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From:	SLegislation
Sent:	Tuesday, March 24, 2026 9:46 AM
To:	Senate Finance
Subject:	FW: S2844 - ACS CAN - Oppose - 3.24.26
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Subject: S2844 - ACS CAN - Oppose - 3.24.26

Greetings –

I wish to submit the attached documents demonstrating the American Cancer Society Cancer Action Network's (ACS CAN) opposition to Senate Bill 2844, which is up for a hearing in the Senate Finance Committee on Tuesday March 24th.

I am happy to answer any questions. Thank you!

Warmest Regards,
Ryan

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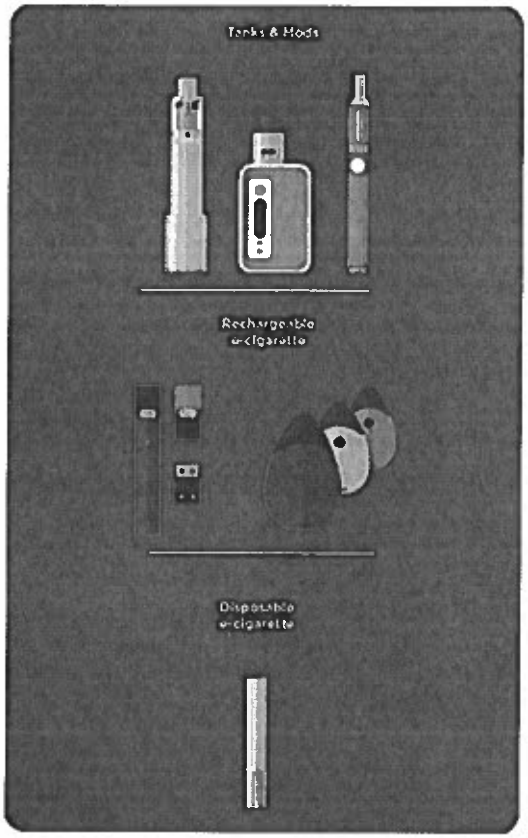
E-cigarettes: Preventing Youth & Young Adult Use

The U.S. Surgeon General declared youth e-cigarette use to be an epidemic.[i] E-cigarettes are the most used tobacco product among youth and, like any tobacco product, are unsafe.[ii] E-cigarette use is also most common among younger adults.[iii] Action is urgently needed to reverse these dangerous trends.



Source: CDC.

WHAT ARE E-CIGARETTES?

E-cigarettes are battery-operated devices that heat a liquid to inhale an aerosol usually made of nicotine and other chemicals.

- E-cigarettes can come in many shapes and sizes, resembling other tobacco products, or look like everyday items likes USB drives. E-cigarettes that are easy to conceal, like those that look like USB drives, are popular with youth.
- E-cigarettes can be disposable, one-time use products, or rechargeable, and can come in mod or tank systems that allow for more customization. Cartridges or pods of e-liquids are used in the devices.
- E-cigarettes can have other names including e-cigs, e-pen, e-hookah, mods, and Juul – a brand with high youth popularity.
- Using an e-cigarette can also be called "vaping" or "Juuling."

