these factors. Stratification also controls any potential differential sample attrition by these factors. The multivariable models include additional controls for demographics as well as baseline levels of marijuana use and binge drinking, which serve as measures of proclivity for general substance use. The second component of the analyses examines vaping as a predictor of decreases in perceived risk of smoking, to examine whether vaping desensitises youth to the dangers of smoking cigarettes.

RESULTS

Table 1 presents the proportions and definitions of the study variables. The prevalence of vaping ranked among the highest of all substance use,[19] and prevalence of recent vaping (in the past 30 days) was about 50% higher than prevalence of recent smoking (smoked combustible cigarettes in the past 30 days). Cigarette smoking was considered harmful by most, with the percentage seeing great risk in smoking one or more packs of cigarettes per day over 80% at both the baseline and follow-up surveys.

Table 2 presents incidence of cigarette smoking among respondents who had never smoked a cigarette up to the time of the 12th grade survey. For this group, the incidence of smoking within the past 12 months in 2015 was about four times higher for youth who vaped at baseline as compared with those who did not, at 31% and 7%, respectively (model 1). This difference remained after statistically controlling the potential confounders of sex, race, and parental education. Among the group of new smokers at follow-up who had recently vaped at baseline, all reported that they had smoked cigarettes at the level of 'once or twice' in the past 12 months at follow-up.

Model 2 of table 2 presents results for the subgroup of never-smokers who at baseline saw great risk in cigarette smoking. This group would presumably be the least likely to consider cigarette smoking in the future. Even among this group, recent vaping at baseline strongly predicted incidence of cigarette smoking in the following year.

Table 3 presents prevalence of any cigarette smoking in the past 12 months among respondents who had ever smoked a cigarette by the time of the 12th grade survey. For this group the prevalence of past 12-month smoking at follow-up was more than twice as high for baseline recent vapers compared with non-vapers at baseline, at 80% and 37%, respectively. This difference was statistically significant in bivariate and multivariable analyses.

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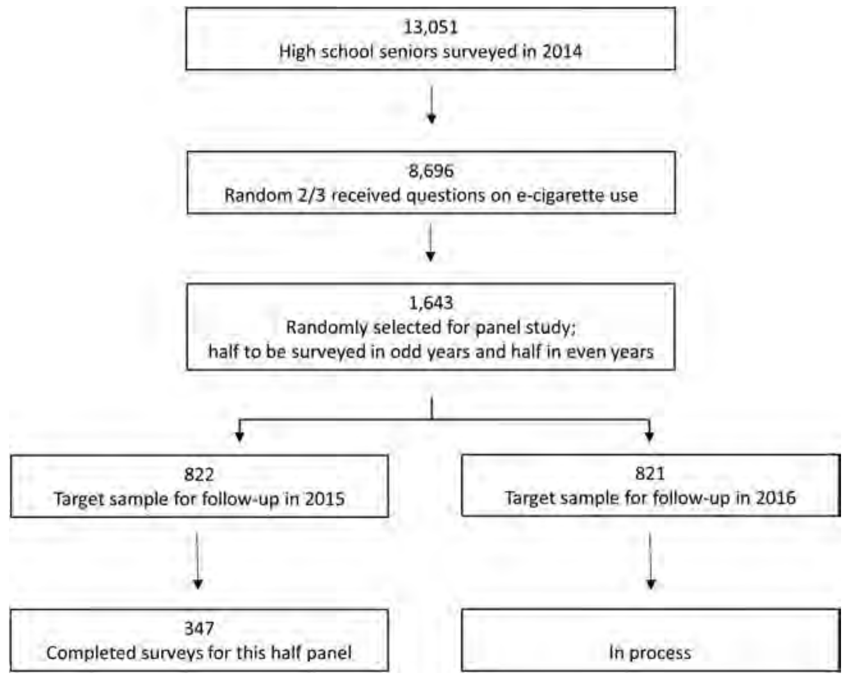

Figure 1 Flow chart for selection in the panel study.

Table 3 also presents results stratified by smoking activity in the 30 days prior to the 12th grade survey. Vaping significantly predicted cigarette smoking in the past 12 months at follow-up among youth who had smoked in the past but not recently (63% vs 27%), but did not reach significance among youth who had smoked recently (95% vs 77%). To test whether the predictive power of vaping was significantly different across these two groups of youth we modelled past 12-month prevalence at follow-up as a function of baseline recent vaping, baseline recent smoking, and the multiplicative interaction between these two dichotomies. The significance level of the interaction term was $p<0.062$, which meets criteria as 'statistically significant' to the extent that multiplicative interaction terms warrant higher probability cut-offs.[20]

Among youth with past smoking experience the analysis examined potential differences by level of past cigarette use (analyses not presented in the tables). About half (50.73%, SE=5.06) of the non-recent smokers in 12th grade were experimental smokers who reported that they had smoked a cigarette just 'once or twice' in their life. For this subgroup vaping was a significant predictor of past-year smoking at the follow-up survey (bivariate relative risk=2.75; 95% CI 1.17 to 6.76). The other half of youth with past smoking experience reported that before 12th grade they smoked 'occasionally but not regularly' or 'regularly in the past'. For this subgroup vaping was not a significant predictor of past-year smoking in the follow-up survey (bivariate relative risk=1.60; 95% CI 0.88 to 2.91). However, the relative risk estimates did not significantly differ across the two groups, making these differences across the two groups only suggestive (relative risk differences tested with a multiplicative interaction term in a model that included all past smokers).

Table 4 presents baseline recent vaping as a predictor of changes in perception of cigarette smoking away from 'great risk' to a lower level during the study period. Among respondents who had never smoked a cigarette by the 12th grade survey, recent vapers compared with non-vapers were four times more likely to move away from the view that cigarette smoking poses a 'great risk'. This predictive association was statistically significant in bivariate and multivariable models both of all never-smokers as well as never-smokers who saw 'great risk' in cigarette smoking at the baseline survey. No predictive association for recent vaping on risk perception was present among respondents who had ever smoked cigarettes at the baseline survey.

DISCUSSION

Two aims motivated this study. The first was to examine vaping in 12th grade as a predictor of future smoking of traditional combustible cigarettes, among youth with and without smoking experience at baseline. The second was to examine whether youth who vaped later downgraded their perception of the risks of smoking. Study participants were drawn from a nationally representative sample of students in US private and public schools in 2014 and followed up 1 year later in 2015.

Among 12th grade students who had never smoked combustible cigarettes, vaping strongly predicted smoking initiation a year later. First use of a combustible cigarette at follow-up was reported by 31% of those who had recently vaped at the baseline survey, as compared with 7% among those who did not. The analysis also examined the group of non-smokers who at baseline reported the highest level of perceived risk for smoking; these adolescents would be expected to have the lowest predisposition to start smoking cigarettes. Even among this group, recent vaping was a strong predictor of smoking initiation, which was 33% for vapers as compared with 7% among non-vapers.

Desensitisation to the dangers of smoking may play a role in explaining how vaping can progress to smoking among youth who have no history of cigarette use. Youth who begin to vape primarily to experiment and because vaping tastes good (the most common reasons for vaping[21]) may detect no immediate health consequences and conclude that the dangers of smoking are exaggerated. Empirical support for a desensitisation process comes from this study's finding that youth who vaped were significantly more likely to change their perception of the dangers of smoking away from 'great risk', among those who had never smoked at baseline.

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Table 1 Definitions and sample proportions for analysis variables (SEs in brackets)*

Variable	Percentage of follow-up subsample n=347
Variables measured at baseline in 2014	
Recently vaped	15.60
Coded 1 for response of at least 1 to the question 'During the last 30 days, on how many days (if any) have you used electronic cigarettes (e-cigarettes)?'.	(1.97)
See 'great risk' in smoking	80.88
Coded 1 for the response of 'great risk' to the question 'How much do you think people risk harming themselves (physically or in other ways) if they smoke 1 or more packs of cigarettes per day?'.	(2.28)
Never smoked a cigarette	71.05
Coded 1 for the response 'never' to the question 'Have you ever smoked cigarettes?'.	(2.49)
Recently smoked	10.13
Coded 1 for a response of '<1 cigarette a day' or more to the question 'How frequently have you smoked cigarettes in the past 30 days?'.	(1.68)
Female	56.26
Coded 1 for female respondents	(2.80)
Non-white†	39.89
Coded 1 for respondents who did not report that they were 'white (Caucasian)'.	(2.77)
Binge drinking in past 2 weeks	16.12
Coded 1 for a response of at least one to the question 'Think back over the last 2 weeks. How many times (if any) have you had 5 or more drinks in a row?'.	(2.00)
Recently smoked marijuana	18.93
Coded 1 for a response of at least 1 to the question 'On how many occasions (if any) have you used marijuana (weed, pot) or hashish (hash, hash oil) during the last 30 days?'.	(2.09)
Variables measured at follow-up in 2015	
See 'great risk' in smoking	83.05
Coded 1 for the response of 'great risk' to the question 'How much do you think people risk harming themselves (physically or in other ways) if they smoke one or more packs of cigarettes per day?'.	(2.13)
Changed perception of risk of smoking away from 'great risk'	11.12
Coded 1 for respondents who saw 'great risk' in smoking at baseline but not at follow-up.	(1.82)
Smoked in last 12 months at 1-year follow-up	21.75
Coded 1 for respondents who responded 'smoked once or twice', or more, to the question 'What best describes your cigarette smoking in the last 12 months?'.	(2.27)

Baseline questions on cigarettes ask about lifetime and past 30-day smoking, but not smoking in the past year.
*Estimates weighted for oversample of 12th grade students with high levels of drug use and for attrition.
†More detailed measures of race/ethnicity are precluded by small sample size.

Table 2 Smoking incidence at 1-year follow-up among 12th grade students who had never smoked traditional, combustible cigarettes, by baseline vaping (SEs and 95% relative risk CIs in brackets)†

Model	(1) All	(2) See 'great risk' in smoking cigarettes
n (weighted)	246	204
Recently vaped at time of 12th grade survey		
No	6.75 (1.70)	7.15 (1.96)
Yes	31.07 (14.00)	32.92 (14.99)
Bivariate relative risk‡	4.60** (1.71 to 12.34)	4.59** (1.67 to 12.63)
Adjusted relative risk‡	4.78** (1.91 to 11.96)	4.64** (1.66 to 12.93)

**p<0.01.
†Estimates weighted.
‡Differences across e-cigarette use groups modelled in a binomial regression with a log link. See online supplementary table A4 for detailed presentation of the controls in the models for adjusted relative risk.

The analysis also examined vaping as a predictor of cigarette smoking among students with smoking experience by 12th grade. Among those who had not recently smoked at the baseline survey, vaping strongly predicted any cigarette smoking in the past 12 months at the follow-up. In contrast, among students who were recent smokers at the baseline survey, the prevalence of past 12-month smoking at the follow-up did not differ significantly by vaping at baseline.

Health policy implications

Developing a rationale to regulate youth access to e-cigarettes will require more than a simple extension of the arguments used to regulate combustible cigarettes. Currently lacking for e-cigarettes is a developed body of scientific evidence documenting their health dangers, a body of evidence that exists for combustible cigarettes and plays a central role in the rationale for their regulation. The development of such evidence for the direct effects of

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Table 3 Prevalence of past 12-month smoking at 1-year follow-up among 12th grade students who had ever smoked, by baseline vaping status (SEs and 95% relative risk CIs in brackets)†

n (weighted)	All 101	Non-recent smoking at 12th grade survey‡ 66	Recent smokers at 12th grade survey‡ 35
Recently vaped at time of 12th grade survey			
No	37.44 (6.73)	27.45 (6.78)	76.93 (13.72)
Yes	80.18 (5.78)	62.70 (10.62)	94.86 (3.69)
Bivariate relative risk§	2.14** (1.46 to 3.14)	2.28** (1.27 to 4.10)	1.23 (0.87 to 1.73)
Adjusted relative risk§	2.15* (1.49 to 3.12)*	2.26** (1.22 to 4.18)	1.32 (0.89 to 1.96)

*p<0.05; **p<0.01.
†Estimates weighted.
‡Non-recent smoking defined as youth who smoked at some time in the past but not in 30 days prior to the 12th grade survey, and recent smokers defined as those who smoked in the 30 days prior to the 12th grade survey.
§Differences across e-cigarette use groups modelled in a binomial regression with a log link. Not all controls could be included in each adjusted model due to convergence issues; see online supplementary table A4 for detailed presentation of multivariable models.

e-cigarettes may require many years or even decades (as it did for regular cigarettes), and once this body is developed e-cigarette manufacturers could change their ingredients and the process may need to start all over again. In addition, recent research shows that the majority of youth who vape report that they vape 'just flavouring' and not nicotine.[22] Consequently, regulations and policies based on a rationale of nicotine regulation may not necessarily apply to youth e-cigarette use in a straightforward way.

One important rationale to regulate e-cigarettes is that they lead to use of combustible cigarettes among youth. This rationale builds on the already-existing consensus and political will to reduce youth cigarette smoking, given that most people would favour age restrictions on sale of devices that lead youth to smoke.

This study strengthens the evidence that vaping is a risk factor for cigarette smoking among youth in three ways. First, it contributes the first findings based on a sample of schools selected to be nationally representative of the USA to the growing body of evidence linking vaping to later smoking incidence among youth who had never smoked at baseline. Now four studies have used school-based samples of adolescents to investigate this topic longitudinally, and all support vaping as an independent predictor of smoking incidence, taking into account predisposition to smoke at baseline.[3 4 6] These findings are particularly important given that vaping is one of the most common forms of substance use among youth who have never smoked, with a current prevalence of 4% for this group.

Second, the study's evidence for a potential role for perceived risk is an important step in the identification of mechanisms that link vaping to later smoking incidence among never smokers. The intervening mechanisms at work may not necessarily be linked to chemical addiction and may operate even if the substance vaped in e-cigarettes is not addictive or physically harmful. Other candidate intervening mechanisms include smoking expectancies, peer smoker affiliations, and attitudes toward smokers.[23] The planned, future addition of a third wave of data will allow testing of a formal mediation model.

Finally, this study is one of few to consider the possibility that vaping may lead youth with past smoking experience to return to smoking. Among youth who had smoked in the past but had not recently smoked at the time of survey, those who vaped were about twice as likely to have smoked at least one cigarette in the past 12 months at the follow-up. Vaping did not divert this group away from smoking.

We note four limitations of this study. First, the analyses do not take into account what substances youth vaped in their e-cigarettes. Such questions were asked in more recent surveys, so in the future it will be possible to test if the overall predictive power of vaping for future smoking incidence differs among subgroups who vape different types of substances.

A second limitation is that the sample size of the analysis did not allow detailed examination of important subgroups. For example, analysis of racial/ethnic categories beyond white and non-white led to groupings that were too small to support

Table 4 Percentage who changed their perceived risk of smoking away from 'great risk' at follow-up wave (SEs and 95% relative risk CIs in brackets)†

Smoking status:	Never smoked by 12th grade		Smoked by 12th grade
	All	See 'great risk' in smoking cigarettes	All
n (weighted)	246	204	101
Recently vaped at time of 12th grade survey			
No	9.01 (2.04)	10.92 (2.44)	14.12 (5.05)
Yes	41.27 (16.58)	41.73 (16.68)	11.65 (5.70)
Bivariate relative risk‡	4.56** (1.87 to 11.11)	3.81** (1.57 to 9.21)	0.82 (0.29 to 2.83)
Adjusted relative risk‡	4.73** (2.07 to 10.82)	3.74** (1.57 to 8.89)	0.69 (0.19 to 2.49)

Analysis includes five cases with imputed data for the dependent variable. Results changed only trivially when these five cases were removed from the analysis. See online supplementary table A5 for detailed presentation of multivariable models.
**p<0.01.
†Estimates weighted.
‡Differences across e-cigarette use groups modelled in a binomial regression with a log link. Adjusted relative risk controls sex, parental education, and race (white vs non-white).

statistical analysis. The sample size also did not allow analysis by different frequency of vaping in the past 30 days at baseline. In future years, the sample size will grow considerably with the addition of new cohorts that can be combined with this one, which will allow more detailed analysis of possible differences in the overall findings across specific subgroups.

A third limitation is that not all target follow-up respondents returned surveys, which introduces the possibility of response bias. Subgroups that are more likely to respond may exert a larger influence than their size warrants on the study results. In particular, for this study any differential sampling response by groups with high predisposition to smoke cigarettes at baseline or smoking experience at baseline have potential to confound the results. To address this possibility the analyses stratify by these factors, with perceived risk of smoking as an indicator of predisposition to smoke. Stratification of analyses by key groups takes into account both substantive confounding as well as any confounding that results from their potentially different levels of survey response. Confidence that response bias does not seriously confound the study results is strengthened both by the stratification procedure as well as the finding from the attrition analyses that the stratified subgroups showed no major difference in proportionate size among follow-up responders as compared with the target panel sample. To be thorough, the study's attrition weighting addresses the small differences in response rates by groups, and this attrition weighting did not change the study's substantive results or conclusions.

A fourth limitation is that the data do not contain specific questions related to tobacco use such as smoking susceptibility, smoking expectations, rebelliousness, affiliation with smokers in the community, and perception of friends' attitudes toward smoking. Such questions would allow more comprehensive, statistical control of the predisposition of youth to smoke cigarettes. The analyses control for these influences in part by controlling general substance use at baseline, through which many of these influences would act, and still find support for vaping as an independent predictor of future smoking. These results are consistent with other school-based studies in this literature that include controls for these factors[3 4 6] and still find that vaping significantly predicts future smoking. Taken together, existing studies suggest that it is unlikely that predisposition to smoke can 'explain away' the association of vaping with future cigarette smoking.

In conclusion, these results bolster findings for vaping as a one-way bridge to cigarette smoking among adolescents. To the best of our knowledge, the risk for future cigarette smoking is currently one of the strongest, scientifically-based rationales for restricting youth access to e-cigarettes.

What this paper adds

This paper contributes to the growing body of evidence that e-cigarette use is an independent risk factor for future smoking, both among youth who are non-smokers and also among youth with past smoking experience. Results support a desensitisation process, whereby youth who vape lower their perceived risk of cigarette smoking.

Contributors LDJ is the principal investigator of the Monitoring the Future Study, and the other authors are all co-investigators. RM developed the paper plan, performed the data analysis, and drafted the manuscript, assisted by MEP. All authors contributed to drafts of the manuscript.

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Competing interests None declared.

Ethics approval University of Michigan Institutional Review Board, approval number HUM00063656.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The data are drawn from a wider survey that examines trends in the use of a variety of substances among adolescents, as well as trends in many substance use related variables. Each year a de-identified version of the previous year's data is made publicly available and can be downloaded for no charge at: http://www.icpsr.umich.edu/icpsrweb/NAHDAP/index.jsp. Researchers wishing to use sensitive data that cannot be publicly released should send a request to mtfinformation@umich.edu to start the application process.

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Annals of Internal Medicine — Original Research

Association of E-Cigarette Use With Smoking Cessation Among Smokers Who Plan to Quit After a Hospitalization

A Prospective Study

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Background: Many smokers report using e-cigarettes to help them quit smoking, but whether e-cigarettes aid cessation efforts is uncertain.

Objective: To determine whether e-cigarette use after hospital discharge is associated with subsequent tobacco abstinence among smokers who plan to quit and are advised to use evidence-based treatment.

Design: Secondary data analysis of a randomized controlled trial. (ClinicalTrials.gov: NCT01714323 [parent trial])

Setting: 3 hospitals.

Participants: 1357 hospitalized adult cigarette smokers who planned to stop smoking, received tobacco cessation counseling in the hospital, and were randomly assigned at discharge to a tobacco treatment recommendation (control) or free tobacco treatment (intervention).

Measurements: Self-reported e-cigarette use (exposure) was assessed 1 and 3 months after discharge; biochemically validated tobacco abstinence (outcome) was assessed 6 months after discharge.

Results: Twenty-eight percent of participants used an e-cigarette within 3 months after discharge. In an analysis of 237 propensity score–matched pairs, e-cigarette users were less likely than nonusers to abstain from tobacco use at 6 months (10.1% vs. 26.6%; risk difference, −16.5% [95% CI, −23.3% to −9.6%]). The association between e-cigarette use and quitting varied between intervention patients, who were given easy access to conventional treatment (7.7% vs. 29.8%; risk difference, −22.1% [CI, −32.3% to −11.9%]), and control patients, who received only treatment recommendations (12.0% vs. 24.1%; risk difference, −12.0% [CI, −21.2% to 2.9%]) (*P* for interaction = 0.143).

Limitations: Patients self-selected e-cigarette use. Unmeasured confounding is possible in an observational study.

Conclusion: During 3 months after hospital discharge, more than a quarter of smokers attempting to quit used e-cigarettes, mostly to aid cessation, but few used them regularly. This pattern of use was associated with less tobacco abstinence at 6 months than among smokers who did not use e-cigarettes. Additional study is needed to determine whether regular use of e-cigarettes aids or hinders smoking cessation.

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E-cigarettes are battery-operated nicotine delivery devices that produce an aerosol that users inhale (1). Use of an e-cigarette is often called "vaping." Because the devices do not burn tobacco, users avoid exposure to the harmful products of combustion. However, they are exposed to the heated aerosol, which generally includes a humectant (such as propylene glycol or vegetable glycerine), nicotine, and a flavoring agent. Small amounts of potentially toxic compounds, such as volatile organic compounds and heavy metals, have also been detected in e-cigarette aerosol (2). E-cigarette use has increased dramatically since 2010 (3). Among adults, they are primarily used by cigarette smokers, most of whom report that they use them to stop smoking or reduce their health risks (3–5).

The health risks and benefits of e-cigarettes are uncertain (6), but the scientific consensus is that cigarette smokers who completely switch to e-cigarettes are likely to reduce their tobacco-related health risks (7–9). E-cigarettes could benefit smokers by helping them to quit smoking conventional cigarettes, but whether e-cigarettes are effective cessation aids is uncertain due to a lack of sufficient high-quality data from randomized controlled trials (10–12).

Despite this uncertainty, e-cigarettes are readily available to consumers and are used by smokers who are trying to quit and who may also be using evidence-based smoking cessation medications (13, 14). Whether e-cigarette use in this context helps or hinders smoking cessation is a critical question. The results of observational studies done to answer this question are summarized in several systematic reviews whose methods and conclusions vary (10–12, 15). In 1 meta-analysis, the odds that smokers using e-cigarettes would quit smoking were 28% lower than those of smokers not using e-cigarettes (15). However, the analysis had several limitations (16). Three other systematic reviews found insufficient evidence from observational studies to make a definitive conclusion about the relationship between e-cigarette use and tobacco cessation (10–12).

We addressed this question in a secondary analysis of data from a large randomized controlled trial of hospitalized smokers who planned to quit smoking after discharge. The trial compared the effectiveness of free

See also:

Summary for Patients I-24

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Table 1. E-Cigarette Use After Hospital Discharge*

E-Cigarette Use	Month 1				Month 3			
	All (*n* = 1100)	Intervention (*n* = 560)	Control (*n* = 540)	*P* Value	All (*n* = 1040)	Intervention (*n* = 518)	Control (*n* = 522)	*P* Value
Any use since discharge	18.3	16.2	20.6	0.058	28.0	24.9	31.1	0.026
Use in the past 30 d	16.6	14.0	19.3	0.019	15.8	13.7	17.8	0.069
Use in the past 7 d	10.7	8.3	13.2	0.008	11.3	9.8	12.7	0.150
At 1 and 3 mo								
Use in the past 30 d	–	–	–		9.0	7.4	10.5	0.079
Use in the past 7 d	–	–	–		5.6	4.3	7.0	0.057

* Values are percentages among the 1100 (81%), 1040 (77%), and 1021 (75%) participants who completed follow-up surveys at 1, 3, and 6 mo, respectively.

evidence-based tobacco cessation treatment versus standard care after hospital discharge. The analysis reported here examined whether e-cigarette use in the 3 months after discharge was associated with more or less tobacco abstinence at 6 months. The randomized design of the parent trial also allowed us to explore how the effect of e-cigarette use on cessation success varied by access to conventional smoking cessation treatment. We hypothesized that smokers with easy access to evidence-based tobacco cessation treatment might be less likely to use e-cigarettes during a quit attempt and that this might moderate the relationship between e-cigarette use and cessation success.

METHODS

Setting

We analyzed data from Helping HAND 2, a 2-group, 3-site, randomized controlled trial that enrolled hospitalized cigarette smokers who planned to quit smoking and compared a postdischarge smoking cessation intervention versus standard care. A detailed study protocol and main outcomes have been published (17, 18). The study, conducted from 2012 to 2015 at Massachusetts General Hospital (Boston, Massachusetts), North Shore Medical Center (Salem, Massachusetts), and the University of Pittsburgh Medical Center (Pittsburgh, Pennsylvania), was approved by the Institutional Review Boards of Partners HealthCare and the University of Pittsburgh and was registered at ClinicalTrials.gov (NCT01714323). Use of tobacco products and e-cigarettes was prohibited in all hospitals.

Participants

Each hospital routinely identified patients' smoking status at admission. A tobacco treatment counselor visited inpatients identified as smokers to offer brief bedside counseling and encourage use of nicotine replacement therapy in the hospital. Counselors did not recommend e-cigarettes to smokers; rather, when asked, they advised that the safety and efficacy of e-cigarettes were unknown, and they encouraged smokers to use tobacco cessation medications approved by the U.S. Food and Drug Administration (FDA). Adult (aged ≥18 years) daily smokers who received the inpatient counseling session and planned to quit smoking after discharge were eligible for the study.

Interventions

Patients were randomly assigned to postdischarge standard care (control) or sustained care (intervention). Standard care participants were advised to call a free telephone quitline and received an individualized postdischarge medication recommendation. Sustained care participants received an intervention that included a free 30-day supply of their choice of FDA-approved cessation medication at discharge (refillable for a total of 90 days) and 5 automated telephone calls using interactive voice-response technology over 90 days. At each automated call, recorded messages tailored to participants' responses encouraged participants to remain abstinent or make another quit attempt and offered to transfer smokers directly to a telephone quitline, where they could receive counseling or refill a study medication.

Measures and Assessments

Baseline measures included demographic factors (age, sex, race/ethnicity, and education), health insurance status, nicotine dependence (number of cigarettes per day and time to first cigarette after awakening [19]), prior use of tobacco cessation treatment, perceived importance of and confidence in quitting (5-point Likert scales), postdischarge intention to quit (plan to remain abstinent vs. plan to try to remain abstinent), presence of another smoker at home, screening for alcohol abuse (Alcohol Use Disorders Identification Test), illicit drug use in the past 30 days, and depression and anxiety symptoms (Patient Health Questionnaire-4 [PHQ-4]) (20, 21). Hospital records provided primary discharge diagnosis and length of stay.

Participants were called 1, 3, and 6 months after discharge to assess abstinence from tobacco in the past 7 days and current use of smoking cessation treatments. Participants received $20 per completed survey. The primary outcome was biochemically validated tobacco abstinence in the past 7 days at 6 months, but the measure permitted exclusive use of e-cigarettes. To verify self-reported abstinence at 6 months, patients were asked to mail a saliva sample to be tested for cotinine (a nicotine metabolite), for which they were compensated $50 (22). Participants using nicotine replacement therapy or e-cigarettes were asked to provide an in-person measurement of expired-air carbon

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Table 1–Continued

Month 6			
All (*n* = 1021)	**Intervention (*n* = 508)**	**Control (*n* = 513)**	***P* Value**
37.0	34.3	39.6	0.085
16.9	16.2	17.6	0.55
11.9	11.8	11.9	0.97
5.5	5.2	5.7	0.72
3.6	3.6	3.5	0.97

monoxide and were compensated $50 for the sample. Self-reported abstinence was verified if the saliva cotinine concentration was 10 ng/mL or less or the carbon monoxide level was less than 9 ppm (23).

E-cigarette use in the past 30 days was assessed at baseline ("In the 30 days before you entered the hospital, did you use an electronic cigarette [or e-cigarette]?"). At 1, 3, and 6 months, participants were asked about any e-cigarette use since hospital discharge, in the past 30 days, and in the past 7 days. Additional questions about the pattern and reason for e-cigarette use were added to our assessments in August 2013, 9 months after the start of the 20-month enrollment, when it became clear that e-cigarette use in the community was increasing (24). The new questions asked about the number of days of e-cigarette use in the past 7 days and the past 30 days and the primary reason for e-cigarette use. Response options were "help me to quit smoking cigarettes," "give me something to use in non-smoking area," "use a less risky product than cigarettes," or "other."

Statistical Analysis

Our goal was to examine the association between e-cigarette use in the 3 months after discharge and tobacco abstinence at 6 months. To avoid misclassification of e-cigarette use, primary analyses were limited to the subset of participants who completed postdischarge e-cigarette assessments. The primary dependent variable was biochemically validated abstinence at 6 months. Participants with missing or nonvalidated tobacco use outcomes were counted as smokers.

The independent variable of interest was e-cigarette use. Because different patterns of e-cigarette use may have different relationships with tobacco cessation, we calculated the prevalence of any e-cigarette use since discharge, in the past 30 days, and in the past 7 days at 3 months. We also combined data from the 1- and 3-month follow-up periods to calculate persistent use, defined as use in the past 7 or 30 days at both 1 and 3 months.

To adjust for baseline differences between participants who did and did not use e-cigarettes in the 3 months after discharge, we conducted a propensity score analysis, matching participants in a 1:1 ratio according to study group and their propensity to use e-cigarettes after discharge. We included baseline variables of age, sex, race/ethnicity, education level, number of cigarettes per day, time to first cigarette after awakening, e-cigarette use in the 30 days before hospitalization, perceived importance of quitting, confidence in ability to quit, alcohol use, marijuana use in the past year, smoking-related disease as the primary discharge diagnosis, baseline PHQ-4 score, length of hospital stay, use of medication or counseling after discharge, and study site in the propensity score models. We matched e-cigarette users (case patients) with nonusers (control patients) on the logit scale of the propensity score and used calipers of width equal to two tenths of the SD (25). Among all pairs of potential matches, we first calculated the number of possible matches for each case patient and allowed the one with the fewest match options to select first. We selected the control patient with the shortest distance to the case patient for the matched pair. We then repeated the process for all remaining case patients. We report the risk differences and 95% CIs from the matched samples.

To examine whether the effect of e-cigarette use on smoking cessation varied by study group, we repeated the analysis with stratification by study group and tested for an interaction between the effects of study group and each e-cigarette measure.

To quantify the effect of unmeasured potential confounding factors, we report the E-value, which represents the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure (e-cigarette use) and the outcome (smoking abstinence) to fully explain away an association between the two, associated with each e-cigarette measure (26).

Analyses were done using SAS, version 9.4 (SAS Institute). The E-value and 95% CI were calculated using an online calculator (27). A 2-sided *P* value less than 0.05 was considered statistically significant.

Role of the Funding Source

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RESULTS

The Helping HAND 2 study enrolled 1357 smokers who were randomly assigned to sustained care (n = 680) or standard care (n = 677) after discharge. Follow-up rates were 81% (n = 1100) at 1 month, 77% (n = 1040) at 3 months, and 75% (n = 1021) at 6 months and did not differ significantly between groups. Participants who were lost to follow-up at 3 months were younger (mean age, 46 vs. 51 years; $P < 0.001$) and were less likely to have a smoking-related disease as their primary discharge diagnosis (24% vs. 37%; $P < 0.001$) but did not differ in the number of cigarettes smoked per day. At 6 months, 69% of self-reported nonsmokers provided a sample for validation. Abstinence was con-

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Table 2. Characteristics of Participants Who Did and Did Not Use E-Cigarettes Within 3 Months After Discharge

Variable	Full Sample (n = 1022)*				Propensity Score-Matched Sample†			
	Any E-Cigarette Use ≤3 Months After Discharge		Standardized Difference	P Value	Any E-Cigarette Use ≤3 Months After Discharge		Standardized Difference	P Value
	Yes (n = 286)	No (n = 736)			Yes (n = 237)	No (n = 237)		
Demographic characteristics								
Mean age (SD), y	49 (12)	52 (12)	−2.0	0.005	50 (12)	50 (12)	0.03	0.76
Male, %	43.4	51.9	−0.17	0.014	42.6	42.6	0	1.00
Nonwhite race/ethnicity, %	21.7	30.7	−0.21	0.004	22.4	21.9	0.01	0.91
High school diploma or less, %	45.8	51.1	−0.11	0.129	48.9	45.1	0.08	0.41
Tobacco use								
Mean cigarettes per day (SD), n	17 (9)	15 (10)	0.20	0.003	17 (10)	17 (11)	0.02	0.79
Smoke ≤30 min after awakening, %	80.8	73.0	0.18	0.012	81.4	76.4	0.12	0.177
E-cigarette use ≤30 d before hospitalization, %	46.5	12.0	0.82	<0.001	35.4	35.4	0	1.00
Mean perceived importance of quitting (SD)‡	3.9 (0.4)	3.9 (0.4)	−0.01	0.83	3.9 (0.4)	3.9 (0.4)	−0.08	0.40
Mean confidence in quitting (SD)‡	3.0 (0.9)	3.2 (1.0)	−0.18	0.009	3.1 (1.1)	3.0 (0.9)	−0.05	0.61
Other substance use								
Median AUDIT-C score (IQR)§	1 (0 to 4)	1 (0 to 4)	−0.05	0.47	1 (0 to 4)	1 (0 to 4)	0.04	0.66
Marijuana use in past year, %	24.8	24.3	0.01	0.81	24.1	24.9	−0.02	0.83
Medical history								
Smoking-related disease as primary discharge diagnosis, %‖	35.7	37.0	−0.03	0.70	38.0	38.0	0	1.00
Median PHQ-4 score at baseline (IQR)¶	5 (2 to 8)	4 (2 to 7)	0.18	0.015	5 (2 to 8)	4 (2 to 7)	0.02	0.88
Median length of hospital stay (IQR), d	4 (3 to 6)	5 (3 to 7)	−0.07	0.131	4 (3 to 6)	4 (3 to 7)	0	0.30
Tobacco cessation treatment use after discharge, %								
Medication	78.7	77.4	0.03	0.67	77.6	77.2	0.01	0.91
Counseling	33.9	29.9	0.09	0.20	34.2	30.8	0.07	0.43
Study group, %				0.026				1.00
Control	55.6	47.8	−0.16		56.1	56.1	0	
Intervention	44.4	52.2	0.16		43.9	43.9	0	
Study site, %				0.137				0.63
Massachusetts General Hospital	36.7	41.8	−0.11		36.3	35.4	0.02	
North Shore Medical Center	16.1	17.8	−0.05		16.9	20.3	−0.09	
University of Pittsburgh Medical Center	47.2	40.4	0.14		46.8	44.3	0.05	

AUDIT-C = Alcohol Use Disorders Identification Test; ICD-9 = International Classification of Diseases, Ninth Revision; IQR = interquartile range; PHQ-4 = Patient Health Questionnaire-4.
* 1040 randomly assigned participants completed 3-mo follow-up, but information on e-cigarette use since discharge was not available for 18 participants.
† Matching was based on study group and participants' propensity to use e-cigarettes after discharge. Variables in the propensity score model were age, sex, race/ethnicity, education level, number of cigarettes per day, time to first cigarette after awakening, e-cigarette use in 30 d before hospitalization, perceived importance of quitting, confidence in ability to quit, alcohol use, marijuana use in the past year, smoking-related disease as primary discharge diagnosis, baseline PHQ-4 score, length of hospital stay, use of medication or counseling after discharge, and study site.
‡ Based on a 5-point Likert scale ranging from 0 ("not at all") to 4 ("very").
§ Scores range from 0 to 12, with higher scores indicating a greater likelihood that the patient's alcohol consumption has adverse health and safety effects.
‖ Diseases were those specified in the 2014 U.S. Surgeon General's report (28). These include neoplasms (ICD-9 codes 140–151, 157, 161, 162, 180, 188, 189, and 204–208), cardiovascular diseases (ICD-9 codes 410–414, 390–398, 415–417, 420–429, 430–438, and 440–448), respiratory diseases (ICD-9 codes 480–492 and 496), and perinatal conditions (ICD-9 codes 765, 769, and 798.0).
¶ Screens for symptoms of depression (2 questions) and anxiety (2 questions). Scores range from 0 to 12, with higher scores indicating more symptoms.

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firmed in 73% of these samples (sustained care, 72%; standard care, 74%).

E-Cigarette Use

E-cigarette use in the 30 days before hospitalization was reported by 290 (21.4%) of 1357 participants and did not differ significantly between the intervention (20.7%) and control (22.0%) groups. Table 1 shows the prevalence of e-cigarette use among participants who completed each follow-up survey. The reported rate of any e-cigarette use after hospital discharge increased from 18.3% at 1 month to 28.0% at 3 months and 37.0% at 6 months ($P < 0.001$), but current use at each follow-up was stable over time (16% to 17% for use in the past 30 days and 11% to 12% for use in the past 7 days), suggesting that different people were using e-cigarettes at different follow-up times. Persistent use, defined as use in the 7 or 30 days before both the current and previous follow-up periods, was uncommon; only 5.6% and 9.0% of participants, respectively, reported it at 1 and 3 months and only 3.6% and 5.5%, respectively, reported it at 1, 3, and 6 months. E-cigarette use was more frequent in the control group than the intervention group at 1 and 3 months.

At 3 months, 68% of the 178 e-cigarette users who were asked why they used an e-cigarette gave quitting smoking as their primary reason. Among 114 of 164 participants who had used e-cigarettes in the past 30 days and were asked about frequency of use, the median was 10 of the past 30 days (interquartile range, 5 to 30 days). Among 83 of 117 participants who reported using an e-cigarette in the past 7 days and were asked about frequency of use, the median was 5 of the past 7 days (interquartile range, 2 to 7 days).

Association With Smoking Cessation

Table 2 compares the characteristics of participants who completed the 3-month follow-up assessment, stratified by their report of e-cigarette use in the 3 months after discharge. Among participants who completed this survey, those who did and did not use e-cigarettes differed by several demographic and tobacco use characteristics. These imbalances were reduced in the propensity score–matched sample. Among the 286 participants reporting any e-cigarette use in the 3 months after discharge, we found 237 participants with a similar propensity score who did not use e-cigarettes. Table 2 illustrates the similarity of the matched groups on baseline characteristics.

Table 3 shows the relationship between e-cigarette use at 3 months and smoking status at 6 months. In the propensity score–matched sample, participants who reported any e-cigarette use in the 3 months since hospital discharge were less likely to be biochemically abstinent at 6 months than those not using e-cigarettes (10.1% vs. 26.6%; risk difference, −16.5% [95% CI, −23.3% to −9.6%]). The E-value was 4.7 for the estimated difference and 2.9 for the lower confidence limit. The risk differences were consistently below 0 but were not statistically significant for alternative measures of e-cigarette use after discharge (use in the past 30 or 7 days at 3 months and in the past 30 or 7 days at both 1 and 3 months). In contrast, there was almost no difference in cessation rates at 6 months between 223 propensity score–matched pairs of participants who did or did not use e-cigarettes in the 30 days before hospitalization (Table 3).

Table 4 summarizes the analysis stratified by study group. Participants who reported using e-cigarettes at any time in the 3 months after hospital discharge were less likely to achieve biochemically validated tobacco cessation at 6 months if they were in the sustained care group (7.7% vs. 29.8%). The risk difference (−22.1% [CI, −32.3% to −11.9%]) was larger than if they were in the standard care group (12.0% vs. 24.1%; risk difference, −12.0% [CI, −21.2% to 2.9%]) (P for interaction = 0.143). The same pattern of association was observed

Table 3. Propensity Score Analysis for Biochemically Verified Tobacco Abstinence at 6-Month Follow-up, by E-Cigarette Use

E-Cigarette Use	E-Cigarette Users, *n*		Biochemically Confirmed Tobacco Abstinence in the Past 7 Days at 6-Month Follow-up			
	Full Sample	Matched Sample*	E-Cigarette Use, %		Risk Difference (95% CI), %	*P* Value
			Yes	No		
Before hospitalization						
Use in the past 30 d	224	223	19.7	18.4	1.3 (−5.9 to 8.6)	0.72
At 3 mo						
Any use since discharge	286	237	10.1	26.6	−16.5 (−23.3 to −9.6)	<0.001
Use in the past 30 d	164	162	11.7	18.5	−6.8 (−14.6 to 1.0)	0.088
Use in the past 7 d	117	117	13.7	17.9	−4.3 (−13.6 to 5.1)	0.37
At 1 and 3 mo						
Use in the past 30 d	92	91	14.3	24.2	−9.9 (−21.3 to 1.5)	0.091
Use in the past 7 d	58	57	17.5	21.1	−3.5 (−18.0 to 11.0)	0.64

PHQ-4 = Patient Health Questionnaire-4.
* Matching was based on study group and participants' propensity to use e-cigarettes after discharge. Variables in the propensity score model were age, sex, race/ethnicity, education level, number of cigarettes per day, time to first cigarette after awakening, e-cigarette use in the 30 d before hospitalization, perceived importance of quitting, confidence in ability to quit, alcohol use, marijuana use in the past year, smoking-related disease as primary discharge diagnosis, baseline PHQ-4 score, length of hospital stay, use of medication or counseling after discharge, and study site.

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Table 4. Propensity Score Analysis for Biochemically Verified Tobacco Abstinence at 6-Month Follow-up, by E-Cigarette Use: Stratified by Study Group

E-Cigarette Use	Standard Care (Control)				Sustained Care (Intervention)				P Value*
	Matched Pairs, *n*	Biochemically Confirmed Tobacco Abstinence in the Past 7 Days at 6-Month Follow-up, %		Risk Difference (95% CI), %	Matched Pairs, *n*	Biochemically Confirmed Tobacco Abstinence in the Past 7 Days at 6-Month Follow-up, %		Risk Difference (95% CI), %	
		Yes	No			Yes	No		
Before hospitalization									
Use in the past 30 d	117	17.9	14.5	3.4 (−6.0 to 12.9)	106	21.7	22.6	−0.9 (−12.1 to 10.2)	0.53
At 3 mo									
Any use since discharge	113	12.0	24.1	−12.0 (−21.2 to 2.9)	104	7.7	29.8	−22.1 (−32.3 to −11.9)	0.143
Use in the past 30 d	93	14.0	18.3	−4.3 (−14.9 to 6.3)	69	8.7	18.8	−10.1 (−21.5 to 1.2)	0.39
Use in the past 7 d	66	16.7	19.7	−3.0 (−16.2 to 10.1)	51	9.8	15.7	−5.9 (−18.8 to 7.0)	0.66
At 1 and 3 mo									
Use in the past 30 d	53	15.1	26.4	−11.3 (−26.6 to 4.0)	38	13.2	21.1	−7.9 (−24.7 to 8.9)	0.86
Use in the past 7 d	33	17.1	17.1	0 (−17.7 to 17.7)	22	18.2	27.3	−9.1 (−33.7 to 15.5)	0.59

* For interaction between study group and e-cigarette use measure.

for measures of e-cigarette use in the past 7 days and the past 30 days at 3 months.

DISCUSSION

In this secondary analysis of a large randomized controlled trial, more than one quarter of recently hospitalized smokers who planned to quit smoking after discharge and were advised to use conventional tobacco cessation treatment reported using an e-cigarette in the 3 months after discharge. Although most smokers said that they used e-cigarettes to help them quit, those who used an e-cigarette after discharge were less likely to be abstinent from tobacco at 6 months than smokers who did not use e-cigarettes. In our propensity score analysis, the negative association between e-cigarette use and smoking cessation was large, with confidence bounds spanning meaningful effects.

Because e-cigarette use was self-selected, unmeasured confounding in the observed relationship between e-cigarette use and smoking cessation is possible, and a causal relationship cannot be inferred. However, sensitivity analyses to assess unmeasured confounding using the E-value indicated that the observed association between any e-cigarette use in the 3 months since hospital discharge and smoking cessation at 6 months could be explained away by an unmeasured confounder that was associated with both e-cigarette use and smoking cessation by a risk ratio of 4.7-fold each beyond the measured confounders. Weaker confounding could not do so. The CI for the observed association could be moved to include the null by an unmeasured confounder that was associated with both e-cigarette use and smoking cessation by a risk ratio of 2.9-fold each beyond the measured confounders, but weaker confounding could not do so. Thus, the evidence of association seems reasonably strong because substantial unmeasured confounding would be needed to explain away the observed association.

Conducting our study within a randomized controlled trial permitted us to make several novel observations about e-cigarette use among smokers who were trying to quit. Smokers in the intervention group, who received immediate free access to conventional cessation treatment for 3 months, were less likely to use e-cigarettes in the month after discharge than those assigned to the control group, who received a treatment recommendation only (Table 1). Access to conventional cessation aids may influence a smoker's decision about whether to use e-cigarettes when attempting to quit.