E-cigarette Use

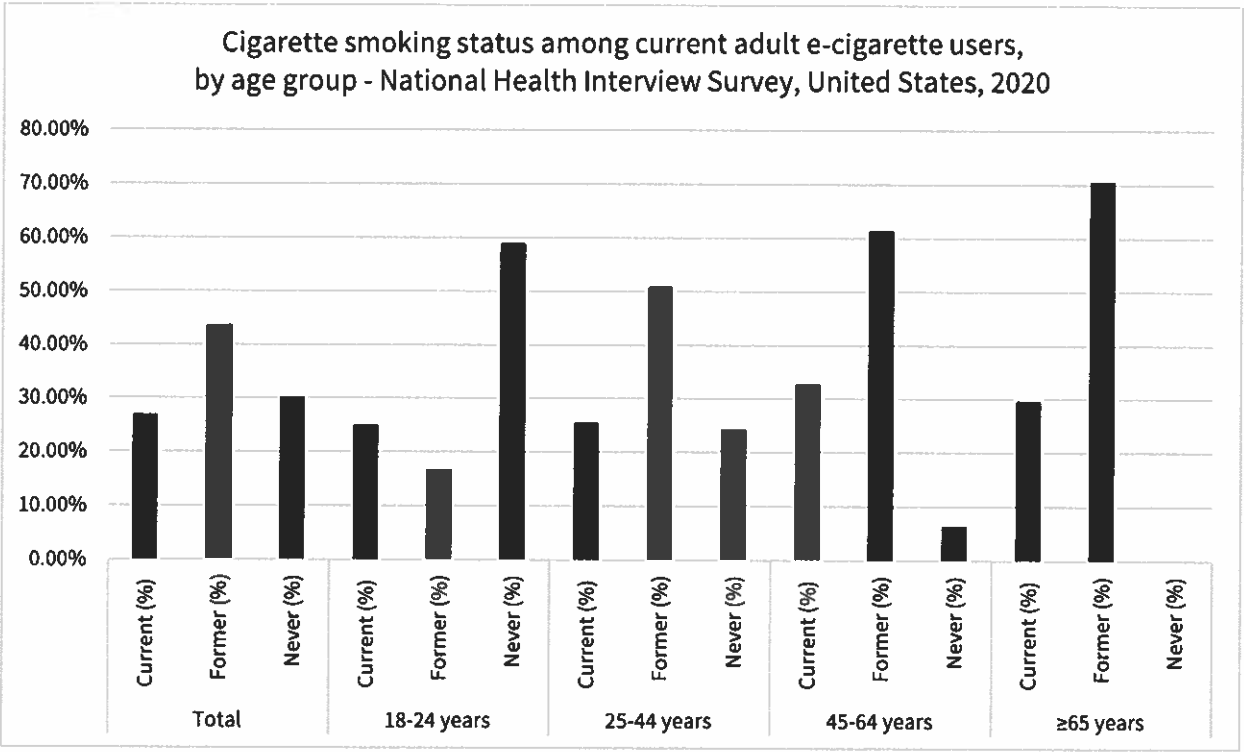
Nationwide, the use of e-cigarettes by youth has rapidly increased. In 2011, 1.5% of high school students and 0.6% of middle school students reported using e-cigarettes.[iv] By 2019, those numbers rose dramatically to 27.5% of high school students and 10.5% of middle school students.[v] In 2022, more than 2.5 million youth reported current e-cigarette use, 14.1% of high school students and 3.3 % of middle school students.[vi]

Frequency of e-cigarette use can be an indication of dependence. Among high school students who currently use e-cigarettes, 46% used on 20 or more of the past 30 days.[vii] Among middle school students who currently use e-cigarettes, 20.8% used e-cigarettes on 20 or more of the past 30 days.

Students also use a variety of e-cigarette types.[viii] Among all students who used e-cigarettes, disposable e-cigarettes were the most common (55.3%). Among high school students who currently use e-cigarettes,

57.2% used disposables, 25.7% used prefilled pods or cartridges, and 6.7% used tank systems. Among middle school students who currently use e-cigarettes, 45.8% used disposables, 21.6% used prefilled pods or cartridges, and 9.8% used tank systems. While 2022 survey results cannot be compared to previous years, this is the second year that disposable e-cigarettes were the most popular among students. From 2019 to 2020, the use of disposable e-cigarettes increased approximately 1,000% (from 2.4% to 26.5%) among high school students who currently use e-cigarettes and approximately 400% (from 3.0% to 15.2%) among middle school students who currently use e-cigarettes.[ix] A possible reason for the dramatic increase in youth disposable e-cigarette use during this time could be related to FDA an announcement in that they would prioritize the removal of illegal flavored tobacco products off the market, but excluded flavored disposable e-cigarettes. It is important to track how youth product popularity changes if policymakers are considering regulating types of products differently.

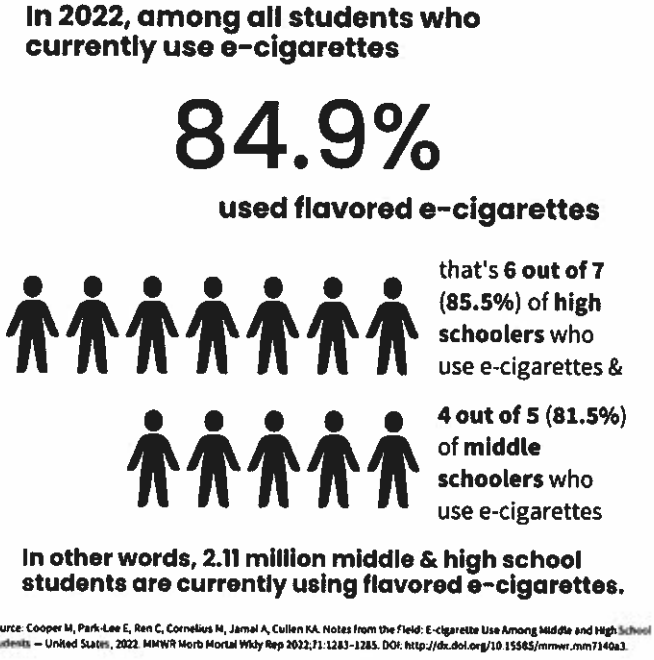
E-cigarettes were also the most commonly used tobacco product among young adults aged 18-25 (9.4% of young adults reporting using e-cigarettes); and young adults were more likely to use e-cigarettes than older age groups in 2020.[x] In fact, current e-cigarette use declined with age. Young adults who have never smoked cigarettes were also more likely to have used e-cigarettes as compared to older adults. Contrary to claims from e-cigarette manufacturers that these products transition people off cigarettes, 58.81% of young adults who were current users of e-cigarettes in 2020 had never smoked cigarettes.[xi]



Source: National Health Interview Survey, 2020. American Cancer Society, Inc., Surveillance Research.

Flavors Encourage E-cigarette Use

Flavors are a key tactic the tobacco industry uses to lure new users, especially youth, into using their highly addictive products. According to the 2022 National Youth Tobacco Survey, among all students who currently use e-cigarettes, 84.9% used flavored e-cigarettes, including 85.5% of high schoolers who use and 81.5% of middle schoolers who use e-cigarettes.[xii] In other words, 2.11 million middle and high school students are currently using flavored e-cigarettes.



The most used flavors of e-cigarettes among middle and high school students who were currently using e-cigarettes were fruit (69.1%), candy, desserts, or other sweets (38.3%), mint (29.4%), and followed by menthol (26.6%).[xiii] Importantly, menthol is derived from mint products and can be found naturally or developed synthetically.[xiv] While these reports asked youth separately about mint and menthol, the user may not necessarily distinguish between these flavors since one is a derivative of the other. Menthol and mint flavors are also often combined with fruit, dessert, or other sweet flavors. **Policies to prohibit flavors in tobacco products or to prohibit the sale of flavored tobacco products, including e-cigarettes, should not distinguish between mint and menthol and instead include all flavors.**

E-cigarette Use Associated with Cigarette and Cigar Use

The 2016 Surgeon General's Report concluded that "e-cigarette use is strongly associated with the use of other tobacco products among youth and young adults, particularly combustible tobacco products.[xv]" In 2018, a National Academies of Science, Engineering, and Medicine report concluded that: "There is substantial evidence that e-cigarette use increases risk of ever using combustible tobacco cigarettes among youth and young adults.[xvi]" Furthermore, the report concluded that there was moderate evidence that e-cigarette use increases the intensity and frequency of cigarette smoking.