The strength of the negative association between e-cigarette use and smoking cessation may have been related to study group. In the propensity score analysis, any e-cigarette use was associated with an absolute 22% lower rate of cessation at 6 months for smokers in the intervention group but only an absolute 12% lower rate of cessation for those in the control group (Table 4). One interpretation is that smokers with easy access to cessation aids may have initiated e-cigarette use primarily when conventional aids failed. If so, e-cigarette users in this study might represent a subgroup of smokers who have more difficulty quitting. This could contribute to the negative association between e-cigarette use and cessation seen in many observational trials (10, 11, 14, 15). To our knowledge, this is the first study to assess an interaction between treatment and e-cigarette use. This relationship should be tested in future studies.

This study had notable methodological strengths. These include a large, geographically diverse sample of smokers who were trying to quit; a prospective de-

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sign with repeated measures to permit exposure assessment before outcome assessment; several measures of e-cigarette exposure; biochemical validation of tobacco abstinence; and detailed assessments of sociodemographic, clinical, and tobacco use factors that allowed us to compare samples that were propensity score–matched on multiple factors.

Because of the study's observational design, in which e-cigarette use was self-selected, unmeasured confounding could explain the findings, and a causal relationship cannot be inferred from these data. However, as noted earlier, the E-value calculation indicated that the effect could be explained away only by a strong, unmeasured confounder. The analysis was also limited by a lack of data on e-cigarette type and detailed data on frequency of use. Prior studies have suggested that the effect of e-cigarettes on quitting may depend on the type of product and frequency of use (15, 29–31), which we could not explore. Further, detailed timing of e-cigarette use, especially in relation to use of conventional cessation aids, was beyond the scope of this study. Finally, our results apply to recently hospitalized smokers and may not apply to other groups of smokers.

In conclusion, this large prospective study of recently hospitalized smokers who planned to quit found a negative association between any use of e-cigarettes after discharge and subsequent tobacco abstinence. The association must be interpreted in the context in which the e-cigarettes were used: intermittently; often concomitantly with evidence-based tobacco cessation treatment; and more often by smokers without easy, free access to evidence-based cessation aids. Despite the limitations inherent in its observational design, this study illustrates how e-cigarettes, which are widely available commercially, are being used in a common clinical situation (a cessation attempt after hospitalization). In this setting, the use of e-cigarettes intermittently and concurrently with other cessation aids did not seem to aid quitting and may have hampered it. The possibility remains that e-cigarettes can promote tobacco cessation if they are used regularly and as a complete replacement for cigarettes, which is how conventional cessation medications are recommended for use. Future research, particularly randomized controlled trials, is needed to address this critical question.

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Reproducible Research Statement: *Study protocol, statistical code, and data set:* Available through written agreement with the authors (e-mail, nrigotti@partners.org).

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Documentation of e-cigarette use and associations with smoking from 2012 to 2015 in an integrated healthcare delivery system

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ABSTRACT

It is unclear whether use of electronic nicotine delivery systems (ENDS) precedes cigarette smoking initiation, relapse, and/or quitting. Healthcare systems with electronic health records (EHRs) provide unique data to examine ENDS use and changes in smoking.

We examined the incidence of ENDS use (2012–2015) based on clinician documentation and tested whether EHR documented ENDS use is associated with twelve-month changes in patient smoking status using a matched retrospective cohort design. The sample was Kaiser Permanente Northern California (KPNC) patients aged ≥12 with documented ENDS use ($N = 7926$); 57% were current smokers, 35% former smokers, and 8% never-smokers. ENDS documentation incidence peaked in 2014 for current and former smokers and in 2015 for never-smokers. We matched patients with documented ENDS use to KPNC patients without documented ENDS use ($N = 7926$) on age, sex, race/ethnicity, and smoking status.

Documented ENDS use predicted the likelihood of smoking in the following year. Among current smokers, ENDS use was associated with greater odds of quitting smoking (OR = 1.17, 95%CI = 1.05–1.31). Among former smokers, ENDS use was associated with greater odds of smoking relapse (OR = 1.53, 95%CI = 1.22–1.92). Among never-smokers, ENDS use was associated with greater odds of initiating smoking (OR = 7.41, 95%CI = 3.14–17.5). The overall number of current smokers at 12 months was slightly higher among patients with ($N = 3931$) versus without ($N = 3850$) documented ENDS use.

Results support both potential harm reduction of ENDS use (quitting combustibles among current smokers) and potential for harm (relapse to combustibles among former smokers, initiation for never-smokers).

1. Introduction

Cigarette smoking, including exposure to secondhand smoke, is linked to > 520,000 deaths in the US each year, and smoking-related illnesses result in nearly $170 billion in direct medical costs and $156 billion attributable to lost work productivity annually (Xu et al., 2015). Alternatives to smoking, such as electronic nicotine delivery systems (ENDS), which include electronic cigarettes, have become increasingly popular in recent years (McMillen et al., 2015; Pearson et al., 2012; Regan et al., 2013; King et al., 2015). Regulated as a tobacco product by the U.S. Food and Drug Administration (FDA) since May 2016 (*Fed. Regist.*, 2016), data on the potential of ENDS for harm enhancement and harm reduction are limited. Given the substantial harms of combustible cigarettes, ENDS are thought to be safer nicotine delivery products. Similarly, there is some evidence of health benefits among smokers who fully switch to vaping ENDS (Farsalinos and Polosa, 2014; McRobbie et al., 2014; Farsalinos et al., 2016; Nolan et al., 2016). Further, ENDS may help some smokers cut down on or quit cigarette smoking, although dual use remains common (Hartmann-Boyce et al., 2016). There is concern, however, that these products may serve as a gateway to smoking initiation (Primack et al., 2015; Leventhal et al., 2015; Chatterjee et al., 2016) and encourage relapse among those who have recently quit smoking (U.S. Department of Health and Human Services, 2016; Bhatnagar et al., 2014). Simulation-based models indicate that the potential net effects of ENDS use on population health depend on a number of factors, including the impact of ENDS on cigarette smoking

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initiation and cessation, ENDS toxicity, and patterns of use (Kalkhoran and Glantz, 2015; Levy et al., 2017a).

As patients increasingly turn to their healthcare providers for information about ENDS (Nickels et al., 2017; Steinberg et al., 2015; El-Shahawy et al., 2016; Kandra et al., 2014), research is critically needed to increase the surveillance of their use in healthcare settings (Young-Wolff et al., 2017). To fill this gap in the literature, we analyzed data from a large, integrated healthcare delivery system to describe the incidence of patients' ENDS use based on clinician documentation in the EHR from 2012 to 2015 and to test whether ENDS use was associated with changes in patients' smoking status (i.e., starting, quitting, relapsing) in the subsequent year using a matched retrospective cohort design.

2. Methods

2.1. Setting

Kaiser Permanente Northern California (KPNC) is a nonprofit, multi-specialty healthcare delivery system providing comprehensive health services to > 4 million members (Kaiser Permanente, 2011) and covering ~40% of the region's commercially insured population (Report, 2013). KPNC provides integrated medical and behavioral health treatment and is a recognized leader in establishing tobacco treatment quality-of-care standards (Goldstein et al., 2005). Members are racially and socio-economically diverse, and highly representative of the population in the geographic catchment area (Selby et al., 2005). KPNC institutional review board approval was obtained for this study.

2.2. Study participants

Our study population comprised 3,680,549 patients aged ≥12 with KPNC membership and ≥1 clinical contact between January 1, 2012 and December 31, 2015. Within this population, $N = 8256$ patients had ≥1 valid instance of documented ENDS use in the EHR during this timeframe.

For the matched-case analyses examining changes in smoking status over the subsequent year, we matched each patient with documented ENDS use to a patient without documented ENDS use on age, sex, race/ethnicity, and smoking status in the same month and year as the first documented ENDS use. For matched patients without documented ENDS use who had multiple recorded smoking statuses at different times during the study period, we randomly sampled one smoking status before employing the matching algorithm to ensure that each patient was matched only once. Of documented ENDS users, 646 of the 664 never-smokers (97%), 2752 of the 2857 former smokers (96%), and 4528 of the 4735 current smokers (96%) were successfully matched to patients without documented ENDS use, resulting in samples of $n = 7926$ documented ENDS users and $n = 7926$ matched patients without documented ENDS use.

2.3. Measures

2.3.1. Identification of documented ENDS use

We used natural language processing techniques to identify instances of ENDS use, based on clinicians' documentation in the tobacco-use free text field within the social history section of the Epic EHR. We created a set of specific "shorthand" text strings (i.e., a series of characters one would expect to find within the keywords, such as "e-cig," "electronic," or "vape") and used the SAS INDEX function (substring matches) to capture suspected variations of ENDS keywords in the tobacco comments. When we found new, potential flags, we manually reviewed the full comments for inclusion, alternative candidate strings, and exclusionary criteria (Appendix 1). We included only keywords that referenced ENDS (e.g., electronic cigarette but not electronic signature). We included the first (earliest) documented ENDS reference for each patient to estimate the number of *new* documented ENDS users in each year (2012–2015).

2.3.2. Smoking status

KPNC has several systems in place to ensure that smoking status is routinely asked about and documented, including an EHR prompt that triggers staff to ask about patients' smoking status and management oversite of staff documentation of patient smoking. Overall, tobacco screening rates are about 90%, with the highest rates in primary care. We obtained patient-reported smoking status (i.e., current, former, or never-smoker) from the EHR (Goldstein et al., 2005). Prior studies support the validity of EHR-based smoking status data (McGinnis et al., 2011; McVeigh et al., 2016; Marston et al., 2014). KPNC clinicians began consistently documenting "former smoking" status in 2012, and our study included years 2012–2015. We included the smoking status from the same encounter as the earliest ENDS documentation. If no smoking status was associated with that encounter (19%), we included the last recorded smoking status preceding ENDS documentation.

We categorized current smokers as "quitting" if they had ≥1 "former smoker" status during the year following ENDS documentation. Quitting did not have to be sustained in future records to be coded as "quitting." We categorized former smokers and never-smokers as starting smoking if they had ≥1 "current smoker" status during the year following ENDS documentation.

2.3.3. Demographic variables

Data on patient sex, race/ethnicity, age, and neighborhood median household income were from the EHR. Neighborhood median household income was geocoded from census data using patients' addresses and was dichotomized as 1 (≤median household salary) or 0 (> median household salary).

2.3.4. Comorbidity diagnoses

We identified the most common psychiatric disorders (depressive disorders, anxiety disorders, attention deficit hyperactivity disorders, bipolar spectrum disorders, substance use disorders and psychotic disorders) in our sample based on current ICD-9 and ICD-10 diagnoses recorded in the EHR during the year after ENDS use documentation.

2.3.5. Tobacco cessation medications

Use of tobacco cessation medication was determined by dispensation of any FDA-approved tobacco cessation medication (i.e., nicotine replacement therapy (NRT) gum, lozenge, inhaler, patch, nasal spray, or varenicline) from a KPNC pharmacy in the year following earliest recorded ENDS use, or the date of the matched recorded smoking status. Because bupropion is commonly prescribed to treat depressive disorders and not solely as a smoking cessation aid, it was not included in analyses. Data were extracted from the KPNC Pharmacy Information Management System database, which contains all data related to prescriptions dispensed at a KPNC pharmacy.

2.4. Analysis

Analyses were conducted in 2016 and 2017 using SAS© software, version 9.3. We first calculated the annual incidence rate of ENDS-use documentation in the EHR, defined as the number of newly documented ENDS users per 1000 KPNC patients with a documented clinical encounter in a given year, from 2012 to 2015. We plotted annual incidence rates by smoking status to visualize the relative increases in documentation among current smokers, former smokers, and never-smokers.

We calculated the percentage of ENDS users and matched non-users of each smoking status with a 12-month change in smoking status (i.e., quit smoking, initated smoking, or relapsed) and used chi-square tests to assess statistical significance. We then estimated the association between ENDS-use documentation and a 12-month change in smoking

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status using matched odds ratios from conditional logistic regression models, stratified by smoking status. We also computed the total number of current smokers at 12 months among ENDS users and matched non-users.

For all analyses, we adjusted for median income and the presence of a psychiatric or substance use disorder in the year following documented ENDS use. For analyses with current and former smokers, we also adjusted for use of tobacco cessation medications in the year following documented ENDS use.

For analyses with former smokers, we adjusted for "time since quitting smoking" in the event that newly documented ENDS users quit cigarette smoking more recently than those without documented ENDS use and may be at greater risk of relapsing to smoking. For documented ENDS users, we calculated time since quitting as the difference between their most recent quit date (i.e., date of the most recent 'former smoker' status that was immediately preceded by a 'current smoker' status) and the date of their first documented ENDS use. For patients without documented ENDS use, we calculated time since quitting as the difference between their most recent quit date and the date of their reported status as a former smoker that was used to match each patient with an ENDS user. We dichotomized this variable into "quit within a 6-month period" or "quit more than 6 months ago."

If a patient did not have a recorded smoking status in the year following the index date, we considered his or her smoking status to be unchanged. As this was a potential cause of outcome misclassification, we conducted a probabilistic bias analysis to assess the degree to which this misclassification could affect our estimates and conclusions (Fox et al., 2005; Fox et al., 2009) (Appendix 2).

3. Results

Each year, current smokers, and former smokers to a lesser extent, had higher rates of ENDS-use documentation relative to never-smokers. The number of patients with ENDS-use documentation peaked in 2014 for current (n = 1723; 9.21 per 1000 current smokers) and former smokers (n = 1043; 2.19 per 1000 former smokers) and in 2015 for never-smokers (n = 242; 0.18 per 1000 never-smokers) (Fig. 1). At the time of first ENDS-use documentation, 57% of patients were current smokers, 35% were former smokers, and 8% were never-smokers. The majority of patients with ENDS-use documentation were non-Hispanic White and male. Compared with current and former smokers, never-smokers with documented ENDS use were younger and more likely to be Hispanic (Table 1).

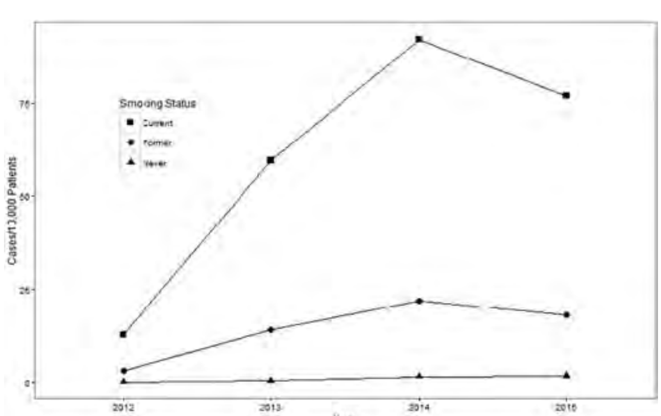

Fig. 1. Unadjusted annual incidence rate of ENDS-use documentation by patient smoking status, Kaiser Permanente Northern California, 2012–2015

Table 1
Characteristics of ENDS users at the time of first ENDS-use documentation (N = 7926), Kaiser Permanente Northern California, 2012–2015.

Variable	Smoking status at first documented ENDS use		
	Current	Former	Never
	N (%)		
Total	4528	2752	646
Age			
12–17	16 (0.35)	10 (0.36)	22 (3.4)
18–24	665 (15)	250 (9.1)	228 (35)
25–44	1885 (42)	1280 (47)	300 (46)
45–64	1545 (34)	959 (35)	81 (13)
65 +	417 (9.2)	253 (9.2)	15 (2.3)
Sex			
Male	2543 (56)	1478 (54)	342 (53)
Female	1985 (44)	1274 (46)	304 (47)
Race			
White	3015 (67)	1929 (70)	390 (60)
Hispanic	479 (11)	237 (8.6)	113 (17)
Black	270 (6.0)	148 (5.4)	31 (4.8)
Asian/Hawaiian Pacific Islander	557 (12)	306 (11)	80 (12)
Multiracial/American Indian	207 (4.6)	132 (4.8)	32 (5.0)
Median household income	68,333	68,690	73,298
Tobacco cessation medication use[a]	415 (9.2)	160 (5.8)	NA
Year of first documented use			
2012	221 (4.9)	134 (4.9)	26 (4.0)
2013	1073 (24)	647 (24)	81 (13)
2014	1723 (38)	1043 (38)	242 (37)
2015	1511 (33)	928 (34)	297 (46)
Psychiatric disorders[a]			
Depression	972 (21)	589 (21)	93 (14)
Anxiety	917 (20)	572 (21)	114 (18)
Bipolar disorder	233 (5.2)	154 (5.6)	28 (4.3)
Psychotic disorders	161 (3.6)	60 (2.2)	9 (1.4)
ADHD[b]	128 (2.8)	96 (3.5)	28 (4.3)
Any	1611 (36)	971 (35)	176 (27)
Substance use disorders[a]			
Alcohol	306 (6.8)	148 (5.4)	31 (4.8)
Drug	336 (7.4)	182 (6.6)	33 (5.1)
Any	537 (12)	283 (10)	52 (8.1)

[a] Recorded in the year following ENDS use documentation.
[b] ADHD = Attention Deficit Hyperactivity Disorder.

3.1. ENDS use and changes in smoking status among matched patients

Results from bivariate matched case analyses (using Chi-square tests) comparing patients with and without documented ENDS use (N = 7926 each group) indicated that among initially identified current smokers, 23% (n = 1028) of ENDS users and 19% (n = 863) of matched non-users (based on EHR documentation) reported quitting smoking during the following year ($p < 0.0001$ for group comparison). Among the initially identified former smokers, 14% (n = 382) of ENDS users and 7% (n = 179) of matched non-users reported returning to smoking in the following year ($p < 0.0001$). Among initially identified never-smokers, 8% (n = 49) of ENDS users and 1% (n = 6) of non-users reported initiating smoking in the next year ($p < 0.0001$). Current smokers with documented ENDS use (9%) did not differ from matched smokers without documented ENDS use (8%) in their utilization of tobacco cessation medications during the subsequent year. However, among former smokers, those with documented ENDS use (6%) had significantly greater prevalence of tobacco cessation medication use during the subsequent year relative to matched former smokers without documented ENDS use (2%) ($p < 0.01$).

Results from multivariable conditional logistic regression analyses demonstrated that among current smokers, ENDS users had 16% greater odds of quitting smoking in the next year relative to matched current smokers who were non-users during the same time period

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Table 2
Associations between documented ENDS use and change in smoking status within one-year follow-up.

Smoking status at baseline	Change in smoking status *N* (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Current smokers (*N* = 9056)			
ENDS users	1028 (22.7)	1.26 (1.13, 1.40)	1.16[a,b] (1.04, 1.29)
Matched non-users	863 (19.1)		
Former smokers (*N* = 5504)			
ENDS users	382 (13.9)	2.35 (1.94, 2.85)	1.53[a,b,c] (1.22, 1.92)
Matched non-users	179 (6.5)		
Never-smokers (*N* = 1292)			
ENDS users	49 (7.6)	8.17 (3.50, 19.06)	7.41[a] (3.14–17.46)
Matched non-users	6 (0.93)		

Notes. Change in smoking status is defined as quitting smoking for current smokers, and initiating smoking among former and never-smokers. ENDS users were matched to non-ENDS users on sex, race/ethnicity, exact age, and month and year of concordant smoking status documentation.
[a] Adjusted for median household income and psychiatric/substance use disorder diagnoses in the year following ENDS use documentation.
[b] Adjusted for use of tobacco cessation medication (Nicotine replacement therapy or varenicline).
[c] Adjusted for time since quitting smoking.

(OR = 1.16, 95% CI = 1.04–1.29) (Table 2). Among former smokers, ENDS users had 53% greater odds of relapsing to smoking in the following year compared to non-users during the same time period (OR = 1.53, 95% CI = 1.22–1.92). Finally, among never-smokers, ENDS users had greater than seven times the odds of becoming current smokers in the next year relative to non-users during the same time period (OR = 7.41, 95% CI = 3.14–17.5). Odds ratios and 95% confidence intervals for the covariates for these regression analyses are provided in Appendix 3. Greater median household income and psychiatric or substance use disorders were associated with a greater likelihood of initiating smoking among never-smokers. Greater median household income, having a psychiatric disorder, tobacco cessation medication use, and being quit for < 6 months were associated with a greater likelihood of smoking relapse among former smokers. Psychiatric and substance use disorders and tobacco cessation medication use were associated with greater odds of quitting smoking among current smokers. Probabilistic bias analysis showed that the effects of misclassification due to imperfect follow-up data were likely to be minimal, resulting in odds ratio changes of 2% or less (Appendix 2).

At 12 months, there were 3931 current smokers among the patients with documented ENDS use compared with 3850 current smokers among matched patients without documented ENDS use: a difference of 81 current smokers with documented ENDS use.

4. Discussion

Incidence rates of patients' ENDS use based on clinician documentation in the EHR have increased dramatically in recent years, likely reflecting both surges in patient uptake of ENDS and greater patient-provider discussions about ENDS (Young-Wolff et al., 2017; Brown-Johnson et al., 2016). As expected, current smokers—and former smokers, to a lesser extent—had higher incidence rates of ENDS-use documentation each year than never-smokers. This finding likely reflects both greater use of ENDS and greater self-disclosure or patient-clinician discussion about ENDS use among current and former smokers relative to never-smokers. From 2012 to 2015, the number of patients with ENDS-use documentation peaked in 2014 for current and former smokers, and in 2015 for never-smokers. The peak among current and former smokers in 2014 may be explained by the simultaneous implementation of the Affordable Care Act and the influx of high-priority populations for tobacco control (e.g., men, adults aged 19–34, low-income enrollees) into the healthcare system in 2014 via the California insurance exchange and Medicaid expansion (McAfee et al., 2015; Reichard, 2014; Satre et al., 2016; Covered California, 2014). While our text-based assessment of ENDS-use documentation is novel and represents how the incidence of ENDS documentation has increased over time, results substantially understimate the true incidence of ENDS use (Young-Wolff et al., 2017). Standard ENDS documentation practices and discrete EHR fields for mandatory ENDS documentation that would allow for an enhanced estimate of ENDS incidence and prevalence are recommended.

Notably, among current smokers, documented ENDS use was associated with increased odds of quitting smoking in the next year, even after adjusting for utilization of tobacco cessation medications. ENDS use may directly help some smokers quit smoking (Hartmann-Boyce et al., 2016). In the literature, there are observational findings that smokers who use e-cigarettes are more likely to make a quit attempt and to succeed in quitting (Zhu et al., 2017; Levy et al., 2017b), particularly with a greater number of days of ENDS use in the past month (Levy et al., 2017b). There also are studies indicating that ENDS use is associated with a lower likelihood of quitting (Kalkhoran and Glantz, 2016). The potential for harm reduction may depend on patterns of ENDs use (e.g., intensity/frequency of use). Clinician inquiry and ENDS documentation in the EHR should quantify ENDs use. Most existing research on ENDS for quitting smoking is observational and, therefore, lacking the empirical strength of randomization that controls for inherent differences between exposure groups. ENDS users tend to have greater motivation to quit smoking and report more recent quit attempts (Biener and Hargraves, 2015; Schoenborn and Gindi, 2014). It may be that ENDS use (and discussion of ENDS with a healthcare provider) is a relevant marker for motivation to quit as well as receptivity to clinical intervention. Because quitting did not have to be sustained in future records to be coded as 'quitting', the potential for harm reduction in the long-run may be overestimated if patients did not quit for good. Notably, having a psychiatric or substance use disorder was also associated with greater odds of quitting smoking. These patients may have greater interactions with the healthcare system, providing more opportunities to receive clinician advice to quit and more opportunities to have a quit documented in the EHR.

Conversely, ENDS use was associated with increased odds of relapsing to smoking among former smokers, even after adjusting for tobacco cessation medication use. ENDS use may directly increase the risk for smoking relapse (e.g., via reinstating nicotine addiction, mimicking hand-to-mouth smoking behavior, re-normalizing smoking) or may be a marker for relapse risk. That is, former smokers who are at greater risk for smoking relapse may also be more likely to try ENDS or to talk to their healthcare providers about their ENDS use. ENDS use was associated with a greater likelihood of using tobacco cessation medication among former smokers, suggesting that this group may be

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fundamentally different and more actively attempting to stave off relapse. Randomized controlled trials are needed to further explore these associations.

Of concern, although the incidence of documented ENDS use was low among never-smokers, documented ENDS use was associated with more than seven times greater odds of initiating smoking in the next year. These findings are consistent with prior longitudinal survey research indicating that ENDS use is associated with subsequent initiation of cigarette smoking among youth and young adult never-smokers in the US (Primack et al., 2015; Leventhal et al., 2015; Wills et al., 2017; Barrington-Trimis et al., 2016; Unger et al., 2016). ENDS are the most commonly used tobacco product among US youth. Addressing this use, the US Surgeon General has issued a call to action to reduce ENDS use and related harms among young people (U.S. Department of Health and Human Services, 2016). Interestingly, nearly two-thirds of never-smokers in our study with documented ENDS use were age 25 or older, suggesting that the increased risk for smoking initiation among ENDS users may not be limited to youth and young adults. Again, while the association could be causal, never-smokers who use ENDS, and those who choose to discuss ENDS use with their clinicians, may have already been at elevated risk for smoking initiation regardless of ENDS use. Additional research is needed to evaluate these possibilities and illuminate the potential harms and benefits of ENDS use.

4.1. Limitations and strengths

Interpretations of study findings are limited by those data available in the EHR. Smoking status was self-reported and subject to social desirability bias. We are unable to determine the frequency or quantity with which patients used ENDS, duration of ENDS use, type of product used, level of nicotine, reasons for ENDS use, or motivation to initiate or quit smoking. These important details could be collected as part of more comprehensive routine ENDS inquiry and inclusion of discrete ENDS data elements in the EHR (Winden et al., 2015). The prevalence and quit rate of ENDS use cannot be reliably estimated from the EHR; thus, we focused on the earliest reference per person. It is possible that some matched patients without documented ENDS use were ENDS users; however, we would expect that patients with versus without documented ENDS use are more likely to be regular vs. single trial users. Further, if ENDS users are misclassified as non-users, this would bias results toward the null (i.e., no difference between groups). Our measure of quitting smoking focused on successful quit attempts in the short term. Patients may have returned to smoking over time. While ENDS documentation was associated with smoking status changes, we cannot determine the causal nature of these associations. Lastly, we lack data on ENDS use at 12 months, which prohibits our application of recently developed formulas (Kalkhoran and Glantz, 2015) to estimate the net health effects of ENDS use in our patient population. Major study strengths included examining smoking transitions in a large sample and wide age span of patients (ages 12+ years) that included current, former, and never smokers. This allowed us to examine cessation, relapse, and smoking initiation relative to ENDS use over a 12-month period and calculate changes in the number of smokers among patients with and without documented ENDS use. Notably, prior research has been more circumscribed, typically examining only adult current smokers or young never smokers. A novel use of KPNC's rich longitudinal data, we developed a comprehensive matching algorithm and utilized a cohort design, thereby minimizing residual confounding in assessing smoking status changes. We also conducted a bias analysis to examine the expected validity of our findings despite outcome misclassification, increasing confidence in our results.

5. Conclusions

Patients' use of ENDS, based on healthcare providers' documentation in the EHR, has increased dramatically in recent years. Large, integrated healthcare delivery systems with EHRs collect longitudinal clinical data that can reveal novel insights in use patterns of emerging drug products over time. To achieve this, healthcare systems should implement more consistent and standardized documentation of the behavior (i.e., ENDS use) in the EHR with required discrete fields. Results from this matched retrospective cohort study corroborate earlier observational research and provide new evidence suggesting both the harm-reduction potential of ENDS among current smokers and the potential for harm (initiation and relapse to smoking) for never-smokers and former smokers. However, we cannot infer causality from these data.

The overall impact of ENDs on smoking behavior at a population level will depend on whether the number of current smokers who successfully quit smoking with ENDS is greater than the number of former and never-smokers who relapse or initiate smoking following ENDS use. In this study, the overall number of current smokers was slightly higher at 12 months among patients with versus without documented ENDS use. Given our study limitations in defining quits (not necessarily sustained) and detecting ENDS use (likely under-detected in young people, i.e., never smokers), we anticipate this differential may be even greater and believe further investigation is warranted. Worth considering, are the clinical, regulatory and policy strategies that could influence the balance (e.g., by extending Tobacco 21 policies to ENDS, banning kid-friendly ENDS flavors, restricting marketing/advertising of ENDS to youth, and banning indoor use). Further research among nationally representative samples is needed to determine how safe ENDS are relative to cigarettes and whether the long-term effects of ENDS on smoking cessation, relapse, and initiation represent a net benefit or a net risk for population health.

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All authors contributed to this work. KCYW designed the study, drafted the manuscript and guided interpretation of the results. DK, BF and VS participated in the data extraction, analysis and editing of the paper. RF, AT and JJP assisted in study design, advised on analysis methods, and assisted with editing of the paper.

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All other authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ypmed.2018.01.012.

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TABLE 2—Support Among Blacks for Banning Cigarettes With Menthol: United States, 2009

Demographic Variables	Percentage of Sample (Unweighted)	Support Ban on Menthol (Weighted), % (95% CI)	Support Ban on Menthol, AOR (95% CI)
Overall (n = 303)		75.8 (70.9, 80.7)	
Smoking status**			
Never smoker	64.4	83.4 (78.0, 88.8)	3.83 (1.74, 8.45)
Former smoker	17.8	71.4 (57.7, 85.1)	1.95 (0.74, 5.15)
Current smoker (Ref)	17.8	52.8 (39.4, 66.2)	1.00
Age, y			
18–24 (Ref)	12.5	87.5 (78.1, 96.9)	1.00
25–44	31.0	77.6 (70.0, 85.2)	0.58 (0.21, 1.60)
45–64	38.9	67.1 (56.9, 77.3)	0.39 (0.14, 1.11)
≥ 65	17.5	75.9 (60.3, 91.5)	0.54 (0.15; 1.97)
Education			
< High school[a]	12.2	62.5 (43.1, 81.9)	0.61 (0.19, 1.97)
High school diploma/GED	30.0	83.3 (75.3, 91.3)	1.65 (0.71, 3.81)
Some college	30.7	69.4 (59.6, 79.2)	0.66 (0.31, 1.42)
College (Ref)	27.1	78.3 (69.4, 87.2)	1.00
Gender			
Women	69.3	80.9 (74.7, 87.1)	1.74 (0.95, 3.20)
Men (Ref)	30.4	69.1 (60.9, 77.3)	1.00

Note. AOR = adjusted odds ratio; CI = confidence interval; GED = Graduate Educational Development Exam.
[a]n < 30.
***P* < .001.

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Modeling the Future Effects of a Menthol Ban on Smoking Prevalence and Smoking-Attributable Deaths in the United States

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We used a validated smoking simulation model and data from the 2003 Tobacco Use Supplement to the Current Population Survey to project the impact that a US menthol ban would have on smoking prevalence and smoking-attributable deaths. In a scenario in which 30% of menthol smokers quit and 30% of those who would have initiated as menthol smokers do not initiate, by 2050 the relative reduction in smoking prevalence would be 9.7% overall and 24.8% for Blacks; deaths averted would be 633 252 overall and 237 317 for Blacks. (*Am J Public Health.* 2011;101:1236–1240. doi:10.2105/AJPH.2011.300179)

The Family Smoking Prevention and Tobacco Control Act[1] authorized the Food and Drug Administration to establish the Center for Tobacco Products to regulate tobacco for the protection of the public health. The Center for

Tobacco Products is charged with considering a ban on the menthol flavoring in cigarettes (menthols). The act specifies that in considering the impact of a ban, a broad public health standard is to be applied rather than a narrow individual standard of whether there is more or less harm to individual users of menthols. Although there is evidence that menthol plays a role in smoking initiation and cessation,[2–6] little is known about the anticipated impact of such a ban on population-level smoking behavior and subsequent deaths that may be averted. Of particular interest is the effect of a ban on the Black population, which has substantially higher rates of menthol use than do other racial/ethnic groups.[7]

In the absence of an experimental or actual ban on menthols, simulation modeling can be a useful tool to understand the potential pathways and predict the anticipated effect of such a policy intervention.[8] In the current study, we used a validated smoking simulation model, SimSmoke,[9–14] in conjunction with plausible ranges of change in patterns of smoking behavior, to examine the potential impact of a menthol ban on future smoking prevalence and smoking-attributable deaths.

METHODS

We extended previous versions of the SimSmoke model to explicitly distinguish menthol and nonmenthol smokers. Separate models were developed for males and females, both for the total population and for Blacks. The model uses self-reported data from the 2003 Tobacco Use Supplement to the Current Population Survey (TUS-CPS) as well as initial population data for the year 2003.

We first distinguished among never, current, and former smokers. Current smokers were those who had smoked at least 100 cigarettes in their lifetime and smoked some or all days. Former smokers were those who had smoked at least 100 cigarettes in their lifetime but did not currently smoke, further distinguished by how many years ago they had quit smoking. Current and former smokers were also differentiated by cigarette type into menthol, nonmenthol, and no usual type, as defined by the TUS-CPS.[15] We averaged data over 3-age-year groups (e.g., people aged 18–20 years) and then smoothed.

The smoking model simulates groups of individuals as they transition into and out of smoking through initiation, cessation, and relapse rates, following a discrete first-order Markov process. We measured initiation for each cigarette type through age 24 years as the change in smoking prevalence between successive age-year groups; this figure thus represents initiation net of cessation and switching between types for each age. We applied cessation rates after age 24 years in the model, measured as smokers who had quit in the past year but not in the past 3 months as a percentage of smokers 1 year ago.[16] We constructed separate cessation rates by gender and type for 3-age-year groups and then smoothed. We applied the same relapse rates to former smokers by type, distinguished by age and gender on the basis of various sources.[17–20]

The influence of tobacco-control policies on initiation and cessation through the year 2010 were incorporated into the model by using measures of price, smoke-free air, and expenditure policies obtained from the Impacteen Web site (http://www.impacteen.org). We calibrated the model by comparing smoking rates from the model predicted for 2006 to smoking rates from the 2006 TUS-CPS.

We used the calibrated model to estimate the effect of banning menthol cigarettes as of the year 2011. A ban on menthol cigarettes may have 3 types of effects. First, some former menthol smokers may simply switch to smoking nonmenthol cigarettes (switching effect). However, in a recent preliminary analysis of 2010 TUS-CPS data, only 36.2% of all menthol smokers and 25.7% of Black menthol smokers predicted that they would switch to a nonmenthol brand if menthol cigarettes were no longer available.[21] A second effect is that some menthol smokers may quit soon after the ban as a response to the unavailability of their preferred cigarette, that is, the cigarette viewed as more safe or less harsh (cessation effect). Tauras et al.[22] did not find close substitutability of the 2 products; in fact, they found that nonmenthol cigarettes were less of a substitute for menthol cigarettes than was the reverse. Indeed, in 2010 TUS-CPS data, 39.0% of all menthol smokers and 46.8% of Black menthol smokers reported that they would quit if menthol cigarettes were not available.[21] Although intentions do not always translate into actual behavior, this suggests that menthol smokers are dedicated to menthol flavoring and do not see nonmenthol cigarettes as a suitable substitute.

Finally, some individuals who would have initiated smoking menthol cigarettes may not initiate (initiation effect). Studies have not directly considered the effects of a menthol ban on smoking initiation, but the proportion of menthol smokers is inversely related to age, suggesting that menthol cigarettes are the preferred starter cigarette and that they facilitate initiation.[7]

Former menthol smokers who remain smokers in the switching effect are assumed to take on the cessation rate of nonmenthol smokers. This rate is directly estimated from the TUS-CPS and has been found to be relatively stable for the years 2003 and 2006.[15] Direct estimates were not available for the cessation and initiation effects. On the basis of the studies cited above, we considered 3 conservative, plausible scenarios: (1) 10% of the menthol smokers permanently quit, and 10% of those who would have initiated as menthol smokers do not initiate; (2) 20% quit, and 20% do not initiate; and (3) 30% quit, and 30% do not initiate.

For each scenario, we projected the effect on smoking prevalence, the absolute number of smokers, and the number of smoking-attributable deaths 40 years forward, to the year 2050. We calculated the percentage change in smoking prevalence relative to the baseline case (status quo scenario, i.e., no ban is enacted) and the deaths averted because of a menthol ban as the difference between smoking-attributable deaths in the baseline case and those under a ban. Previous studies do not clearly distinguish mortality risks of menthol and nonmenthol smokers, so we applied the same relative risks to menthol and nonmenthol that have been applied to all smokers in previous SimSmoke models.[10,11,23,24]

In the baseline scenario, the model incorporates switching between menthols and nonmenthols up through age 24 years through our measure of net initiation by type, but the model does not consider switching after age 24 years. The few studies that examine switching yield mixed results.[4,25,26] In the model, those smokers maintaining no preference for either menthol or nonmenthol—who are probably most likely to switch—are conservatively assumed to continue as nonmenthol smokers after the ban.

RESULTS

In the absence of a menthol ban, the model predicts a slow downward trend in overall smoking prevalence from 18.1% (20.3% for males and 16.1% for females) in 2003 to 8.2% in 2050. Smoking rates decline, but the percentage of those smoking menthols is projected to increase. From 2003 to 2050, menthol use increases from about 23% to 27% among all males and from 65% to 77% among Black males. For females, the menthol rate stays flat for all smokers, but it increases from 76% in 2003 to 83% in 2050 among Blacks (results not shown).

Figure 1 presents the projected smoking prevalence of all smokers under the status quo and the projected changes in population prevalence under a scenario of 10% change (10% reduction in initiation and 10% increase in cessation), a scenario of 20% change, and a scenario of 30% change. At 10 years following the hypothetical ban on menthol in cigarettes, the model projects a 4% relative reduction in smoking prevalence compared with the status quo under the 10% scenario, increasing to 4.6% at 20 years and 4.8% at 40 years. At 40 years, the model projects a 7.2% decrease under the 20% scenario and a 9.7% decrease under the 30% scenario. For Blacks in 2050, the projected relative reduction is a 9.1% decrease under the 10% scenario, a 17.0% decrease under the 20% scenario, and a 24.8% decrease under the 30% scenario.

Table 1 presents the projected number of smoking-attributable deaths at 10-year intervals through 2050 for each scenario and computes deaths averted at 2050 relative to status quo estimates. In 2020, the menthol ban results in 1.06 million fewer smokers under the most conservative scenario, increasing slightly through 2030 and then declining (results not shown). In 2020 alone, there are 4764 smoking-attributable deaths averted, increasing to 11 355 in 2040. From 2011 to 2050, a total of 323 107 deaths are averted under the 10% scenario, 478 154 under the 20% scenario, and 633 252 under the 30% scenario. Almost one third of the deaths averted are among Blacks, for whom 91 744 deaths are averted under the 10% scenario, 164 465 under the 20% scenario, and 237 317 under the 30% scenario.

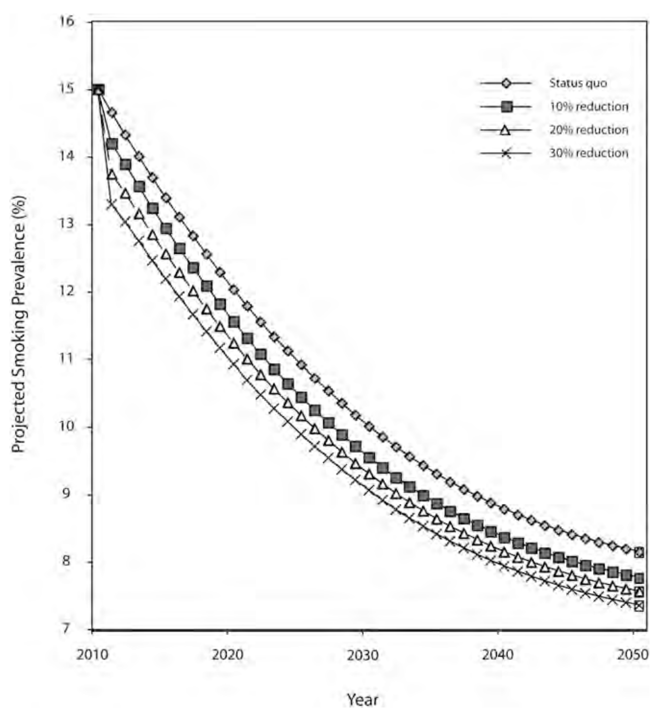

FIGURE 1—Smoking prevalence if menthol is banned under 3 scenarios (10%, 20%, and 30% change in initiation and cessation), projected from 2010 to 2050: United States.

DISCUSSION

This application of SimSmoke modeling suggests that a menthol ban would have large population-level benefits in reducing smoking prevalence, the number of smokers, and the number of smoking-attributable deaths in the United States over a 40-year period. We have provided 3 plausible scenarios to address the lack of data on the proportion of menthol smokers who would quit or never start smoking in the case of a ban on menthol, and our results suggest that somewhere between 323 000 and 633 000 deaths could be avoided under a ban, almost one third of which would be among Blacks. Even under the most conservative scenario, the model predicts a substantial public health benefit of a ban on menthols consistent with the broad public health standard specified by the Family Smoking Prevention and Tobacco Control Act of 2009.[1]

As is typically the case with simulated projections, the models are limited by current evidence regarding switching and initiation behaviors, assumptions inherent in the model, and the reliability of the data. The model uses data from the 2003 TUS-CPS, which yields smoking prevalence rates below those from the National Health Interview Survey (NHIS). We used TUS-CPS data to calibrate our model to predict well between 2003 and 2006. The 2009 TUS-CPS data were not yet available, but the model overpredicts the percentage change in smoking rates from 2006 to 2009 implied by NHIS data. Still, the lower initial smoking level seen in TUS-CPS data relative to NHIS data and the greater projected change in smoking prevalence than is observed in the NHIS data between 2006 and 2009 can both be expected to reduce the estimated number of smoking-attributable deaths and consequently increase the number of deaths averted as a result of the ban. Therefore, the estimate of deaths averted is likely to be conservative.

The immediate effects of a ban are simulated as occurring through cessation in the first year of the ban. The results of a gradual change, either because the ban is implemented in steps or because reactions to the ban occur over

TABLE 1—Smoking-Attributable Deaths (SADs) and Deaths Averted if Menthol is Banned Under 3 Scenarios (10%, 20%, and 30% Change in Initiation and Cessation), Projected From 2010 to 2050: Total Population and Black Population, United States

Menthol Ban Scenarios	SADs, 2010	SADs, 2020	SADs, 2030	SADs, 2040	SADs, 2050	Total SADs	Total SADs Averted Compared With Status Quo
Total population							
Status quo	386 732	410 809	399 028	342 472	272 424	17 923 889	-
10% change	386 732	406 046	388 347	331 117	262 574	17 600 782	323 107
20% change	386 732	402 568	382 621	326 799	259 002	17 445 735	478 154
30% change	386 732	399 091	376 893	322 478	255 424	17 290 637	633 252
Black population							
Status quo	53 836	57 056	53 382	45 022	37 475	2 433 536	-
10% change	53 836	55 234	50 086	42 175	35 320	2 341 792	91 744
20% change	53 836	53 706	47 562	40 044	33 340	2 269 071	164 465
30% change	53 836	52 177	45 036	37 908	31 347	2 196 219	237 317

Note. Total SADs averted include all years from 2010 through 2050 and therefore include years not represented in the table.

a longer period than 1 year, would yield slightly different results in the earlier years but almost identical results by 2020 and certainly identical results by 2050.

SimSmoke incorporates the effect of tobacco-control policies through 2010, assuming that policies have the same percentage effects on menthol and nonmenthol smokers. Evidence on these effects is limited, but some evidence suggests that price and clean-air policies may be less effective among menthol smokers. In the absence of a ban, the percentage of menthol smokers might be expected to increase with stricter tobacco-control policies.[22] We have assumed that relative mortality risks are equal for menthol and nonmenthol smokers, and for Black smokers relative to other racial/ethnic groups. Although the higher lung cancer risk among Black smokers suggests a link to menthol use,[27,28] studies fail to find a clear association between menthol smoking and increased risk for lung cancer or other disease.[29–31] If a menthol ban increases smoking cessation and reduces initiation, Blacks would experience even greater health benefits, which could serve to reduce health disparities.

Given the tremendous harms associated with smoking,[32] public health efforts are needed to positively influence population-level smoking behavior and reinvigorate the stalled decline in adult smoking prevalence in the United States.[33] Such efforts are especially important for populations at increased risk, such as Blacks, who disproportionately smoke menthols. If a menthol ban were accompanied by effective mass-media campaigns and increased access to evidence-based cessation services, additional reductions in smoking prevalence would be likely, further contributing to the public health impact of this policy intervention.

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Contributors

D.T. Levy developed the model and wrote the article. K. Blackman conducted the data analysis. J.L. Pearson, A.C. Villanti, R.S. Niaura, D.M. Vallone, and D.B. Abrams suggested the original idea and contributed to the writing of the article.

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Human Participant Protection

No protocol approval was necessary because the study used secondary data from a public-use data set.

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Federal Trade Commission

Cigarette Report

for 2011

ISSUED: 2013

I. INTRODUCTION

This report is the latest in a series on cigarette sales, advertising, and promotion that the Federal Trade Commission ("Commission") has prepared since 1967.

The statistical tables appended to this report provide information on domestic sales and advertising and promotional activity by the five largest U.S. cigarette manufacturers. The tables were compiled from data contained in special reports submitted to the Commission pursuant to compulsory process by: Altria Group, Inc.; Commonwealth Brands, Inc.; Lorillard, Inc.; Reynolds American, Inc.; and Vector Group Ltd.

II. TOTAL CIGARETTE SALES AND ADVERTISING AND PROMOTIONAL EXPENDITURES

The total number of cigarettes reported sold or given away by the major manufacturers decreased by 8.1 billion units (2.9 percent) from 2010 to 2011. Advertising and promotional expenditures, by contrast, increased, rising from $8.046 billion to $8.366 billion. The largest single category of these expenditures in 2011 was price discounts paid to cigarette retailers or wholesalers in order to reduce the price of cigarettes to consumers, which accounted for $6.997 billion (83.6 percent of total advertising and promotional expenditures).[1]

III. CIGARETTES SOLD AND GIVEN AWAY

Tables 1 and 1A display annual cigarette sales by the manufacturers to wholesalers and retailers. Table 1A displays the total number of cigarettes sold and given away in the years 2001 through 2011.[2] In 2011, the five major domestic cigarette manufacturers sold 273.6 billion

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[1] The advertising and promotion expenditure figures contained in this report are in nominal dollars and have not been adjusted for inflation.

[2] Cigarettes given away include all cigarettes distributed for free, whether through sampling, coupons for free product, "buy 3 packs, get 1 free" type offers, or otherwise, as long as those cigarettes were not reported as sold. For years prior to 2001, the Commission required the

cigarettes domestically, down from 281.6 billion in 2010. The Commission is not reporting the number of cigarettes given away in 2011, because only one company reported such giveaways.

IV. ADVERTISING AND PROMOTIONAL EXPENDITURES BY CATEGORY

Tables 2 through 2D show the amounts spent on cigarette advertising and promotion for the years 1970, and 1975 through 2011.[3] These tables list the amounts spent on the different types of media advertising (*e.g.*, magazines) and sales promotion activities (*e.g.*, distribution of cigarette samples), and also give the percentage of the total amount spent for the various types of advertising and promotion.

Table 2E shows that overall, the major manufacturers spent $8.366 billion on cigarette advertising and promotion in 2011, an increase from the $8.046 billion reported in 2010.[4]

The companies reported spending $549,000 on newspaper advertising in 2011. This is the first year since 2008 that the Commission is reporting spending on newspaper advertising.

The companies reported spending $23.3 million on magazine advertising in 2011, down from $46.5 million in 2010.

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manufacturers to report the number of cigarettes they sold but not the number they gave away. It is possible that in those earlier years, some manufacturers included in their sales figures some cigarettes that were actually given away.

[3] The reported figures include all advertising, merchandising, and promotional expenditures related to cigarettes, regardless of whether such expenditures would constitute "commercial speech" or would be protected from law enforcement action under the First Amendment.

[4] Definitions of the advertising and promotional expenditure categories currently used are reported in the Appendix to this report. If only one company reported spending money on a particular type of advertising or promotion, that category is shown as "N/A" on Table 2D and its expenditures are included in the "All Others" category, to avoid potential disclosure of individual company data. For this reason, the Commission is not separately reporting the specific amounts spent in 2011 on promotional allowances paid to persons other than retailers and wholesalers, on Internet advertising (other than the company's own website), or on telephone advertising.

Spending on "outdoor" advertising increased from $1.7 million in 2010 to $3.1 million in 2011. Since 2002, "outdoor" advertising has been defined to mean billboards; signs and placards in arenas, stadiums, and shopping malls (whether they are open air or enclosed); and any other advertisements placed outdoors, regardless of their size, including those on cigarette retailer property. Before 2002, "outdoor" advertising was not precisely defined and it was not clear that signs in arenas, stadiums, shopping malls, or on retailer property would have been reported in this category.

As they have since 2001, the companies reported no expenditures on transit advertising (*i.e.*, advertising in or on private or public vehicles or any transportation facility) in 2011.

Spending on point-of-sale materials (ads posted at the retail location but excluding outdoor ads on retailer property) fell from $106.6 million in 2010 to $76.6 million in 2011.

Since 2002, the "promotional allowance" category has been replaced by four separate categories: price discounts, promotional allowances paid to retailers, promotional allowances paid to wholesalers, and other promotional allowances. As noted above, the largest of these categories was price discounts paid to cigarette retailers or wholesalers in order to reduce the price of cigarettes to consumers (*e.g.*, off-invoice discounts, buy downs, and voluntary price reductions), which accounted for expenditures of $7.00 billion in 2011 (up from $6.49 billion in 2010).

In addition, the industry spent $357.0 million in 2011 (down from $370.0 million in 2010) on promotional allowances paid to cigarette retailers in order to facilitate the sale or placement of cigarettes (*e.g.*, payments for stocking, shelving, displaying, and merchandising brands, volume rebates, and incentive payments); and $401.0 million on promotional allowances paid to cigarette wholesalers (*e.g.*, payments for volume rebates, incentive payments, value-added services, and promotional executions). When these three promotional allowance categories are combined, they total $7.75 billion, and account for 92.7 percent of all 2011 spending; in 2010, they totaled $7.27 billion, 90.4 percent of all spending. The Commission is not separately reporting the amount spent on promotional allowances paid to persons other than retailers and wholesalers.

Money spent giving cigarette samples to the public ("sampling distribution") decreased from $22.2 million in 2010 to $4.5 million in 2011. "Sampling" includes the distribution of cigarettes for consumer testing or evaluation outside the company's facility, and the distribution of coupons for free cigarettes when no purchase or payment is required to obtain the coupons or cigarettes.

In 2010, $6.3 million was spent on branded specialty item distribution through the mail, at promotional events, or by any means other than at the point-of-sale with the purchase of cigarettes; $65.6 million was spent distributing non-branded, non-cigarette items in connection with the marketing or promotion of cigarettes.[5] In 2011, those figures were $5.6 million and $44.4 million, respectively.

Expenditures for the adult-only public entertainment category declined from $138.9 million in 2010 to $129.8 million in 2011. This category includes public entertainment events (*e.g.*, sponsorship of bar nights or concerts) that take place in an adult-only facility and display the name or logo of a company's cigarettes or otherwise refer to cigarettes. The companies reported no expenditures on public entertainment events in non-adult-only facilities that display the name or logo of a company's cigarettes or otherwise refer to cigarettes.

All reporting companies stated that no money had been spent on endorsements and testimonials, or on audio-visual advertising, in 2011.

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[5] Specialty item distribution includes the practice of selling or giving to consumers non-cigarette items, such as T-shirts, caps, sunglasses, key chains, lighters, and sporting goods.

The companies reported spending $51.5 million for direct mail advertising in 2011, down from $56.5 million in 2010.[6]

The industry reported spending $171.2 million on coupons to reduce the retail cost of cigarettes in 2011 (a decrease from the $235.8 million reported in 2010).[7]

Retail-value-added expenditures are the costs associated with offers such as “buy one, get one free” and “buy three, get a free T-shirt,” where the bonus item is distributed at retail when the cigarettes are purchased. The companies reported spending no money on either category of retail-value-added in 2011. In 2010, the companies had reported spending no money on retail-value-added involving free non-cigarette items, and the Commission did not separately report the amount spent on retail-value-added involving free cigarettes.

In 2011, the companies reported spending $21.9 million on advertising on company websites, up slightly from the $20.8 million they reported in 2010.

The compulsory process orders that the Commission issued in 2011 for 2009 and 2010 data specifically asked for the first time for spending on “social media marketing on Web sites or other online services or communities, including but not limited to social networking sites, microblogging sites, content-sharing sites, and blogs.” The companies reported no spending in those two years. The orders issued in 2012 for 2011 data also included this expenditure category, and the companies, again, reported no such spending.

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[6] This category does not include direct mail containing coupons, which is reported separately.

[7] As noted above, when coupons are distributed for free cigarettes and no purchase is required to redeem them, such activities are reported as “sampling,” not as “coupons.”

The Commission requires the cigarette manufacturers to report the amounts they spent advertising and promoting sports and sporting events.[8] This question is separate from, and duplicative of, the reporting of the individual various advertising and promotion categories. For example, money spent on a magazine advertisement promoting a cigarette-branded sports tournament open to those of all ages is reported under the category "general-audience public entertainment" and is also reported as an expenditure on "sports and sporting events." The companies reported that they did not spend any money on sports and sporting events in 2011.

Since 2001, the Commission has required the manufacturers to report expenditures on advertisements directed to youth or their parents that are intended to reduce youth smoking. The companies reported spending $2.9 million in 2011.[9] Over the previous five years, they had reported expenditures of $57.7 million (2006), $20.7 million (2007), $11.5 million (2008), $8.1 million (2009), and $4.4 million (2010). These figures do not include contributions to third parties that engage in such programs.

Cigarette manufacturers reported that neither they nor anyone working for them or on their behalf paid money or any other form of compensation in connection with the production or filming of any motion picture or television show in 2011, or paid money or any other form of compensation to anyone engaged in product placement in motion pictures or television shows. The companies

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[8] This includes expenditures for: (1) the sponsoring, advertising, or promotion of sports or sporting events; support of an individual, group, or sports team; and purchase of or support for equipment, uniforms, sports facilities, and/or training facilities; (2) all expenditures for advertising in the name of the cigarette company or any of its brands in a sports facility, on a scoreboard, or in conjunction with the reporting of sports results; and (3) all expenditures for functional promotional items (clothing, hats, etc.) connected with a sporting event.

[9] These expenditures are not included in the $8.366 billion reported in Table 2E (cigarette and smokeless tobacco expenditures by category for 2011).

also reported that neither they nor anyone working for them or on their behalf: sought, solicited, granted approval, or otherwise gave permission for the appearance of any cigarette product or cigarette brand imagery in any motion picture, television show, or video appearing on the Internet, although one company reported having video advertising on a website restricted to age-verified smokers 21 or older.

The expenditure data reported in Tables 2 through 2D were not collected in their present form until 1975. Therefore, Table 3 reports advertising expenditures from 1963 through 1974.

V. TAR RATINGS, FILTERS, LENGTH, AND FLAVOR

Tables 4 and 4A give the domestic market share of cigarettes with tar ratings of 15 milligrams (mg.) or less for the years 1967 through 2011. The data for the years since 1982 are further broken down into sub-categories according to tar ratings, *e.g.*, 3 mg. or less, 6 mg. or less, etc. (categories are presented cumulatively). In 2011, cigarettes with tar ratings of 15 mg. or less constituted 94.7 percent of the domestic cigarette market, while cigarettes with tar ratings of 3 mg. or less – the lowest rated portion of the market – made up 0.2 percent of the market.

As shown in Tables 5 and 5A, filtered cigarettes have dominated the market since the Commission began collecting this information in 1963. Filtered cigarettes account for 99.8 percent of the market in 2011.

Table 6 provides the market share of the various cigarette length categories. The King-size (79-88 mm.) category continues to be the biggest seller, with 59 percent of the market in 2011, down from 62 percent in 2010. This category is followed by the Long (94-101 mm.) group, which rose from 33 percent in 2010 to 37 percent in 2011.

Table 7 gives the market share of menthol and non-menthol cigarettes. In 2008, menthol cigarettes were 27 percent of the market, while non-menthols held 73 percent of the market. In

2009 and 2010, the market share of menthol cigarettes reported by the companies were 21 percent and 22 percent, respectively. In 2011, menthol cigarettes rose to 32 percent of the market.

Table 8 shows the percentage of cigarettes that disclosed both tar and nicotine ratings on their packs during the years 1994 through 2001. Table 8A shows the percentage that disclosed tar ratings from 2002 to 2011.

In 2008, the Commission rescinded guidance issued in 1966 that generally permitted statements concerning tar and nicotine yields if they were based on the Cambridge Filter Method. The Commission took this action because the scientific consensus was that machine-based measurements of tar and nicotine yields based on this testing methodology did not provide meaningful information on the amounts of tar and nicotine smokers receive from cigarettes, and that the test method was sufficiently flawed to make statements of tar and nicotine yields as measured by the method unlikely to help consumers make informed decisions. The Commission also believed that statements of tar and nicotine yields as measured by this test method were likely to mislead consumers who believe they will get proportionately less tar and nicotine from lower-rated cigarettes than from higher-rated brands.

Table 8A shows that, for the fourth consecutive year, 0.0 percent of all cigarettes sold in 2011 printed tar ratings on their packs. Given this recent history, the Commission has decided to discontinue the updating of Table 8A. The Commission will continue to require the companies to report these data, however, and will publish the data if the companies resume printing tar ratings on packs.

TABLE 1
TOTAL DOMESTIC CIGARETTE UNIT SALES
(IN BILLIONS OF INDIVIDUAL CIGARETTES)

YEAR	TOTAL SALES REPORTED BY CIGARETTE MANUFACTURERS*	UNIT CHANGE FROM PRIOR YEAR	% CHANGE FROM PRIOR YEAR	USDA CIGARETTE CONSUMPTION ESTIMATES
1963	516.5	---	---	523.9
1964	505.0	(11.5)	(2.2)	511.2
1965	521.1	16.1	3.2	528.7
1966	529.9	8.8	1.7	541.2
1967	525.8	5.9	1.1	549.2
1968	540.3	4.5	.8	545.7
1969	527.9	(12.4)	(2.3)	528.9
1970	534.2	6.3	1.1	536.4
1971	547.2	13.0	2.4	555.1
1972	561.7	14.5	2.7	566.8
1973	584.7	23.0	4.1	589.7
1974	594.5	9.8	1.7	599.0
1975	603.2	8.7	1.5	607.2
1976	609.9	6.7	1.1	613.5
1977	612.6	2.7	.4	617.0
1978	615.3	2.7	.4	616.0
1979	621.8	6.5	1.1	621.5
1980	628.2	6.4	1.0	631.5
1981	636.5	8.3	1.3	640.0
1982	632.5	(4.0)	(.6)	634.0
1983	603.6	(28.9)	(4.6)	600.0
1984	608.4	4.8	.8	600.4
1985	599.3	(9.1)	(1.5)	594.0
1986	586.4	(12.9)	(2.2)	583.8
1987	575.4	(11.0)	(1.9)	575.0
1988	560.7	(14.7)	(2.6)	562.5
1989	525.6	(35.1)	(6.3)	540.0
1990	523.7	(1.9)	(.4)	525.0
1991	510.9	(12.8)	(2.4)	510.0
1992	506.4	(4.5)	(.9)	500.0
1993	461.4	(45.0)	(8.9)	485.0
1994	490.2	28.8	6.2	486.0
1995	482.3	(7.9)	(1.6)	487.0
1996	484.1	1.8	0.4	487.0
1997	478.6	(5.5)	(1.1)	480.0
1998	458.6	(20.1)	(4.2)	465.0
1999	411.3	(47.2)	(10.3)	435.0
2000	413.9	2.6	.6	430.0

* Cigarettes sold by manufacturers to wholesalers and retailers within the U.S. and to armed forces personnel stationed outside the U.S.

TABLE 1A

TOTAL DOMESTIC CIGARETTE UNITS SOLD AND GIVEN AWAY

(IN BILLIONS OF INDIVIDUAL CIGARETTES)

YEAR	UNITS SOLD*	UNITS GIVEN AWAY**	TOTAL NUMBER SOLD AND GIVEN AWAY AS REPORTED BY MANUFACTURERS	UNIT CHANGE IN SOLD AND GIVEN AWAY FROM PRIOR YEAR	PERCENT CHANGE IN SOLD AND GIVEN AWAY FROM PRIOR YEAR	USDA CIGARETTE CONSUMPTION ESTIMATES
2001	398.3	3.9	402.2	***	***	425.0
2002	376.4	11.1	387.4	(14.8)	(3.7)	415.0
2003	360.5	7.1	367.6	(19.8)	(5.1)	400.0
2004	361.3	2.1	363.4	(4.2)	(1.1)	388.0
2005	351.6	3.0	354.6	(8.8)	(2.4)	376.0
2006	343.3	7.2	350.5	(4.1)	(1.2)	371.0
2007	337.7	5.0	342.8	(7.7)	(2.2)	****
2008	320.0	2.7	322.6	(20.2)	(5.9)	****
2009	290.2	0.1	290.3	(32.3)	(10.0)	****
2010	281.6	0.05	281.7	(8.6)	(3.0)	****
2011	273.6	N/A†	273.6	(8.1)†	(2.9)†	****

* Cigarettes sold by manufacturers to wholesalers and retailers within the U.S. and to armed forces personnel stationed outside the U.S.

** Cigarettes given away within the U.S. and to armed forces personnel stationed outside the U.S.

*** Prior to 2001, the Commission did not ask about cigarettes given away, although some cigarettes given away may have been reported as sold.

**** USDA no longer reports these data.

† The Commission is not reporting the number of cigarettes given away, to avoid potential disclosure of individual company data.

TABLE 2

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES FOR YEARS 1970, 1975-1985 (DOLLARS IN THOUSANDS)*

	1970	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985
Newspapers	$14,026	$104,460	$155,808	$190,677	$186,947	$240,978	$304,380	$358,096	$282,897	$200,563	$193,519	$203,527
	3.9%	21.3%	24.4%	24.5%	21.4%	22.2%	24.5%	23.1%	15.8%	10.6%	9.2%	8.2%
Magazines	$50,018	$131,199	$148,032	$173,296	$184,236	$257,715	$266,208	$291,227	$349,229	$388,365	$425,912	$395,129
	13.9%	26.6%	23.2%	22.2%	21.1%	23.8%	21.4%	18.8%	19.5%	20.4%	20.3%	16.0%
Outdoor	$7,338	$84,329	$102,689	$120,338	$149,010	$162,966	$193,333	$228,081	$266,925	$295,226	$284,927	$300,233
	2.0%	17.2%	16.1%	15.4%	17.0%	15.0%	15.6%	14.7%	14.9%	15.5%	13.6%	12.1%
Transit	$5,354	$10,852	$19,341	$21,530	$22,899	$21,151	$26,160	$21,931	$24,135	$26,652	$25,817	$33,136
	1.5%	2.2%	3.0%	2.8%	2.6%	2.1%	2.0%	1.4%	1.3%	1.4%	1.2%	1.3%
Point-of-Sale	$11,663	$35,317	$44,176	$46,220	$57,384	$66,096	$79,799	$98,968	$116,954	$170,059	$167,279	$142,921
	3.2%	7.2%	6.9%	5.9%	6.6%	6.1%	6.4%	6.4%	6.5%	8.9%	8.0%	5.8%
Promotional Allowances	$33,789	$72,018	$82,523	$108,227	$125,148	$137,111	$179,094	$229,077	$272,269	$366,153	$363,247	$548,877
	9.4%	14.7%	12.9%	13.9%	14.3%	12.7%	14.4%	14.8%	15.2%	19.3%	17.3%	22.2%
Sampling Distribution	$11,775	$24,196	$40,390	$47,683	$47,376	$64,286	$50,459	$81,522	$141,178	$125,968	$148,031	$140,565
	3.3%	4.9%	6.3%	6.1%	5.4%	5.9%	4.1%	5.3%	7.9%	6.6%	7.1%	5.7%
Specialty Item Distribution	$5,652	$10,088	$20,030	$35,797	$48,281	$62,029	$69,248	$115,107	$95,246	$127,186	$140,431	$211,429
	2.6%	2.1%	3.1%	4.6%	5.5%	5.7%	5.6%	7.5%	5.3%	6.6%	6.7%	8.5%
Public Entertainment	$544	$8,484	$7,946	$9,538	$11,590	$10,783	$16,914	$37,423	$63,168	$76,648	$59,988	$57,581
	0.2%	1.7%	1.3%	1.2%	1.3%	1.0%	1.4%	2.4%	3.5%	4.0%	2.9%	2.3%
Other**	$220,841	$10,311	$18,182	$26,157	$42,100	$60,310	$56,694	$86,226	$181,813	$123,951	$286,035	$443,043
	61.1%	2.0%	2.8%	3.4%	4.8%	5.6%	4.6%	5.6%	10.1%	6.5%	13.7%	17.9%
Total	$361,000	$491,254	$639,117	$779,463	$874,971	$1,083,425	$1,242,289	$1,547,658	$1,793,814	$1,900,771	$2,095,231	$2,476,441
	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

* Because of rounding, sums of percentages may not equal 100 percent.

** Includes TV and Radio advertising expenditures of $207,324,000 and $12,492,000, respectively, for 1970. Broadcast advertising was banned after January 1, 1971. Expenditures for direct mail, endorsements, testimonials, and audio-visual are included in the "All Others" category to avoid potential disclosure of individual company data.

TABLE 2A

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES FOR YEARS 1986-1995 (DOLLARS IN THOUSANDS)*

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995
Newspapers	$119,629	$95,810	$105,783	$76,993	$71,174	$48,212	$35,467	$36,220	$24,143	$19,122
	5.0%	3.7%	3.2%	2.1%	1.8%	1.0%	0.7%	0.6%	0.5%	0.4%
Magazines	$340,160	$317,748	$355,055	$380,393	$328,143	$278,110	$237,061	$235,253	$251,644	$248,848
	14.3%	12.3%	10.8%	10.5%	8.2%	6.0%	4.5%	3.9%	5.2%	5.1%
Outdoor	$301,822	$269,778	$319,293	$358,583	$375,627	$386,165	$295,657	$231,481	$240,024	$273,664
	12.7%	10.5%	9.7%	9.9%	9.4%	8.3%	5.7%	3.8%	5.0%	5.6%
Transit	$34,725	$35,822	$44,379	$52,294	$60,249	$60,163	$53,293	$39,117	$29,323	$22,543
	1.5%	1.4%	1.4%	1.4%	1.5%	1.3%	1.0%	0.6%	0.6%	0.5%
Point-of-Sale	$135,541	$153,494	$222,289	$241,809	$303,855	$344,580	$366,036	$400,943	$342,650	$259,035
	5.7%	5.9%	6.8%	6.7%	7.6%	7.4%	7.0%	6.6%	7.1%	5.3%
Promotional Allowances	$630,036	$702,430	$879,703	$999,843	$1,021,427	$1,156,280	$1,514,026	$1,557,635	$1,678,917	$1,865,657
	26.4%	27.2%	26.9%	27.6%	25.6%	24.9%	28.9%	25.8%	34.7%	38.1%
Sampling Distribution	$98,866	$55,020	$74,511	$57,771	$100,893	$56,970	$49,315	$40,202	$6,974	$13,836
	4.1%	2.1%	2.3%	1.6%	2.5%	1.2%	0.9%	0.7%	0.1%	0.3%
Specialty Item Distribution	$210,128	$391,351	$190,003	$262,432	$307,037	$184,348	$339,997	$755,780	$850,810	$665,173
	8.8%	15.2%	5.8%	7.3%	7.7%	4.0%	6.5%	12.5%	17.6%	13.6%
Public Entertainment	$71,439	$71,389	$88,072	$92,120	$125,094	$118,622	$89,739	$84,276	$81,292	$110,669
	3.0%	2.8%	2.7%	2.5%	3.1%	2.6%	1.7%	1.4%	1.7%	2.3%
Direct Mail	$187,057	$187,931	$42,545	$45,498	$51,875	$65,002	$34,345	$31,463	$31,187	$34,618
	7.9%	7.3%	1.3%	1.3%	1.3%	1.4%	0.7%	0.5%	0.7%	0.7%
Endorsements & Testimonials	$384	$376	$781	$0	$0	$0	$0	$0	$0	$0
	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Coupons & Retail-Value-Added	**	**	$874,127	$959,965	$1,183,798	$1,882,905	$2,175,373	$2,559,387	$1,248,896	$1,348,378
			26.7%	26.5%	29.6%	40.4%	41.6%	42.4%	25.8%	27.5%
Other***	$252,570	$299,355	$78,366	$89,290	$62,917	$68,758	$41,608	$63,680	$47,672	$33,680
	10.0%	11.6%	2.4%	2.5%	1.6%	1.5%	0.8%	1.2%	1.0%	0.7%
Total	$2,382,357	$2,580,504	$3,274,853	$3,616,993	$3,992,008	$4,650,114	$5,231,917	$6,035,437	$4,833,532	$4,895,223
	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

* Because of rounding, sums of percentages may not equal 100 percent.

** Prior to 1987, the Commission did not specifically collect information on Coupons & Retail-Value-Added.

*** Expenditures for audio-visual are included in the “All Others” category to avoid potential disclosure of individual company data.

TABLE 2B

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES FOR YEARS 1996-2001 (DOLLARS IN THOUSANDS)*

	1996	1997	1998	1999	2000	2001
Newspapers	$14,067 0.3%	$16,980 0.3%	$29,444 0.4%	$50,952 0.6%	$51,652 0.5%	$31,676 0.3%
Magazines	$243,046 4.8%	$236,950 4.2%	$281,296 4.2%	$377,364 4.6%	$294,916 3.1%	$172,853 1.5%
Outdoor	$292,261 5.7%	$295,334 5.2%	$294,721 4.4%	$53,787 0.7%	$9,262 0.1%	$8,241 0.1%
Transit	$28,865 0.6%	$26,407 0.5%	$40,158 0.6%	$5,573 0.1%	$4 0.0%	$0 0.0%
Point-of-Sale	$252,619 4.9%	$305,360 5.4%	$290,739 4.3%	$329,429 4.0%	$347,038 3.6%	$284,319 2.5%
Promotional Allowances	$2,150,838 42.1%	$2,438,468 43.1%	$2,878,919 42.8%	$3,542,950 43.0%	$3,913,997 40.8%	$4,452,709 39.7%
Sampling Distribution	$15,945 0.3%	$22,065 0.4%	$14,436 0.2%	$33,711 0.4%	$22,330 0.2%	$17,175 0.2%
Specialty Item Distribution	$544,345 10.7%	$512,602 9.6%	$355,835 5.3%	$335,680 4.1%	$327,826 3.4%	$333,394 3.0%
Public Entertainment	$171,177 3.4%	$195,203 3.4%	$248,536 3.7%	$267,379 3.3%	$309,610 3.2%	$312,366 2.8%
Direct Mail	$38,703 0.8%	$37,310 0.7%	$57,772 0.9%	$94,610 1.2%	$92,902 1.0%	$133,947 1.2%
Endorsements & Testimonials	$0 0.0%	$0 0.0%	$0 0.0%	$0 0.0%	$0 0.0%	$0 0.0%
Coupons	$1,308,708** 25.6%	$552,550 9.8%	$624,199 9.3%	$531,004 6.5%	$705,299 7.4%	$602,110 5.4%
Retail-Value-Added		$970,363 17.1%	$1,555,391 23.1%	$2,559,883 31.1%	$3,453,446 36.0%	$4,761,792 42.5%
Internet	$432 0.0%	$215 0.0%	$125 0.0%	$651 0.0%	$949 0.0%	$841 0.0%
Other***	$46,696 0.9%	$50,207 1.0%	$61,584 0.9%	$54,658 0.7%	$63,395 0.7%	$104,797 0.9%
Total	$5,107,700 100%	$5,660,014 100%	$6,733,157 100%	$8,237,631 100%	$9,592,627 100%	$11,216,220 100%

* Because of rounding, sums of percentages may not equal 100 percent.

** Prior to 1997, Coupons and Retail-Value-Added were reported as a single category.

*** Expenditures for audio-visual are included in the "All Others" category to avoid potential disclosure of individual company data.

TABLE 2C

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES
FOR YEARS 2002-2005 (DOLLARS IN THOUSANDS)*

	2002	2003	2004	2005
Newspapers	$25,538	$8,251	$4,913	$1,589
	0.2%	0.1%	0.0%	0.0%
Magazines	$106,852	$156,394	$95,700	$44,777
	0.9%	1.0%	0.7%	0.3%
Outdoor	$24,192	$32,599	$17,135	$9,821
	0.2%	0.2%	0.1%	0.0%
Transit	$0	$0	$0	$0
	0.0%	0.0%	0.0%	0.0%
Point-of-Sale	$260,902	$165,573	$163,621	$182,193
	2.1%	1.1%	1.2%	1.4%
Price Discounts	$7,873,835	$ 10,808,239	$10, 932,199	$9,776,069
	63.2%	71.4%	77.3%	74.6%
Promotional Allowances – Retailers	$1,333,097	$1,229,327	$542,213	$435,830
	10.7%	8.1%	3.8%	3.3%
Promotional Allowances – Wholesalers	$446,327	$683,067	$387,758	$410,363
	3.6%	4.5%	2.7%	3.1%
Promotional Allowances – Other	$2,767	$2,786	$1,323	$1,493
	0.0%	0.0%	0.0%	0.0%
Sampling Distribution	$28,777	$17,853	$11,649	$17,211
	0.2%	0.1%	0.0%	0.1%
Specialty Item Distribution – Branded	$49,423	$9,195	$8,011	$5,255
	0.4%	0.1%	0.0%	0.0%
Specialty Item Distribution - Non-Branded	$174,201	$254,956	$216,577	$225,279
	1.4%	1.7%	1.5%	1.7%
Public Entertainment – Adult-Only	$219,016	$150,889	$140,137	$214,075
	1.8%	1.0%	1.0%	1.6%
Public Entertainment – General-Audience	$34,089	$32,849	$115	$152
	0.3%	0.2%	0.0%	0.0%
Sponsorships	$54,247	$31,371	$28,231	$30,575
	0.4%	0.2%	0.2%	0.2%
Endorsements & Testimonials	$0	$0	$0	$0
	0.0%	0.0%	0.0%	0.0%
Direct Mail	$111,319	$92,978	$93,836	$51,844
	0.9%	0.6%	0.7%	0.0%
Coupons	$522,246	$650,653	$751,761	$870,137
	4.2%	4.3%	5.3%	6.6%
Retail-Value-Added – Bonus Cigarettes	$1,060,304	$677,308	$636,221	$725,010
	8.5%	4.5%	4.5%	5.5%
Retail-Value-Added – Non-Cigarette Bonus	$24,727	$20,535	$14,343	$7,526
	0.2%	0.1%	0.1%	0.0%
Company Website	$940	$2,851	$1,401	$2,675
	0.0%	0.0%	0.0%	0.0%
Internet – Other	$0	$0	$0	$0
	0.0%	0.0%	0.0%	0.0%
Telephone	$679	$760	$346	$59
	0.0%	0.0%	0.0%	0.0%
Other**	$112,879	$117,563	$102,369	$99,025
	0.9%	0.8%	0.7%	0.8%
Total	$12,466,358	$ 15,145,998	$14, 149,859	$ 13,110,958
	100.0%	100.0%	100.0%	100.0%

* Because of rounding, sums of percentages may not equal 100 percent.

** Expenditures for audio-visual are included in the “All Others” category to avoid potential disclosure of individual company data.

TABLE 2D

CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES FOR 2006-2010 (DOLLARS IN THOUSANDS)*

	2006	2007	2008	2009	2010
Newspapers	N/A	N/A	$169	N/A	N/A
	– –	– –	0.0%	– –	– –
Magazines	$50,293	$47,203	$25,478	$36,680	$46,463
	0.0%	0.4%	0.3%	0.4%	0.6%
Outdoor	$935	$3,041	$2,045	$1,812	$1,744
	0.0%	0.0%	0.0%	0.0%	0.0%
Transit	$0	$0	$0	$0	$0
	0.0%	0.0%	0.0%	0.0%	0.0%
Point-of-Sale	$242,625	$198,861	$163,709	$110,311	$106,634
	1.9%	1.8%	1.0%	1.3%	1.3%
Price Discounts	$9,205,106	$7,699,362	$7,171,092	$6,672,428	$6,490,832
	73.7%	70.9%	72.1%	78.2%	80.7%
Promotional Allowances – Retailers	$434,239	$454,139	$481,500	$428,675	$369,992
	3.5%	4.2%	4.8%	5.0%	4.6%
Promotional Allowances – Wholesalers	$471,204	$479,032	$448,461	$449,006	$410,370
	3.8%	4.4%	4.5%	5.3%	5.1%
Promotional Allowances – Other	N/A	N/A	$1,245	$965	$210
	– –	– –	0.0%	0.0%	0.0%
Sampling Distribution	$29,431	$48,719	$54,261	$23,784	$22,166
	0.2%	0.4%	0.5%	0.3%	0.3%
Specialty Item Distribution – Branded	$5,546	$8,070	$7,188	$7,472	$6,322
	0.0%	0.0%	0.1%	0.1%	0.1%
Specialty Item Distribution - Non-Branded	$163,761	$160,047	$93,798	$74,956	$65,574
	1.3%	1.5%	0.9%	0.9%	0.8%
Public Entertainment – Adult-Only	$168,098	$160,104	$154,749	$134,328	$138,889
	1.3%	1.5%	1.5%	1.6%	1.7%
Public Entertainment – General-Audience	N/A	N/A	N/A	N/A	N/A
	– –	– –	– –	– –	– –
Sponsorships	N/A	N/A	N/A	N/A	$0
	– –	– –	– –	– –	0.0%
Endorsements & Testimonials	$0	$0	$0	$0	$0
	0.0%	0.0%	0.0%	0.0%	0.0%
Direct Mail	$102,353	$81,929	$89,920	$68,891	$56,482
	0.8%	0.8%	0.9%	0.8%	0.7%
Coupons	$625,777	$366,779	$359,793	$371,028	$235,802
	5.0%	3.4%	3.6%	4.3%	2.9%
Retail-Value-Added – Bonus Cigarettes	$817,792	$981,566	$721,818	$11,736	N/A
	6.5%	9.0%	7.3%	0.1%	– –
Retail-Value-Added – Non-Cigarette Bonus	$14,642	$17,720	$10,983	N/A	$0
	0.1%	0.1%	0.1%	– –	0.0%
Company Website	$6,497	$2,351	$13,172	$18,300	$20,829
	0.1%	0.0%	0.1%	0.2%	0.3%
Internet – Other	$0	N/A	N/A	N/A	N/A
	0.0%	– –	– –	– –	– –
Telephone	N/A	N/A	N/A	N/A	N/A
	– –	– –	– –	– –	– –
Audio-Visual	$0	$0	$0	$0	$0
	0.0%	0.0%	0.0%	0.0%	0.0%
Social Media	– –	– –	– –	$0	$0
				0.0%	0.0%
All Others**	$151,392	$155,843	$143,688	$122,002	$73,291
	1.2%	1.4%	1.4%	1.4%	0.9%
Total	$12,489,692	$10,864,767	$9,943,068	$8,531,375	$8,045,602

* Because of rounding, sums of percentages may not equal 100 percent.

** Expenditures denoted "N/A" are included in the "All Others" category to avoid potential disclosure of individual company data.

TABLE 2E

CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES FOR 2011 (DOLLARS IN THOUSANDS)*

	2011
Newspapers	$549 0.0%
Magazines	$23,254 0.3%
Outdoor	$3,100 0.0%
Transit	$0 0.0%
Point-of-Sale	$76,613 0.9%
Price Discounts	$6,996,942 83.6%
Promotional Allowances – Retailers	$356,991 4.3%
Promotional Allowances – Wholesalers	$401,006 4.8%
Promotional Allowances – Other	N/A – –
Sampling Distribution	$4,515 0.0%
Specialty Item Distribution – Branded	$5,607 0.0%
Specialty Item Distribution - Non-Branded	$44,394 0.5%
Public Entertainment – Adult-Only	$129,822 1.6%
Public Entertainment – General-Audience	$0 0.0%
Sponsorships	$0 0.0%
Endorsements & Testimonials	$0 0.0%
Direct Mail	$51,491 0.6%
Coupons	$171,222 2.0%
Retail-Value-Added – Bonus Cigarettes	$0 0.0%
Retail-Value-Added – Non-Cigarette Bonus	$0 0.0%
Company Website	$21,898 0.3%
Internet – Other	N/A – –
Telephone	N/A – –
Audio-Visual	$0 0.0%
Social Media	$0 0.0%
All Others**	$78,220 0.9%
Total	$8,365,624

* Because of rounding, sums of percentages may not equal 100 percent.
** Expenditures denoted “N/A” are included in the “All Others” category to avoid potential disclosure of individual company data.

TABLE 3

DOMESTIC CIGARETTE ADVERTISING EXPENDITURES
BY MEDIA FOR YEARS 1963 - 1974*
(MILLIONS OF DOLLARS)

YEAR	TV	RADIO	NEWSPAPER	MAGAZINES	DIRECT	BILLBOARD/ POSTER/ OUTDOOR/ TRANSIT	OTHER	TOTAL
1963	$151.7	31.6	45.6		13.2	NA	7.4	249.5
1964	170.2	25.5	45.2		14.6	NA	5.8	261.3
1965	175.6	24.8	41.9		14.7	NA	6.0	263.0
1966	198.0	31.3	43.4		17.9	NA	6.9	297.5
1967	226.9	17.5	41.2		20.3	NA	6.0	311.5
1968	217.2	21.3	44.6		21.6	NA	6.0	310.7
1969	221.3	13.6	48.7		13.4	NA	8.9	305.9
1970	205.0	12.4	14.7	49.5	16.9	11.7	4.5	314.7
1971	2.2	0	59.3	98.3	27.0	60.6	4.2	251.6
1972	0	0	63.1	96.1	22.9	67.5	8.0	257.6
1973	0	0	65.3	92.4	15.2	63.2	11.4	247.5
1974	0	0	80.5	114.6	31.1	71.4	9.2	306.8

* The data reported in Tables 2 through 2E were not collected in their present form until 1975. Thus, Table 3, which reports cigarette advertising expenditures from 1963 through 1974, has been retained in this report for comparative purposes.

TABLE 4 DOMESTIC MARKET SHARE OF CIGARETTES BY TAR YIELD					
Year	Market share of cigarettes having tar yields of:				
	15 mg. or less	12 mg. or less	9 mg. or less	6 mg. or less	3 mg. or less
1967	2.0%	NA	NA	NA	NA
1968	2.5%	NA	NA	NA	NA
1969	3.0%	NA	NA	NA	NA
1970	3.6%	NA	NA	NA	NA
1971	3.8%	NA	NA	NA	NA
1972	6.6%	NA	NA	NA	NA
1973	8.9%	NA	NA	NA	NA
1974	8.9%	NA	NA	NA	NA
1975	13.5%	NA	NA	NA	NA
1976	15.9%	NA	NA	NA	NA
1977	22.7%	NA	NA	NA	NA
1978	27.5%	NA	NA	NA	NA
1979	40.9%	NA	NA	NA	NA
1980	44.8%	NA	NA	NA	NA
1981	56.0%	NA	NA	NA	NA
1982	52.2%	43.8%	27.8%	8.9%	2.9%
1983	53.1%	44.9%	27.9%	9.4%	3.1%
1984	51.0%	43.4%	26.3%	9.4%	2.9%
1985	51.9%	43.1%	25.3%	8.4%	2.3%
1986	52.6%	44.5%	22.3%	9.9%	2.6%
1987	55.4%	47.8%	20.2%	10.0%	2.5%
1988	54.2%	48.7%	20.1%	10.7%	3.1%
1989	55.1%	48.4%	21.5%	11.4%	2.4%
1990	60.6%	51.5%	25.5%	12.2%	2.8%

TABLE 4A DOMESTIC MARKET SHARE OF CIGARETTES BY TAR YIELD					
Year	Market share of cigarettes having tar yields of:				
	15 mg. or less	12 mg. or less	9 mg. or less	6 mg. or less	3 mg. or less
1991	60.5%	52.6%	22.0%	12.7%	2.6%
1992	68.7%	52.9%	24.9%	12.7%	2.5%
1993	66.5%	53.3%	23.4%	12.6%	1.9%
1994	71.2%	53.7%	23.1%	12.3%	2.1%
1995	72.7%	53.6%	27.1%	12.2%	2.2%
1996	67.4%	55.5%	22.3%	11.9%	1.9%
1997	70.2%	55.6%	21.9%	11.5%	1.7%
1998	81.9%	56.8%	22.9%	13.2%	1.6%
1999	86.6%	57.4%	25.3%	13.6%	1.6%
2000	87.1%	50.4%	23.7%	13.6%	1.3%
2001	85.2%	58.1%	22.6%	13.2%	1.0%
2002	84.9%	58.2%	22.5%	12.9%	0.9%
2003	84.9%	59.5%	22.5%	12.6%	0.8%
2004	84.8%	57.7%	19.2%	11.5%	0.8%
2005	83.5%	58.4%	18.7%	11.5%	0.6%
2006	84.4%	57.7%	19.5%	11.1%	0.5%
2007	82.7%	57.3%	19.6%	10.7%	0.4%
2008	82.6%	57.5%	17.8%	9.4%	0.1%
2009	82.3%	61.6%	17.6%	11.0%	0.4%
2010	91.3%	62.7%	14.3%	9.7%	0.4%
2011	94.7%	54.1%	12.5%	7.9%	0.2%

TABLE 5

DOMESTIC MARKET SHARE OF FILTER
AND NON-FILTER CIGARETTES

YEAR	NON-FILTER	FILTER	CHARCOAL	NON-CHARCOAL
1963	42%	58%	*	*
1964	39%	61%	*	*
1965	36%	64%	*	*
1966	32%	68%	*	*
1967	28%	72%	*	*
1968	26%	74%	6%	68%
1969	23%	77%	6%	71%
1970	20%	80%	6%	74%
1971	18%	82%	6%	76%
1972	16%	84%	6%	77%
1973	15%	85%	5%	80%
1974	14%	86%	5%	81%
1975	13%	87%	5%	82%
1976	12%	88%	4%	84%
1977	10%	90%	4%	86%
1978	10%	90%	3%	87%
1979	9%	91%	3%	88%
1980	8%	92%	3%	89%
1981	8%	92%	2%	90%
1982	7%	93%	2%	91%
1983	7%	93%	2%	91%
1984	7%	93%	2%	91%
1985	6%	94%	1%	93%
1986	6%	94%	1%	93%
1987	4%	96%	**	**

* Figures for charcoal filter cigarettes for the years 1963 through 1967 were not obtained.
** Beginning with 1987, figures for charcoal filter cigarettes have no longer been reported.

TABLE 5A

DOMESTIC MARKET SHARE OF FILTER AND NON-FILTER CIGARETTES

YEAR	NON-FILTER	FILTER
1988	5%	95%
1989	5%	95%
1990	5%	95%
1991	4%	96%
1992	3%	97%
1993	3%	97%
1994	3%	97%
1995	3%	97%
1996	3%	97%
1997	2%	98%
1998	2%	98%
1999	2%	98%
2000	2%	98%
2001	2%	98%
2002	2%	98%
2003	1%	99%
2004	1%	99%
2005	1%	99%
2006	1%	99%
2007	1%	99%
2008	1%	99%
2009	0.5%	99.5%
2010	0.5%	99.5%
2011	0.2%	99.8%

TABLE 6

DOMESTIC MARKET SHARE OF CIGARETTES
BY LENGTH IN MILLIMETERS (mm.)

YEAR	68-72 mm.	79-88 mm.	94-101 mm.	110-121 mm.
1967	14%	77%	9%	---
1968	12%	74%	13%	---
1969	11%	74%	16%	---
1970	9%	73%	18%	---
1971	8%	72%	20%	---
1972	8%	71%	21%	---
1973	7%	71%	22%	---
1974	6%	71%	23%	--- *
1975	6%	69%	24%	1%
1976	5%	69%	24%	2%
1977	5%	67%	26%	2%
1978	5%	65%	27%	2%
1979	4%	65%	30%	2%
1980	3%	63%	32%	2%
1981	3%	62%	33%	2%
1982	3%	61%	34%	2%
1983	3%	60%	34%	2%
1984	3%	59%	36%	2%
1985	3%	58%	37%	2%
1986	2%	58%	37%	3%
1987	2%	57%	38%	3%
1988	2%	57%	38%	2%
1989	2%	57%	39%	2%
1990	2%	57%	39%	2%
1991	2%	56%	40%	2%
1992	2%	56%	41%	2%
1993	1%	55%	42%	2%
1994	1%	56%	41%	2%
1995	1%	57%	40%	2%
1996	1%	57%	40%	2%
1997	1%	58%	39%	2%
1998	1%	59%	38%	2%
1999	1%	59%	38%	2%
2000	1%	60%	37%	2%
2001	1%	60%	38%	1%
2002	1%	61%	37%	2%
2003	1%	61%	36%	2%
2004	1%	62%	35%	2%
2005	1%	62%	35%	2%
2006	1%	62%	35%	2%
2007	1%	65%	32%	2%
2008	2%	66%	30%	2%
2009	3%	64%	32%	2%
2010	4%	62%	33%	2%
2011	3%	59%	37%	2%

* The 110-121 mm. length was combined with 94-101 mm. length.