More recent studies have quantified the association between e-cigarette and cigarette use among youth. A 2019 study concluded that youth who use e-cigarettes are more than 4 times as likely to try cigarettes and nearly 3 times as likely to currently smoke cigarettes than those youth who never tried e-cigarettes.[xvii] Cigarette use by the end of the study was higher among youth who had previously used e-cigarettes (20.5%) and youth who previously used other tobacco products (21.1%), compared with those who had not used tobacco before (3.8%). Also concerning, the link between prior e-cigarette use and trying cigarette smoking was stronger for youth who would be considered "low-risk" for smoking. The researchers estimated that more than 43,000 youth ages 12-15 years who currently smoke got their start with e-cigarettes.

A 2021 study analyzed longitudinal data from the PATH study to look at youth and young adults who progressed to daily cigarette smoking from 2013-2014 to 2017.[xviii] Youth who had ever tried an e-cigarette were three times more at risk of later daily cigarette smoking than those youth who had never used an e-cigarette.

In addition to the connections between e-cigarette use and cigarette use, research has shown associations between e-cigarette use and cigar use among youth and young adults. A longitudinal analysis of e-cigarette use and cigar, little cigar or cigarillo (CLCC) initiation among youth and youth adults between 2017-2019, found that young people who previously used e-cigarettes had a three times higher odds of using flavored CLCC compared to individuals who had never used e-cigarettes, with a slightly higher odds among young people who used of the Juul brand e-cigarette.[xix]

The 2022 National Youth Tobacco Survey found that 30.3% of any tobacco product users in high school and 33.3% of any tobacco product users in middle school currently used a combination of two or more tobacco products.[xx] After e-cigarettes, cigars were the most commonly used tobacco product (2.8%) followed by cigarettes (2.0%) among high school students who currently used tobacco products.[xxi]

E-CIGARETTES & MARIJUANA

E-cigarettes can be used to inhale marijuana as well as nicotine. Not surprisingly, youth use of e-cigarettes for marijuana has a similar trend to youth use of e-cigarettes for nicotine. In fact, "vaping" of marijuana increased from 2017 to 2019 by two-fold among 8th, 10th, and 12th graders and remained level in 2020.[xxvii] There is some evidence that youth who use e-cigarettes and other tobacco products are more likely to use marijuana than youth who don't use tobacco products.[xxviii]

Like nicotine, marijuana can have a negative and lasting impact on brain development, including cognitive impairment.[xxix] In addition, 2019 saw a multistate outbreak of e-cigarette, or vaping, product use-associated lung injuries (EVALI) which resulted in dozens of deaths. Most patients with EVALI reported using an e-cigarette product containing THC, the main psychotropic ingredient in marijuana, but some reported using nicotine alone. Vitamin E acetate was identified as a chemical of concern among people with EVALI, although no conclusive cause was determined. The CDC and FDA recommend no youth use an e-cigarette product.[xxx]

Adverse Health Effects of E-cigarettes

E-cigarettes can vary in the amount of nicotine present, and they often contain nicotine at much higher levels than cigarettes.[xxii] Nicotine exposure during adolescence and young adulthood can affect the developing brain and may have lasting effects on cognitive function, decision-making, and impulse control.[xxiii] The brain develops until about age 25. Exposure to nicotine during adolescence puts the user at greater risk for a lifelong addiction, as the developing brain is more susceptible to addiction than an adult brain. In addition, nicotine exposure, through maternal use can also negatively affect fetal development leading to sudden infant death syndrome (SIDS), brain alterations, deficits in auditory processing, and obesity.

E-cigarette aerosol poses potential risk to both users and nonusers. The most recent Surgeon General's report concluded that "e-cigarette aerosol is not harmless. It can contain harmful and potentially harmful constituents, including nicotine."[xxiv] Studies have found the aerosol to contain ultrafine particles that can be inhaled deeply into the lungs, heavy metals, volatile organic compounds and cancer-causing chemicals, among other potentially harmful chemicals.[xxv, xxvi, xxvii] E-cigarettes can vary on whether or how much of these chemicals are present in the products, and such information is often not known to consumers.[xxviii]

Industry Targeting Youth and Young Adults

E-cigarette manufacturers are using the same marketing practices effectively used by other tobacco manufacturers to target youth and mislead consumers about the effects of their products.[xxix] These practices include celebrity endorsements, sports and musical sponsorships, use of images of e-cigarettes as rebellious, glamorous and cool, and the use of flavorings in their products.[xxx] Particularly troubling is that e-cigarettes are not subject to the legal marketing restrictions to which cigarettes and other tobacco products are required to adhere. E-cigarettes are widely advertised on television, streaming, radio, online, in print magazines, including those with high youth readership, and at sports and music events.