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TABLE 7

DOMESTIC MARKET SHARE OF MENTHOL AND NON-MENTHOL CIGARETTES

YEAR	MENTHOL	NON-MENTHOL
1963	16%	84%
1964	16%	84%
1965	18%	82%
1966	19%	81%
1967	20%	80%
1968	21%	79%
1969	22%	78%
1970	23%	77%
1971	24%	76%
1972	24%	76%
1973	25%	75%
1974	27%	73%
1975	27%	73%
1976	28%	72%
1977	28%	72%
1978	28%	72%
1979	29%	71%
1980	28%	72%
1981	28%	72%
1982	29%	71%
1983	28%	72%
1984	28%	72%
1985	28%	72%
1986	28%	72%
1987	28%	72%
1988	28%	72%
1989	27%	73%
1990	26%	74%
1991	27%	73%
1992	26%	74%
1993	26%	74%
1994	25%	75%
1995	25%	75%
1996	25%	75%
1997	25%	75%
1998	26%	74%
1999	26%	74%
2000	26%	74%
2001	26%	74%
2002	27%	73%
2003	27%	73%
2004	27%	73%
2005	27%	73%
2006	28%	72%
2007	29%	71%
2008	27%	73%
2009	21%	79%
2010	22%	78%
2011	32%	68%

TABLE 8

DISCLOSURE OF TAR AND NICOTINE RATINGS
ON CIGARETTE PACKS (1994 - 2001)

		1994	1995	1996	1997	1998	1999	2000	2001
% of overall market that discloses ratings on the pack		6.3%	6.3%	6.1%	5.8%	5.3%	4.1%	3.6%	1.8%
more than 15 mg. tar	market share of varieties in tar group	28.8%	27.3%	32.7%	29.8%	18.0%	13.4%	12.9%	14.8%
	% that discloses ratings on pack	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
12-15 mg. tar	market share of varieties in tar group	19.3%	21.0%	15.3%	16.7%	29.1%	32.5%	39.0%	29.7%
	% that discloses ratings on pack	0.0%	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%	0.0%
8-11 mg. tar	market share of varieties in tar group	38.6%	38.7%	39.2%	41.0%	39.4%	40.3%	33.9%	42.1%
	% that discloses ratings on pack	2.4%	2.8%	2.6%	2.3%	3.2%	1.6%	0.7%	1.0%
4-7 mg. tar	market share of varieties in tar group	11.2%	10.8%	10.9%	10.8%	11.9%	12.2%	12.9%	12.5%
	% that discloses ratings on pack	30.7%	30.1%	29.3%	28.6%	20.7%	16.2%	16.5%	3.7%
3 mg. tar or less	market share of varieties in tar group	2.1%	2.2%	1.9%	1.7%	1.6%	1.6%	1.3%	1.0%
	% that discloses ratings on pack	91.8%	89.1%	97.2%	97.3%	97.4%	92.3%	92.0%	87.9%

TABLE 8A

DISCLOSURE OF TAR RATINGS ON CIGARETTE PACKS (2002-2011)

		2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
% of overall market that discloses ratings on the pack		1.4%	1.2%	1.2%	0.9%	0.8%	0.8%	0.0%	0.0%	0.0%	0.0%
more than 15 mg. tar	market share of varieties in group	15.1%	15.1%	15.2%	16.5%	15.5%	17.3%	17.4%	17.7%	8.7%	5.3%
	% that discloses ratings on pack	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
12-15 mg. tar	market share of varieties in group	28.8%	28.9%	30.3%	28.3%	28.4%	27.4%	26.9%	23.9%	29.4%	46.5.%
	% that discloses ratings on pack	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
8-11 mg. tar	market share of varieties in group	43.0%	43.2%	42.5%	43.3%	44.5%	44.3%	45.9%	47.0%	52.1%	39.4%
	% that discloses ratings on pack	0.9%	0.8%	0.7%	0.6%	0.5%	0.5%	0.0%	0.0%	0.0%	0.0%
4-7 mg. tar	market share of varieties in group	12.2%	12.0%	11.2%	11.3%	10.9%	10.5%	9.7%	11.0%	9.4%	8.5.%
	% that discloses ratings on pack	1.8%	1.5%	1.5%	1.2%	1.0%	0.8%	0.0%	0.0%	0.0%	0.0%
3 mg. tar or less	market share of varieties in group	0.9%	0.8%	0.8%	0.6%	0.5%	0.4%	0.1%	0.4%	0.4%	0.0%
	% that discloses ratings on pack	88.7%	89.9%	91.6%	90.7%	94.9%	100.0%	0.0%	0.0%	0.0%	0.0%

APPENDIX

2011 Advertising and Promotional Expenditure Categories

Newspapers: Newspaper advertising; but excluding expenditures in connection with sampling, specialty item distribution, public entertainment, endorsements, sponsorships, coupons, and retail-value-added.

Magazines: Magazine advertising; but excluding expenditures in connection with sampling, specialty item distribution, public entertainment, endorsements, sponsorships, coupons, and retail-value-added.

Outdoor: Billboards; signs and placards in arenas, stadiums, and shopping malls, whether they are open air or enclosed; and any other advertisements placed outdoors, regardless of their size, including those on cigarette retailer property; but excluding expenditures in connection with sampling, specialty item distribution, public entertainment, endorsements, sponsorships, coupons, and retail-value-added.

Audio-visual: Audio-visual or video advertising on any medium of electronic communication not subject to the Federal Communications Commission's jurisdiction, including screens at motion picture theaters, video cassettes or DVDs, and television screens or monitors in stores; but excluding expenditures in connection with Internet advertising.

Transit: Advertising on or within private or public vehicles and all advertisements placed at, on or within any bus stop, taxi stand, transportation waiting area, train station, airport, or any other transportation facility; but excluding expenditures in connection with sampling, specialty item distribution, public entertainment, endorsements, sponsorships, coupons, and retail-value-added.

Point-of-Sale: Point-of-sale advertisements; but excluding expenditures in connection with outdoor advertising, sampling, specialty item distribution, public entertainment, endorsements, sponsorships, coupons, and retail-value-added.

Price discounts: Price discounts paid to cigarette retailers or wholesalers in order to reduce the price of cigarettes to consumers, including off-invoice discounts, buy downs, voluntary price reductions, and trade programs; but excluding retail-value-added expenditures for promotions involving free cigarettes and expenditures involving coupons.

Promotional Allowances – Retail: Promotional allowances paid to cigarette retailers in order to facilitate the sale or placement of any cigarette, including payments for stocking, shelving, displaying and merchandising brands, volume rebates, incentive payments, and the cost of cigarettes given to retailers for free for subsequent sale to consumers; but excluding expenditures in connection with newspapers, magazines, outdoor, audio-visual, transit, direct mail, point-of-sale, and price discounts.

Promotional Allowances – Wholesale: Promotional allowances paid to cigarette wholesalers in order to facilitate the sale or placement of any cigarette, including payments for volume rebates, incentive payments, value added services, promotional execution and satisfaction of reporting requirements; but excluding expenditures in connection with newspapers, magazines, outdoor, audio-visual, transit, direct mail, point-of-sale, price discounts, and retail promotional allowances.

Promotional Allowances – Other: Promotional allowances paid to any persons other than retailers, wholesalers, and full-time company employees who are involved in the cigarette distribution and sales process in order to facilitate the sale or placement of any cigarette; but excluding expenditures in connection with newspapers, magazines, outdoor, audio-visual, transit, direct mail, point-of-sale, price discounts, and retail and wholesale promotional allowances.

Sampling: Sampling of cigarettes, including the cost of the cigarettes, all associated excise taxes and increased costs under the Master Settlement Agreement, and the cost of organizing, promoting, and conducting sampling. Sampling includes the distribution of cigarettes for consumer testing or evaluation when consumers are able to smoke the cigarettes outside of a facility operated by the Company, but not the cost of actual clinical testing or market research associated with such cigarette distributions. Sampling also includes the distribution of coupons for free cigarettes, when no purchase or payment is required to obtain the coupons or cigarettes.

Specialty Item Distribution – Branded: All costs of distributing any item (other than cigarettes, items the sole function of which is to advertise or promote cigarettes, or written or electronic publications), whether distributed by sale, redemption of coupons, or otherwise, that bears the name, logo, or an image of any portion of the package of any brand or variety of cigarettes, including the cost of the items distributed but subtracting any payments received for the item. The costs associated with distributing non-cigarette items in connection with sampling or retail-value-added programs are reported in those categories, not as specialty item distribution.

Specialty Item Distribution – Non-Branded: All costs of distributing any item (other than cigarettes, items the sole function of which is to advertise or promote cigarettes, or written or electronic publications), whether distributed by sale, redemption of coupons, or otherwise, that does not bear the name, logo, or an image of any portion of the package of any brand or variety of cigarette, including the cost of the items distributed but subtracting any payments received for the item. The costs associated with distributing non-cigarette items in connection with sampling or retail-value-added programs are reported in those categories, not as specialty item distribution.

Direct Mail: Direct mail advertising; but excluding expenditures in connection with sampling, specialty item distribution, public entertainment, endorsements, sponsorships, coupons, retail-value-added, and Internet advertising.

Public Entertainment – Adult-Only: Public entertainment events bearing or otherwise displaying the name or logo or an image of any portion of the package of any of a company's cigarettes or otherwise referring or relating to cigarettes, which take place in an adult-only facility, including all expenditures made by the company in promoting and/or sponsoring such events.

Public Entertainment – General-Audience: Public entertainment events bearing or otherwise displaying the name or logo or an image of any portion of the package of any of a company's cigarettes or otherwise referring or relating to cigarettes, which do not take place in an adult-only facility, including all expenditures made by the company in promoting and/or sponsoring such events.

Retail-Value-Added – Bonus Cigarettes: Retail-value-added expenditures for promotions involving free cigarettes (*e.g.*, buy two packs, get one free), whether or not the free cigarettes are physically bundled together with the purchased cigarettes, including all expenditures and costs associated with the value added to the purchase of cigarettes (*e.g.*, excise taxes paid for the free cigarettes and increased costs under the Master Settlement Agreement).

Retail-Value-Added – Non-Cigarette Bonus: Retail-value-added expenditures for promotions involving free non-cigarettes items (*e.g.*, buy two packs, get a cigarette lighter), including all expenditures and costs associated with the value added to the purchase of cigarettes.

Coupons: All costs associated with coupons for the reduction of the retail cost of cigarettes, whether redeemed at the point-of-sale or by mail, including all costs associated with advertising or promotion, design, printing, distribution, and redemption. However, when coupons are distributed for free cigarettes and no purchase or payment is required to obtain the coupons or the cigarettes, these activities are considered to be sampling and not couponing.

Sponsorships: Sponsorships of sports teams or individual athletes, but excluding endorsements.

Endorsements & Testimonials: Endorsements, testimonials, and product placement.

Company Website: All expenditures associated with advertising on any company Internet website.

Internet – Other: Internet advertising other than on the Company's own Internet website, including on the World Wide Web, on commercial on-line services, and through electronic mail messages; but excluding costs associated with social media marketing.

Telephone: Telephone advertising, including costs associated with the placement of telemarketing calls or the operation of incoming telephone lines that allow consumers to participate in any promotion or hear pre-recorded product messages; but excluding costs associated with having customer service representatives available for responding to consumer complaints or questions.

Social Media Marketing: All expenditures for social media marketing on Web sites or other online services or communities, including but not limited to social networking sites, microblogging sites, content-sharing sites, and blogs.

All Other: Advertising and promotional expenditures not covered by another category.

Trajectories of E-Cigarette and Conventional Cigarette Use Among Youth

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abstract

BACKGROUND: Electronic cigarette (e-cigarette) use is common among youth, and there are concerns that e-cigarette use leads to future conventional cigarette use. We examined longitudinal associations between past-month cigarette and e-cigarette use to characterize the stability and directionality of these tobacco use trajectories over time.

METHODS: High school students (N = 808, 53% female) completed surveys across 3 waves (2013, 2014, and 2015) in 3 public schools in Connecticut. Using autoregressive cross-lagged models, we examined bidirectional relationships between past-month cigarette and e-cigarette use over time. Models were adjusted for covariates related to tobacco use (ie, sex, race/ethnicity, socioeconomic status, and use of other tobacco products).

RESULTS: Past-month e-cigarette use predicted future cigarette use (wave 1–2: odds ratio [OR] = 7.08, 95% confidence interval [CI] = 2.34–21.42; wave 2–3: OR = 3.87, 95% CI = 1.86–8.06). However, past-month cigarette use did not predict future e-cigarette use (wave 1–2: OR = 2.02, 95% CI = 0.67–6.08; wave 2–3: OR = 1.90, 95% CI = 0.77–4.71). Additionally, frequency of cigarette and e-cigarette use increased over time. By wave 3, 26% of cigarette users and 20.5% of e-cigarette users reported using 21–30 days out of the past month.

CONCLUSIONS: E-cigarette use was associated with future cigarette use across 3 longitudinal waves, yet cigarette use was not associated with future e-cigarette use. Future research needs to examine mechanisms through which e-cigarette use leads to cigarette use. E-cigarette regulation and prevention programs may help prevent future use of cigarettes among youth.

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Dr Bold contributed to the conceptualization of the study, developed and tested the hypotheses reported in the manuscript, ran all statistical analyses, and wrote the primary manuscript draft; Drs Kong, Camenga, Simon, Cavallo, and Morean contributed to the conceptualization of the study and the development of the self-report survey and critically reviewed drafts of the manuscript; Dr Krishnan-Sarin secured study funding, led the conceptualization of the study and the development of the self-report survey, and critically reviewed drafts of the manuscript; and all authors approved the final manuscript as submitted.

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WHAT'S KNOWN ON THIS SUBJECT: Electronic cigarette (e-cigarette) use rates are high among youth, and there are concerns that e-cigarette use confers risk for future conventional cigarette use. Prospective research is needed to characterize the stability and directionality of these tobacco use trajectories over time.

WHAT THIS STUDY ADDS: Past-month e-cigarette use predicted future conventional cigarette use across 3 longitudinal waves among high school youth. Cigarette use did not predict subsequent e-cigarette use. E-cigarette regulation and prevention programs are needed to reduce future use of conventional cigarettes among youth.

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Electronic cigarettes (e-cigarettes) are battery-operated devices used to vaporize liquid solutions that may contain nicotine, flavors, and other chemicals. E-cigarettes are now the most commonly used tobacco product among youth; an estimated 3 million US adolescents currently use e-cigarettes,[1] including many who have never used conventional cigarettes.[2,3] There are concerns that e-cigarette use among youth may lead to conventional cigarette smoking, which is a leading cause of morbidity and mortality in the United States.[4]

Longitudinal cohort studies provide some of the strongest scientific evidence to assess the prospective relationship between e-cigarette use and future cigarette use. To date, results from several longitudinal studies indicate that e-cigarette use among nonsmoking youth increases the likelihood of future use of conventional cigarettes.[5–10] Specifically, the pooled odds ratio (OR) in a recent meta-analysis of studies of adolescents and young adults (aged 14–30) indicates that those who had ever used e-cigarettes were 3.62 times more likely to report using cigarettes at follow-up compared with those who had not used e-cigarettes.[11] This finding was robust and remained significant when adjusting for known risk factors associated with cigarette smoking, including demographic, psychosocial, and behavioral variables such as cigarette susceptibility.

Thus, there is growing evidence to support the concern that e-cigarette use is associated with future cigarette use. However, previous studies have focused on the unidirectional relationship between 2 time points, examining the association between baseline e-cigarette use and future cigarette use but not the stability of these relationships over time or the potential reverse directionality. E-cigarette and cigarette use may be highly correlated over time such that the use of either product is associated with the use of the other, in which case cigarette use would also confer risk for future e-cigarette use.

To better understand the stability and directionality of these associations over time, we used a cross-lagged model to examine the direct and reciprocal relationships between e-cigarette and cigarette use across 3 waves (2013, 2014, and 2015) using longitudinal survey evidence from high school students in Connecticut. With this analytic approach, we can simultaneously model cross-lagged effects (ie, relationships between e-cigarette use at 1 wave predicting cigarette use at a future wave and vice versa) while controlling for previous levels of the variables across waves (ie, direct effects of earlier use on future use of the same product),[12] thereby ruling out the possibility that a cross-lagged effect is merely representing a strong correlation between the likelihood of e-cigarette and cigarette use at a given point in time. If the cross-lagged relationship is unidirectional over multiple waves such that e-cigarette use predicts future cigarette use but not vice versa, this would further support the notion that e-cigarette use is a risk factor for future conventional cigarette smoking.

METHODS

Longitudinal data were collected in school-wide surveys across 3 time points (wave 1: fall 2013; wave 2: spring 2014; and wave 3: spring 2015). Surveys were repeated across 3 Connecticut high schools that were selected across different district reference groups (ie, school groupings that vary on the basis of characteristics such as family income levels, parental education and occupation levels, and the use of a non-English language in the home)[13] to include diverse demographic and socioeconomic characteristics. Individual paper-and-pencil surveys were distributed during homeroom periods at each wave of the survey administration. Parents were contacted in advance of the study and could indicate if they did not want their child to participate. Students were informed that their participation was voluntary and that data were anonymous. Study procedures were approved by the Yale University Institutional Review Board and school administrators.

It has been suggested that more accurate reports of youth substance use are obtained from anonymous surveys, so all surveys were anonymous to encourage honest responding.[14,15] Unique 5-factor identification codes (eg, day value from date of birth, school, sex) were used to match student responses longitudinally by following previously validated procedures.[16,17] Out of 1408 students, n = 1098 were matched from wave 1 to 2, and n = 972 were matched from wave 2 to 3. These match rates are comparable to those observed in other regional and national longitudinal surveys that used procedures for either anonymous[16] or identifiable survey matching.[5,6] Those who were matched across all 3 waves (n = 808) did not significantly differ from those who were not matched longitudinally in terms of sociodemographic characteristics (eg, sex, race) or substance use (eg, ever or past-month use of cigarettes or e-cigarettes), and comparable match rates were observed across schools and grades, reducing potential concerns about attrition bias.

Baseline Covariates

In Table 1, we present sample characteristics, including sociodemographic variables and baseline use of other tobacco products.

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TABLE 1 Baseline Characteristics for the Matched Longitudinal Sample (*N* = 808)

Variable	Value
Sex, No. (%)	
Male	380 (47.0)
Female	428 (53.0)
Age[a], mean (SD)	15.04 (0.90)
SES[b], mean (SD)	5.92 (1.38)
Race/ethnicity[c], No. (%)	
White	708 (87.6)
Asian	46 (5.7)
Hispanic and/or Latino	41 (5.1)
Black or African American	21 (2.6)
American Indian or Alaskan Native	8 (1.0)
Native Hawaiian or Pacific Islander	6 (0.7)
Middle Eastern	7 (0.9)
Other	3 (0.4)
Ever use of other tobacco products[d], No. (%)	
Yes	157 (19.4)
No	651 (80.6)

[a] Age data available for *n* = 769; range: 13–17 y old.
[b] SES was assessed by using the Family Affluence Scale (Boyce et al[18]), data were available for *n* = 795, and there was a possible range of 0 (low) to 8 (high).
[c] Race/ethnicity values add up to >100% because students could select >1 category.
[d] Ever use of other tobacco products (ie, cigars, hookah, blunts, smokeless tobacco).

Demographics

Students reported demographic characteristics including sex (male or female), age, and race/ethnicity (white, black or African American, Hispanic and/or Latino, Asian, American Indian or Alaskan Native, Native Hawaiian or other Pacific Islander, Middle Eastern, or other). Socioeconomic status (SES) was assessed by using the Family Affluence Scale, which has been shown to be a reliable and valid measure of SES among adolescents.[18] The 4-item Family Affluence Scale assessed the following: (1) whether an adolescent's family owns a car, van, or truck (no = 0, yes = 1); (2) whether an adolescent has his or her own bedroom (no = 0, yes = 1); (3) the number of laptops and/or computers an adolescent's family owns (none = 0, 1 = 1, 2 = 2, >2 = 3); and (4) whether an adolescent's family had vacationed in the past 12 months (not at all = 0, once = 1, twice = 2, more than twice = 3). Responses were added to create a total SES score.

Ever Use of Other Tobacco Products

Ever use of other tobacco products (ie, cigars, hookah, blunts, smokeless tobacco) was assessed by asking students if they had ever tried each product (yes or no) at wave 1.

Longitudinal Outcome Measures

E-Cigarette Use

E-cigarette use was measured at each wave by asking, "Have you ever tried an e-cigarette?" (yes or no) and, "How many days out of the past 30 days did you use e-cigarettes?" (open-ended response, 0–30).

Cigarette Use

Cigarette use was measured at each wave by asking, "Have you ever tried a cigarette, even just 1 or 2 puffs?" (yes or no) and, "During the past 30 days, on how many days did you smoke a cigarette (even just 1 or 2 puffs)?" Categorical response options included the following: "none," "1 day," "2 days," "3 to 5 days," "6 to 10 days," "11 to 20 days," "21 to 28 days," and "everyday."

Primary Outcomes

To capture recent use, which may be less prone to recall bias, the primary outcomes of interest were past-month use (1 = yes, 0 = no) of cigarettes and e-cigarettes at each wave. If data on past-month use were missing and youth reported never trying the product in their lifetime, past-month use was imputed as 0 = no use (*n* = 10 records, 0.4% of cases).

Data Analysis

Analyses were run by using Mplus (version 7.4). Outcome data were missing for 6.5% of cases across waves and were handled by using maximum likelihood estimation with robust standard errors. Past-month cigarette and e-cigarette use outcomes were modeled as binary variables with a logit link function. School was included as a covariate across all waves to account for potential school cohort effects. Path models were used to simultaneously estimate the following: (1) the autoregressive direct effects within cigarette and e-cigarette use across waves (ie, the association between e-cigarette and cigarette use at each wave and use of the same product at the next wave) and (2) the reciprocal predictive pathways between e-cigarette and cigarette use at each wave to use of the other product at the next wave (eg, e-cigarette use at wave 1 predicting cigarette use at wave 2 and vice versa) (see Fig 1).

Baseline variables such as sociodemographic characteristics and use of other tobacco products (ie, cigars, hookah, blunts, smokeless tobacco) were selected a priori as covariates on the basis of previous literature.[19,20] Results were consistent across the models in which the direct and reciprocal effects were estimated without including any covariates (*n* = 808) and the model in which the effects were estimated including all baseline covariates (ie, sex, race/ethnicity, SES, use of other tobacco products; *n* = 795). Therefore, results are presented from adjusted models including all covariates.

Lastly, frequencies of e-cigarette and cigarette product use were examined at each wave (Table 2). The

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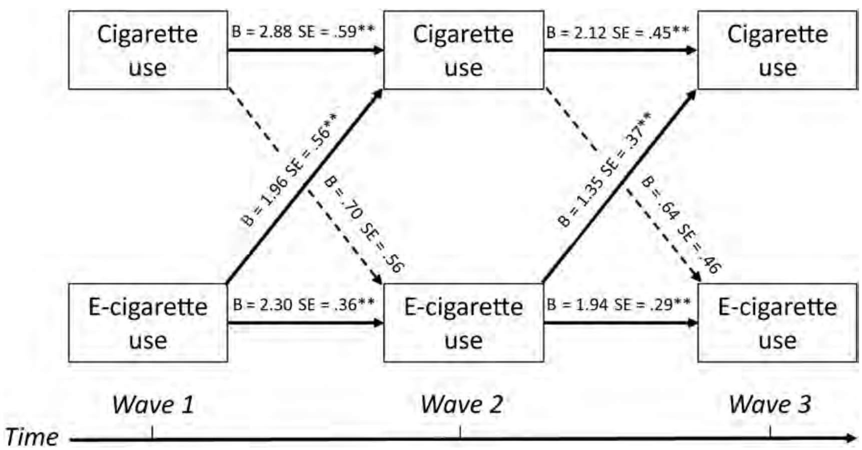

FIGURE 1

Relationships between past-month cigarette and e-cigarette use among youth across 3 longitudinal waves (*N* = 808). Values represent unexponentiated path estimates (B) and SEs. Path estimates can be exponentiated to obtain ORs. Past-month use is coded as yes or no. Estimates are adjusted for covariates (ie, sex, race, SES, other tobacco use, and school). Significant paths are denoted in a solid line (** *P* < .01) and nonsignificant paths are denoted in a dashed line.

TABLE 2 Descriptive Statistics of Past 30-Day Cigarette and E-Cigarette Use by Wave (*N* = 808)

Variable	Wave 1: 2013	Wave 2: 2014	Wave 3: 2015
Age, mean (SD)	15.0 (0.9)	15.5 (1.0)	16.4 (1.0)
Past-month cigarette use, No. (%)	39 (4.8)[a]	44 (5.4)[a]	69 (8.5)[b]
Past-month e-cigarette use, No. (%)	72 (8.9)[a]	97 (12.0)[b]	117 (14.5)[b]
Days of cigarette use, No. (%)			
1–5 d	29 (3.6)[a]	27 (3.3)[a]	38 (4.7)[a]
6–10 d	2 (0.2)[a]	6 (0.7)[a]	8 (1.0)[a]
11–20 d	4 (0.5)[a]	7 (0.9)[a]	5 (0.6)[a]
21–30 d	4 (0.5)[a]	4 (0.5)[a]	18 (2.2)[b]
Days of e-cigarette use,[c] No. (%)			
1–5 d	42 (5.2)[a]	60 (7.4)[a,b]	69 (8.5)[b]
6–10 d	16 (2.0)[a]	14 (1.7)[a]	11 (1.4)[a]
11–20 d	3 (0.4)[a]	12 (1.5)[b]	13 (1.6)[b]
21–30 d	11 (1.4)[a]	11 (1.4)[a]	24 (3.0)[b]

Frequency values are expressed as the number (and percent) of the total matched longitudinal sample (*N* = 808). [a,b] superscripts denote column proportions that differ significantly from one another (p<.05) calculated using a chi-square test. [c] Number of days of e-cigarette use was recoded into numerical categories to match categorical responses of cigarette use frequency.

number of days of e-cigarette use was recoded into numerical categories to match categorical responses of cigarette use frequency. χ^2 analyses were used to explore changes in frequencies over time.

RESULTS

Results from the path models (Fig 1) indicated significant autoregressive direct effects (ie, stability in use over time). As expected, past-month use of e-cigarettes and cigarettes at wave 1 predicted greater odds of past-month use of that same product at wave 2 (cigarette: OR = 17.74, 95% confidence interval [CI] = 5.56–56.56; e-cigarette: OR = 9.95, 95% CI = 4.92–20.13). Similarly, past-month use of e-cigarettes and cigarettes at wave 2 predicted greater odds of past-month use of that same product at wave 3 (cigarette: OR = 8.30, 95% CI = 3.43–20.10; e-cigarette: OR = 7.00, 95% CI = 3.96–12.40).

Additionally, our results indicated that there were significant reciprocal pathways between past-month e-cigarette use at each wave and future cigarette use. Specifically, individuals using e-cigarettes in the past month at wave 1 were >7 times more likely to report subsequent cigarette use at wave 2 (OR = 7.08, 95% CI = 2.34–21.42) when compared with those not using e-cigarettes. Furthermore, those using e-cigarettes in the past month at wave 2 were close to 4 times more likely to report subsequent cigarette use at wave 3 (OR = 3.87, 95% CI = 1.86–8.06) when compared with those not using e-cigarettes. Conversely, past-month cigarette use at each wave was not significantly predictive of future e-cigarette use (wave 1–2: OR = 2.02, 95% CI = 0.67–6.08; wave 2–3: OR = 1.90, 95% CI = 0.77–4.71). Thus, the effects were unidirectional such that youth using e-cigarettes were at greater risk for future cigarette use compared with those not using e-cigarettes, whereas the reverse relationship (cigarette use predicting future e-cigarette use) was not observed.

To further characterize cigarette and e-cigarette use, rates of product use were examined over time (Table 2). Overall, the rates of past-month use of both cigarettes and e-cigarettes significantly increased in the longitudinal sample over time (cigarettes: χ^2 [*N* = 2424], *P* = .001; e-cigarettes: χ^2 [*N* = 2424], *P* = .001), almost doubling from wave 1 (2013) to wave 3 (2015). Frequency of use (measured as the number of days of use in the past month) also increased significantly over time for both cigarettes (χ^2 [*N* = 2424], *P* = .003) and e-cigarettes (χ^2 [*N* = 2424], *P* = .001). By wave 3, a greater proportion of youth reported using cigarettes on most days in the past month (ie, 21–30 days) when compared with waves 1 or 2. Additionally, significantly higher rates of low (1–5 days), moderate (11–20 days), and heavy (21–30 days) e-cigarette use were observed in wave 3 compared with earlier waves. By 2015, 26% of past-month

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cigarette users and 20.5% of past-month e-cigarette users reported heavy use, characterized by using on the majority of the days during the month (21–30 days), which is an increase from 10.3% (cigarette) and 15.3% (e-cigarette) of users in 2013.

DISCUSSION

This study is the first to examine reciprocal relationships between past-month e-cigarette and cigarette use among high school youth using 3 waves of matched longitudinal data. We found that e-cigarette use is prospectively associated with a greater risk of future conventional cigarette use, while controlling for the autoregressive effects of stability of use over time. Importantly, we also observed that this risk is unidirectional, such that cigarette use was not significantly associated with e-cigarette use over time. The observed relationships were consistent across unadjusted models and when including covariates known to relate to cigarette and e-cigarette use (eg, sociodemographic characteristics, other tobacco use). Furthermore, rates of past-month cigarette and e-cigarette use increased significantly across our 3 waves of assessment, indicating more youth were using these products over time, which is consistent with epidemiologic evidence of higher rates of tobacco use as youth age.[1,21] The rising frequency of recent e-cigarette use among youth over time is concerning, especially in light of evidence that e-cigarette use is a significant risk factor for future conventional cigarette use.

In future studies, researchers should examine potential mediators to better understand possible mechanisms that account for the observed directionality of the association between e-cigarette use and future cigarette use. For example, adolescents may be more likely to use e-cigarettes before conventional cigarettes because of factors unique to e-cigarette products, such as perceptions that e-cigarettes are less harmful than conventional cigarettes,[2,22] the widespread availability of unique e-cigarette liquid flavors that may be especially appealing to youth,[23,24] and limited enforcement or restrictions on youth access to e-cigarettes (eg, through online sales).[25,26] At the same time, there is evidence that the adolescent brain is highly sensitive to the rewarding effects of nicotine,[27,28] so e-cigarette use may provide early exposure to the reinforcing pharmacological effects of nicotine, which may increase the likelihood of transitioning to conventional cigarettes. Furthermore, nicotine may be delivered more efficiently through cigarettes than e-cigarettes depending on the e-cigarette device,[29,30] so youth who use conventional cigarettes may find e-cigarettes less reinforcing and be less likely to transition in the reverse direction: from cigarette to e-cigarette use over time. Given the observational nature of the current survey study, we are unable to ascertain the specific causal mechanisms accounting for the association between e-cigarette use and future cigarette use. Yet our findings suggest that early prevention and intervention efforts as well as policies targeting youth e-cigarette use may be needed to reduce future conventional cigarette use among youth. Prevention efforts may include new e-cigarette regulatory policies given that the deeming rule now extends the regulatory authority of the Food and Drug Administration to other tobacco products, including e-cigarettes.[31] As e-cigarette regulatory policies are enforced and product regulations change, continued research will be needed to understand how these strategies influence youth e-cigarette and cigarette use behaviors.

The current study has several important strengths, including the use of matched longitudinal data from the same high school students across 3 time points (2013, 2014, and 2015) and a cross-lagged model with which we assessed the stability and directionality of associations between e-cigarettes and cigarettes over time. Furthermore, we used anonymous survey procedures that are known to improve the validity of substance use reporting among youth. With the current results, we extend previous longitudinal research that is focused on ever use of cigarettes and e-cigarettes, which may primarily capture youth who experiment with the product a single time, by examining past-month rates and frequencies to better quantify recent product use over time.

Several limitations should also be noted. For example, the sample comprised high school students from Connecticut, with the majority identifying as white, so our results may not generalize to other geographic or more diverse sociodemographic areas. Additionally, there may be other product characteristics (eg, nicotine strength) or covariates (eg, advertisement exposure, parental tobacco use) not assessed in this study that may relate to cigarette and e-cigarette use over time that should be considered in future investigations. Although we controlled for use of other tobacco products at baseline in the current study, it will be important for researchers to also consider how use patterns change across multiple tobacco products longitudinally. In our study, we intended to focus on adolescents during high school given the unique vulnerability to tobacco product use during this developmental period, and further research is needed to characterize trajectories between e-cigarette

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and cigarette use among people of other ages, including persistence of use into adulthood. Lastly, we focused on binary outcomes of past-month use of the products given the small sample sizes across the full range of use frequency. However, our preliminary analyses indicated higher rates of e-cigarette and cigarette use over time, consistent with national samples. Future large-scale longitudinal studies are needed to address the question of how frequency of use of 1 product relates to future use of another product.

CONCLUSIONS

This study is the first to examine reciprocal associations between cigarette and e-cigarette use among youth across 3 longitudinal waves. The observed relationship between cigarette and e-cigarette use over time was unidirectional. E-cigarette use was associated with future cigarette use across 3 longitudinal waves, yet cigarette use was not associated with future e-cigarette use. Potential mediators of this effect should be examined in future research to better understand the mechanisms through which e-cigarette use increases the risk for future cigarette use. Prevention and intervention efforts and policies targeting youth e-cigarette use may be needed to reduce future conventional tobacco use among youth.

ABBREVIATIONS

CI: confidence interval
e-cigarette: electronic cigarette
OR: odds ratio
SES: socioeconomic status

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Electronic Cigarette Use and Progression From Experimentation to Established Smoking

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abstract

BACKGROUND: It has been shown that never-smoking adolescents who try electronic cigarettes (e-cigarettes) are at increased risk of subsequent conventional cigarette smoking. We evaluated associations between e-cigarette use and progression to established smoking among adolescents who had already tried cigarettes.

METHODS: Among participants (age 12–17 years) in the nationally representative Population Assessment of Tobacco and Health survey who had smoked a cigarette (≥1 puff) but not yet smoked 100 cigarettes ($N = 1295$), we examined 3 outcomes at 1-year follow-up as a function of baseline e-cigarette use: (1) having smoked ≥100 cigarettes (established smoking), (2) smoking during the past 30 days, and (3) both having smoked ≥100 cigarettes and past 30-day smoking (current established smoking). Survey-weighted multivariable logistic regression models were fitted to obtain odds ratios (ORs) and 95% confidence intervals (CIs) adjusted for smoking risk factors.

RESULTS: Versus e-cigarette never use, having ever used e-cigarettes was positively associated with progression to established cigarette smoking (19.3% vs 9.7%), past 30-day smoking (38.8% vs 26.6%), and current established smoking (15.6% vs 7.1%). In adjusted models, e-cigarette ever use positively predicted current established smoking (OR: 1.80; 95% CI: 1.04–3.12) but did not reach statistical significance ($\alpha = .05$) for established smoking (OR: 1.57; 95% CI: 0.99–2.49) and past 30-day smoking (OR: 1.32; 95% CI: 0.99–1.76).

CONCLUSIONS: Among adolescent cigarette experimenters, using e-cigarettes was positively and independently associated with progression to current established smoking, suggesting that e-cigarettes do not divert from, and may encourage, cigarette smoking in this population.

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Dr Chaffee contributed to the design and conceptualization of the study and the analysis plan, conducted statistical analyses, and prepared the initial manuscript draft; Dr Watkins contributed to the design and conceptualization of the study and the analysis plan and conducted statistical analyses; Dr Glantz contributed to the design and conceptualization of the study and the analysis plan; and all authors revised and reviewed the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: In previous studies of youth who have never smoked cigarettes, those who tried electronic cigarettes (e-cigarettes) were more likely to initiate conventional cigarette smoking compared with e-cigarette never users. In cross-sectional studies, e-cigarette use is associated with established youth smoking.

WHAT THIS STUDY ADDS: Among youth who already experimented with cigarettes but were not yet established smokers, having used e-cigarettes was prospectively associated with onset of current established cigarette smoking. For these youth, e-cigarettes appear to encourage progression to established smoking.

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Electronic cigarettes (e-cigarettes) are increasingly popular among youth; from 2014 to 2016, more US middle and high school students used e-cigarettes than any other tobacco product, including conventional cigarettes.[1] All currently available longitudinal studies have revealed that among never-smoking adolescents and young adults, e-cigarette use is associated with subsequent cigarette smoking.[2–6] This association was shown in studies taking place in California,[3] Hawaii,[2] and the Mid-Atlantic region,[7] as well as in nationally representative US samples,[6,8] Canada,[4] and the United Kingdom.[5] Seven of these studies were summarized in a recent meta-analysis, revealing more than a threefold increase in the risk of cigarette smoking initiation when comparing youth e-cigarette ever users to never users.[9] Although this association between e-cigarettes and smoking initiation has been consistent across the literature and could be explained by using a proposed "catalyst" model,[10] some have argued that the relationship partly reflects a shared propensity for experimentation with different nicotine-containing products.[11]

Many individuals at low risk of smoking initiation may be included in studies of baseline cigarette never-users. In contrast, youth who have already begun cigarette experimentation represent a population at high risk of progression to greater levels of cigarette use later in adolescence and into adulthood. Although smoking even 1 cigarette is concerning, becoming an established smoker in adolescence is of substantial clinical and public health concern and is strongly associated with continuing to smoke regularly.[12] Therefore, in the present investigation we consider high-risk youth, as evident by having already tried smoking (ever smoked ≥1 puff) but not yet smoked 100 cigarettes, and evaluate whether e-cigarette use in this population predicts progression from experimentation to established cigarette smoking 1 year later.

In a previous cross-sectional analysis of the 2011 and 2012 National Youth Tobacco Surveys (NYTSs), among youth who had ever smoked a cigarette, ever use of e-cigarettes was associated with being an established smoker (lifetime smoked ≥100 cigarettes), including after adjusting for socio-demographic variables.[13] However, the cross-sectional design of that analysis precluded causal conclusions because of uncertain temporal sequencing between e-cigarette use and established smoking.

In the current study, we used the nationally representative Population Assessment of Tobacco and Health (PATH) Study[14] Waves 1 (2013–2014) and 2 (2014–2015) to examine these same relationships prospectively. We hypothesized that among PATH youth participants who had already tried cigarette smoking but not yet smoked a total of 100 cigarettes, use of e-cigarettes would be positively associated with becoming an established cigarette smoker within 1 year.

METHODS

Researchers from the PATH Study selected participants using a 4-stage stratified probability design with oversampling for tobacco users, African Americans, and young adults (ages 18–24 years). The PATH youth sample consisted of adolescents (up to 2 per household) whose parents were selected for the PATH adult sample.[14] Researchers from the PATH Youth Study enrolled 13 651 US adolescents ages 12 to 17 years at baseline (2013–2014), with 87.9% retention (unweighted) at Wave 2 (2014–2015).

In-home in-person computer-assisted interviews were conducted in administering the PATH questionnaire. In separate sections, participants were asked about their tobacco use (eg, ever use, number of lifetime uses, and number of days used in the past 30 days) for 8 types of tobacco and nicotine-containing products, including cigarettes and e-cigarettes. Tobacco use questions were repeated during the Wave 2 interview, including for individuals who reached age 18 before follow-up and were therefore administered the Wave 2 adult questionnaire.

In the present analysis, we included youth who had smoked ≥1 cigarette puff but had not yet smoked 100 cigarettes at baseline (smoking experimenters), with known smoking status at follow-up ($N = 1295$). We examined 3 outcomes at follow-up as a function of baseline e-cigarette use: (1) having smoked ≥100 cigarettes (established smoking), (2) smoking during the past 30 days, and (3) both having smoked ≥100 cigarettes and past 30-day smoking (current established smoking). We categorized e-cigarette use in 2 ways: (1) ever use or never use, and (2) never use, nonpast 30-day use (former use), or past 30-day use.

Logistic regression models (Stata 14; StataCorp, College Station, TX) were used to adjust for hypothesized confounding variables in 3 stages. First, 6 separate unadjusted models were fitted to cover each combination of independent variable (Wave 1 e-cigarette never or ever use and e-cigarette never or former or past 30-day use) and dependent variable (Wave 2 established smoking, current smoking, and current established smoking). In the second stage, we added sex, age (in years), and race and/or ethnicity (Hispanic and/or Latino, non-Hispanic white, non-Hispanic African American, other) as covariables in all models, matching the confounders used in a previous cross-sectional analysis of NYTS data.[13] In the third stage, parent education (≥1 parent with a

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TABLE 1 Progression From Cigarette Experimentation to Established Smoking, According to Baseline E-cigarette Use

	n	Weighted % With Outcome	Unadjusted		Adjusted[a]		Adjusted[b]	
			OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Outcome: smoked 100 cigarettes								
Wave 1 predictors								
E-cigarette never	646	9.7	Reference	—	Reference	—	Reference	—
E-cigarette ever	582	19.3	2.23 (1.55–3.21)	<.001	2.07 (1.41–3.04)	<.001	1.57 (0.99–2.49)	.05
E-cigarette never	646	9.7	Reference	—	Reference	—	Reference	—
E-cigarette former	406	18.6	2.13 (1.43–3.18)	<.001	2.04 (1.33–3.12)	.001	1.55 (0.94–2.56)	.09
E-cigarette in the past 30 d	171	21.5	2.56 (1.58–4.14)	<.001	2.22 (1.31–3.74)	.003	1.69 (0.93–3.05)	.08
Outcome: smoked during the past 30 d								
Wave 1 predictors								
E-cigarette never	699	26.6	Reference	—	Reference	—	Reference	—
E-cigarette ever	596	38.8	1.75 (1.35–2.27)	<.001	1.65 (1.26–2.15)	<.001	1.32 (0.99–1.76)	.06
E-cigarette never	699	26.6	Reference	—	Reference	—	Reference	—
E-cigarette former	415	36.1	1.56 (1.15–2.12)	.004	1.48 (1.09–2.02)	.01	1.20 (0.86–1.68)	.29
E-cigarette in the past 30 d	176	45.3	2.29 (1.64–3.19)	<.001	2.10 (1.47–2.99)	<.001	1.64 (1.12–2.41)	.01
Outcome: smoked 100 cigarettes and smoked during the past 30 d								
Wave 1 predictors								
E-cigarette never	644	7.1	Reference	—	Reference	—	Reference	—
E-cigarette ever	580	15.6	2.43 (1.55–3.80)	<.001	2.23 (1.39–3.59)	<.001	1.80 (1.04–3.12)	.03
E-cigarette never	644	7.1	Reference	—	Reference	—	Reference	—
E-cigarette former	406	15.5	2.41 (1.46–3.97)	<.001	2.29 (1.35–3.89)	.002	1.85 (1.02–3.36)	.04
E-cigarette in the past 30 d	171	16.3	2.56 (1.52–4.32)	<.001	2.19 (1.24–3.88)	.007	1.76 (0.92–3.37)	.09

ORs and CIs corresponding to model covariates are shown in Supplemental Table 2. —, not applicable.

[a] Model covariates include the following: sex, age, and race and/or ethnicity.

[b] Model covariates additionally include the following: parent education, urban residence, household tobacco use, alcohol ever use, tobacco advertisement receptivity, sensation-seeking score, cigarette warning label exposure, interview time of year, and ever use of any other tobacco product.

bachelor degree or greater), urban residence (based on sampling units), household tobacco use (lives with ≥1 tobacco user), alcohol ever use, tobacco advertisement receptivity[15] (can recall brand of favorite advertisement), sensation-seeking score (scale from 3 to 15), cigarette warning label exposure (Likert-type scale), interview time of year (summer versus all other months), and ever use of any other tobacco product (ie, cigars, pipes, hookah, bidis, kreteks, snus, dissolvable tobacco, and conventional moist snuff or chewing smokeless tobacco) were also included in additional adjusted models. A sensation-seeking score was a composite of 3 Likert-type items (liking frightening things, willingness to break rules, and preference for exciting and unpredictable friends) and has been shown to correlate with youth tobacco use.[16] Interview time of year was included because, for youth, the scholastic calendar may play a role both in opportunity and social pressure to experiment with tobacco products.

All models were weighted for sampling design and nonresponse by using balanced repeated replication to be representative of the Wave 1 target population.[17] Multiple imputation was performed for missing observations (0.7% of data), with variance estimates adjusted accordingly.

An institutional review board at the University of California, San Francisco reviewed and designated the study protocol exempt for this analysis of deidentified survey data. The PATH Study protocol received a National Institutes of Health Certificate of Confidentiality and approval from the Westat Institutional Review Board. Parental consent was requested on behalf of participating youth. Youth who completed the questionnaire were given $25.

RESULTS

Among baseline cigarette experimenters (mean age: 15.5 years; 48.3% girls), having ever used e-cigarettes was positively associated with progression to established cigarette smoking in Wave 2 (Table 1). Compared with e-cigarette never users, e-cigarette ever users were twice as likely to report Wave 2 established smoking (19.3% vs 9.7%; $P < .001$) and current established smoking (15.6% vs 7.1%; $P < .001$) and were more likely to report past 30-day smoking (38.8% vs 26.6%; $P < .001$).

In models adjusted for sex, age, and race and/or ethnicity (Table 1), Wave 1 e-cigarette ever use (versus never use) was associated with approximately twice the odds of progression to Wave 2 established cigarette smoking (odds ratio [OR]: 2.23; 95% confidence interval [CI]: 1.55–3.21; $P < .001$), past 30-day smoking (OR: 1.75; 95% CI: 1.35–2.27; $P < .001$), and current

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established smoking (OR: 2.43; 95% CI: 1.55–3.80; $P < .001$). Associations were attenuated in fully adjusted models (Table 1), but e-cigarette ever use remained a positive and statistically significant predictor of current established smoking (OR: 1.80; 95% CI: 1.04–3.12; $P = .035$). Associations did not reach the threshold for statistical significance for established smoking (OR: 1.57; 95% CI: 0.99–2.49; $P = .055$) and past 30-day smoking (OR: 1.32; 95% CI: 0.99–1.76; $P = .059$).

When baseline e-cigarette former use (tried but not used in past 30 days) and past 30-day use were considered separately, there was a stepwise increase in the probability of progression to future established smoking from never to former to past 30-day e-cigarette use (Table 1). For example, the probability of Wave 2 past 30-day cigarette smoking rose from baseline e-cigarette never use (26.6%) to former use (36.1%) to past 30-day use (45.3%). Both e-cigarette former use and past 30-day use remained statistically significantly associated with all 3 Wave 2 cigarette outcomes in models adjusted for sex, age, and race and/or ethnicity (Table 1). In fully adjusted models, baseline e-cigarette former use remained a statistically significant predictor of progression to current established smoking (OR: 1.85; 95% CI: 1.02–3.36; $P = .042$), and baseline e-cigarette past 30-day use statistically significantly predicted progression to past 30-day smoking (OR: 1.64; 95% CI: 1.12–2.41; $P = .010$). Adjustment variables that were consistently associated with greater progression to established smoking included household tobacco use and tobacco advertisement receptivity (Supplemental Table 2).

DISCUSSION

In this study, among youth who had experimented with cigarettes but had not progressed to established smoking, additional use of e-cigarettes was positively associated with future onset of current established smoking. Across 3 different definitions of established smoking and 2 different specifications of e-cigarette use, baseline e-cigarette users were at 1.5 to 2 times greater odds of progression to established smoking than e-cigarette never users, after adjustment for confounding variables. Fully adjusted associations with e-cigarette ever use were statistically significant for 1 definition of established smoking (current established smoking; $P = .035$) but fell just short of the a priori threshold for statistical significance for established smoking ($P = .055$) and past 30-day smoking ($P = .059$). The ORs in the present longitudinal analysis were in the same direction but smaller in magnitude than in the previous cross-sectional analysis of NYTS data[13] in which new trials of e-cigarettes among previously established smokers could have been captured.

Regardless of how Wave 1 e-cigarette and Wave 2 smoking variables were specified, positive associations persisted after statistical adjustment for sex, age, and race and/or ethnicity. Adding the full set of confounding variables to models, such as household tobacco use, warning label exposure, and baseline use of other tobacco products, reduced the strength of some of the observed associations to below the threshold for statistical significance. However, all associations remained positive in direction and similar in magnitude across different definitions of e-cigarette exposure and the smoking outcome.

Suggested in these results is that e-cigarette use is more likely to encourage youth smoking than to divert youth from smoking when considering individuals who have already experimented with cigarette use. Unlike adults, particularly cigarette smokers, who commonly report a desire to quit smoking as a main motivator for e-cigarette use,[18] youth are more likely to cite curiosity as a reason to try e-cigarettes.[19] E-cigarette use was not associated with cigarette quit attempts or with quit contemplation among US middle and high school students in any NYTS wave from 2011 to 2015.[20]

In existing studies of youth who had never smoked a cigarette at baseline, those who tried e-cigarettes were more likely to initiate cigarette smoking in the future.[2–6,9] In addition to smoking initiation among youth never-smokers, we demonstrate in the current study that e-cigarette use was also associated with progression to current established smoking among youth smoking experimenters.

In a study of California 10th grade students that included never smokers and current smokers at baseline, greater frequency of e-cigarette use at baseline was associated with subsequently greater levels of smoking frequency (days smoked in past month) and heaviness (cigarettes smoked per day) 6 months later.[21] Similarly, in a school-based study of adolescent never and current smokers in Canada, baseline past 30-day e-cigarette use was associated with initiation of daily smoking 1 year later.[4] In the results of a school-based study of baseline cigarette ever smokers in Hawaii, a statistically significant change at follow-up in smoking frequency (measured as numerical categories) between baseline e-cigarette ever and never users was not yielded.[2] However, in a school-based study of adolescents in the United Kingdom, ever use (versus never use) of e-cigarettes was associated with “escalation” to smoking sometimes or usually among baseline nonsmokers who had used cigarettes in the past.[5] Authors of that study reported an adjusted OR that was similar to the current study

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(OR: 1.89; 95% CI: 0.82–4.33) but not statistically significant (P = .13) in a smaller sample (n = 318).[5]

The smoking outcomes evaluated in the current study represent intensity levels of clear clinical and public health concern. Although smoking as infrequently as 1 day in the past month in adolescence is predictive of adult smoking,[22] youth who reach higher levels of smoking are even more likely to continue to smoke.[12] Additionally, although more recent (past 30-day) e-cigarette use was a stronger predictor of future established smoking than former e-cigarette use in unadjusted models, this pattern did not necessarily persist in fully adjusted models. We suggest that any level of e-cigarette use among adolescent cigarette experimenters may be a meaningful risk indicator of smoking progression.

Several study advantages strengthened the conclusions that can be drawn from this research. The large, prospective, and nationally representative nature of the PATH Study enhanced generalizability and certainty regarding the temporal sequence between exposure and outcome. The PATH questionnaire was rigorously pilot tested and administered under a consistent protocol.[14] Furthermore, the magnitude of associations found in this study was largely consistent across different specifications of e-cigarette and cigarette use. Among other study aspects to consider, in-home administration of the PATH questionnaire could have led to differences in estimated tobacco use compared with school-based surveys. However, results of this analysis were qualitatively similar to previous work in which NYTS data was used.[13] As with all observational studies, residual confounding from unmeasured variables cannot be ruled out, although associations remained positive and at the threshold for statistical significance after adjustment for an extensive set of variables known to predict youth cigarette smoking.[23]

In July 2017, the US Food and Drug Administration announced a plan for tobacco and nicotine regulation that delayed federal e-cigarette regulation from 2018 until 2022.[24] However, local governments have taken regulatory action of e-cigarettes. For example, a 2017 San Francisco, California, ordinance prohibits the sale of flavored tobacco products, including e-cigarettes, with the intention of reducing the appeal of tobacco products to youth.[25] It is indicated in our results that among youth cigarette experimenters, those who have also used e-cigarettes are more likely to progress to current established smoking than those who tried cigarettes alone. As long as e-cigarettes remain attractive to youth, concern persists that these products contribute to greater combustible cigarette smoking among adolescents.

CONCLUSIONS

Among youth cigarette experimenters, using e-cigarettes was positively and independently associated with future onset of current established smoking, suggesting that e-cigarettes do not divert from, and may encourage, cigarette smoking in this population. In weighing the overall public health impact of e-cigarette availability, regulation, and use, the potential to increase combustible cigarette smoking by youth deserves special consideration.

ABBREVIATIONS

CI: confidence interval
e-cigarette: electronic cigarette
NYTS: National Youth Tobacco Survey
OR: odds ratio
PATH: Population Assessment of Tobacco and Health

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Original article

The Association Between Smoking and Electronic Cigarette Use in a Cohort of Young People

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ABSTRACT

Purpose: Electronic cigarette (e-cigarette) use is associated with smoking initiation among young people; however, it is also possible that smoking is associated with e-cigarette initiation. This study explores these associations among young people in Great Britain.
Methods: A longitudinal survey of 1,152 11- to 18-year-olds was conducted with baseline in April 2016 and follow-up between August and October 2016. Logistic regression models and causal mediation analyses assessed whether (1) ever e-cigarette use and escalation were associated with smoking initiation (ever smoking at follow-up) among baseline never smokers (n = 923), and (2) ever smoking and escalation were associated with e-cigarette initiation (ever e-cigarette use at follow-up) among baseline never e-cigarette users (n = 1,020).
Results: At baseline, 19.8% were ever smokers and 11.4% were ever e-cigarette users. Respondents who were ever e-cigarette users (vs. never users, 53% vs. 8%, odds ratio [OR] = 11.89, 95% confidence interval [CI] = 3.56–39.72) and escalated their e-cigarette use (vs. did not, 41% vs. 8%, OR = 7.89, 95% CI = 3.06–20.38) were more likely to initiate smoking. Respondents who were ever smokers (vs. never smokers, 32% vs. 4%, OR = 3.54, 95% CI = 1.68–7.45) and escalated their smoking (vs. did not, 34% vs. 6%, OR = 5.79, 95% CI = 2.55–13.15) were more likely to initiate e-cigarette use. There was a direct effect of ever e-cigarette use on smoking initiation (OR = 1.34, 95% CI = 1.05–1.72), and ever smoking on e-cigarette initiation (OR = 1.08, 95% CI = 1.01–1.17); e-cigarette and smoking escalation, respectively, did not mediate these effects.

IMPLICATIONS AND CONTRIBUTION

This study employs a causal inference approach to provide further support for the association between ever e-cigarette use and smoking initiation, and additionally finds that ever smoking is associated with e-cigarette initiation, among young people.

Conflicts of Interest: Katherine East, Sara Hitchman, and Ann McNeill are members of the UK Centre for Tobacco and Alcohol Studies. Ioannis Bakolis is supported by the National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and by the NIHR Collaboration for Leadership in Applied Health Research and Care South London at King's College Hospital NHS Foundation Trust. Sarah Williams is an employee at Public Health England and was previously an employee at Action on Smoking and Health at the time this study was conducted. Hazel Cheeseman and Deborah Arnott are employees of Action on Smoking and Health, which receives funding from the British Heart Foundation, Cancer Research UK (CRUK), and the Department of Health. This study was funded by CRUK grant code A21559. CRUK was not involved in the study design, data collection, analysis or interpretation of the data, the write up of the manuscript, or decision to submit the article for publication. The views expressed are those of the author(s) and not necessarily those of Public Health England, CRUK, Action on Smoking and Health, the NHS, the NIHR or the Department of Health.
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Conclusions: Among young people in Great Britain, ever e-cigarette use is associated with smoking initiation, and ever smoking is associated with e-cigarette initiation.
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There are an estimated 2.9 million current adult electronic cigarette (e-cigarette) users in Great Britain [1]. Concerns have been expressed about the impact of e-cigarette use on cigarette smoking, particularly among young people [2–4]. There is some evidence that trial of e-cigarettes among young people aged 11–18 years in Great Britain is rising (from 3.7% in 2013 to 9.3% in 2016) [5]. However, regular (at least monthly) use among young people is low, and increases in regular use are mainly restricted to current smokers (from 20.2% in 2015 to 27.2% in 2016), with regular use by never smokers remaining rare (.6% in 2015 to .4% in 2016) [5].

Cross-sectional studies have found that young people who use e-cigarettes are more likely to smoke [6,7], intend to smoke [8,9], and be susceptible to smoking [10] than those who do not. On the other hand, among young people in Great Britain, ex- and current smokers are more likely to intend to use e-cigarettes than never smokers [11]. It is therefore difficult to determine whether there is any causality, and it is likely that there is an underlying factor driving both smoking and e-cigarette use.

Several longitudinal studies of U.S. youth have found baseline e-cigarette use is associated with smoking initiation [12–17], past six-month smoking [18], and past-month smoking [19] at follow-up. A meta-analysis of these studies has confirmed the strength and consistency of these associations [4], and the association between ever e-cigarette use and smoking initiation has since been replicated in England [20] and Scotland [21].

Although each of the above studies exploring the association between e-cigarette use and smoking control for a variety of factors associated with smoking, there remains the presence of extraneous variables, which may be related to both smoking and e-cigarette use. Furthermore, some researchers propose that certain psychosocial processes lead to vulnerability to any drug use [22,23]. One study [18] explored whether the association between smoking and e-cigarettes works both ways, and found that not only was use of e-cigarettes at baseline associated with past six-month smoking at follow-up, but also smoking at baseline was associated with past six-month e-cigarette use at follow-up. Furthermore, among young people in Argentina, current smoking was associated with e-cigarette initiation one and a half years later [24].

Despite the above research, the relative contributions of e-cigarette use to smoking initiation, and smoking to e-cigarette initiation, have not been formally assessed. All studies in this field with the exception of Wills and colleagues [15] have relied on standard regression models [12–14,16–21,24], which allow only limited conclusions to be drawn regarding the pathways between these products. Therefore, in this study, we have included causal mediation analyses [25] to investigate the causal influence of e-cigarette use on smoking initiation, and smoking on e-cigarette initiation.

This study is the first to our knowledge to explore the longitudinal association between (1) ever e-cigarette use and smoking initiation (ever smoking at follow-up) among baseline never smokers, and (2) ever smoking and e-cigarette initiation (ever e-cigarette use at follow-up) among baseline never e-cigarette users, among young people in Great Britain. We additionally explore whether escalation of each product between baseline and follow-up is associated with initiation of the alternative product, and employ causal mediation analyses for the identification of mediating factors [25] to investigate specific pathways between the two products.

Methods

Design

This study used data from the 2016 Action on Smoking and Health Great Britain Youth longitudinal survey. A non-probability quota sampling approach was adopted using Ipsos MORI's online panels to recruit respondents aged 11–18 years. Quotas were set in respect of age, gender, and Government Office Region (GOR) using data from Eurostat 2012 to ensure sample representativeness. Respondents were invited by email to participate in an online survey about smoking between April 6 and 20 with follow-up between August 5 and October 7, 2016. Up to eight email reminders were sent to maximize follow-up rates. Each wave took approximately 10 minutes to complete, and financial incentives were provided via a prize draw. Informed consent to take part in the surveys was provided either by the parents of those aged 11–15 years or by those individuals aged 16–18 years. Ethical approval for the analyses in this paper was not required as this study used secondary pre-existing data.

Ipsos MORI's online panel applicants consist of volunteers from the general public. These panel applicants are validated by a means of sophisticated vetting procedures using a variety of recruitment channels. Shortly after joining, panelists' survey-taking behavior is tested, with those most likely to make intentional or unintentional errors on future surveys deactivated. Subsequently, panelists' behavior is monitored and tracked across all surveys for quality reasons.

Sample

The baseline survey was completed by 2,916 respondents aged 11–18 years, of whom 1,469 (50%) successfully completed the follow-up survey. We excluded 317 respondents (22%) who had never heard of e-cigarettes and selected "don't know" or "prefer not to say" to some questions (see full breakdown in Figure 1). This left a final study sample of 1,152, of whom 923 (80%) were baseline never smokers and 1,020 (89%) were baseline never e-cigarette users (Figure 1).

Measures

Smoking and e-cigarette status. At baseline, respondents were classified as never smokers (never smoked, not even a puff) or ever smokers; at follow-up, respondents were classified as never smokers or initiated smoking (never smokers at baseline but ever

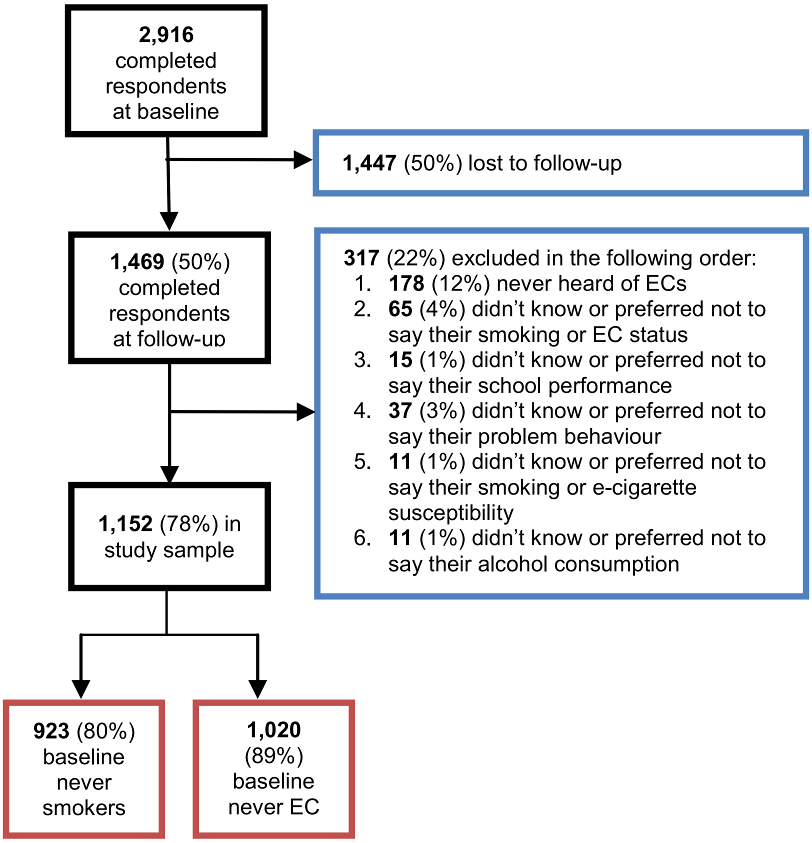

Figure 1. Flow diagram illustrating the respondent selection process. EC = electronic cigarette.

smokers at follow-up). At follow-up, respondents were further classified as having escalated smoking (increased their smoking between baseline and follow-up, e.g., escalating from never smoking to trying smoking, from smoking sometimes to smoking between one and six cigarettes a week) or not escalated smoking. Respondents were classified using the same procedure for e-cigarette use. Respondents who had never heard of e-cigarettes (n = 178), and those who responded with "Prefer not to say" or "Don't know" to the smoking or e-cigarette question at either baseline or follow-up (n = 65) were excluded from all analyses. Full item wording and response options are available in Table A1 (Supplementary Data).

Covariates (assessed at baseline only). Age (11–13, 14–15, 16–18), gender (male, female), school performance (1–4, below average to excellent), problem behavior (2–8, 8 = greater problem behavior), monthly alcohol use (yes, no), smoking susceptibility (susceptible, not susceptible) [26], e-cigarette susceptibility (susceptible, not susceptible—to mirror smoking susceptibility [26]), some friends smoke (yes, no, not applicable/don't know), some friends use e-cigarettes (yes, no, not applicable/don't know), at least one parent smokes (yes, no), at least one parent uses e-cigarettes (yes, no), sibling(s) smoke (yes, no, not applicable/don't know), sibling(s) use e-cigarettes (yes, no, not applicable/don't know), public approve of smoking (yes, no), and public approve of e-cigarettes (yes, no) [27]. For school performance, problem behavior, monthly alcohol use, and smoking and e-cigarette susceptibility, "Don't know" and "Prefer not to say" responses were excluded from all analyses. Covariates specific to smoking were selected based on the previous literature [12,15,18,26–28] and friend, parental, and sibling e-cigarette use and public approval of e-cigarettes were also included to mirror the similar smoking measures and to explore potential shared risk factors for each product. Full item wording, response options, and further details on coding for all covariates are available in Table A1 (Supplementary Data).

Statistical analysis

We used unadjusted logistic regressions to compare respondents lost to follow-up with those retained and included in the study sample. We then used chi-square tests to compare smoking and e-cigarette status at baseline and follow-up. We used unadjusted and adjusted logistic regressions to explore the associations between (1) ever e-cigarette use at baseline and e-cigarette escalation between baseline and follow-up with smoking initiation at follow-up among baseline never smokers (n = 923), and (2) ever smoking at baseline and smoking escalation between baseline and follow-up with e-cigarette initiation at follow-up among baseline never e-cigarette users (n = 1,020). In adjusted models, we adjusted for all covariates described in the Measures section.

To decompose the causal effect of e-cigarette use on smoking initiation, and smoking on e-cigarette initiation, we used causal mediation analyses using the parametric g-computation procedure [25]. Mediation analyses go beyond standard regression models, which can estimate the associations between use of both products, by disentangling different pathways that could explain the effect of an exposure on an outcome. Furthermore, when a potential mediator is treated as confounder in standard regression models, spurious associations may arise. The most commonly used mediation analysis in epidemiology is based on the Baron and Kenny approach [29], in which the total effect of an exposure on an outcome, the effect of the exposure explained by a given set of mediators (indirect effect), and the effect of the exposure unexplained by those same mediators (direct effect) can be defined. This approach has four main problems as it (1) assumes no unmeasured confounding between mediator and outcome, (2) assumes no interactions between exposure and mediator on outcome, (3) does not extend to nonlinear models, and (4) assumes correctly specified models.

Causal mediation analysis has arisen from the causal inference literature [30] and addressed problems of the Baron and Kenny approach [29] under the potential outcomes framework, first by defining (using potential outcomes) precisely what is meant by direct and indirect effects, second by giving clear assumptions under which they can be identified, and third by generalizing the statistical methods available for carrying out such analyses to allow for nonlinearities, interactions, discrete outcomes, and semiparametric estimation [31]. We therefore use the parametric g-computation procedure under this framework as it can quantify reliable direct and indirect causal effects for binary variables, and produces narrow confidence intervals to allow for stronger conclusions to be made regarding observed associations [25,32]. The g-computation procedure is discussed in detail elsewhere [25,31,32], but primarily relies on the parametric modeling assumptions shared with logistic regression and, to infer causality, assumes no unmeasured confounding. It has been applied to survey data previously [33].

To assess the causal influence of e-cigarette use on smoking initiation, we specified a direct effect from ever e-cigarette use at baseline to smoking initiation at follow-up and an indirect effect acting through e-cigarette escalation between baseline and follow-up (mediator). We used the same approach to assess the causal influence of ever smoking on e-cigarette initiation at follow-up with smoking escalation between baseline and follow-up acting as a mediator. The causal diagrams for each model are shown in Figure 2. In the causal mediation analyses, all covariates described in the Measures section were specified as baseline confounders. The g-computation estimates were converted to odds ratios via exponentiation.

For attrition analysis and causal mediation analyses, we used unweighted data; for all other analyses, we used weighted data unless otherwise specified. Data were weighted according to age, gender, and GOR using data from the Eurostat 2012, and adjusted for attrition on age, gender, GOR, ever smoking, and ever e-cigarette use. Missing data were excluded listwise from all analyses (see Figure 1).

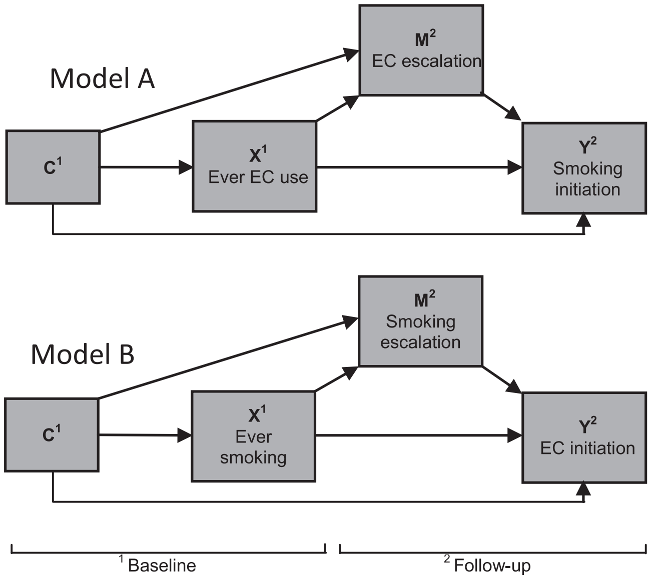

Figure 2. Conceptual causal diagrams for mediation and confounding. C = Covariate(s); X = Exposure; M = Mediator; Y = Outcome, EC = E-cigarette. Model A specifies baseline ever e-cigarette use as the exposure, e-cigarette escalation at follow-up as the mediator, and smoking initiation at follow-up as the outcome. Model B specifies baseline ever smoking as the exposure, smoking escalation at follow-up as the mediator, and e-cigarette initiation at follow-up as the outcome.

Results

Table 1 shows the characteristics of the study sample at baseline (n = 1,152) compared with respondents lost to follow-up and who would have otherwise been excluded (because of not having heard of e-cigarettes or selecting "don't know" or "prefer not to say" on key variables and covariates) (n = 1,225). Respondents were more likely to be lost to follow-up if they had ever smoked and ever used an e-cigarette, and also differed on all covariates included in the study except smoking susceptibility and having at least one parent who uses e-cigarettes.

At baseline, 229 respondents (19.9%) had ever smoked (Table 1), and this increased to 301 (26.0%) at follow-up ($\chi^2 = 834.32$, $p < .001$). Of the 229 baseline ever smokers, 111 (48.5%) were also ever e-cigarette users; of the 923 baseline never smokers, 21 (2.3%) were ever e-cigarette users. At baseline, 132 respondents (11.5%) had ever used an e-cigarette (Table 1), increasing to 204 (17.6%) at follow-up ($\chi^2 = 761.74$, $p < .001$). Of the 132 baseline ever e-cigarette users, 111 (84.0%) were also ever smokers; of the 1,020 baseline never e-cigarette users, 118 (11.6%) were ever smokers. At baseline, only 56 (4.9%) respondents smoked monthly or more and 24 (2.1%) used an e-cigarette monthly or more.

Compared with baseline never e-cigarette users, ever e-cigarette users were more likely to initiate smoking at follow-up (Table 2). Furthermore, respondents who escalated e-cigarette use between baseline and follow-up were also more likely to initiate smoking at follow-up compared with those who did not (Table 2).

Compared with baseline never smokers, ever smokers were more likely to initiate e-cigarette use at follow-up (Table 3). Furthermore, respondents who escalated smoking between baseline and follow-up were also more likely to initiate e-cigarette use at follow-up compared with those who did not (Table 3).

Having some friends who use an e-cigarette reduced the likelihood of smoking initiation (Table 2) but increased the likelihood of e-cigarette initiation (Table 3). Being older, susceptible to smoking, and having at least one parent who smokes were associated with an increased likelihood of smoking initiation (Table 2). Monthly alcohol use and no perceived public approval of smoking were associated with an increased likelihood of e-cigarette initiation (Table 3).

Table 1
Respondent characteristics of the study sample at baseline (n = 1,152) and comparison with those lost to follow-up who would have otherwise been excluded (n = 1,225)

	Study sample (n = 1,152)	Lost to follow-up and excluded (n = 1,225)	OR (95% CI)
Ever smoked	229 (19.88)	382 (31.18)	**.55 (.45–.66)**
Ever used e-cigarettes	132 (11.46)	297 (24.24)	**.40 (.32–.51)**
Female	620 (53.82)	564 (46.04)	**1.37 (1.16–1.61)**
Age			
11–13	438 (38.02)	375 (30.61)	
14–15	338 (29.34)	263 (21.47)	1.10 (.89–1.36)
16–18	376 (32.64)	587 (47.92)	**.55 (.45–.66)**
School performance (1–4, 4 = excellent), mean (SD)	3.05 (.8)	2.97 (.8)	**1.11 (1.01–1.22)**
Problem behavior (2–8, 8 = high), mean (SD)	2.93 (1.2)	3.30 (1.4)	**.80 (.75–.86)**
Monthly alcohol use	269 (23.35)	407 (33.22)	**.61 (.51–.73)**
Susceptible to smoking	146 (12.67)	151 (12.33)	.86 (.67–1.11)
Susceptible to using e-cigarettes	264 (22.92)	330 (26.94)	**.63 (.52–.77)**
Some friends smoke			
No	371 (32.2)	279 (22.78)	
Yes	727 (63.11)	894 (72.98)	**.61 (.51–.73)**
DK/NA	54 (4.69)	52 (4.24)	.78 (.52–1.18)
Some friends use e-cigarettes			
No	684 (59.38)	526 (42.94)	
Yes	399 (34.64)	620 (50.61)	**.49 (.42–.59)**
DK/NA	69 (5.99)	79 (6.45)	**.67 (.48–.95)**
At least one parent smokes	343 (29.77)	413 (33.71)	**.83 (.70–.99)**
At least one parent uses e-cigarettes	182 (15.8)	221 (18.04)	.85 (.69–1.06)
Sibling(s) smokes			
No	918 (79.69)	935 (76.33)	
Yes	127 (11.02)	191 (15.59)	**.68 (.53–.86)**
NA/DK	107 (9.29)	99 (8.08)	1.10 (.83–1.47)
Sibling(s) use e-cigarettes			
No	992 (86.11)	1016 (82.94)	
Yes	54 (4.69)	119 (9.71)	**.46 (.33–.65)**
NA/DK	106 (9.20)	90 (7.35)	1.21 (.90–1.62)
Public approve of smoking	33 (2.86)	62 (5.06)	**.55 (.36–.85)**
Public approve of e-cigarettes	43 (3.73)	90 (7.35)	**.49 (.34–.71)**

All data are unweighted. Significant associations ($p < .05$) are highlighted in **bold.**
N (%) of the samples are reported unless otherwise stated.

In the causal mediation analysis (Figure 2, model A), baseline ever e-cigarette use had a direct causal effect on smoking initiation at follow-up (odds ratio [OR] = 1.34, 95% confidence interval [CI] = 1.05–1.72, $p = .018$), and there was a significant total causal effect of the model (OR = 1.35, 95% CI = 1.04–1.74, $p = .022$). However, there was no indirect effect of baseline ever e-cigarette use on smoking initiation at follow-up mediated by e-cigarette escalation between baseline and follow-up (OR = 1.00, 95% CI = .91–1.11, $p = .983$).

In the causal mediation analysis (Figure 2, model B), baseline ever smoking had a direct causal effect on e-cigarette initiation at follow-up (OR = 1.08, 95% CI = 1.01–1.17, $p = .034$), and there was a significant total causal effect of the model (OR = 1.11, 95% CI = 1.03–1.20, $p = .006$). However, there was no indirect effect of baseline ever smoking on e-cigarette initiation at follow-up mediated by smoking escalation between baseline and follow-up (OR = 1.03, 95% CI = .99–1.06, $p = .106$).

Discussion

This study was the first to explore the longitudinal association between e-cigarette use and smoking initiation, and smoking and e-cigarette initiation among young people in Great Britain, and to assess the relative contribution of these associations using a causal inference approach. In the logistic regression analyses, we found evidence for a prospective association between ever e-cigarette use and smoking initiation, and between ever smoking and e-cigarette initiation. We also found that escalation of each product (e-cigarettes and smoking) between baseline and follow-up was associated with initiation of the alternative product. The causal mediation analyses confirmed the direct effect of baseline ever e-cigarette use on smoking initiation, and baseline ever smoking on e-cigarette initiation, but found that e-cigarette and smoking escalation, respectively, did not mediate these effects.

This study provides insight into the impact of e-cigarette use on smoking and vice versa in young people; however, the findings must be considered in the light of some limitations. Attrition was high and respondents lost to follow-up differed substantially from those retained, potentially reducing generalizability to ever smokers, ever e-cigarette users, males, older respondents, and those with poorer school performance and greater problem behavior.

Although this study controlled for a variety of factors previously associated with smoking and e-cigarette use to enhance approximation of the models, there are still several factors that were not included that may contribute to the observed association between these products [28]. Examples may include curiosity, sensation seeking, liking, or disliking the effects of smoking/e-cigarettes, expectancies of smoking/e-cigarettes, mental ill health, and use of other drugs [28]. Furthermore, there are likely to be contributing factors that cannot be easily measured in surveys such as biological or genetic vulnerabilities, although drug use and parent's smoking and e-cigarette use may act as an indicator of these. Larger sample sizes are required to enable this substantial number of covariates to be assessed and meaningfully interpreted.

Table 2
Associations between smoking initiation at follow-up and e-cigarette use and all covariates, among baseline never smokers (n = 923)

	n (% initiated smoking)	Unadjusted		Adjusted model 1[a]		Adjusted model 2[b]	
		OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Baseline EC use							
Never	902 (8.2)	1.00		1.00		1.00	
Ever	21 (52.6)	**12.41 (4.53–33.99)**	**<.001**	**10.57 (3.33–33.50)**	**<.001**	**11.89 (3.56–39.72)**	**<.001**
Follow-up EC use							
No escalation	882 (8.1)	1.00		—	—	1.00	
Escalation	41 (41.0)	**7.94 (3.75–16.82)**	**<.001**	—	—	**7.89 (3.06–20.38)**	**<.001**
Age							
11–13	397 (4.4)	1.00		1.00		1.00	
14–15	270 (6.3)	1.45 (.71–2.97)	.312	1.22 (.54–2.73)	.636	1.35 (.58–3.15)	.485
16–18	256 (16.1)	**4.12 (2.19–7.76)**	**<.001**	**4.02 (1.72–9.40)**	**.001**	**4.98 (2.07–12.00)**	**<.001**
Gender							
Male	428 (10.8)	1.00		1.00		1.00	
Female	495 (8.5)	.77 (.46–1.30)	.331	.90 (.48–1.68)	.738	.91 (.47–1.76)	.786
School perf. (1–4, 4 = excellent)[c]	2.93 (.9)	.76 (.53–1.08)	.124	.91 (.64–1.29)	.596	.90 (.64–1.29)	.579
Problem beh. (2–8, 8 = high)[c]	3.05 (1.3)	**1.31 (1.03–1.66)**	**.028**	1.06 (.82–1.37)	.659	1.05 (.81–1.36)	.705
Monthly alcohol use							
No	790 (7.8)	1.00		1.00		1.00	
Yes	133 (18.1)	**2.61 (1.42–4.80)**	**.002**	1.64 (.82–3.30)	.165	1.32 (.61–2.86)	.480
Smoking susceptibility							
No	777 (7.9)	1.00		1.00		1.00	
Yes	146 (19.8)	**2.88 (1.57–5.29)**	**.001**	**2.38 (1.17–4.84)**	**.016**	**2.61 (1.23–5.52)**	**.012**
Some friends smoke							
No	355 (5.4)	1.00		1.00		1.00	
Yes	515 (12.9)	**2.60 (1.34–5.07)**	**.005**	1.48 (.66–3.34)	.341	1.28 (.57–2.87)	.555
NA/DK	53 (1.9)	.35 (.04–2.76)	.317	.30 (.04–2.43)	.258	.29 (.04–2.36)	.246
Some friends use EC							
No	598 (8.6)	1.00		1.00		1.00	
Yes	264 (11.0)	1.32 (.73–2.40)	.358	**.47 (.24–.93)**	**.029**	**.35 (.17–.75)**	**.007**
NA/DK	61 (15.1)	1.90 (.73–4.94)	.188	1.99 (.78–5.10)	.150	1.80 (.72–4.51)	.212
At least one parent smokes							
No	676 (6.8)	1.00		1.00		1.00	
Yes	247 (18.0)	**2.99 (1.72–5.20)**	**<.001**	**2.97 (1.62–5.44)**	**<.001**	**2.65 (1.37–5.12)**	**.004**
At least one parent uses EC							
No	802 (8.4)	1.00		1.00		1.00	
Yes	121 (18.8)	**2.54 (1.35–4.76)**	**.004**	1.47 (.70–3.07)	.304	1.33 (.65–2.73)	.437
Sibling(s) smoke							
No	761 (8.5)	1.00		1.00		1.00	
Yes	71 (20.8)	**2.83 (1.23–6.51)**	**.015**	.75 (.30–1.84)	.527	.84 (.33–2.16)	.723
NA/DK	91 (10.4)	1.25 (.56–2.82)	.584	1.65 (.56–4.92)	.365	1.94 (.66–5.69)	.226
Sibling(s) use EC							
No	810 (9.3)	1.00		1.00		1.00	
Yes	28 (24.3)	**3.13 (1.09–9.01)**	**.034**	2.16 (.54–8.58)	.274	1.59 (.35–7.27)	.551
NA/DK	85 (9.3)	1.00 (.41–2.41)	.998	.72 (.20–2.53)	.604	.67 (.19–2.41)	.543
Public approve of smoking							
No	903 (9.5)	1.00		1.00		1.00	
Yes	20 (20.5)	2.45 (.60–9.96)	.209	1.33 (.34–5.16)	.676	1.87 (.48–7.19)	.365
Public approve of ECs							
No	907 (9.7)	1.00		1.00		1.00	
Yes	16 (9.8)	1.00 (.20–4.99)	.997	.39 (.07–2.05)	.263	.40 (.08–1.92)	.252

Adjusted model 1 constant OR = .02 (95% CI = .00–.11) $p < .001$. Adjusted model 2 constant OR = .02 (95% CI = .00–.10), $p < .001$. N and % illustrate the number and percentage of individuals who initiated smoking at follow-up. All n use unweighted data, % and analyses use weighted data.
Significant associations ($p < .05$) are highlighted in **bold.**
beh. = behavior; EC = e-cigarette; perf. = performance.
[a] Adjusted model 1 is adjusted for all variables listed except follow-up EC use.
[b] Adjusted model 2 is adjusted for all variables listed.
[c] Mean(SD) reported, mean (SD) for never smoked at follow-up: school performance = 3.12 (.8), problem behavior = 2.71 (1.0).

Another important limitation is that this study uses the outcomes smoking initiation and e-cigarette initiation defined as progressing from never to ever use of each product. This is similar to some previous studies [12–16,21,24], yet the use of such broad measures has been criticized for providing limited evidence of progression to any significant smoking behavior [28,34]. However, because of low prevalence rates of monthly or more smoking (5%) and e-cigarette use (2%) in this study's sample, options for refining the measures were limited. Therefore, although the present study found an association between ever smoking and ever e-cigarette use, these cannot be generalized to current or regular use, and it cannot be determined whether e-cigarette experimentation leads to regular smoking. Such questions are critical in this area of research. Surveys with multiple waves across several years with larger sample sizes are needed to enable higher numbers of ever and current smokers and e-cigarette users, and further dissect the association between the two products.

Table 3
Associations between e-cigarette initiation at follow-up and smoking and all covariates, among baseline never e-cigarette users (n = 1,020)

	n (% initiated EC use)	Unadjusted		Adjusted model 1[a]		Adjusted model 2[b]	
		OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Baseline smoking							
Never	902 (4.1)	1.00		1.00		1.00	
Ever	118 (32.4)	**9.48 (5.36–16.76)**	**<.001**	**3.69 (1.88–7.23)**	**<.001**	**3.54 (1.68–7.45)**	**.001**
Follow-up smoking							
No escalation	932 (5.9)	1.00		—	—	1.00	
Escalation	88 (33.5)	**8.00 (4.36–14.69)**	**<.001**	—	—	**5.79 (2.55–13.15)**	**<.001**
Age							
11–13	413 (5.6)	1.00		1.00		1.00	
14–15	294 (6.1)	1.11 (.54–2.27)	.779	.65 (.29–1.43)	.285	.57 (.25–1.27)	.168
16–18	313 (12.5)	**2.41 (1.29–4.51)**	**.006**	.69 (.31–1.55)	.374	.48 (.19–1.18)	.109
Gender							
Male	468 (10.2)	1.00		1.00		1.00	
Female	552 (7.3)	.70 (.41–1.17)	.171	.77 (.41–1.43)	.404	.73 (.39–1.37)	.331
School perf. (1–4, 4 = excellent)[c]	2.67 (.9)	**.57 (.42–.78)**	**<.001**	.81 (.58–1.14)	.226	.79 (.55–1.12)	.183
Problem beh. (2–8, 8 = high)[c]	3.51 (1.4)	**1.62 (1.30–2.03)**	**<.001**	1.20 (.93–1.53)	.154	1.13 (.87–1.47)	.352
Monthly alcohol use							
No	824 (5.0)	1.00		1.00		1.00	
Yes	196 (20.6)	**4.93 (2.87–8.47)**	**<.001**	**2.66 (1.27–5.61)**	**.010**	**2.40 (1.08–5.33)**	**.032**
EC susceptibility							
No	756 (5.1)	1.00		1.00		1.00	
Yes	264 (18.9)	**4.39 (2.51–7.67)**	**<.001**	1.53 (.83–2.83)	.173	1.67 (.86–3.27)	.131
Some friends smoke							
No	363 (2.4)	1.00		1.00		1.00	
Yes	603 (12.3)	**5.58 (2.44–12.73)**	**<.001**	1.97 (.86–4.50)	.107	1.95 (.87–4.36)	.105
NA/DK	54 (5.5)	2.34 (.56–9.84)	.247	3.24 (.60–17.36)	.170	4.31 (.88–21.13)	.071
Some friends use EC							
No	660 (5.7)	1.00		1.00		1.00	
Yes	293 (15.9)	**3.14 (1.81–5.45)**	**<.001**	**2.69 (1.48–4.87)**	**.001**	**3.03 (1.63–5.64)**	**<.001**
NA/DK	67 (6.4)	1.15 (.31–4.19)	.835	1.10 (.20–6.14)	.915	.78 (.14–4.54)	.785
At least one parent smokes							
No	733 (6.6)	1.00		1.00		1.00	
Yes	287 (14.9)	**2.47 (1.45–4.23)**	**.001**	1.88 (.91–3.91)	.090	1.45 (.61–3.46)	.405
At least one parent uses EC							
No	884 (7.6)	1.00		1.00		1.00	
Yes	136 (17.3)	**2.54 (1.38–4.67)**	**.003**	2.34 (1.00–5.47)	.051	2.1 (.87–5.07)	.097
Sibling(s) smoke							
No	830 (7.4)	1.00		1.00		1.00	
Yes	94 (24.0)	**3.94 (2.00–7.75)**	**<.001**	1.49 (.66–3.36)	.332	1.64 (.69–3.91)	.266
NA/DK	96 (3.9)	.51 (.16–1.61)	.251	.36 (.06–2.11)	.258	.27 (.04–1.93)	.193
Sibling(s) use EC							
No	899 (8.3)	1.00		1.00		1.00	
Yes	31 (29.9)	**4.69 (1.50–14.66)**	**.008**	1.46 (.39–5.43)	.576	.92 (.28–3.09)	.895
NA/DK	90 (5.6)	.66 (.23–1.83)	.420	1.03 (.21–5.11)	.969	1.10 (.19–6.27)	.917
Public approve of smoking							
No	1000 (9.0)	1.00		1.00		1.00	
Yes	20 (2.8)	.29 (.04–2.22)	.233	**.09 (.01–.88)**	**.038**	.15 (.02–1.22)	.076
Public approve of ECs							
No	995 (8.5)	1.00		1.00		1.00	
Yes	25 (20.9)	2.84 (.95–8.50)	.061	.99 (.31–3.15)	.987	1.32 (.34–5.15)	.689

Adjusted model 1 constant OR = .02 (95% CI = .00–.07) $p < .001$. Adjusted model 2 constant OR = .02 (95% CI = .00–.10), $p < .001$. N and % illustrate the number and percentage of individuals who initiated EC use at follow-up. All n use unweighted data, % and analyses use weighted data.
Significant associations ($p < .05$) are highlighted in **bold.**
beh. = behavior; EC = e-cigarette; perf. = performance.
[a] Adjusted model 1 is adjusted for all variables listed except follow-up smoking.
[b] Adjusted model 2 is adjusted for all variables listed.
[c] Mean (SD) reported, mean (SD) for never used EC at follow-up: school performance = 3.08 (.8), problem behavior = 2.77 (1.0).

Despite the above limitations, this study has several strengths. It was the first to explicitly explore the association not only between e-cigarette use at baseline and smoking initiation at follow-up but additionally smoking at baseline and e-cigarette initiation at follow-up. Moreover, a novel statistical approach (causal mediation analysis [25]) was used to explore whether the association between baseline ever e-cigarette use and smoking initiation at follow-up was mediated by escalation of e-cigarette use between survey waves; the same procedure was also used to explore further the association between smoking and e-cigarette initiation. To our knowledge this has not been done previously. Finally, the sample was drawn from the general population in Great Britain using a quota sampling approach to enhance representativeness.