Therefore, it is no surprise that youth are exposed to e-cigarette advertising. In 2021, 70.3% of middle and high school students – 17.7 million youth - reported seeing e-cigarette advertising and promotions.[xxxi] Almost two-thirds of students reported seeing these advertisements in retail stores (58.7%), 36.0% on the Internet, 21.7% on TV, streaming or movies, and 34.8% in newspapers and magazines. Recent research shows that youth exposed to e-cigarette advertising are more likely to ever and currently use e-cigarettes, with a dose-response effect, even among youth who had never used an e-cigarette.[xxxii]

ACS CAN'S Position

The epidemic of e-cigarette use by youth and young adults, aggressive marketing tactics by their manufacturers, including the use of flavors appealing to youth, and under-regulation of these products requires the public health community to take action to protect youth, young adults, and the public at-large. ACS CAN supports evidence-based strategies to reduce youth use of e-cigarettes:

- **Strong Federal Regulation:** The FDA should use its full authority over all tobacco products, including e-cigarettes to:
  - Enforce premarket review, continuing to issue marketing denial orders for flavored e-cigarettes.
  - Restrict the marketing of these products to youth,
  - Prohibit all characterizing flavors in any tobacco products,
  - Enforce the prohibition on unsubstantiated health claims, and
  - Require sound scientific evidence when evaluating marketing applications and proposing product standards for the protection of public health.

- **Strengthen State and Local Tobacco Control Measures:** Many states and localities are enacting regulations on the sale and use of e-cigarettes. E-cigarettes should be included in evidence-based state and local tobacco control laws.
  - E-cigarettes should be defined as tobacco products and included in the definitions of smoking to:
    - Prohibit e-cigarette use where smoking and/or tobacco use is prohibited.
    - End the sale of all flavored tobacco products including e-cigarettes.
    - Include e-cigarettes in tobacco sales restrictions, including retailer licensing requirements.
    - Tax e-cigarettes based on their price at a rate parallel to the tax on cigarettes and all other tobacco products.
  - Include education about e-cigarettes in all evidence-based state tobacco control programs.

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Health Care Cost Savings Associated with the Massachusetts Flavored Tobacco Restriction on Menthol Cigarettes

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March 25, 2024

Key Takeaways

Background

- In June 2020, Massachusetts became the first state in the United States to restrict the sale of all flavored tobacco products, including menthol cigarettes.
- The Massachusetts Tobacco Cessation and Prevention Program (MTCP) conducted a comprehensive evaluation of the impact of the policy on tobacco use, access, and cessation.
- As part of this evaluation MTCP collaborated with economists John Tauras, Ph.D. and Frank Chaloupka, Ph.D. at the University of Illinois Chicago ("economists")to examine the impact of the policy on the retail environment and health care costs.

Healthcare Cost Savings

- Simulations conducted by economists show that restricting menthol cigarettes reduced smoking prevalence in Massachusetts by 1.37 percentage points between June 2020 and January 2023.
- As a result of reduced smoking prevalence, economists projected reductions in chronic disease and smoking-related birth/pregnancy complications, which would lead to healthcare cost savings.
    - Table 1. Direct cost savings (inclusive of inpatient and outpatient services and prescription drugs) due to reductions in lung cancer, heart attack, and stroke; and smoking-related birth/pregnancy complications and related health care costs for their children in their first year of life. All projected cost savings have been adjusted for inflation. Overall, 10-year costs savings were projected to be close to $200 million.