The rate of ever smoking in this study was 19.9% at baseline, which is lower than other findings in Great Britain in 2016 [5], but could be because of those lost at follow-up being more likely to smoke. The rate of ever e-cigarette use (11.5% at baseline) and findings that ever e-cigarette use was largely confined to those who had ever smoked, with a low proportion of never smokers having ever used e-cigarettes, was consistent with other findings in Great Britain [5,35]. Furthermore, only 4% of never smokers initiated e-cigarette use (vs. 32% of ever smokers). This suggests that e-cigarettes are attracting few who have never smoked. Furthermore, monthly or more smoking and e-cigarette use was low, at 5% and 2%, respectively.

In the logistic regression analyses, e-cigarette escalation between baseline and follow-up was associated with smoking initiation, even when controlling for ever e-cigarette use; likewise, smoking escalation was associated with e-cigarette initiation when controlling for ever smoking. This represents a novel contribution to the literature, and further suggests the need for multiwave surveys to explore dynamic changes in use of both products over time. Despite this, the causal mediation analyses, which as discussed allow for stronger conclusions to be made regarding observed observations, suggest that it is primarily ever use of that product that contributes to initiation of the alternative product.

Our findings are consistent with previous studies that found a prospective association between e-cigarette use at baseline and smoking at follow-up [4,12–21], and also with those who found a prospective association between smoking at baseline and e-cigarette use at follow-up [18,24]. There are several possible reasons for the strong and reliable association between e-cigarettes and smoking in young people [18,28,36]. One interpretation is that e-cigarettes act as a "gateway" to smoking [3,37]; however, this has been contested [28,36], and our findings suggest that the association between e-cigarette initiation and smoking initiation may work both ways. Certain psychological processes ("common liabilities") may lead to vulnerability of any drug use [22,23]. Specifically, young people who exhibit curiosity, rebelliousness, and sensation-seeking may be more likely to experiment with both smoking and e-cigarettes. Future research should explore potential common liabilities pertaining to experimentation of both products, some of which were included in this study and others are proposed above.

Despite potential common liabilities and our findings that e-cigarette use is associated with smoking and vice versa, there are several important differences to consider between these products and the contexts in which they may be used. Among young people, e-cigarettes, compared with conventional cigarettes, have been described as more accessible and convenient [38,39], have a greater capacity for continual novelty in terms of flavors and devices [39], and are perceived as less harmful in the UK [5,39]. On the contrary, smoking is highly stigmatized in some societal groups [40]. Indeed, some have reported that e-cigarettes appeal to those who do not want to smoke but want to try the experience of "smoking" [38,39].

Interestingly, friend's e-cigarette use increased the likelihood of e-cigarette initiation but reduced the likelihood of smoking initiation in adjusted models. This first association is unsurprising given the important role of peer influence on behavior. However, the protective effect of friend's e-cigarette use on smoking initiation warrants further investigation.

In conclusion, this study provides further support for the association between ever e-cigarette use and smoking initiation, and additionally finds that ever smoking is associated with e-cigarette initiation, among young people. Better understanding of these associations will aid policy makers with their efforts to develop an appropriate regulatory framework for both tobacco products and e-cigarettes.

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Supplementary Data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jadohealth.2017.11.301.

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May 9, 2018

BY OVERNIGHT MAIL AND E-MAIL

Mayor Peter Lindstrom
City Hall
2077 Larpenteur Avenue West
Falcon Heights, MN 55113
peter.lindstrom@falconheights.org

Dear Mayor Lindstrom:

I am a partner at Jones Day, which represents R.J. Reynolds Tobacco Company, American Snuff Company, LLC, Santa Fe Natural Tobacco Company, Inc., and R.J. Reynolds Vapor Company. It has come to our clients' attention that the Falcon Heights City Council is considering a proposed ordinance that would effectively ban the sale of "flavored tobacco products."

As explained below, we believe that this ban violates the Supremacy Clause and the First Amendment of the United States Constitution. In light of these legal infirmities, we urge the Council to reject the proposed ordinance.

I. The Proposed Ban Violates The Supremacy Clause Of The United States Constitution.

As you are aware, state and local laws that conflict with federal law are invalid under the Supremacy Clause of the United States Constitution. U.S. Const. art. VI, cl. 2. By banning the sale of flavored tobacco products, the proposed ordinance squarely conflicts with the Family Smoking Prevention and Tobacco Control Act, Pub. L. No. 111-31, 123 Stat. 1776 (June 22, 2009) (the "Tobacco Control Act").

The Tobacco Control Act provides that "[n]o State or political subdivision of a State may establish … with respect to a tobacco product any requirement which is different from, or *in addition to*, any requirement under [the Act] relating to tobacco product standards." 21 U.S.C. § 387p(a)(2)(A) (emphasis added). Under that Act, "tobacco product standards" govern (among other things) "the construction, components, ingredients, additives, constituents, including smoke constituents, and properties of the tobacco product." *Id.* § 387g(a)(4)(B)(i). Notably, the Act establishes two tobacco product standards, one of which is a "special rule" banning cigarettes with characterizing flavors (other than menthol). *Id.* § 387g(a)(a)(A) (prohibiting "a cigarette or any of its component parts" from "contain[ing], as a constituent … or additive, an artificial or natural flavor (other than tobacco or menthol) or an herb or spice, … that is a characterizing flavor of the tobacco product or tobacco smoke"). Although Congress generally banned cigarettes with characterizing flavors, it expressly chose *not* to ban menthol cigarettes; instead, it directed the Secretary of the U.S. Department of Health and Human Services to refer this subject to the Tobacco Products Scientific Advisory Committee. *See id.* § 387g(e)(1). In addition, the U.S. Food and Drug Administration ("FDA") has not banned additional types of flavored tobacco products at this time.[1] And recently, FDA issued an advance notice of proposed rulemaking regarding potential regulatory actions that it might take with respect to flavored tobacco products.[2]

Falcon Heights's proposed ordinance ignores these provisions of the Tobacco Control Act. If the Council bans the sale of all flavored tobacco products except in adult-only tobacco stores, it would do what the Tobacco Control Act prohibits—establish what amounts to a tobacco product standard that is "in addition to" existing federal standards. The proposed ordinance is therefore preempted by the Tobacco Control Act.

Moreover, the Council cannot dispute that its proposed ordinance effects a *de facto* ban on flavored tobacco products. Although the Council has framed its proposed ordinance so that it does not apply to adult-only tobacco stores, the ordinance has the practical effect of flatly banning the sale of all flavored tobacco products. According to information available to us, there are *no* retailers in Falcon Heights that meet the definition of an adult-only tobacco store. Thus, the proposed ordinance is in fact a total ban on flavored tobacco products, which is preempted by the Tobacco Control Act.

The Tobacco Control Act's saving clause does not alter that conclusion. Under the saving clause, the Act's preemption provision does not apply to certain types of requirements relating to tobacco products, including certain requirements relating to the sale of such products. *Id.* § 387p(a)(2)(B). As the Supreme Court and the Eighth Circuit have "repeatedly" made clear, however, a saving clause must be narrowly construed to avoid "upset[ting] the careful regulatory scheme established by federal law." *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 870 (2000) (quoting *United States v. Locke*, 529 U.S. 89, 106–07 (2000)); *see also Qwest Corp. v. Minn. Pub. Utilities Comm'n*, 684 F.3d 721, 727 (8th Cir. 2012) (interpreting the Telecommunications Act and explaining that the court "decline[s] to give broad effect to saving clauses where doing so would upset the careful regulatory scheme established by federal law"). More specifically,

---

[1] *Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products*, 81 Fed. Reg. 28,974, 29,055 (May 10, 2016) ("FDA is not banning flavored tobacco products with this final rule. … FDA is announcing here that it intends to issue in the future a proposed product standard that would prohibit characterizing flavors in all cigars, including cigarillos and little cigars.").

[2] *Regulation of Flavors in Tobacco Products*, 83 Fed. Reg. 12,294 (Mar. 21, 2018).

the exceptions set forth in the saving clause cannot be interpreted to swallow the terms of the preemption provision itself. *Lorillard Tobacco Co. v. Reilly*, 533 U.S. 525, 542 (2001). But that is precisely what Falcon Heights's apparent interpretation would do, since it would allow a municipality to impose a preempted tobacco product standard so long as it was artfully drafted to bear a tenuous relationship to the saving clause's exceptions. Clear Supreme Court authority forecloses that result.

II. The Proposed Ban Violates The First Amendment To The United States Constitution.

Not only does the proposed ordinance run afoul of the Supremacy Clause, it also violates the First Amendment to the United States Constitution. By prohibiting the "offer for sale" of flavored tobacco products except in adult-only tobacco stores, the proposed ordinance restricts constitutionally-protected commercial speech. In particular, the proposed ordinance goes beyond merely restricting the physical sale of flavored tobacco products; it also restricts *what is said* about a proposed sale. The proposed ordinance therefore restricts fully protected commercial speech. *See Va. Bd. of Pharmacy v. Va. Citizens Consumer Council, Inc.*, 425 U.S. 748, 762–64 (1976).[3]

Because the proposed ordinance restricts commercial speech, it must be justified under the legal standard articulated by the United States Supreme Court in *Central Hudson Gas & Electric Corp. v. Public Service Commission*, 447 U.S. 557, 566 (1980). But the proposed ordinance cannot possibly meet this standard. First, the Supreme Court has held that any restriction on protected commercial speech is invalid unless the government proves it will directly and materially advance a substantial government interest. *See 44 Liquormart, Inc. v. Rhode Island*, 517 U.S. 484, 504–05 (1996) (plurality opinion). Here, the Council seeks to ban the sale of flavored tobacco products outside of adult-only tobacco shops, which suggests that the purpose of the proposed ordinance is to reduce the use of tobacco by minors. But the sale of tobacco products to minors is already prohibited, so the proposed ordinance adds very little to existing law. Thus, the Council could not prove that the proposed ordinance will reduce youth tobacco use "to a material degree." *Id.* at 505 (plurality opinion) (quotation marks omitted); *see also Brown v. Entm't Merchants Ass'n*, 131 S. Ct. 2729, 2741 n.9 (2011) (noting that "the government does not have a compelling interest in each marginal percentage point by which its goals are advanced").

Second, the Supreme Court has held that commercial speech restrictions must be "narrowly tailored to achieve the desired objective." *Bd. of Trustees of the State Univ. of N.Y. v. Fox*, 492 U.S. 469, 480 (1989). The proposed ordinance fails on this score because it is not tailored to restricting the flow of information to *minors*. Instead, it broadly restricts the flow of information to *adults* as well. As the Supreme Court explained, "so long as the sale and use of

[3] The First Amendment argument about *offers* to sell flavored products assumes that the proposed ordinance's ban on *selling* flavored products is invalid on preemption or other grounds.

tobacco is lawful for adults, the tobacco industry has a protected interest in communicating information about its products and adult customers have an interest in receiving that information." *Lorillard Tobacco Co. v. Reilly*, 533 U.S. 525, 571 (2001). Nor can the Council prove that the proposed ordinance is necessary to further any interest in reducing youth tobacco use. To the contrary, there are numerous non- and less-speech restrictive alternatives to achieving that interest; for example, the Council could engage in its own speech by launching an educational campaign against underage tobacco use. Under the First Amendment, the Council bears the burden of proving that such alternative "possibilities, alone or in combination, would be insufficient" to further the asserted government interest. *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 373 (2002). The Council could not carry that burden.

* * *

Given the legal infirmities discussed above, we urge the Council to reject the proposed ordinance. I appreciate your immediate attention to this matter, and ask that you raise our legal concerns with the full Council at the earliest opportunity. Please feel free to contact me should you have any questions.

Sincerely,

Ryan J. Watson /grs

Ryan J. Watson

cc: Joe Brown Thunder, joe.brownthunder@falconheights.org
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September 26, 2016

BY OVERNIGHT MAIL AND FACSIMILE

Elizabeth S. Dunn, R.N., Chairman, Board of Health
John B. Howard, M.D., Vice-Chair, Board of Health
Dr. Jason Reynolds, Clerk, Board of Health
Jonathan E. Dickerson, Chairman, Board of Selectmen
Stephen M. Cushing, Vice Chairman, Board of Selectmen
Stephen C. Gonsalves, Clerk, Board of Selectmen
Town of Marion
2 Spring Street
Marion, MA 02738
Facsimile: (508) 748-2545

Dear Members of the Marion Board of Health and Marion Board of Selectmen:

I am a partner at Jones Day, which represents R.J. Reynolds Tobacco Company, American Snuff Company, LLC, Santa Fe Natural Tobacco Company, Inc., and R.J. Reynolds Vapor Company. It has come to our clients' attention that the Marion Board of Health has proposed regulations that would ban flavored tobacco products and prohibit the sale of tobacco products at "health care institutions."

We believe that the flavors ban violates the United States Constitution and that the health-institutions provision contravenes state law. In light of these legal infirmities, explained further below, we urge Marion to refrain from adopting the proposed regulation. If Marion instead chooses to adopt these provisions, we will have no choice but to consider the initiation of litigation challenging the regulation.

I. The Proposed Flavors Ban Violates The Supremacy Clause Of The United States Constitution.

As you are aware, state and local laws that conflict with federal law are invalid under the Supremacy Clause of the United States Constitution. U.S. Const. art. VI cl. 2. By banning the sale or distribution of flavored tobacco products, the proposed regulation squarely conflicts with the Family Smoking Prevention and Tobacco Control Act ("Tobacco Control Act"), Pub. L. No. 111-31, 123 Stat. 1776 (June 22, 2009).

The Tobacco Control Act provides that "[n]o State or political subdivision of a State may establish . . . with respect to a tobacco product any requirement which is different from, or *in addition to*, any requirement . . . relating to tobacco product standards." 21 U.S.C. § 387p(a)(2)(A) (emphasis added). Under the Tobacco Control Act, "tobacco product standards" govern, among other things, "the construction, components, ingredients, additives, constituents, including smoke constituents, and properties of the tobacco product." *Id.* § 387g(a)(4)(B)(i). Notably, this federal statute establishes two tobacco product standards, one of which is a "special rule" banning flavored cigarettes, which prohibits "a cigarette or any of its component parts" from "contain[ing], as a constituent . . . or additive, an artificial or natural flavor (other than tobacco or menthol) or an herb or spice, . . . that is a characterizing flavor of the tobacco product or tobacco smoke." *Id.* § 387g(a)(1)(A). Although Congress banned flavored cigarettes, it expressly chose not to ban menthol products; instead, it directed the Secretary of the U.S. Department of Health and Human Services to refer this subject to the Tobacco Products Scientific Advisory Committee. *See id.* § 387g(e)(1). Moreover, the U.S. Food and Drug Administration recently decided *not* to ban additional types of flavored tobacco products.[1]

Marion's proposed regulation ignores the above-described provisions of the Tobacco Control Act. By prohibiting the sale or distribution of any "flavored tobacco product," the County has done what the Tobacco Control Act says it cannot do—it has enacted what amounts to a tobacco product standard that is "in addition to" existing federal standards.

Marion cannot dispute that its proposed flavors regulation effects a *de facto* ban on flavored tobacco products. Although Marion framed its proposed regulation so that it superficially resembles Providence's flavors ordinance, those two flavors provisions are not, in fact, analogous. Providence's ordinance does not impose a blanket ban on flavored tobacco products but, instead, allows such sales in certain locales throughout the city. In contrast, Marion's regulation has the practical effect of flatly banning the sale of all flavored tobacco products. Thus, while Section G of Marion's proposed regulation prohibits the sale or distribution of flavored tobacco products "except in smoking bars and adult-only retail tobacco stores," according to information available to us, there has not been, nor are there, *any* smoking bars or adult-only retail tobacco stores located in Marion. Thus, unlike in Providence, Marion's flavors provision is in fact a total ban on flavored tobacco products, which is preempted by the Tobacco Control Act.

---

[1] *Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products*, 81 Fed. Reg. 28,974, 29,055 (May 10, 2016) ("FDA is not banning flavored tobacco products with this final rule. . . . FDA is announcing here that it intends to issue in the future a proposed product standard that would prohibit characterizing flavors in all cigars, including cigarillos and little cigars.").

The Tobacco Control Act's saving clause does not alter the conclusion that Marion's proposed flavors regulation is preempted. The saving clause provides that the statute's preemption provision does not apply to certain types of requirements relating to tobacco products. *Id.* § 387p(a)(2)(B). But as the Supreme Court has "repeatedly" made clear, a saving clause must be narrowly construed to avoid "'upset[ting] the careful regulatory scheme established by federal law.'" *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 870 (2000) (quoting *United States v. Locke*, 529 U.S. 89, 106–07 (2000)). More specifically, the exceptions set forth in the saving clause cannot be interpreted to swallow the terms of the preemption provision itself. *Lorillard Tobacco Co. v. Reilly*, 533 U.S. 525, 542 (2001). That, however, is precisely what Marion's apparent interpretation would do, since it would allow a municipality to impose *any* requirement on tobacco products so long as it bore some tenuous relationship to the saving clause's exceptions. Clear Supreme Court authority, however, forecloses that result.

II. <u>The Proposed Ban On Sales Of Tobacco Products In "Health Care Institutions" Exceeds The Board Of Health's Authority Under State Law.</u>

Section N of the proposed regulations would prohibit the sale of tobacco products at "health care institutions." According to Section A, the purpose of this ban stems from the "incompatib[ility]" of the sale of tobacco products "with the mission of health care institutions because these products are detrimental to the public health and their presence in health care institutions undermines efforts to educate patients on the safe and effective use of medication, including cessation medication." However, Section C of the proposed regulations defines the term "health care institutions" to include retail establishments that provide pharmaceutical goods and services and are regulated by the state's Board of Registration in Pharmacy. Thus, according to the Board of Health's proposed definition, supermarkets, general stores, and big-box retailers (hereinafter "general stores") that contain pharmacies would all be considered "health care institutions," despite the fact that the central purpose of such stores is unrelated to health care.

Pursuant to a Massachusetts state statute, local boards of health have the authority to make "*reasonable* health regulations." Mass. Gen. Law ch. 111, § 31 (emphasis added). Under this law, courts must overturn regulations when they find that they are not rationally related to a legitimate government purpose. *See, e.g.*, *RYO Cigar Ass'n, Inc. v. Boston Pub. Health Comm'n*, 79 Mass. App. Ct. 822, 827 (2011) (noting, in case involving a challenge to a tobacco regulation, that courts must overturn regulations where "there is no rational connection between the regulation and the public purpose to be achieved"). Here, even if the Board's purpose—namely, eliminating tobacco product sales at institutions whose mission is to promote health—is legitimate, it is not rationally connected to a ban on selling tobacco products in general stores. As long as tobacco products are not sold within the pharmacy department itself, there is no reason to think that the sale of tobacco products at general stores would "undermine efforts to educate patients on the safe and effective use of medication." Such stores do not exist to provide health care or health services, but rather to provide a single convenient location for customers to buy what they need.

In short, no one would confuse a general store that contains a pharmacy with a "health care institution," and as applied to such stores, "there is no rational connection between the regulation and the public purpose to be achieved." *Id.* The definition of "health care institutions" in the proposed regulations therefore exceeds the Board of Health's authority to make "reasonable health regulations." Mass. Gen. Law ch. 111, § 31.

* * *

Given the legal infirmities discussed above, we urge Marion to reject the proposed regulation. Otherwise, we will have no choice but to consider the initiation of litigation challenging the regulation.

I appreciate your immediate attention to this matter. Please feel free to contact me should you have any questions.

Sincerely

Noel J Francisco /rjw

Noel J. Francisco

cc: Karen Walega, Health Director, Town of Marion
(via Overnight Mail and e-mail kwalega@marionma.gov)
Paul Dawson, Administrator, Town of Marion
(via Overnight Mail and e-mail pdawson@marionma.gov)

MINNEAPOLIS

Lobbyists descend on Minneapolis to fight menthol restriction

Tobacco companies and retailers are pushing back against Minneapolis leaders' move to restrict the sales of menthol cigarettes in the city.

By Emma Nelson (http://www.startribune.com/emma-nelson/261800211/) Star Tribune

JULY 20, 2017 — 10:28PM

Tobacco companies and retailers are pushing back against Minneapolis leaders' move to restrict the sales of menthol cigarettes in the city, bringing in lobbyists and appealing to the public.

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KAYLEE EVERLY, SPECIAL TO THE STAR TRIBUNE

Tobacco companies and retailers are pushing back against Minneapolis leaders' move to restrict the sales of menthol cigarettes in the...

Lobbyists visiting City Hall are telling council members about the losses local convenience stores will face. Gas stations across the city are hanging up banners in opposition. And last week, a former Florida congressman and a former Virginia police chief with ties to tobacco giant Reynolds American Inc. (RAI), which sells popular menthol brand Newport, visited the Twin Cities to speak against the proposed menthol restriction.

Anti-smoking advocates say the fight against this restriction is bigger than they've previously seen at the local level.

"It's a national presence that we haven't quite seen like that, of tobacco companies sending in somebody from outside," said Betsy Brock, director of research at the Association for Nonsmokers Minnesota. "We see that at the state, but never really at the local level much."

The proposed policy, which is scheduled for a public hearing July 24, would limit menthol cigarette sales in Minneapolis to adult-only tobacco shops. The City Council passed a similar restriction on flavored tobacco products in 2015, limiting sales of products such as fruit-flavored chewing tobacco and candy-flavored cigarillos to specialty shops. St. Paul followed suit last year.

The Coalition of Neighborhood Retailers, a local trade group, says restricting menthol in addition to flavored tobacco is too much.

Clay and Mia Lambert, who have owned Metro Petro on University Avenue for 14 years, said they're still not sure what impact the flavored tobacco restriction has had on their business — and now the city is talking about restricting menthol.

As small business owners, the Lamberts said, they rely on local trade associations to lobby for their interests. If the menthol restriction passes, they said, they're not sure how they'll compensate for the lost revenue.

Thomas Briant, executive director of the National Association of Tobacco Outlets — a member of the retailers' coalition — has visited City Hall to raise small business' concerns. He said if a menthol sales restriction passes, the city's tobacco retailers will lose $73 million as Minneapolis smokers leave the city to buy menthol products, or buy them illegally.

"We're so concerned that this opens up the opportunity for criminals to now come into the city and start selling out of their car trunks, in back alleys, to anyone who has cash," he said.

Menthol restrictions are relatively new — Chicago and San Francisco have passed them, but San Francisco's ordinance hasn't yet taken effect — so it's not clear that restricting menthol creates an underground market.

Council Member Cam Gordon, the lead author of the Minneapolis menthol ordinance, said he is taking business owners' worries into account and working on getting new data showing what the financial impact will be on tobacco retailers. But he's also concerned about lobbyists spreading false information about how a menthol restriction will affect tobacco retailers and smokers, he said.

Tobacco companies have historically marketed menthol cigarettes to black smokers, and today nearly 90 percent of black smokers ages 12 and up prefer menthol, according to the Centers for Disease Control and Prevention. The tobacco industry's push against

Minneapolis' menthol restriction is targeting that group.

"They are the masters of strategy and marketing," said LaTrisha Vetaw of NorthPoint Health and Wellness Center. "It's even so low that they're using what we're going through in the world at this time — they're using the fact that black men are dying at the hands of the police."

In January, the Rev. Al Sharpton visited Greater Friendship Missionary Baptist Church in Minneapolis for a talk on "decriminalizing the black community" and "banning of menthol cigarettes." The visit, which was sponsored by RAI (http://www.startribune.com/tobacco-industry-looks-for-political-wins-in-minnesota-usually-unfriendly-turf/413548993/) , included two panelists who returned to the Twin Cities last week: former U.S. Rep. Kendrick Meek, D-Fla., and former Petersburg, Va., Police Chief John Dixon, a past president of the National Organization of Black Law Enforcement Executives.

In a meeting with black leaders in St. Paul and a radio interview with Al McFarlane, owner of black community newspaper Insight News, Meek and Dixon said restricting menthol sales will criminalize black smokers by creating an underground tobacco market.

McFarlane said he connected with Meek and Dixon through the National Newspaper Publishers Association, a group of black newspapers that RAI sponsors. They said in advance that they were working for RAI, McFarlane said. McFarlane said he's planning a show for next week with guests who support the menthol restriction.

As a member of Congress, Meek received tens of thousands of dollars in donations from the tobacco industry and lobbyists for tobacco companies, including RAI, according to data from the Center for Responsive Politics.

Reached by phone, Meek would not specify RAI's role in last week's visit. Dixon described RAI as a sponsor, but said the company does not control what he says.

"They don't script me at all," Dixon said. "They don't script anybody."

A spokeswoman for RAI said in an e-mail that the company works with both Meek and Dixon, but "did not pay them to be there or sponsor the event."

"That said, we are happy that meaningful conversations are being had on this important issue and hope that there will continue to be an open dialogue going forward," she said.

The City Council is expected to vote on the menthol sales restriction in August.

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The New York Times

San Francisco Voters Uphold Ban on Flavored Vaping Products

The measure is considered the strictest in the nation. Voters backed it despite an expensive advertising campaign funded by a major tobacco company.

By Jan Hoffman

June 6, 2018

Voters in San Francisco on Tuesday upheld a ban on all flavored tobacco products, from colorfully packaged e-liquids to menthol cigarettes. Mike Segar/Reuters

Despite a $12 million ad blizzard by a giant tobacco company, voters in San Francisco resoundingly supported a new ban on the selling of flavored tobacco products, including vaping liquids packaged as candies and juice boxes, and menthol cigarettes.

The measure, known as Proposition E, is said to be the most restrictive in the country, and health groups predicted it could serve as a model for other communities.

The vote had been expected to be close, but the final tally was 68 percent to 32 percent in support of the ban. Those results reflected a big miscalculation by R. J. Reynolds Tobacco Company, which had saturated the city with multimedia ads in four languages, likening the ban to Prohibition and invoking a black market crime wave.

“They had a strategic chance there to show that they are actually walking the walk and talking the talk about moving smokers to nonsmoker tobacco products,” said Eric Lindblom, a Georgetown Law professor and former Food and Drug Administration tobacco official. “Instead they took this scorched earth approach, trying to eliminate the entire flavor ban. They failed and now other jurisdictions can say, ‘Why should we compromise?’”

Although using electronic cigarettes, or vaping, is touted as a means of smoking cessation, parents, public health advocates and federal regulators have expressed deepening concern as some studies show that the products are gateways to smoking for teenagers. E-cigarettes give users a powerful hit of nicotine, but without the mix of toxins contained in traditional, combustible cigarettes.

Schools across the country have grown increasingly alarmed about the growing use of e-cigarettes among middle- and high school students, and some are taking harsh disciplinary measures, including suspensions, to curtail it.

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Dr. Melissa Welch, a spokeswoman for the American Heart Association, one of several national organizations that fought to uphold the ban, said she hoped the San Francisco vote would be a first step toward ending “the sale of candy-flavored tobacco before nicotine addiction claims a new generation of young people.”

Proponents of the ban pointed to some 7,000 products, including those with flavors said to be particularly alluring to young users like bubble gum, chicken and waffles, and unicorn milk.

San Francisco’s Board of Supervisors unanimously approved the ban last year. It was to take effect in April. But R. J. Reynolds, which makes popular vaping products called Vuse, as well as Newport menthol cigarettes, propelled the campaign to block it by getting the initiative on Tuesday’s ballot.

Jacob McConnico, a spokesman for R. J. Reynolds, called the vote “a setback for tobacco harm reduction efforts because it removes from the market many potentially reduced-risk alternatives.”

Nevertheless, he added, the company would urge federal officials to draft regulations to restrict youths' access to the products while "preserving choice for adult smokers who are looking for alternatives to help them switch."

Juul Labs, maker of the top-selling vaping devices, which is based in San Francisco, did not have a prominent voice in the debate. The company did not respond to requests for comment.

A coalition of groups, including the American Cancer Society, the American Heart Association, the American Lung Association and Tobacco-Free Kids Action Fund, conducted a vigorous drive to uphold the ban. Their war chest was significantly smaller — $2.3 million, including a $1.8 million personal contribution from Michael R. Bloomberg, the former mayor of New York City.

In a statement, Mr. Bloomberg said the vote "shows that the tobacco industry, no matter how much money it spends on misleading ads, can be defeated. This vote should embolden other cities and states to act."

The United States has lagged behind other nations in regulating menthol cigarettes. The inclusion of menthol in the San Francisco ban was hailed by numerous groups, concerned about the booming sales of menthol cigarettes among minorities, who have seen disproportionately high mortality rates related to smoking.

"The ban on menthol cigarettes is a monumental step forward for health equity and social justice for communities of color," said Dr. Phil Gardiner, a co-chairman of the African-American Tobacco Control Leadership Council.

Canada banned the sale of menthol cigarettes last fall, and a similar measure for the European Union will take effect in 2020. In the United States, the F.D.A. banned cigarettes with flavors like chocolate, cinnamon and vanilla in 2009 and said it would look at menthol cigarettes. Though it has taken steps to regulate them as well, the agency has continued to allow them on the market.

A handful of other cities, including Chicago, New York and Providence, R.I., have some restrictions on flavored tobacco products, such as limiting their sale to adults-only stores.

Matthew Myers, president of the Campaign for Tobacco-Free Kids, said that some cities, including Duluth and St. Paul in Minnesota, have instituted more circumscribed bans than San Francisco's, but held off widening their reach when they saw the pushback from R. J. Reynolds.

"When Reynolds paid to put this on the ballot, other jurisdictions were cautious," he said. "The resounding vote in San Francisco is going to lead a lot of cities to take a closer look."

Such policies can be tough to manage, said Mark D. Meaney, a senior lawyer for the Public Health Law Center, which has helped draft tobacco restrictions. "But San Francisco certainly has the expertise and capacity to enforce them."

Oakland recently passed restrictions that will soon take effect, and outreach workers are contacting small retailers to educate them about the new ordinance. Just this week, the San Mateo County, Calif., Board of Supervisors unanimously approved a ban that very much resembles San Francisco's and one in small, rural Yolo County, Calif.

Although R. J. Reynolds led the attack on the ban, other groups joined in. Libertarians took up the protest, saying that the government was overreaching. Small business owners also fought back, saying that the ban would sharply reduce their profits.

"Anchor products allow us to stay competitive to big-box stores, and we will lose regular customers that keep our doors open," said Miriam Zouzounis, a board member of the Arab American Grocers Association, which represents over 400 businesses in San Francisco. She said the law would disproportionately affect Arab, Sikh and Asian store owners.

The ban is expected to take effect within days after the vote is officially certified.

Sheila Kaplan contributed reporting.

Jan Hoffman has been a Science reporter since 2013. Before that she wrote about young adolescence and family dynamics for Styles and was the legal affairs correspondent for Metro. She joined The Times in 1992.

A version of this article appears in print on June 6, 2018, on Page A1 of the New York edition with the headline: Voters in San Francisco Banish Flavored Tobacco From Shelves

PLOS ONE

RESEARCH ARTICLE

Quantifying population-level health benefits and harms of e-cigarette use in the United States

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Abstract

Background

Electronic cigarettes (e-cigarettes) may help cigarette smokers quit smoking, yet they may also facilitate cigarette smoking for never-smokers. We quantify the balance of health benefits and harms associated with e-cigarette use at the population level.

Methods and findings

Monte Carlo stochastic simulation model. Model parameters were drawn from census counts, national health and tobacco use surveys, and published literature. We calculate the expected years of life gained or lost from the impact of e-cigarette use on smoking cessation among current smokers and transition to long-term cigarette smoking among never smokers for the 2014 US population cohort.

Results

The model estimated that 2,070 additional current cigarette smoking adults aged 25±69 (95% CI: -42,900 to 46,200) would quit smoking in 2015 and remain continually abstinent from smoking for ≥7 years through the use of e-cigarettes in 2014. The model also estimated 168,000 additional never-cigarette smoking adolescents aged 12±17 and young adults aged 18±29 (95% CI: 114,000 to 229,000), would initiate cigarette smoking in 2015 and eventually become daily cigarette smokers at age 35±39 through the use of e-cigarettes in 2014. Overall, the model estimated that e-cigarette use in 2014 would lead to 1,510,000 years of life lost (95% CI: 920,000 to 2,160,000), assuming an optimistic 95% relative harm reduction of e-cigarette use compared to cigarette smoking. As the relative harm reduction decreased, the model estimated a greater number of years of life lost. For example, the model estimated-1,550,000 years of life lost (95% CI: -2,200,000 to -980,000) assuming an

Competing interests: The authors have declared that no competing interests exist.

approximately 75% relative harm reduction and -1,600,000 years of life lost (95% CI: -2,290,000 to -1,030,000) assuming an approximately 50% relative harm reduction.

Conclusions

Based on the existing scientific evidence related to e-cigarettes and optimistic assumptions about the relative harm of e-cigarette use compared to cigarette smoking, e-cigarette use currently represents more population-level harm than benefit. Effective national, state, and local efforts are needed to reduce e-cigarette use among youth and young adults if e-cigarettes are to confer a net population-level benefit in the future.

Introduction

The use of electronic cigarettes (e-cigarettes) has become intensely controversial since their introduction to the US in 2007 [1±7]. E-cigarettes might help the 40 million current adult cigarette smokers quitÐthe vast majority of whom want to stop smoking completelyÐby delivering nicotine with the same sensory experience as combustible, or traditional, cigarettes but without inhalation of as many toxicants [8±12]. Conversely, e-cigarettes might facilitate the transition to traditional cigarette smoking among never-smoking adolescents and young adults [13±21]. This harm is potentially substantial because youth e-cigarette use has risen rapidly over time [6,22,23]. For example, past 30-day use of e-cigarettes increased from 1.5% in 2011 to 11.3% in 2016 among high school students and exceeded their level of past 30-day use of traditional cigarettes (8.0% in 2016) [24].

The controversy over e-cigarettes persists because we do not yet know if e-cigarette use results in more benefit than harm at the population level [25±27]. This uncertainty creates a quandary for the US Food and Drug Administration (FDA), which recently asserted its regulatory authority over e-cigarettes and developed regulations to promote their safety and limit youth appeal [28]. Quantifying the balance of benefits and harms of e-cigarette use requires simultaneous accounting of the additional number of (1) current cigarette smokers who will quit through the use of e-cigarettes and (2) never-cigarette smokers who will initiate cigarette smoking through the use of e-cigarettes, a substantial proportion of whom may become long-term daily cigarette smokers. A recent study concluded a net population-level health benefit under a scenario in which e-cigarette use increases in the future only among cigarette smokers interested in quitting, and net harm under a scenario in which e-cigarette use increases in the future only among youth who would have never smoked [29]. A second study modeled future cigarette and e-cigarette use patterns over the next decade for young adults aged 18±24 years and concluded that e-cigarette use would have a limited impact on the prevalence of current cigarette smoking [30]. However, this study did not assess the effect of e-cigarette use among adolescents or adults aged ≥25 years. A third study estimated the population impact of e-cigarettes on smoking cessation and found e-cigarettes could increase the number of smokers who successfully quit for one year. However, this study also did not assess the effect of e-cigarette use among adolescents [31]. Thus, these last two studies could not determine the balance of benefits and harms of e-cigarette use at the population level.

In this study, we developed a Monte Carlo stochastic simulation model that extends prior research in two ways. First, we simultaneously consider multiple population subgroups including current cigarette smokers and never cigarette smokers. Second, we quantify the net population benefits (or harms) of e-cigarette use in terms of the total number of years of life gained among additional current cigarette smokers who quit smoking and years of life lost among additional cigarette smoking initiators who become long-term daily cigarette smokers, both through the use of e-cigarettes. We base our calculations on 2014 US census data, national health or tobacco use surveys on e-cigarette use, and published randomized trials and cohort studies on the e-cigarette associated transition probabilities of cigarette smoking cessation and initiation.

Methods

Analytic model

Our analytic approach consists of two main steps (Fig 1). The first step estimates the number of years of life gained among the additional number of current cigarette smokers who quit smoking through the use of e-cigarettes as a cessation tool, compared to those who did not use e-cigarettes as a cessation tool, and remain continually abstinent from smoking for ≥7 years. We set the threshold for continual abstinence at 7 years because cohort studies found that relapse beyond this point is rare [32,33]. Additionally, the risk of death among former cigarette smokers who quit for this long begins to approximate the risk of death among never cigarette smokers [34]. We began with the US adult population of 25±69 year olds in 2014 (in five-year age groups) and multiplied these counts by the: (1) age-group-specific prevalence of current cigarette smoking, (2) age-group-specific prevalence of trying to quit smoking within the past year among current cigarette smokers, (3) age-group-specific prevalence of current e-cigarette use among current cigarette smokers who tried quitting within the past year, (4) difference in the transition probability of ≥6-month cigarette smoking cessation between current smokers who used e-cigarettes as a cessation tool and current smokers who did not use e-cigarettes as a cessation tool, (5) probability of 1 year of cigarette smoking abstinence from cigarette smoking given ≥6 months of cigarette smoking abstinence, (6) probability of ≥6 years of abstinence

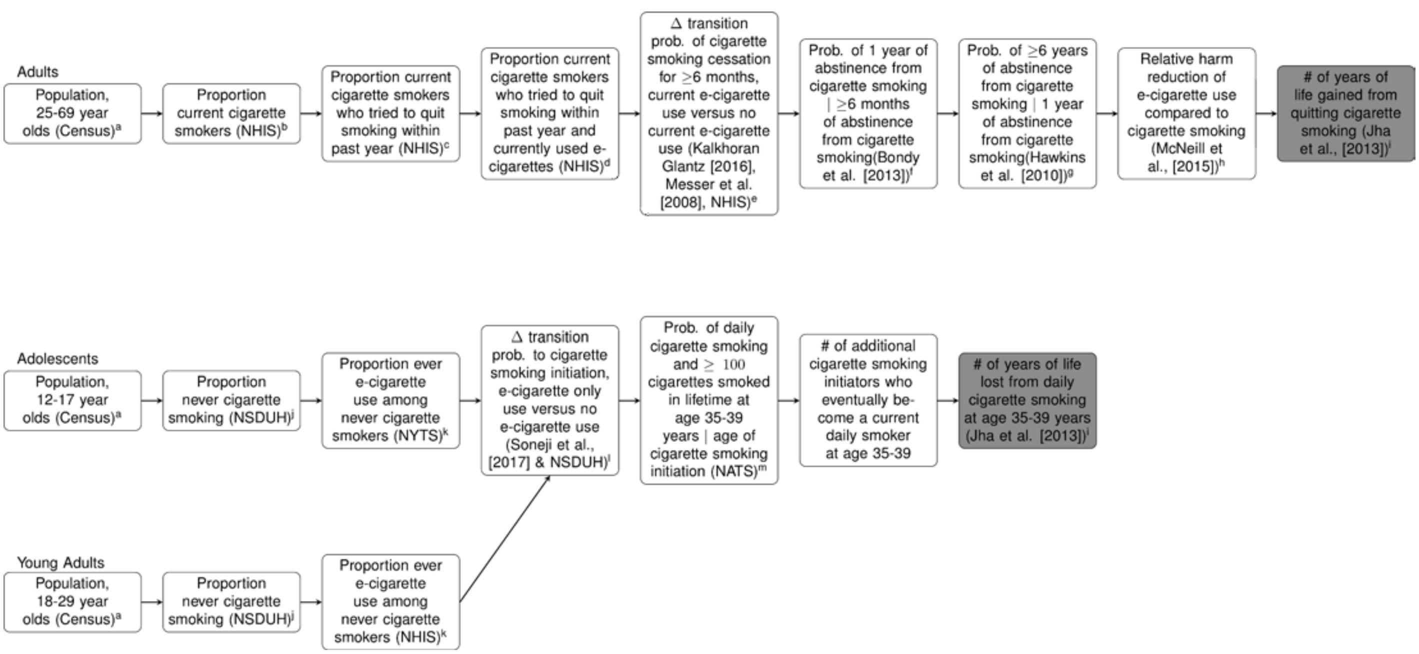

Fig 1. Population-level model to quantify benefits and harms of E-cigarette use. Superscripted letters refer to the columns in Tables A and B in S3 Appendix for age- and age-group-specific parameter point estimates and 95% confidence intervals. Note: Δ = Change in; | = Conditional On; NATS = National Adult Tobacco Survey; NHIS = National Health Interview Survey; NSDUH = National Survey on Drug Use and Health; NYTS = National Youth Tobacco Survey; and Prob. = Probability.

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from cigarette smoking given 1 year of cigarette smoking abstinence, and (7) age-group-specific number of years of life gained from quitting cigarette smoking. We assumed 95% relative harm reduction of e-cigarette use, compared to cigarette smoking, among current cigarette smokers who used e-cigarettes as a cessation tool and quit smoking [35]. As described below, we vary the relative harm of e-cigarette use, compared to cigarette smoking, to include the levels of relative harm inferred from in vitro and mouse model studies [36,37].

The second step estimates the number of years of life lost among the additional number of never-cigarette smoking adolescents and young adults who eventually become current daily cigarette smokers (and also smoked ≥100 cigarettes in lifetime) at age 35±39 through the use of e-cigarettes. We began with the US adolescent and young adult population of 12±29 year olds in 2014 (by single year of age) and multiplied these counts by the: (1) age-specific prevalence of never cigarette smoking, (2) age-specific prevalence of ever having tried e-cigarettes among never cigarette smokers, (3) the difference in the transition probability of cigarette smoking initiation among never cigarette smoking adolescents and young adults who had ever used e-cigarettes, compared to the corresponding probability among those who had never used e-cigarettes, (4) probability of becoming a current daily cigarette smoker at age 35±39 based on the age of cigarette smoking initiation, and (5) age-specific number of years of life lost from current daily cigarette smoking at age 35±39.

We assessed three outcomes of interest: (1) the additional number of current cigarette smokers who will quit smoking through the current use of e-cigarettes and abstain from smoking for ≥7 years, compared to those who do not currently use e-cigarettes and (2) the additional number of adolescents and young adults who will initiate cigarette smoking through the ever use of e-cigarettes and eventually become daily cigarette smokers at age 35±39, compared to those who never used e-cigarettes; and (3) the total number of expected years of life gained or lost across all these population subgroups.

Table 1 describes the data source of each model parameter. S1 Appendix describes how the difference in transition probabilities of ≥6-month cigarette smoking cessation between current e-cigarette users and non-current e-cigarette users was estimated based on various parameters such as the proportion of current cigarette smokers who used pharmaceutical aids during quit attempt and the pooled odds ratio of quitting smoking among smokers interested in quitting reported by the meta-analysis of Kalkhoran & Glantz [38]. S2 Appendix describes the estimation of the difference in transition probabilities of cigarette smoking initiation between never cigarette smokers who ever used e-cigarettes compared to those who never used e-cigarettes based on the pooled odds ratio of cigarette smoking initiation reported by the meta-analysis of Soneji et al. [19]. Tables A and B in S3 Appendix show the value of each model parameter.

Validation of model

We validated the model against one-year intermediate outcomes (e.g., the number of adolescents and young adult cigarette smoking initiators). For current adult smokers, we applied the model to 2013 National Health Interview Survey (NHIS) data to predict the number of current cigarette smoking adults (both current and non-current e-cigarette users) who would quit in 2014 and remain continually abstinent from smoking for ≥6 months. We then compared this predicted number with the observed number in 2014, estimated from 2014 NHIS data, by identifying new ≥6-month quitters as respondents who answered six months to one year to the question: ªHow long has it been since you quit smoking cigarettes?º. For adolescent and young adult never smokers, we applied the model to 2013 National Survey on Drug Use and Health (NSDUH) data to predict the number of cigarette smoking initiators in 2014 (both ever and never e-cigarette users). We then compared this predicted number with the observed

Table 1. Data Sources of model parameters.

Parameter	Population Sub-group	Source	Survey Question & Notes
Population	All	2014 US Census	Ð
Current Cigarette Smoking	Current Smokers	2014 NHIS	ªHave you smoked at least 100 cigarettes in your entire life?º (yes). ªDo you now smoke cigarettes every day, some days or not at all?º (every day or some days)
Past-Year Quit Attempt	Current Smokers	2014 NHIS	ªDuring the past 12 months, have you stopped smoking for more than one day because you were trying to quit smoking?º (yes)
Current E-Cigarette Use	Current Smokers	2014 NHIS	ªDo you now use e-cigarettes every day, some days, or not al all?º (every day or some days)
Proportion Of Current Cigarette Smokers With a Past-Year Quit Attempt Who Used a Pharmaceutical Aid During Quit Attempt* (%)	Current Smokers	2010 NHIS	ªThinking back to when you tried to quit smoking in the past 12 months, did you use any of the following products: a nicotine patch; a nicotine gum or lozenge; a prescription pill, such as Zyban, Bupropion, or Wellbutrin; a nicotine containing nasal spray or inhaler; a nicotine patch?º. See S1 Appendix for calculation of e-cigarette associated Δtransition probability of ≥6-months cigarette smoking cessation.
Probability of Cigarette Smoking Cessation ≥6 Months Among Current Cigarette Smokers Who Seriously Tried to Quit and Used a Pharmaceutical Aid During Quit Attempt (%)	Current Smokers	Messer et al. [92]	ªThinking back to the last time you tried to quit smoking in the past 12 months. Did you use any of the following products: a nicotine gum; a nicotine patch; a nicotine nasal spray; a nicotine inhaler; a nicotine lozenge; a nicotine tablet; a prescription pill, such as Zyban, Buproprion, or Wellbutrin?º (2003 TUS-CPS). ªDuring the past 12 months, what is the length of time you stopped smoking because you were trying to quit smoking?º (2003 TUS-CPS). See S1 Appendix for calculation of e-cigarette associated Δtransition probability of ≥6-months cigarette smoking cessation.
Odds Ratio of Quitting Smoking Among Smokers with an Interest in Quitting	Current Smokers	Kalkhoran & Glantz [38]	Meta-analysis of 2 clinical trials [49,93], 4 cohort studies [50,51,63,94], and 1 cross-sectional study [52]. See S1 Appendix for calculation of e-cigarette associated transition probability of ≥6-months cigarette smoking cessation
Relative Risk Of Cigarette Smoking Cessation Among Current Cigarette Smokers Interested In Quitting, E-Cigarette Users Compared With Nicotine Patch Users	Current Smokers	Bullen et al. [49]	Primary outcome was continuous ≥6-month smoking abstinence: self-reported abstinence over the whole follow-up period (allowing ≤5 cigarettes in total) and biochemically verified continuous abstinence at 6 months (exhaled breath carbon monoxide measurement <10 ppm). See S1 Appendix for calculation of e-cigarette associated transition probability of ≥6-months cigarette smoking cessation.
Probability of 1-Year Abstinence from Cigarette Smoking | 6-Months Abstinence	Current Smokers	Bondy et al. [95]	2005±2008 Ontario Tobacco Survey
Probability of Long-Term (≥6-Year) Abstinence from Cigarette Smoking | ≥1-Year Abstinence	Current Smokers	Hawkins et al. [33]	1991±2006 British Household Panel Survey
Relative Harm Reduction of E-Cigarette Use Compared to Cigarette Smoking	Current Smokers	McNeill et al. [35]	Consensus opinion
Never Cigarette Smoking	Adol. & Young Adults	2014 NSDUH	ªHave you ever tried cigarette smoking, even one or two puffs?º (no)
Ever E-Cigarette Use	Adol.	2014 NYTS	ªHave you ever used an electronic cigarette, even just one time in your entire life?º (yes)
Ever E-Cigarette Use	Young Adults	2014 NHIS	ªHave you ever used an electronic cigarette, even just one time in your entire life?º (yes)
Probability of Cigarette Smoking Initiation Among Never E-Cigarette Users	Adol. & Young Adults	2012 Surgeon General's Report [96]	Initiation of cigarette smoking 12- to 17-year-olds and 18- to 25-year olds, 2006 (2006±2010 NSDUH). See S2 Appendix for calculation of e-cigarette associated transition probability of cigarette smoking initiation.

(*Continued*)

Table 1. (Continued)

Parameter	Population Sub-group	Source	Survey Question & Notes
Adjusted Odds Ratio of Cigarette Smoking Initiation, Ever E-Cigarette Users vs. Never E-Cigarette Users	Adol. & Young Adults	Soneji et al. (2017) [19]	Seven cohort studies pooled in random-effects meta-analysis [13±18,97]. Odds ratioÐadjus ted for demographic, psychosocial, and behavioral risk factorsÐof cigarette smoking initiation between never cigarette smokers who ever used e-cigarettes and never cigarette smokers who never used e-cigarettes. See S2 Appendix for calculation of e-cigarette associated Δtransition probability of cigarette smoking initiation.
Probability of Being a Current Daily Cigarette Smoker at Age 35±39 | Age Of Cigarette Smoking Initiation	Adol. & Young Adults	2009±2010 and 2012±2013 NATS	Current daily cigarette smoker at age 35±39: ªHave you smoked at least 100 cigarettes in your entire life?º (yes). ªDo you now smoke cigarettes every day, some days, or not at all?º (every day or some days). Age of cigarette smoking initiation: ªHow old were you when you smoked a whole cigarette for the first time?º
Years of Life Gained or Lost	All	Jha et al.[98]	1997±2004 NHIS data linked to National Death Index. Years of life gained applied to current cigarette smokers who quit for ≥6 years. Years of life lost applied to adolescents and young adults who become current daily cigarette smokers at age 35±39.

Note: Adol. = Adolescents; | = Conditional On; NATS = National Adult Tobacco Survey; NHIS = National Health Interview Survey; NSDUH = National Survey on Drug Use and Health; NYTS = National Youth Tobacco Survey; TUS-CPS = Tobacco Use Supplement, Current Population Survey.

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number of initiators in 2014, estimated from 2014 NSDUH data, by identifying respondents who answered ªyesº to the question: ªHave you smoked part or all of a cigarette?º and whose current age was ≤1 year less than the age at which they first smoked a cigarette (ªHow old were you the first time you smoked part or all of a cigarette?º).

Analytic considerations and sensitivity analyses

To account for uncertainty in the prevalence and transition probability parameters, we utilized Monte Carlo simulation and independently drew from normal distributions with the means and standard deviations equal to the parameters' means and standard errors shown in Tables A and B in S3 Appendix. We repeated this process 100,000 times to create a distribution of each outcome of interest.

We conducted a sensitivity analysis by varying the level of four key parameters: (1) the adjusted odds ratio of smoking cessation, (2) the adjusted odds ratio of cigarette smoking initiation, (3) age-group-specific prevalence of current e-cigarette use among current cigarette smokers who tried quitting within the past year, and (4) age-specific prevalence of ever having tried e-cigarettes among never cigarette smokers. We also calculated the probability of positive total years of life gained across a wide range of possible values for these four parameters. For example, we supposed the adjusted odds ratio of smoking cessation equaled 2.5 times the baseline estimate (2.15 = 2.5 x 0.86) and recalculated the years of life gained, drawing all other parameters from their baseline distributions. The probability of a positive total years of life gained under this supposition equaled the ratio of the (1) number of simulations that yielded a positive value and (2) total number of simulations (100,000). Finally, we varied from 0% to 100% the relative harm of e-cigarette use, compared to cigarette smoking, in terms of the number of years of life gained from quitting cigarette smoking. We used R, Version 3.2.3 for all analyses. Results of years of life gained were determined to be statistical significant if their 95% confidence intervals do not contain zero.

Results

Additional quitters and initiators

In 2014, 3,490,000 current adult cigarette smokers who had attempted to quit smoking in the past year had also currently used e-cigarettes. Additionally, 3,640,000 never-cigarette smoking adolescents and young adults had ever used e-cigarettes.

The model estimated that 2,070 additional current cigarette smoking adults (95% CI: -42,900 to 46,200) who currently used e-cigarettes in 2014 would quit smoking in 2015 and remain continually abstinent from smoking for ≥7 years using e-cigarettes, compared to those who did not currently use e-cigarettes (Fig 2). The model also estimated that an additional 168,000 never-cigarette smoking adolescents and young adults in 2014 (95% CI: 114,000 to 229,000) who had ever used e-cigarettes would initiate cigarette smoking in 2015 and eventually become daily cigarette smokers at age 35±39, compared to those who had never used e-cigarettes.

Years of life gained

The model estimated that the 2,070 additional long-term quitters would gain -3,000 years of life (95% CI: -351,000 to 325,000). The model also estimated the additional 168,000 adolescent and young adult cigarette smoking initiators who eventually become daily cigarette smokers at age 35±39 will lose 1,510,000 years of life (95% CI: 1,030,000 to 2,060,000). Thus, considering

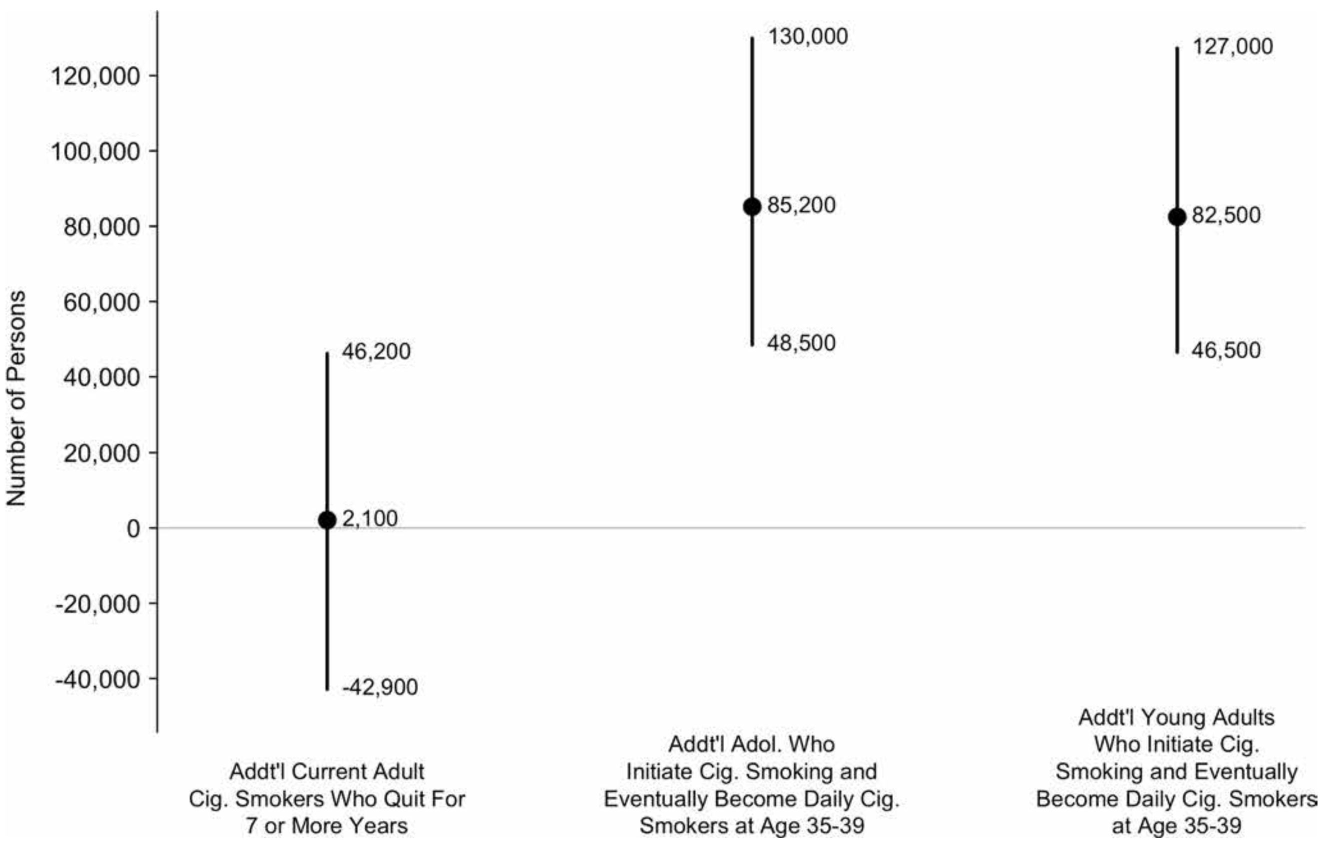

Fig 2. Number of additional adult current cigarette smokers who quit for ≥7 years and additional adolescents and young adults who initiate cigarette smoking and eventually become daily cigarette smokers at age 35±39, all through the use of E-cigarettes. The mean of the distribution is shown as a solid circle and the 95% confidence interval is shown as a vertical line. Source: stochastic simulation (100,000 iterations). Note: Addt'l = Additional; Cig. = Cigarette. Estimates reported as text in the figure rounded to 3 significant digits.

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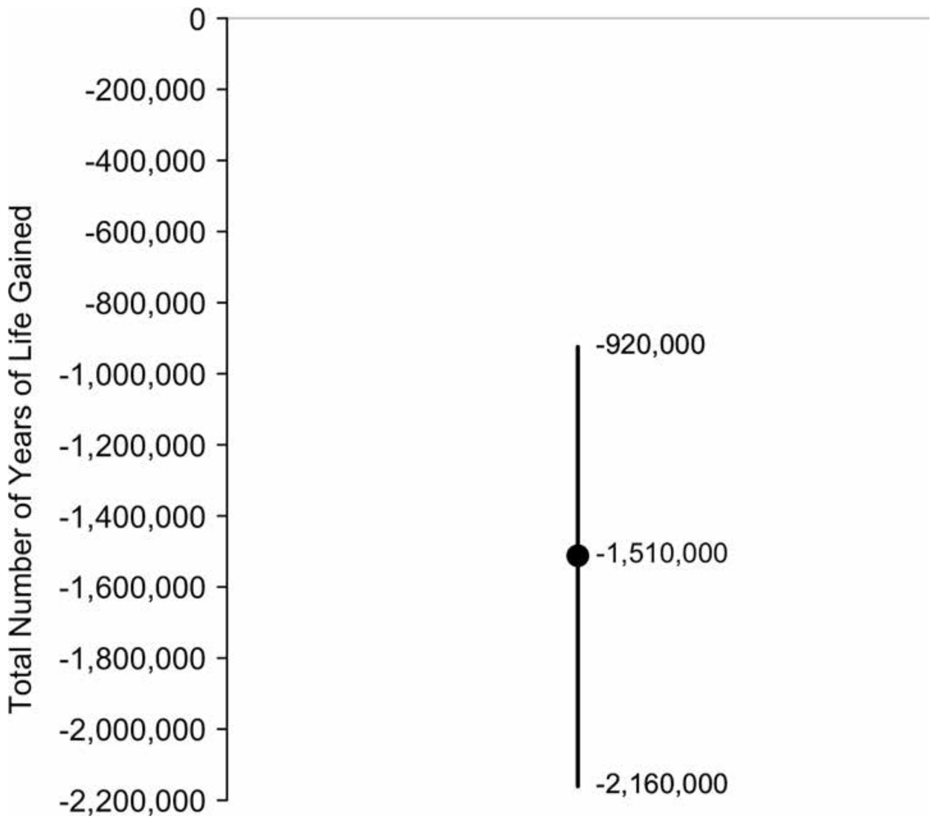

Fig 3. Total number of years of life gained. Negative years of life gained represent years of life lost. The mean of the distribution is shown as a solid circle and the 95% confidence interval is shown as a vertical line. Source: stochastic simulation (100,000 iterations). Estimates reported as text in the figure rounded to 3 significant digits.

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all population subgroups, the model estimated that e-cigarette use in 2014 would lead to 1,510,000 years of life lost (95% CI: 920,000 to 2,160,000; Fig 3) assuming an approximate 95% relative harm reduction of e-cigarette use compared to cigarette smoking.

Sensitivity analysis

Our results were sensitive to the adjusted odds ratios of cigarette smoking cessation and cigarette smoking initiation (Table 2). The model estimated that e-cigarette use in 2014 would lead to 1,150,000 years of life lost (95% CI: 2,130,000 to 242,000) under the relative risk of smoking cessation estimated by Bullen et al. (transformed to an odds ratio). The model estimated that e-cigarette use in 2014 would lead to 1,330,000 years of life lost (95% CI: 1,950,000 to 780,000) and 1,150,000 years of life lost (95% CI: 1,730,000 to 620,000) if the adjusted odds ratio of cigarette smoking initiation decreased by 10% and 20%, respectively. Our results were also sensitive to the prevalence of current e-cigarette use among current cigarette smokers who tried quitting within the past year and ever e-cigarette use and never cigarette smokers. Finally, we varied the health risks of e-cigarette use as a percentage of the risk associated with cigarette smoking. The total number of years of life lost increased as the relative harm of e-cigarette use, compared to cigarette smoking, grew (Fig 4). The model estimated that e-cigarette use in 2014 would lead to 1,530,000 years of life lost (95% CI: 2,180,000 to 960,000) and 1,580,000 years of life lost (95% CI: 2,250,000 to 1,020,000) if the health risks of e-cigarette use were 10%-20% (i.e., 80%-90% safer) and 40%-50% (i.e., 50%-60% safer) of the risks of cigarette smoking, respectively.

Table 2. Results of sensitivity analysis.

Parameter	Scenario	Parameter Pt. Est. (95% CI)	Years of Life Gained (95% CI)[2]
Adjusted Odds Ratio of Cigarette Smoking Cessation	Base Case	0.86 (0.54 to 1.18)	-1,510,000 (-2,160,000 to -925,000)
	Bullen et al.[1]	1.28 (0.42 to 2.24)	-1,150,000 (-2,130,000 to -242,000)
Adjusted Odds Ratio of Cigarette Smoking Initiation	Base Case	3.50 (2.38 to 5.16)	-1,510,000 (-2,160,000 to -925,000)
	10% Reduction	3.15 (2.14 to 4.64)	-1,330,000 (-1,950,000 to -775,000)
	20% Reduction	2.80 (1.90 to 4.13)	-1,150,000 (-1,730,000 to -616,000)
Prevalence of Current E-Cigarette Use Among Current Cigarette Smokers Who Tried to Quit Within the Past Year	Base Case	Age-Group Specific	-1,510,000 (-2,160,000 to -925,000)
	10% Increase	Age-Group Specific	-1,510,000 (-2,180,000 to -906,000)
	20% Increase	Age-Group Specific	-1,510,000 (-2,190,000 to -882,000)
Prevalence of Ever E-Cigarette Use Among Never Cigarette Smokers	Base Case	Age Specific	-1,510,000 (-2,160,000 to -925,000)
	10% Decrease	Age Specific	-1,360,000 (-1,950,000 to -817,000)
	20% Decrease	Age Specific	-1,210,000 (-1,770,000 to -702,000)

Note: Pt. Est. = Point Estimate; CI = Confidence Interval.

[1]Odds ratio and 95% CI converted from reported relative risk and probability of 6-month cessation in the nicotine patch control group (5.8%).

[2]All estimates rounded to 3 significant digits.

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The probability of a positive total number of years of life gained increased with the relative risk of smoking cessation: 6.7%, 44.6%, and 83.3% as the relative risk increased to 2.0, 2.5, and 3.0, respectively (Fig 5, Panel A). The probability also increased with higher prevalence of current e-cigarette use among current cigarette smokers (Fig 5, Panel B). Conversely, the probability increased to 0.0%, 0.0%, and 47.6% as the adjusted odds ratio decreased to 3.0, 2.0, and 1.0, respectively (Fig 5, Panel C). Finally, the probability increased with lower prevalence of ever e-cigarette use among never cigarette smokers (Fig 5, Panel D).

Model validation

Based on 2013 NHIS data, we predicted 1.2 million current cigarette smoking adults would have quit and remained continually abstinent from smoking for ≥6 months in 2014 (95% CI, 1.0 to 1.4 million), which was not statistically different ($p = 0.57$) from the estimated number from the 2014 NHIS data (1.1 million, 95% CI: 0.9 to 1.3 million). Based on 2013 NSDUH data, we predicted that 5.5 million adolescents and young adults would have initiated cigarette smoking in 2014 (95% CI: 4.0 to 6.9 million), which was not statistically different ($p = 0.53$) from the observed number from 2014 NSDUH data (5.0 million, 95% CI: 4.1 to 5.9 million).

Discussion

Our study developed a Monte Carlo stochastic simulation model to assess the balance of health benefits and harms of e-cigarette use at the population level. Based on the most up-to-date published evidence, our model estimated that e-cigarette use in 2014 represents a population-

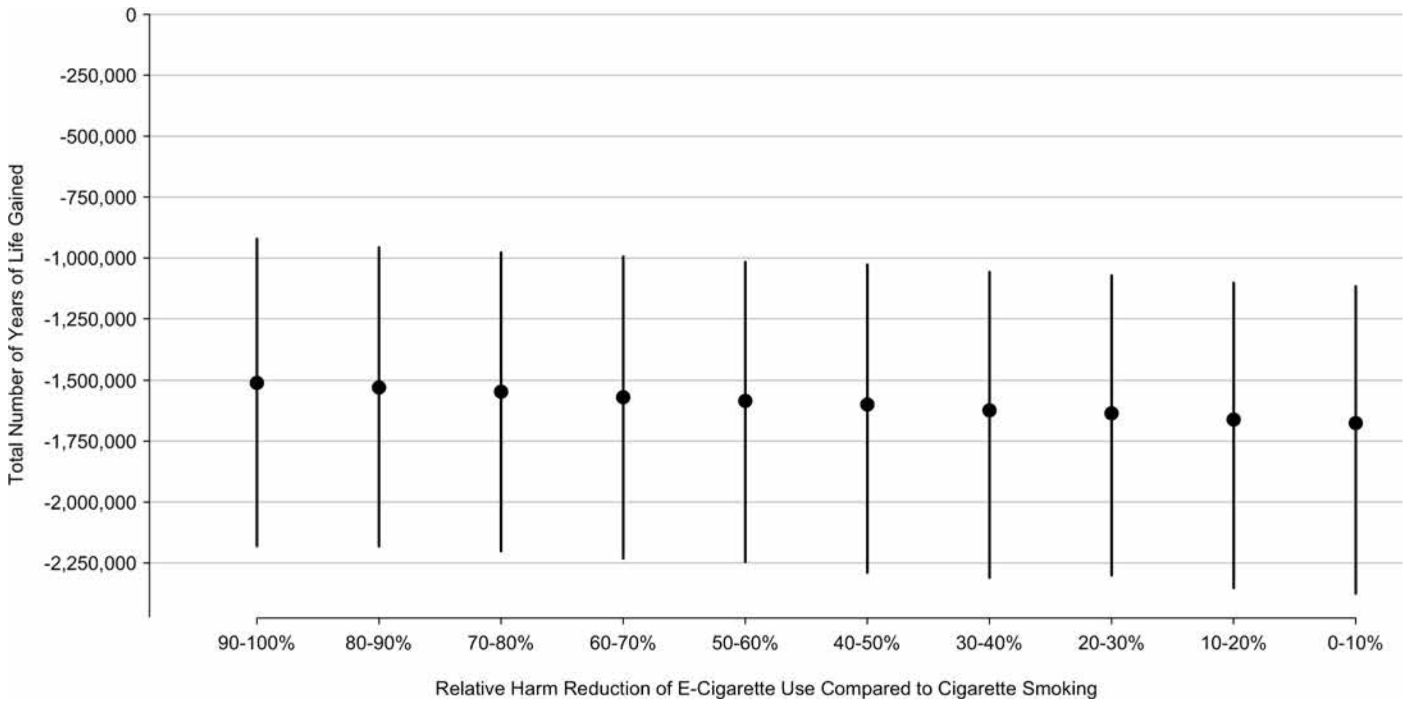

Fig 4. Total number of years of life gained by relative harm of E-cigarette use compared to cigarette smoking.

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level harm of about 1.6 million years of life lost over the lifetime of all adolescent and young adult never-cigarette smokers and adult current cigarette smokers in the 2014 US population. Our model also estimated even greater population-level harm if e-cigarette use confers long-term health risks.

Our study is consistent with Kalkhoran & Glantz (2015), who estimated the effects of e-cigarette use on cessation among smokers and on cigarette smoking initiation by never-smokers under various scenarios [29]. For example, their study found the largest relative health costs occurred in the scenario under which e-cigarette use increased among never-smokers because of the resulting increase in cigarette smoking initiation and the dual use of cigarettes and e-cigarettes, while e-cigarette use remained unchanged among established smokers. Our study also supports the conclusion of Cherng et al. (2016) on the relative effects of e-cigarettes on smoking initiation and cessation [39]. Our model indicates that the odds of smoking initiation among e-cigarette users would need to decrease more than the odds of smoking cessation would need to increase to achieve the same change in the total number of years of life gained.

Our conclusions differ from those of Levy et al. (2016), Levy et al. (2017), and Hill & Camacho (2017)Ða tobacco industry-funded study [40±42]. Hill & Camacho found the use of e-cigarettes would result in a decrease in smoking-related mortality in the UK from 8.4% to 8.1% in 2050 [40]. Levy et al. found that the use of vaporized nicotine products (VNPs; e.g., e-cigarettes) would lead to years of life gained for the US birth cohort of 1997 as it ages over time [41]. Hill & Camacho estimated an ªoverall beneficial effect from launching e-cigarettesº, in part, because they explicitly assumed the transition probability of cigarette smoking initiation among never cigarette smokers who used e-cigarettes equaled 5% [40]. Levy et al. (2016) estimated a ªpositive public health impactº from VNP use, in part, because they implicitly assumed the odds of cigarette smoking initiation was only marginally higher for ever e-cigarette users than never e-cigarette users (odds ratio≈1.16) among adolescents and young adults

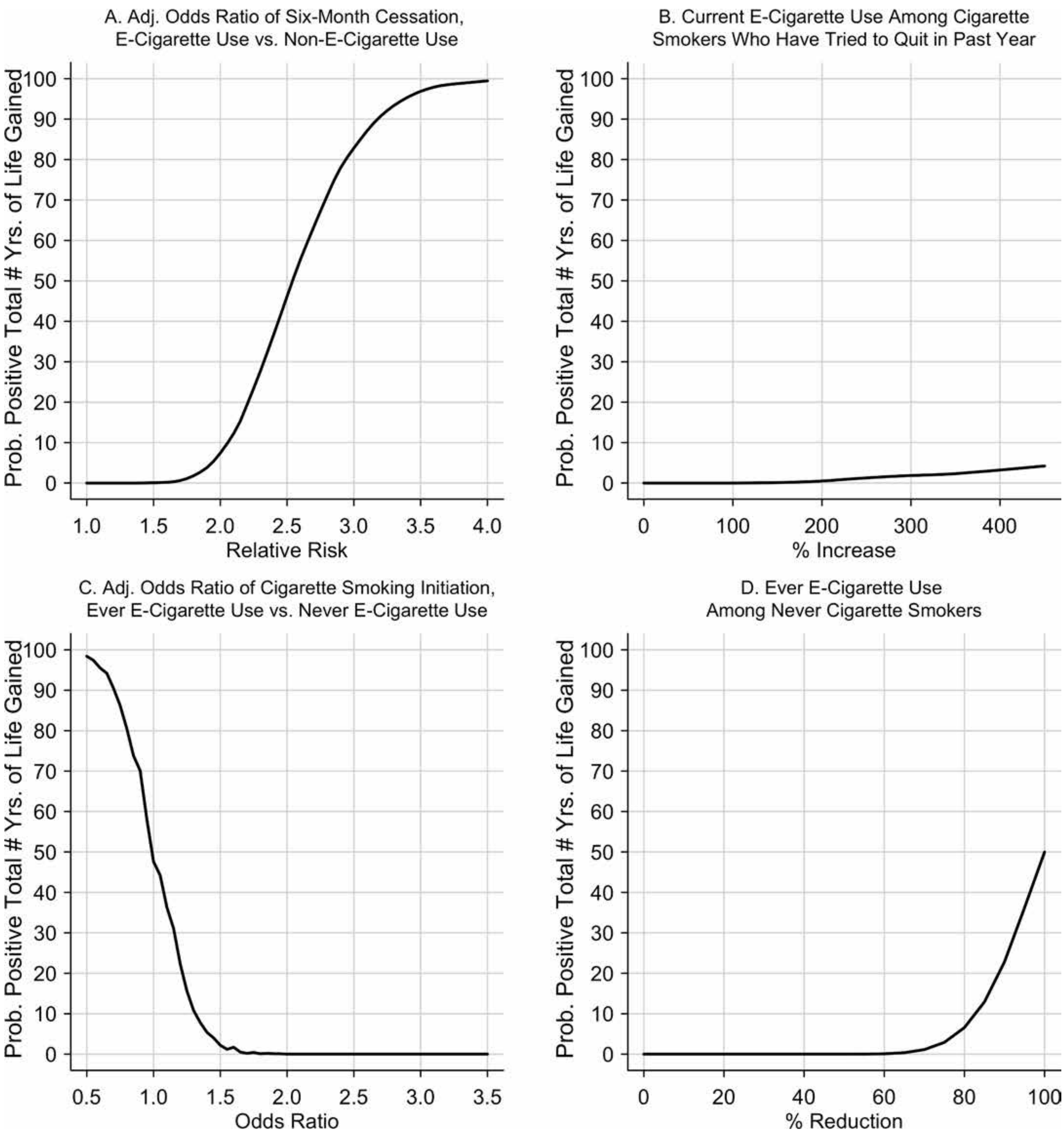

Fig 5. Probability of a positive total number of years of life gained varying the level of four key model parameters. Note: vs. = versus; Adj. = Adjusted.

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who would not have become a cigarette smoker in the absence of VNPs. Yet, both of these assumptions are substantially different from empirical estimates of these parameters from thirteen published cohort studies with a combined sample size of over 44,000 respondents [13±

18,20,21,43±47]. Levy et al. (2017) estimates a substantial number of years of life gained from e-cigarette use, in part, because they explicitly assumed e-cigarette use among never cigarette smokers does not increase the rate of cigarette smoking initiation, whichÐagainÐcontrasts with growing scientific evidence to the contrary. Nevertheless, these models provide useful conceptual frameworks to assess the net benefits of e-cigarette use and would likely yield substantively different conclusions under alternativeÐand empirically basedÐassumptions of e-cigarette use and cigarette smoking initiation.

E-cigarettes could, indeed, confer a positive population benefit if they were more effective as a smoking cessation device. For example, if current smokers who used e-cigarettes as a smoking cessation tool achieved six-month smoking abstinence at a rate of approximately 2.55 times greater than their counterparts who did not use e-cigarettes, then our model estimated that the probability of a positive total number of years of life gained would approach 50%. However, the estimated effectiveness of e-cigarettes for smoking cessation from all published randomized trials and nearly all cohort studies fall well below this threshold including some studies that concluded cigarette smokers who used e-cigarettes were lessÐnot moreÐlikely to quit than those who used standard clinic-based smoking cessation treatments [11,38,48±65]. Three cohort studies of current cigarette smokers did, indeed, estimate relative risks of smoking cessation above this threshold among intensive e-cigarette users (daily use for at least one month), daily tank e-cigarette users, and long-term (i.e., $\geq$2-year) e-cigarette users [59,66,67]. However, the prevalence of intensive e-cigarette use, daily e-cigarette tank use, and long-term e-cigarette use were low in these studies: only 34% of e-cigarette users were intensive users, 12% of e-cigarette users were daily e-cigarette tank users, and 14% of e-cigarette users were long-term users [59,66,67].

A decline in public acceptability of cigarette smoking has been accompanied by proscriptions on where smoking is allowed [68,69]. Nearly two-thirds of e-cigarette users reported using them when and where cigarette smoking was not allowed [70,71]. Further, an analysis of e-cigarette tweets highlighted that e-cigarette vaping was considered social acceptable by many, as opposed to cigarette smoking [72]. However, the lower level of sensation and satisfaction experienced with e-cigarettes, compared to cigarettes, may explain why some individuals who initiate with e-cigarettes then transition to cigarettes even thought this transition is associated with higher nicotine ingestion [73±75].

E-cigarette use among former cigarette smokers may confer health risks. For example, e-cigarette aerosols carry high levels of aldehydes (e.g., formaldehyde) that affect cardiovascular function and high levels of fine particles that accelerate heart disease [76,77]. E-cigarette users experience equivalent reductions in vascular function (e.g., vitamin E levels and flow-mediation dilatation) as cigarette smokers. Furthermore, e-cigarette use suppresses immune and inflammatory-response genes in nasal epithelial cells and injures lung epithelial cells [78,79].

Our study has some potential limitations. First, we do not know if e-cigarette use causes cigarette-smoking initiation in adolescents and young adults. Published cohort studies have found consistent evidence of an increased risk of cigarette smoking initiation among non-smoking youth who had ever used e-cigarettes after accounting for known demographic, psychosocial, and behavioral risk factors [13±18,20,21]. We varied this longitudinal association between e-cigarette use and cigarette smoking initiation and reach similar conclusions. Perhaps more concerning that cigarette smoking initiation, e-cigarette use was independently associated with progression to heaving patterns of cigarette smoking among US adolescents [80]. Second, we do not know the type of e-cigarette currently used by cigarette-smoking adults. Second generation e-cigarettes (e.g., tank-style systems) deliver nicotine more efficiently than the first generation e-cigarettes used in Bullen et al. trial [49,81]. Third generation e-cigarettes (e.g., advanced personal vaporizers) deliver nicotine at approximately the same level and speed as traditional cigarettes [82]. However, we do not yet know the national prevalence of second and third generation e-cigarette use among current cigarette smokers who are trying to quit, and no published trials or cohort studies estimate cessation efficacy or effectiveness of third-generation e-cigarettes.

Third, in our calculation of benefit, we did not consider the possibility that e-cigarette use among current cigarette smokers leads to a reduction in the intensity of cigarettes smoked per day. A trial conducted by Caponnetto et al. found e-cigarette reduced the median number of cigarettes smoked per day among 300 Italian smokers not intending to quit [83]. Yet, similar reductions in the number of cigarettes smoked per day has not been observed in the US between dual users of e-cigarettes and cigarettes and exclusive cigarette smokers [65].

Fourth, we did not consider the potential population-level health benefit or harm of e-cigarette use among former cigarette smokers because no published trials or cohort studies assessed whether e-cigarette use among former cigarette smokers led to higher or lower rates of relapse to cigarette smoking. A recent cross-sectional study suggested long-term former cigarette smokers who use e-cigarettes may not experience any higher rate of relapse to smoking than their counterparts who do not use e-cigarettes [84].

Current public health models may yield substantively different conclusions about the net harm or benefit of e-cigarette use because there is insufficient data on the effect of e-cigarette use on cigarette smoking-related transitions and tobacco-related diseases. Conclusions may also differ because of decisionsÐboth implicit and explicitÐabout the framework and underlying assumptions inherent in the model. The host of decisions required to develop a model produce structural uncertainty that may exceed parameter uncertainty [85,86]. Sensitivity analysis will not capture structural uncertainty because the model, itself, remains constant. Future work could incorporate Bayesian model averaging to account structural, or model-based, uncertainty [87]. Future work could also grade the quality of models based on published best practices [86,88].

In conclusion, based on currently available evidence on the e-cigarette associated transition probabilities of cigarette smoking cessation and initiation, our study suggests that e-cigarettes pose more harm than they confer benefit at the population level. If e-cigarettes are to confer a net population-level benefit in the future, the effectiveness of e-cigarettes as a smoking cessation tool will need to be much higher than it currently is. The US Preventive Services Task Force concludes the existing scientific evidence is insufficient to clinically recommend e-cigarettes as a smoking cessation tool [89]. In the United Kingdom, the National Institute of Clinical Excellence also notes limited evidence on the long-term health effects of e-cigarette use and does not clinically recommend e-cigarettes for smoking cessation, in contrast to Public Health England and the Royal College of Physicians [35,90,91]. Additionally, comprehensive tobacco control efforts are needed to reduce the appeal of e-cigarettes to youth.

Supporting information

S1 Appendix. E-vigarette-associated Δ transition probability of cigarette smoking cessation.
(DOCX)

S2 Appendix. E-cigarette-associated Δ transition probability of cigarette smoking initiation.
(DOCX)

S3 Appendix. Model parameters. S3 Appendix including Tables A and B. Table A shows model parameters for current adult cigarette smokers. Table B shows model parameters for adolescents and young adults.
(DOCX)

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POLITICS

Tobacco industry looks for political wins in Minnesota

Its opponents continue to fight but are finding the lobby still has pull in the state.

By J. Patrick Coolican (http://www.startribune.com/j-patrick-coolican/275328091/) Star Tribune

FEBRUARY 12, 2017 — 10:05PM

The Rev. Al Sharpton and a trio of prominent activists appeared in a Minneapolis church basement in January with a somewhat surprising message: Keep menthol cigarettes legal.

Their visit was sponsored by Reynolds American Inc., the parent company of cigarette brands like Newport that are popular with black smokers and a financial backer of Sharpton's National Action Network. Several of the activists argued that banning menthol cigarettes would create an underground market for the product and a new reason for police to stop and search young black men.

From neighborhood meetings like the Sharpton visit, to the halls of the State Capitol and the powerful House Taxes Committee, the tobacco industry is still finding ways to exert political influence in a state long viewed as hostile to its interests.

By all accounts, that influence has waned since its heyday, when a team of tobacco lobbyists would crowd the bar of the old Lexington on Grand Avenue in St. Paul, sipping lunchtime cocktails as they plotted strategy. That was before a crippling lawsuit brought by former Attorney General Skip Humphrey against big tobacco, the "Freedom to Breathe" law that banned indoor smoking and — perhaps most significant — ushered in a change in culture that has made smoking less socially acceptable, especially among young people.

(http://stmedia.startribune.com/images/ows_14852091902340
(AP PHOTO/GENE J. PUSKAR, FILE)

FILE - In this Friday, July 17, 2015 file photo, Camel and Newport cigarettes, both Reynolds American brands, are on display at a Smoker…

The industry suffered another major defeat in 2013, when the DFL-controlled Legislature raised cigarette taxes an additional $1.60 per pack and included automatic annual increases in the tax going forward. Now Rep. Greg Davids, the influential chairman of the House Taxes Committee, wants to eliminate that automatic yearly hike.

"Tobacco taxation in Minnesota is so far out of the mainstream," said Davids, R-Preston, while stressing he does not like smoking. "This is not about giving money to the tobacco companies. This is about putting money in people's pockets who are being so overtaxed."

One in seven Minnesota adults still smoke, according to a 2014 survey. Those smokers pay tobacco companies for the privilege, which can use the money on advocacy groups like Sharpton's, campaign contributions for sympathetic lawmakers and a stable of skilled lobbyists.

Last year, the state House and Senate passed a sweeping tax bill that cut taxes for farmers, businesses, parents with children and other popular constituencies. It also would have eliminated the automatic annual tax increase on cigarettes. As a tax break for smokers, the measure was widely viewed as a win for the tobacco companies, with research consistently showing a correlation between higher cigarette prices and lower rates of smoking.

The tobacco provision's origins were mysterious, surprising tobacco opponents on the final weekend of the legislative session. It would have cost the state treasury $40 million during the next four years. The bill included another industry-backed measure that would have changed how vaping is taxed — also to the advantage of the big tobacco companies, which have introduced their own vaping products as alternatives to smoking.

Gov. Mark Dayton vetoed the tax bill for an unrelated reason. But he was also critical of the tobacco provisions, recently calling them the result of "a real special interest lobbying effort that got through last year, and I will do what I can to oppose it happening again in this [year's tax] bill."

There is a good chance it will hit his desk again.

Davids said the state's high tobacco taxes, which far exceed those in neighboring states, lead to rampant smuggling and tax evasion.

That assessment of cigarette smuggling was backed by a January report from the Tax Foundation, which found that the percentage of cigarettes smoked in Minnesota that were smuggled from other states rose from 23.6 percent to 35.5 percent after recent tax increases here.

Altria, maker of Marlboro, was a "platinum sponsor" of the Tax Foundation's annual fundraiser last year, known as the Tax Prom. John Buhl, a Tax Foundation spokesman, said the study was funded by the group's operating fund and not specifically financed by industry.

Both Altria and Reynolds are major donors to the Democratic Legislative Campaign Committee and the Republican State Leadership Committee, which in turn funnel money into statehouse races around the country, including Minnesota.

Altria declined to comment.

Brittany Adams, a spokeswoman for Reynolds, which is now known as RAI Services, said the company "participates in the political and public policy process in a manner consistent with the law and interests of their businesses."

The industry-sponsored event in the basement of Greater Friendship Missionary Baptist Church in Minneapolis focused on an issue of overriding concern to black communities: the criminal justice system.

A recording of the meeting was provided to the Star Tribune. Sharpton told the assembled group that he is officially neutral on whether menthol cigarettes should be legal. Sharpton was the star attraction, but three tobacco industry surrogates who joined him — a former congressman and two retired police officers — argued that if menthols are banned, a black market would spring up, exposing black communities to violence, vigorous policing and incarceration.

The speakers were met with a force to be reckoned with in black communities: church ladies.

"We schooled them. That would be the street term," said Ora Hokes, a minister and president of the church's health and social justice ministry.

Hokes, who has been working on tobacco prevention for years, said she was happy for the dialogue: "The more you know the enemy, the more you can prepare for battle."

More than 80 percent of black smokers prefer menthol cigarettes, which are believed to attract and retain customers by cutting down on the harshness of the smoking experience. About 45,000 black Americans die from smoking-related diseases every year, according to the federal Centers for Disease Control and Prevention.

LaTrisha Vetaw, policy manager for Northpoint Health and Wellness, challenged the speakers at the event, which she called "embarrassing."

Vetaw said the entire issue is a red herring: "Someone would have to be working on the [menthol] ban. And no one is. It's a scare tactic. And what better way than through the black church?"

Adams said the company supports events like these "to engage in conversations to work to resolve controversial issues related to tobacco use ... and open a dialogue with community leaders and the members of the community at large on how a potential ban on menthol can affect the community and the criminal justice system."

National Action Network did not reply to an interview request.

Hokes said the battle with tobacco rages on: "When black people stop dying, then I'll stop working."

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U.S. SALES RESTRICTIONS ON FLAVORED TOBACCO PRODUCTS

This chart provides select examples[1] of U.S. cities and counties that restrict the sale of flavored tobacco products. The chart captures variations among these flavor restrictions by noting when (1) flavors are prohibited generally or only within certain "buffer" zones, (2) menthol is prohibited, (3) flavors are restricted in e-cigarettes, and (4) exemptions are provided for certain retailers. This chart also provides links to each jurisdiction's laws and summarizes relevant legal challenges. Beneath this chart is a supplemental list showing these select flavored tobacco restrictions organized by type rather than by state.

A state or local government considering whether to adapt any language from the following policies should take care to ensure that the language is appropriate, practical, and legal for its jurisdiction. Please note that the Tobacco Control Legal Consortium does not endorse or recommend any of the following policies. We have included these examples to illustrate how various jurisdictions regulate the sale of flavored tobacco products and related electronic nicotine delivery devices.

This chart is not comprehensive. Feel free to contact the Public Health Law Center for more information about flavored tobacco restrictions where you live.

Jurisdiction / Berkeley, California[2]

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes — within buffer zone "Effective January 1, 2017, no person shall sell, give away, barter, exchange, or otherwise deal in flavored tobacco products **within six hundred (600) feet of any school** ...." Berkeley, Cal. Code § 9.80.035(D) (2017) (emphasis added).[3]	**Yes** "'Characterizing flavor' means a distinguishable taste or aroma, other than the taste or aroma of tobacco, that is imparted either prior to or during consumption of a tobacco product, **including but not limited to tastes or aromas of menthol** ...." Berkeley, Cal. Code § 9.80.020(A) (2017) (emphasis added). "'Flavored tobacco product' means **any tobacco product** containing, made of, or derived from tobacco or nicotine that contains a constituent **that imparts a characterizing flavor.**" Berkeley, Cal. Code § 9.80.020(F) (2017) (emphasis added).	**Yes** "'Tobacco product' means: 1. any substance containing, made of, or derived from tobacco or nicotine including but not limited to cigarettes, cigars, cigarillos, pipe tobacco, snuff, chewing tobacco, dipping tobacco, bidis, and shisha; 2. any **e-liquid**; 3. any **electronic nicotine delivery system**; and 4. any tobacco paraphernalia." Berkeley, Cal. Code § 9.80.020(K) (2017).	**No**	**No**

Jurisdiction / Contra Costa County, California

Flavored sales restriction not enforced until January 1, 2018, although ordinance is effective August 17, 2017.

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes — within buffer zone "It is a violation of this division for any tobacco retailer to sell or offer for sale any flavored tobacco product or menthol cigarettes **within 1,000 feet of** any parcel occupied by **a public or private school, playground, park, or library.**" Contra Costa County, Cal., Ordinance 2017-01 (July 18, 2017) (to be codified at Contra Costa County, Cal., Code § 445-6.006) (emphasis added).	**Yes** "It is a violation of this division for any tobacco retailer to sell or offer for sale any **flavored tobacco product or menthol cigarettes** within 1,000 feet of any parcel occupied by a public or private school, playground, park, or library." Contra Costa County, Cal., Ordinance 2017-01 (July 18, 2017) (to be codified at Contra Costa County, Cal., Code § 445-6.006) (emphasis added).	**Yes** "'Flavored tobacco product' means any tobacco product, other than cigarettes as defined by federal law, that contains a constituent that imparts a characterizing flavor." Contra Costa County, Cal., Ordinance 2017-01 (July 18, 2017) (to be codified at Contra Costa County, Cal., Code § 445-2.006(g)). "'Tobacco product' means … (1) [a]ny product **containing**, made from, or derived from tobacco or **nicotine** that is intended for human consumption, whether smoked, heated, chewed, absorbed, dissolved, **inhaled**, snorted, sniffed, or **ingested by any other means** … (2) [a]ny **electronic smoking device** . . ." Contra Costa County, Cal., Ordinance 2017-01 (July 18, 2017) (to be codified at Contra Costa County, Cal., Code § 445-2.006(t)) (emphasis added).	**No**	**No.** Note that this ordinance only applies to unincorporated parts of the county.

Jurisdiction / Contra Costa County, California

Flavored sales restriction not enforced until January 1, 2018, although ordinance is effective August 17, 2017. *continued*

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
		"'Menthol cigarettes' means cigarettes as defined by federal law, that have a characterizing flavor of menthol, mint or wintergreen ...." Contra Costa County, Cal., Ordinance 2017-01 (July 18, 2017) (to be codified at CONTRA COSTA COUNTY, CAL., CODE § 445-2.006(j)).		

Jurisdiction / El Cerrito, California

Note: Existing retailers in good standing have until January 1, 2018, to come into compliance.

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "No tobacco retailer, nor any of the retailer's agents or employees, shall sell or offer for sale, or possess with intent to sell or offer for sale, any imitation tobacco products or flavored tobacco product." EL CERRITO, CAL., CODE § 6.100.160 (2017).	**Yes** "'Characterizing flavor' means a distinguishable taste or aroma, other than the taste or aroma of tobacco, imparted by a tobacco product or any byproduct produced by the tobacco product, **including ... menthol**, mint, wintergreen, herb, or spice."	**Yes** (note that traditional cigarettes not included[4]) "'Flavored tobacco product' means any tobacco product (**other than cigarettes as defined by the U.S. Food and Drug Administration**) that contains a constituent that imparts a characterizing flavor. This includes ... **electronic smoking devices containing nicotine**."	**No** "**No tobacco retailer**, nor any of the retailer's agents or employees, **shall sell** or offer for sale, or possess with intent to sell or offer for sale, any imitation tobacco products or flavored tobacco product." EL CERRITO, CAL., CODE § 6.100.160 (2017).	**No**

Jurisdiction / El Cerrito, California

Note: Existing retailers in good standing have until January 1, 2018, to come into compliance.

continued

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
	El Cerrito, Cal., Code § 6.100.020 (2017) (emphasis added).	El Cerrito, Cal., Code § 6.100.020 (2017) (emphasis added).	"'Tobacco retailer' or 'retailer' means **any** person that sells tobacco, tobacco products, electronic smoking devices, smoking paraphernalia. … This definition is **without regard to the quantity** of tobacco, tobacco products or smoking paraphernalia sold, offers for sale, exchanged, or offered for exchange." El Cerrito, Cal., Code § 6.100.020 (2017) (emphasis added).	**No**

Jurisdiction / Hayward, California

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes — within buffer zone "With the exception of Tobacco Retailers whose business included the sale of flavored tobacco products prior to the effective date of this Article, it shall be a violation of these regulations for any	**Yes** "'Characterizing Flavor' means a distinguishable taste or aroma, other than the taste or aroma of tobacco, imparted by a tobacco product or any byproduct produced by the tobacco product, **including, but not**	**Yes** (note that traditional cigarettes not included) "'Tobacco product' includes, but is not limited to cigarettes, cigars, little cigars, chewing tobacco, pipe tobacco, snuff, snus, **or electronic smoking devices (with or without nicotine)**."	**Yes** Exception for "Tobacco Retailers whose business included the sale of flavored tobacco products prior to the effective date of [the flavored tobacco regulation]." Hayward, Cal. Code § 10-1.2783(c) (2017).	**No**

Jurisdiction / **Hayward, California** *continued*

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Tobacco Retailer or any of the Tobacco Retailer's agents or employees to sell or offer for sale, or to possess with intent to sell or offer for sale, any flavored tobacco product **within a 500 foot radius of any private or public kindergarten, elementary, middle, junior high, or high schoo**l. The burden of proof to establish that sales of flavored tobacco products preceded the effective date of these regulations shall be on the Tobacco Retailer." Hayward, Cal. Code § 10-1.2783(c) (2017) (emphasis added).	**limited to, tastes or aromas relating to … menthol** …." Hayward, Cal. Code § 10-1.2782(b) (2017) (emphasis added). "'Flavored Tobacco Product' means **any tobacco product** (other than cigarettes as defined by federal law) that contains a constituent **that imparts a characterizing flavor.**" Hayward, Cal. Code § 10-1.2782(f) (2017).	Hayward, Cal. Code § 10-1.2782(t) (2017) (emphasis added). "'Flavored Tobacco Product' means **any tobacco product (other than cigarettes as defined by federal law)** that contains a constituent that imparts a characterizing flavor." Hayward, Cal. Code § 10-1.2782(f) (2017) (emphasis added).		

Jurisdiction / **Los Gatos, California**

Effective January 1, 2018.

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "[N]o retailer shall sell a tobacco product containing, as a constituent or additive, an **artificial or natural flavor or aroma** (other than tobacco) or an **herb or spice**, including strawberry, grape, orange, clove, cinnamon, pineapple, vanilla, coconut, licorice, cocoa, chocolate, cherry, or coffee, that is a **characterizing flavor or aroma of the tobacco product, smoke or vapor produced by the tobacco product … rebuttable presumption** that the product is prohibited … if: (1) The product's manufacturer or any other person associated with the manufacture or sale of tobacco products makes or disseminates **public statements or claims**	**Yes** "[N]o retailer shall sell a tobacco product containing, as a constituent or additive, an **artificial or natural flavor or aroma** (other than tobacco)" Los Gatos, Cal., Code § 18.60.020(c)(8) (2017) (emphasis added).	**Yes** "[N]o retailer shall sell a **tobacco product** containing, as a constituent or additive, an **artificial or natural flavor or aroma** (other than tobacco)" Los Gatos, Cal., Code § 18.60.020(c)(8) (2017) (emphasis added). "Tobacco product means … : (1) Any product subject to Subchapter IX [21 U.S.C. § 387 et seq. ("Subchapter IX") of the Federal Food, Drug, and Cosmetic Act … Products subject to Subchapter IX include … **electronic nicotine delivery systems** (such as; but not limited to, **electronic cigarettes**, electronic cigars, electronic hookahs, vape pens, personal vaporizers, and electronic pipes). … Products subject to Subchapter IX also include components or parts of tobacco products, such as, but not limited to, **liquids that are for use in**	**Yes** [Flavor prohibition] shall not apply to any **retailer** that meets **all of the following criteria**: (1) Primarily sells tobacco products; (2) Generates **more than sixty (60) percent of its gross revenues annually from the sale of tobacco products; (3) Does not permit any person under twenty-one (21) years of age to be present** or enter the premises at any time, unless accompanied by the person's parent or legal guardian … ; (4) **Does not sell alcoholic beverages or food** for consumption on the premises; and (5) Posts a sign outside the retail location that **clearly, sufficiently, and conspicuously informs the public that persons under twenty-one (21) years of age are prohibited** from entering the premises. Los Gatos, Cal., Code § 18.60.020(c)(8)(c) (2017) (emphasis added).	

Jurisdiction / **Los Gatos, California**
Effective January 1, 2018.
continued

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
to the effect that the product has or produces a characterizing flavor or aroma, other than tobacco; or (2) The **product's label, labeling, or packaging includes a statement or claim including any text and/or images used to communicate information that the product has or produces a characterizing flavor or aroma** other than tobacco." Los Gatos, Cal., Code § 18.60.020(c)(8) (2017) (emphasis added).		**an electronic nicotine delivery system and that contain tobacco or nicotine or are derived from tobacco or nicotine** ("e-liquids"), vials that contain e- liquids, and atomizers. Los Gatos, Cal., Code § 18.60.020(b) (2017) (emphasis added).		

Jurisdiction / Manhattan Beach, California

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "No retailer shall sell a tobacco product, or any product used in an electronic smoking device, containing, as a constituent or additive, an artificial or natural flavor or an herb or spice (with the exception of mint, menthol, spearmint or wintergreen), including but not limited to strawberry, grape, orange, clove, cinnamon, pineapple, vanilla, coconut, licorice, cocoa, chocolate, cherry, or coffee, that is a characterizing flavor of the tobacco product or smoke produced by the tobacco product." Manhattan Beach, Cal., Code § 4.118.030(H) (2017).	**No** "No retailer shall sell a tobacco product, or any product used in an electronic smoking device, containing, as a constituent or additive, an artificial or natural flavor or an herb or spice (**with the exception of** mint, **menthol**, spearmint or wintergreen) ... that is a characterizing flavor of the tobacco product or smoke produced by the tobacco product." Manhattan Beach, Cal., Code § 4.118.030(H) (2017) (emphasis added).	**Yes** "'Tobacco product' means any product containing tobacco leaf, including but not limited to cigarettes ...." Manhattan Beach, Cal., Code § 4.118.020 (2017). "No retailer shall sell a tobacco product, or **any product used in an electronic smoking device**, containing, as a constituent or additive, an artificial or natural flavor or an herb or spice ... that is a characterizing flavor of the tobacco product or smoke produced by the tobacco product." Manhattan Beach, Cal., Code § 4.118.030(H) (2017) (emphasis added).	**Yes** "The prohibition [on flavored tobacco sales] **shall not apply to a retailer that permits only patrons twenty-one (21) years of age or older**, or active duty military personnel who are eighteen (18) years of age or older, to enter the location where the tobacco product is sold." Manhattan Beach, Cal., Code § 4.118.030(H) (2017) (emphasis added).	**No**

Jurisdiction / **Oakland, California**
Effective July 18, 2018.

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "It shall be a violation of this Chapter for any tobacco retailer or any of the tobacco retailer's agents or employees to sell or offer for sale, or to possess with intent to sell or offer for sale, any flavored tobacco product. A tobacco product is presumed to be a flavored tobacco product if a Tobacco Retailer, Manufacturer, or any employee or agent of a Tobacco Retailer or Manufacturer has: a) Made a public statement or claim that the tobacco product has or produces a characterizing flavor, including, but not limited to, text and/or images on the products' labeling or packaging that are used to explicitly or implicitly	**Yes** "'Characterizing Flavor' means a distinguishable taste or aroma, other than the taste or aroma of tobacco, imparted by a Tobacco Product or any byproduct produced by the Tobacco Product, including, but limited to, taste or aromas relating to any fruit, chocolate, vanilla, honey, candy, cocoa, dessert, alcoholic beverage, **menthol**, mint, wintergreen, herb, or spice; provided, however that a tobacco product shall not be determined to have a Characterizing Flavor solely because of the use of additives or flavorings or the provision of ingredient information." OAKLAND, CAL., CODE 5.91 (2017)	**Yes** "'Tobacco Product,' as used in this Chapter means ... b) Any Electronic Smoking Device." OAKLAND, CAL., CODE 5.91 (2017)	**Yes** "This section does not apply to the sale or offer for sale of Flavored Tobacco Products by a 'Tobacco Store.'" "Tobacco Store" is a retail business that primarily sells tobacco products; generates more than 60 percent of its gross revenues annually from the sale of tobacco products and tobacco paraphernalia; does not permit any person under 18 years of age to be present or enter the premises at any time, unless accompanied by the person's parent or legal guardian; and does not sell alcoholic beverages or food for consumption on the premises. OAKLAND, CAL., CODE 5.91 (2017)	**No**

Jurisdiction / Oakland, California

Effective July 18, 2018.

continued

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
communicate information about the flavor, taste or aroma of a tobacco product; b) Taken actions directed to consumers that would be reasonably expected to result in consumers believing that the tobacco product imparts a characterizing flavor." Oakland, Cal., Code 5.91 (2017)				

Jurisdiction / Palo Alto, California

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "No retailer shall sell a tobacco product containing, as a constituent or additive, an artificial or natural flavor or aroma (other than tobacco) or an herb or spice, including strawberry, grape, orange, clove, cinnamon,	Yes "No retailer shall sell a tobacco product containing, as a constituent or additive, an artificial or natural flavor or aroma (other than tobacco) or an herb or spice ... that is a characterizing flavor or aroma of the tobacco product, smoke or vapor	Yes "Tobacco products" include electronic nicotine delivery systems (such as, but not limited to, electronic cigarettes, electronic cigars, electronic hookahs, vape pens, personal vaporizers, and electronic pipes), as well as components or parts of tobacco products, including liquids	Yes Retailers that primarily sell tobacco products; generate more than 60 percent of their gross revenues annually from the sale of tobacco products; do not permit any person under 21 years of age to be present or enter the premises at any time, unless accompanies by the person's	No

Jurisdiction / Palo Alto, California

continued

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
pineapple, vanilla, coconut, licorice, cocoa, chocolate, cherry, or coffee, that is a characterizing flavor or aroma of the tobacco product, smoke or vapor produced by the tobacco product." PALO ALTO, CAL., CODE 4.64 (2017)	produced by the tobacco product." PALO ALTO, CAL., CODE 4.64 (2017)	that are for use in an electronic nicotine delivery system and that contain or are derived from tobacco or nicotine. PALO ALTO, CAL., CODE 4.64 (2017)	parent or legal guardian; do not sell alcoholic beverages or food for consumption on the premises; and post a sign outside the retail location that clearly, sufficiently, and conspicuously inform the public that persons under 21 years of age are prohibited from entering the premises. PALO ALTO, CAL., CODE 4.64 (2017)	

Jurisdiction / San Francisco, California

Takes effect April 1, 2018.

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "The sale or distribution by an Establishment of any Flavored Tobacco Product is prohibited." S.F., Cal., Ordinance 140-17 (July 7, 2017) (to be codified at S.F., CAL., HEALTH CODE § 19Q.3(a)).	**Yes** "'Characterizing Flavor' means a Distinguishable taste *or* aroma or both, **other than the taste or aroma of tobacco** .... Characterizing Flavors include, but are not limited to, tastes or aromas relating to any fruit, chocolate, vanilla, honey, candy,	**Yes** "'Tobacco Product' has the meaning set forth in Health Code Section 19H.2." S.F., Cal., Ordinance 140-17 (July 7, 2017) (to be codified at S.F., CAL., HEALTH CODE § 19Q.2). "'Tobacco Product' means (1) any product containing, made, or	**No**	**No**

Jurisdiction / San Francisco, California

Takes effect April 1, 2018. *continued*

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
"The sale or distribution by an Establishment of any Flavored Cigarette is prohibited." S.F., Cal., Ordinance 140-17 (July 7, 2017) (to be codified at S.F., Cal., Health Code § 19Q.4(a)).	cocoa, dessert, alcoholic beverage, **menthol**, mint, wintergreen, herb, or spice." S.F., Cal., Ordinance 140-17 (July 7, 2017) (to be codified at S.F., Cal., Health Code § 19Q.2) (emphasis added).	derived from tobacco or nicotine that is intended for human consumption ... ; (2) any device or component, part, or accessory that delivers nicotine alone or combined with other substances to the person using the device including but not limited to **electronic cigarettes**, cigars, or pipes ...." S.F., Cal., Health Code § 19H.2 (2017) (emphasis added). "'Flavored Tobacco Product' means any Tobacco Product, **other than a Cigarette**, that contains a Constituent that imparts a Characterizing Flavor." S.F., Cal., Ordinance 140-17 (July 7, 2017) (to be codified at S.F., Cal., Health Code § 19Q.2) (emphasis added).		

Jurisdiction / San Leandro, California

Effective August 15, 2018.

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "No tobacco retailer, nor any of the retailer's agents or employees, shall sell or offer for sale, or possess with intent to sell or offer for sale, **any flavored tobacco product**." San Leandro, Cal., Ordinance 2017-017 (Oct. 2, 2017) (to be codified at San Leandro, Cal., Code § 4.36.150(l) (2017)) (emphasis added).	**Yes (note: Menthol *cigarettes* are not prohibited because the ordinance excludes cigarettes)** "No tobacco retailer, nor any of the retailer's agents or employees, shall sell or offer for sale, or possess with intent to sell or offer for sale, **any flavored tobacco product**." San Leandro, Cal., Ordinance 2017-017 (Oct. 2, 2017) (to be codified at San Leandro, Cal., Code § 4.36.150(l) (2017)) (emphasis added). "'Flavored tobacco product' means any tobacco product (**other than cigarettes** as defined by the U.S. Food and Drug Administration)" San Leandro, Cal., Ordinance 2017-017 (Oct. 2, 2017) (to be codified at San Leandro, Cal., Code § 4.36.100 (2017)) (emphasis added).	**Yes** "'Flavored tobacco product' means any tobacco product .... **This includes ... electronic cigarettes or electronic smoking devices.**" San Leandro, Cal., Ordinance 2017-017 (Oct. 2, 2017) (to be codified at San Leandro, Cal., Code § 4.36.100 (2017)) (emphasis added).	**No** "No **tobacco retailer**, nor any of the retailer's agents or employees, shall sell or offer for sale, or possess with intent to sell or offer for sale, **any flavored tobacco product**." San Leandro, Cal., Ordinance 2017-017 (Oct. 2, 2017) (to be codified at San Leandro, Cal., Code § 4.36.150(l) (2017)) (emphasis added). "Tobacco retailer" means **any person who sells, offers for sale, or does or offers to exchange for any form of consideration**, electronic cigarettes, electronic cigarette products, electronic cigarette paraphernalia, tobacco products or tobacco paraphernalia. ... **This definition is without regard to the quantity ... sold, offered for sale, exchanged, or offered for exchange.**"	**No**

Jurisdiction / **San Leandro, California**

Effective August 15, 2018.

continued

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
			San Leandro, Cal., Ordinance 2017-017 (Oct. 2, 2017) (to be codified at San Leandro, Cal., Code § 4.36.100 (2017)) (emphasis added).	

Jurisdiction / **Santa Clara County, California**

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "*Flavored tobacco products.* (1) Except as permitted in paragraph (3) of this subsection (i), no retailer shall sell a tobacco product containing, as a constituent or additive, an artificial or natural flavor or aroma (other than tobacco) or an herb or spice, including strawberry, grape … that is a characterizing flavor or aroma of the tobacco product, smoke or vapor produced by the tobacco product.	**Yes** "*Flavored tobacco products.* … Except as permitted in paragraph (3) of this subsection (i), **no retailer shall sell a tobacco product containing**, as a constituent or additive, **an artificial or natural flavor or aroma (other than tobacco)** or an herb or spice … that is a characterizing flavor or aroma of the tobacco product, smoke or vapor produced by the tobacco product." Santa Clara County, Cal., Ordinance 300.903 (Oct.	**Yes** "*Tobacco product[s]* … include, but are not limited to, cigarettes, cigarette tobacco, roll-you-own tobacco, … **and electronic nicotine delivery systems** (such as, but not limited to, **electronic cigarettes**, electronic cigars, electronic hookahs, vape pens, personal vaporizers, and electronic pipes)." Santa Clara County, Cal., Ordinance 300.903 (Oct. 18, 2016) (codified at Santa Clara County, Cal., Code § A18-367(e)) (emphasis added).	**Yes** "Paragraph (1) of this subsection (i) **shall not apply to any retailer that meets all of the following criteria**: (i) Primarily sells tobacco products; (ii) Generates more than 60 percent of its gross revenue annually from the sale of tobacco products; (iii) Does not permit any person under 21 … to be present or enter the premises … unless accompanied by … parent or legal guardian … ; (iv) Does not sell alcoholic beverages or food for consumption on the premises; and (v) Posts a sign … that …	**No.** Note that this ordinance only applies to unincorporated parts of the county. However, one town in Santa Clara County — Los Gatos — passed an almost identical flavored tobacco restriction in May 2017.

Jurisdiction / Santa Clara County, California

continued

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
(2) A tobacco product shall be subject to a rebuttable presumption that the product is prohibited by paragraph (1) … if: (i) the product's manufacturer [or an associated person] . . makes or disseminates public statements or claims … that the product has or produces a characterizing flavor or aroma, other than tobacco; or (ii) [t]he product's label, labeling, or packaging includes a statement or claim … that the product has or produces a characterizing flavor or aroma, other than tobacco." Santa Clara County, Cal., Ordinance 300.903 (Oct. 18, 2016) (codified at Santa Clara County, Cal., Code § A18-369(i)).	18, 2016) (codified at Santa Clara County, Cal., Code § A18-369(i)) (emphasis added).		informs the public that persons under 21 … are prohibited from entering …." Santa Clara County, Cal., Ordinance 300.903 (Oct. 18, 2016) (codified at Santa Clara County, Cal., Code § A18-369(i)(3)) (emphasis added). "*Retailer* means **any person who sells, exchanges, or offers to sell or exchange tobacco products** for any form of consideration." Santa Clara County, Cal., Ordinance 300.903 (Oct. 18, 2016) (codified at Santa Clara County, Cal., Code § A18-367(f)) (emphasis added).	

Jurisdiction / Yolo County, California

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "[I]t shall be a violation of this Chapter for any licensee or any of the licensee's agents or employees to sell, offer for sale, or exchange for any form of consideration: (1) Any Flavored Tobacco Product." Yolo County, Cal., Code § 6-15.10(e) (2017).	**Yes** "'Flavored Tobacco Product' means any Tobacco Product that contains a constituent that imparts a characterizing flavor to the tobacco product or smoke produced by the tobacco product, either by the addition of artificial or natural flavors or an herb or space, **including menthol** …." Yolo County, Cal., Code § 6-15.02(f) (2017) (emphasis added).	**Yes** "'Tobacco Product' means: (1) any substance containing tobacco leaf, including but not limited to cigarettes … (3) any electronic device that delivers nicotine or other substances to the person inhaling from the device, **including but not limited to an electronic cigarette**, cigar, pipe, or hookah;" Yolo County, Cal., Code § 6-15.02(m) (2017) (emphasis added).	**No** "[I]t shall be a violation of this Chapter for **any licensee** or any of the licensee's agents or employees to sell, offer for sale, or exchange for any form of consideration: (1) Any Flavored Tobacco Product." Yolo County, Cal., Code § 6-15.10(e) (2017) (emphasis added).	**No.** Note that this ordinance only applies to unincorporated parts of the county.

Jurisdiction / Chicago, Illinois

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes — within buffer zone "No person shall sell, give away, barter, exchange, or otherwise deal in flavored tobacco products, samples of such products, or accessories for such products at any location **within 500 feet of the**	**Yes** "'Flavored tobacco product' means any tobacco product that contains a constituent that imparts a characterizing flavor …. '[C]haracterizing flavor' means a distinguishable taste or aroma, **other than the taste or aroma of**	**Yes** "'Tobacco product' means any product in leaf, flake, plug, **liquid**, or any other form, containing nicotine derived from tobacco, which product is intended to enable human consumption of the tobacco or nicotine, whether chewed, smoked, absorbed,	**Yes** "No person shall sell, give away, barter, exchange, or otherwise deal in flavored tobacco products, samples of such products, or accessories for such products at any location that has a property line within 500 feet of the property line of any public,	**Yes** Gas station association and Quick Pick Food Mart challenged law, arguing it was preempted by the Family Smoking Prevention Tobacco

Jurisdiction / **Chicago, Illinois** *continued*

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
property line of any public, private, or parochial secondary school located in the City of Chicago." CHICAGO, ILL., CODE § 4-64-180(b) (2017) (emphasis added).	**tobacco**, imparted either prior to or during consumption of a tobacco product, **including, but not limited to, tastes or aromas of menthol**, mint, wintergreen, chocolate, vanilla, honey, cocoa, any candy, any dessert, any alcoholic beverage, any fruit, any herb, and any spice ...." CHICAGO, ILL., CODE § 4-64-098 (2017) (emphasis added).	dissolved, inhaled, snorted, sniffed, or ingested by any other means." CHICAGO, ILL., CODE § 4-64-091 (2017) (emphasis added).	private, or parochial secondary school located in the City of Chicago. **This subsection does not apply to retail tobacco stores.** For purposes of this subsection, 'retail tobacco store' has the meaning ascribed to the term in Section 7-32-010." CHICAGO, ILL., CODE § 4-64-180(b) (2017) (emphasis added). "'Retail tobacco store' means a **retail establishment that derives more than 80% of its gross revenue** from the sale of loose tobacco, cigarettes, cigarillos, cigars, pipes, other smoking devices and accessories, hookahs and related products, and/or electronic cigarettes and related products, and in which the sale of other products is merely incidental. 'Retail tobacco store' does not include a tobacco department or section of a larger commercial establishment or any establishment with any type of liquor, food, or restaurant license."	Control Act (FSPTCA). *Indeps. Gas & Serv. Stations Associations, Inc. v. City of Chicago*, 112 F. Supp. 3d 749, 751 (N.D. Ill. 2015). But the FSPTCA deals with how tobacco products are manufactured, and the law only deals with the final product and whether it has a flavor. Id. at 754. The Court found *Smokeless Tobacco* persuasive: "Even if the ordinance has "some effect on manufacturers' production decisions," it is not a command to implement particular manufacturing standards and, accordingly, is exempt from the FSPTCA's

Jurisdiction / **Chicago, Illinois** *continued*

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
			Chicago, Ill., Code § 7-32-010 (2017).	preemption clause." *Indeps. Gas & Serv. Stations Associations, Inc. v. City of Chicago*, 112 F. Supp. 3d 749, 754 (N.D. Ill. 2015) (quoting *U.S. Smokeless Tobacco Mfg. Co. LLC v. City of N.Y.*, 708 F.3d 428, 434 (2d Cir. 2013)). In the same case, the law also survived vagueness and vested rights challenges. *Id.* at 756, 757-58. Although elementary and middle schools were originally part of this restriction, the buffer zone near those sites was lifted in 2016 due to the financial concerns of business owners.

Jurisdiction / Boston, Massachusetts				
Flavor prohibited?	**Menthol prohibited?**	**E-cigs included?**	**Exemption for certain retailers?**	**Case law**
Yes "No retailer, retail establishment, or other individual or entity shall sell or distribute or cause to be sold or distributed or offer for sale any flavored tobacco product to a consumer. This provision shall not apply to a retail tobacco store or smoking bar as defined by this regulation." Boston Public Health Commission, Youth Access Regulation § III(E)(1) (2016).	**No** "**Characterizing Flavor** — A distinguishable taste or aroma, **other than the taste or aroma** of tobacco, **menthol**, mint or wintergreen …." Boston Public Health Commission, Youth Access Regulation § II(4) (2016) (emphasis added). "**Flavored Tobacco Product** — Any tobacco product or any component part thereof that contains a constituent that imparts a characterizing flavor." Boston Public Health Commission, Youth Access Regulation § II(13) (2016) (emphasis added).	**Yes** "Nicotine delivery products include … **e-cigarettes** …." Boston Public Health Commission, Youth Access Regulation § II(14) (2016) (emphasis added). "**Tobacco Product** – A cigarette, cigar, chewing tobacco, pipe tobacco, bidi, snuff, other tobacco or **nicotine delivery product** in any form." *Id.* § II(20) (emphasis added). "**Flavored Tobacco Product** – Any tobacco product or any component part thereof that contains a constituent that imparts a characterizing flavor." *Id.* § II(13) (emphasis added).	**Yes** "No retailer, retail establishment, or other individual or entity shall sell or distribute or cause to be sold or distributed or offer for sale any flavored tobacco product to a consumer. **This provision shall not apply to a retail tobacco store or smoking bar as defined by this regulation.**" Boston Public Health Commission, Youth Access Regulation § III(E)(1) (2016) (emphasis added).	**No**

Jurisdiction / Cambridge, Massachusetts

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "No retailer, or other individual or entity shall sell or distribute or cause to be sold or distributed or offer for sale **any flavored tobacco** to a consumer. This provision shall not apply to a retail tobacco store." Cambridge, Mass., Code § 8.28.030(K) (2017) (emphasis added).	**No** "Characterizing Flavor. A distinguishable taste or aroma, **other than the taste or aroma of** tobacco, **menthol**, mint or wintergreen, imparted either prior to or during consumption of a tobacco product …." Cambridge, Mass., Code § 8.28.020 (2017) (emphasis added).	**Yes** "Nicotine Delivery Product. Any manufactured article or product made wholly or in part of a tobacco substitute or otherwise containing nicotine that is expected or intended for human consumption …. **Nicotine delivery products include, but are not limited to, e-cigarettes.**" Cambridge, Mass., Code § 8.28.020 (2017) (emphasis added). "Tobacco Product. Cigarettes, cigars, chewing tobacco, pipe tobacco, **nicotine delivery product**, snuff or tobacco in any of its forms." *Id.* (emphasis added). "Flavored Tobacco Product. **Any tobacco product** or component part thereof that contains a constituent that imparts a characterizing flavor." *Id.* (emphasis added).	**Yes** "No retailer, or other individual or entity shall sell or distribute or cause to be sold or distributed or offer for sale any flavored tobacco to a consumer. **This provision shall not apply to a retail tobacco store.**" Cambridge, Mass., Code § 8.28.030(K) (2017) (emphasis added).	**No**

Jurisdiction / **Minneapolis, Minnesota**
Menthol ban will be enforced Aug. 1, 2018

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "No person shall sell, offer for sale, give away, barter, exchange, or otherwise deal in flavored tobacco products or samples of such products." Minneapolis, Minn., Ordinance 17-00749 (passed Aug. 4, 2017) (to be codified at Minneapolis, Minn., Code § 281.45(f)).	**Yes** "*Flavored tobacco product* means any tobacco product that contains a **taste or aroma**, other than the taste or aroma of tobacco … **including, but not limited to, tastes or aromas of menthol, mint, wintergreen** …." Minneapolis, Minn., Ordinance 17-00749 (passed Aug. 4, 2017) (to be codified at Minneapolis, Minn., Code § 281.15) (emphasis added).	**Yes** "*Tobacco products* means tobacco, tobacco related devices, **electronic delivery devices**, or nicotine or lobelia delivery products as those terms are defined in this section." Minneapolis, Minn., Ordinance 17-00749 (passed Aug. 4, 2017) (to be codified at Minneapolis, Minn., Code § 281.15) (emphasis added). "Electronic delivery device includes, but is not limited to … **e-cigarettes** …." Minneapolis, Minn., Ordinance 17-00749 (passed Aug. 4, 2017) (to be codified at Minneapolis, Minn., Code § 281.15) (emphasis added). "*Tobacco* means cigarettes and any product containing, made, or derived from tobacco that is intended for human consumption …." Minneapolis, Minn., Ordinance 17-00749 (passed Aug. 4, 2017) (to be codified at Minneapolis, Minn., Code § 281.15).	**Yes** "No person shall sell, offer for sale, give away, barter, exchange, or otherwise deal in flavored tobacco products or samples of such products. **This subsection does not apply to tobacco products shops or to a licensed tobacco dealer** [under certain conditions]. **This subsection does not apply to licensed off sale liquor stores with regard to menthol, mint or wintergreen flavored tobacco products** provided that such an establishment does not permit any persons under the age of twenty-one (21) to be present within the establishment unaccompanied by a parent or guardian." Minneapolis, Minn., Ordinance 17-00749 (passed Aug. 4, 2017) (to be codified at Minneapolis, Minn., Code § 281.45(f)).	**No**

Jurisdiction / Shoreview, Minnesota				
Flavor prohibited?	**Menthol prohibited?**	**E-cigs included?**	**Exemption for certain retailers?**	**Case law**
Yes "No person shall sell, offer for sale, or otherwise distribute any flavored products." Shoreview, Minn., Ordinance 946 (Nov. 21, 2016) (codified at SHOREVIEW, MINN., CODE § 706.065).	**No** "*Flavored Product*. Any tobacco product, tobacco-related device, electronic delivery device, or nicotine or lobelia delivery product that contains a taste or smell, **other than the taste or smell of** tobacco, **menthol**, mint, or wintergreen, that is distinguishable by an ordinary consumer either prior to or during the consumption of the tobacco product, electronic delivery device, or nicotine or lobelia delivery device including, but not limited to, any taste or smell relating to chocolate, cocoa, vanilla, honey, fruit, or any candy, dessert, alcoholic beverage, herb, or spice." Shoreview, Minn., Ordinance 946 (Nov. 21, 2016) (codified at SHOREVIEW, MINN., CODE § 706.020(C)) (emphasis added).	**Yes** "*Flavored Product*. Any **tobacco product**, tobacco-related device, **electronic delivery device**, or nicotine or lobelia delivery product ...." Shoreview, Minn., Ordinance 946 (Nov. 21, 2016) (codified at SHOREVIEW, MINN., CODE § 706.020(C)) (emphasis added). "Tobacco or Tobacco Products. Tobacco or tobacco products includes cigarettes ...." Shoreview, Minn., Ordinance 946 (Nov. 21, 2016) (codified at SHOREVIEW, MINN., CODE § 706.020(M)).	**Yes** "No person shall sell, offer for sale, or otherwise distribute any flavored products. **This restriction does not apply to retail establishments that**: **(1) Prohibit minors from entering at all times; and** **(2) Derive at least ninety (90) percent of their revenues** from the sale of tobacco, tobacco-related devices, electronic delivery devices, or nicotine or lobelia delivery products." Shoreview, Minn., Ordinance 946 (Nov. 21, 2016) (codified at SHOREVIEW, MINN., CODE § 706.065) (emphasis added).	**No**

Jurisdiction / St. Paul, Minnesota

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "No person shall sell, offer for sale, or otherwise distribute any flavored products." St. Paul, Minn., Code § 324.07(f) (2017).	**No** "*Flavored product* means any tobacco product, tobacco-related device, electronic delivery device, or nicotine or lobelia delivery product that contains a taste or smell, **other than the taste or smell of** tobacco, **menthol**, mint, or wintergreen …." St. Paul, Minn., Code § 324.03(3) (2017) (emphasis added).	**Yes** "*Electronic delivery device* means any product containing or delivering **nicotine**, lobelia, or any other substance intended for human consumption that can be used by a person to simulate smoking in the delivery of nicotine or any other substance through **inhalation of vapor** from the product." St. Paul, Minn., Code § 324.03(2) (2017) (emphasis added). "*Tobacco or tobacco product* means any product containing, made, or derived from tobacco … including, but not limited to cigarettes …." St. Paul, Minn., Code § 324.03(7) (2017). "Flavored product means any tobacco product, tobacco-related device, **electronic delivery device**, or nicotine or lobelia delivery product that contains a taste or smell, other than the taste or smell of tobacco, menthol, mint, or wintergreen …." St. Paul, Minn., Code § 324.03(3) (2017) (emphasis added).	**Yes** "This restriction shall **not apply to retail stores that derive at least ninety (90) percent of their revenue** from the sale of tobacco products, tobacco-related devices, electronic delivery devices, or nicotine or lobelia delivery products **and where the retailer ensures that no person under eighteen (18) years of age is permitted** to enter, at any time." St. Paul, Minn., Code § 324.07(f) (2017) (emphasis added).	**No**

Jurisdiction / **New York City, New York**

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "It shall be unlawful for any person to sell or offer for sale, or to possess with intent to sell or offer for sale, any flavored tobacco product except in a tobacco bar." N.Y.C., N.Y., ADMIN. CODE § 17-715(a) (2017).	**No** "'Characterizing flavor' means a distinguishable taste or aroma, **other than the taste or aroma of** tobacco, **menthol**, mint or wintergreen, imparted either prior to or during consumption of a tobacco product or component part thereof ...." N.Y.C., N.Y., ADMIN. CODE § 17-713(b) (2017) (emphasis added). "'Flavored tobacco product' means any tobacco product or any component part thereof that contains a constituent that imparts a characterizing flavor." N.Y.C., N.Y., ADMIN. CODE § 17-713(e) (2017). "Tobacco products that impart a distinguishable taste or aroma of menthol, mint, wintergreen or tobacco, and do not also impart a characterizing flavor, are **not subject**	**No** (note that traditional cigarettes not included) "'Tobacco product' means **any product which contains tobacco that is intended for human consumption**, including any component, part, or accessory of such product. Tobacco product shall include, but not be limited to, any cigar, little cigar, chewing tobacco, pipe tobacco, roll-your-own tobacco, snus, bidi, snuff, tobacco-containing shisha, or dissolvable tobacco product. **Tobacco product shall not include cigarettes** ...." N.Y.C., N.Y., ADMIN. CODE § 17-713(j) (2017) (emphasis added).	**Yes** "It shall be unlawful for any person to sell or offer for sale, or to possess with intent to sell or offer for sale, any flavored tobacco product except in a tobacco bar." N.Y.C., N.Y., ADMIN. CODE § 17-715(a) (2017) (emphasis added). "Only the following entities may sell or offer for sale flavored tobacco products: **(1) Tobacco bars; and** **(2) Tobacco wholesalers**, but only where the sale or offer of sale is made to a tobacco bar or to an entity located outside the City of New York." N.Y.C., N.Y., R. § 28-02(a) (2017) (emphasis added).	**Yes** Manufacturers and distributors alleged that the Family Smoking Prevention Tobacco Control Act (FSPTCA) preempted NYC's flavor restrictions. *U.S. Smokeless Tobacco Mfg. Co. LLC v. City of N.Y.*, 708 F.3d 428, 430 (2d Cir. 2013). The court held that it didn't. Id. at 436 ("[W]e conclude that Administrative Code § 17–715 is a regulation of sale and not a veiled attempt to regulate the manufacture of tobacco products.") This is because the FSPTCA deals with

Jurisdiction / New York City, New York

continued

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
	to the restriction on sale set forth in § 17-715 of the Administrative Code or these rules." N.Y.C., N.Y., R. § 28-02(b) (2017) (emphasis added).			product manufacturing standards — the flavor restrictions only focus on whether the final product has flavoring (not how the flavor got there). *Id.* at 434.

Jurisdiction / Central Falls, Rhode Island[5]

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "No licensee, or employee or agent of such licensee, shall sell **any flavored tobacco product** to a consumer." Central Falls, R.I., Code § 12-421(e) (2017) (emphasis added).	**No** "*Characterizing flavor* means a distinguishable taste or aroma, **other than the taste or aroma of** tobacco, **menthol**, mint, or wintergreen ...." Central Falls, R.I., Code § 12-417 (2017) (emphasis added).	**Yes** (note that traditional cigarettes not included) "*Tobacco product* means: ... (2) any electronic device that delivers nicotine or other substances to the person inhaling from the device, including, but not limited to, an **electronic cigarette**, cigar, pipe, or hookah." Central Falls, R.I., Code § 12-417 (2017) (emphasis added). "*Flavored tobacco product* means any tobacco product, **other than a cigarette**, that contains a	**Yes** "This subsection (e) shall not apply to a **smoking bar** as defined in Section 23-20.10-2(15) of the Rhode Island General Laws[.]" Central Falls, R.I., Code § 12-421(e) (2017) (emphasis added).	**No**

Jurisdiction / Central Falls, Rhode Island

continued

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
		constituent that imparts a characterizing flavor." CENTRAL FALLS, R.I., CODE § 12-417 (2017) (emphasis added).		

Jurisdiction / Providence, Rhode Island

Flavor prohibited?	Menthol prohibited?	E-cigs included?	Exemption for certain retailers?	Case law
Yes "It shall be unlawful for any person to sell or offer for sale any flavored tobacco product to a consumer, except in a smoking bar." PROVIDENCE, R.I., CODE § 14-309 (2016).	**No** "*Characterizing flavor* means a distinguishable taste or aroma, **other than the taste or aroma of** tobacco, **menthol**, mint or wintergreen, imparted either prior to or during consumption of a tobacco product …." PROVIDENCE, R.I., CODE § 14-308 (2016) (emphasis added). "*Flavored tobacco product* means any tobacco product or any component part thereof that contains a constituent that imparts a **characterizing flavor**."	**Yes** (note that traditional cigarettes not included) "*Tobacco product* means **any product containing tobacco or nicotine**, including, but not limited to, cigars, pipe tobacco, snuff, chewing tobacco, dipping tobacco, bidis, snus, dissolvable tobacco products, and **electronic cigarette cartridges**; provided, however, that **such term shall not include**: (1) **Cigarettes**, including those cigarettes subject to the special rule for cigarettes relating to characterizing flavors of the Federal Family Smoking and Tobacco Prevention Act …." PROVIDENCE, R.I., CODE § 14-308 (2016) (emphasis added).	**Yes** "It shall be unlawful for any person to sell or offer for sale any flavored tobacco product to a consumer, **except in a smoking bar**." PROVIDENCE, R.I., CODE § 14-309 (2016) (emphasis added).	**Yes** In regards to flavoring, the ordinance survived First Amendment and preemption challenges. *See Nat'l Ass'n of Tobacco Outlets, Inc. v. City of Providence*, No. CA 12-96-ML, 2012 WL 6128707, at *13 (D.R.I. 2012), *aff'd. Nat'l Ass'n of Tobacco Outlets, Inc. v. City of Providence*, R.I., 731 F.3d 71 (1st Cir. 2013).

Jurisdiction / Providence, Rhode Island				*continued*
Flavor prohibited?	**Menthol prohibited?**	**E-cigs included?**	**Exemption for certain retailers?**	**Case law**
	PROVIDENCE, R.I., CODE § 14-308 (2016) (emphasis added).			

Addendum: Flavored Tobacco Restrictions by Type

This categorized list organizes the cities and counties mentioned in the chart above by restriction type rather than by state. Please note that this list is not intended to be comprehensive and that other types of flavored tobacco policies exist outside of those mentioned here.

Comprehensive

(jurisdiction-wide ban, menthol prohibited, e-cigarettes included, no retailer exemption)

- El Cerrito, CA (traditional cigarettes excluded)
- Oakland, CA
- Palo Alto, CA (exempts tobacco flavor)
- San Francisco, CA
- Yolo County, CA (only in unincorporated parts of the county)

Comprehensive with retailer exemption

(jurisdiction-wide ban, menthol prohibited, e-cigarettes included, certain retailers exempt)

- Santa Clara County, CA (applies only to unincorporated parts of the county, but see also Los Gatos, CA, noted in the Santa Clara County chart)
- Minneapolis, MN

Buffer zone restriction

(flavor sales prohibited around buffer zone, menthol prohibited, e-cigarettes included)

- Berkeley, CA (no exemption for retailers)
- Contra Costa County, CA (only in unincorporated parts of the county, no exemption for retailers)
- Hayward, CA (traditional cigarettes excluded, exemption for certain retailers)
- Chicago, IL (exemption for certain retailers)

Flavor restriction excluding menthol, with retailer exemption

(jurisdiction-wide ban, menthol allowed, e-cigarettes included, exemption for retailers)

- Manhattan Beach, CA
- Boston, MA
- Cambridge, MA
- Shoreview, MN
- St. Paul, MN
- Central Falls, RI (traditional cigarettes excluded)
- Providence, RI (traditional cigarettes excluded)

Other

- New York City (city-wide ban, menthol allowed, e-cigarettes and traditional cigarettes not included, certain retailers exempt)

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Endnotes

1 Due to the large number of jurisdictions in which flavored tobacco products are prohibited, this chart does not include every city or county with flavored tobacco restrictions, even in the states listed. For example, South Miami, Florida, has an interesting flavored tobacco sales law outside of a licensing section, South Miami, Fla., Code § 12-16 (2017), and almost 100 municipalities in Massachusetts also have sales restrictions on flavored cigarettes. See Local Policies Restricting Flavored "Other Tobacco Products" (Otp) To Adult-Only Retailers, Municipal Tobacco Control Technical Assistance Program, Mass. Municipal Assoc., https://static1.squarespace.com/static/528681f8e4b021ccf6d3c997/t/5903c670cd0f68a2400c03ab/1493419633486/muni+list+Flavored+OTP+Restriction+.pdf (last updated April 21, 2017). These jurisdictions have policies that may differ from those listed in this chart. For more information about jurisdictions in your state in which flavored tobacco sales are restricted, feel free to contact the Public Health Law Center.

2 Not all jurisdictions with flavored tobacco ordinances in highlighted states are covered here. For example, Novato, California, also has a limited flavored tobacco ordinance. Novato, Cal., Code § 7-8.3(h) (2017). It should also be noted that some cities and counties, like Oakland, California, are in the process of adopting a flavored tobacco restriction. Oakland's proposed ordinance will appear again on the city agenda in September 2017. For more information on Oakland's ordinance, visit the city's website at https://oakland.legistar.com/LegislationDetail.aspx?ID=3033408&GUID=E5EE4059-550A-4ABB-899D-56548D300D18. For more information about upcoming ordinances in your area, please contact the Public Health Law Center.

3 The years listed in citations in this document reference when the online codes in hyperlinks were last updated, not when the laws were first passed.

4 Flavored (traditional) cigarettes are prohibited under federal law. For more information, visit *Flavored Tobacco*, Food & Drug Admin. (2017), https://www.fda.gov/tobaccoproducts/labeling/productsingredientscomponents/ucm2019416.htm.

5 Tobacco-Free Rhode Island maintains a list of tobacco restrictions in the state. For more information, visit http://tobaccofree-ri.org/local-ordinances.htm.