Table 1

	1 Year Cost Savings	5 Year Cost Savings	10 Year Cost Savings
Pregnancy	$775,742	$3,984,738	$8,191,116
Heart attack & stroke	$3,298,846	$45,644,111	$113,761,026
Lung Cancer	$714,588	$21,657,348	$76,015,640
Total	$4,789,176	$71,286,197	$197,967,782

- Economists also project reduced smoking prevalence would lead to Medicaid cost savings .
    - Table 2. Savings are inclusive of smoking attributable healthcare costs (ex. cancer, emphysema, arteriosclerosis, heart attack, stroke) incurred by Medicaid recipients who smoke in Massachusetts.
    - Medicaid savings may overlap with savings for specific conditions included in Table 1.

Table 2

	1 Year Cost Savings	5 Year Cost Savings	10 Year Cost Savings
Medicaid	$1,052,343	$15,651,763	$43,244,385

Limitations

- These projections are for menthol cigarettes alone and do not include other flavors or tobacco products.
- Projected cost savings are likely underestimates; overall cost savings do not include savings in other conditions that may be impacted by smoking, such as asthma, and the MassHealth cost savings do not account for all possible smoking-attributable conditions.

Introduction

In 2009, Congress enacted the Family Smoking Prevention and Tobacco Control Act, which restricted the use of characterizing flavors in cigarettes, except for menthol. More than a decade later, on October 13, 2023, the Food and Drug Administration (FDA) presented its finalized regulation to the Office of Management and Budget (OMB), prohibiting the sale of menthol cigarettes. Unfortunately, there has been no movement on this regulation since it was submitted to the OMB. Several states did not wait for federal regulation and took independent action to restrict the sale of flavored tobacco, including menthol cigarettes. In 2019, Massachusetts became the first state in the United States (US) to restrict the sale of all flavored tobacco products, including menthol cigarettes. Massachusetts' menthol cigarette restriction became effective June 1, 2020. The only exception to the Massachusetts policy is that flavored tobacco products can still be sold at adult-only licensed smoking bars where consumption must occur on-site. California became the second state to ban the retail sale of menthol cigarettes, effective December 21, 2022. There have also been significant local level efforts to restrict the sale of menthol cigarettes. According to The Campaign for Tobacco-Free Kids (CTFK), more than 190 localities prohibit the sales of all flavored tobacco products, including menthol cigarettes, (CTFK, 2024).

This report examines the effects of the Massachusetts flavor restriction on menthol cigarettes on smoking prevalence in Massachusetts and estimates the health care cost savings attributable to the restriction. Healthcare cost savings related to lung cancer, myocardial infarction and stroke, pregnancy/birth complications are estimated in addition to= Medicaid cost savings for smoking attributable conditions.

Brief Literature Review

Evidence is beginning to emerge on the effects of Massachusetts flavor restrictions on cigarette sales in Massachusetts. A study by Asare and colleagues (2021) found that after the flavor restriction was enacted, the adjusted 4-week sales of cigarettes in Massachusetts compared to the control states decreased by 372.27 packs per 1000 people for menthol cigarettes but increased by 120.25 packs per 1000 people for non-flavored cigarettes. Overall, the adjusted 4-week sales of all cigarettes in Massachusetts compared to the control states decreased by 282.65 packs per 1000 people. A follow-up study by Asare and colleagues (2022) found that following the implementation of the Massachusetts flavor restriction, compared with comparison states, monthly cigarette sales per 1,000 people decreased in Massachusetts by 350.02 packs and increased in bordering states by 9.51 packs per 1000 persons, yielding a net decrease of 340.51 packs per 1,000 persons in Massachusetts and neighboring states combined. This translates into total monthly cigarette sales declines of 2.45 million packs in Massachusetts and an increase of 0.13 million packs in bordering states, resulting in a net decrease of 2.32 million packs in Massachusetts and neighboring states. A study published by the Massachusetts Tobacco Cessation and Prevention Program (Kingsley et al., 2022) found that in the year after the Massachusetts flavor restriction went into effect, overall tobacco sales in Massachusetts decreased by 25.4% as compared with the previous year. The study found total sales of tobacco products in NH, NY, RI, and VT decreased by 1.8% in the year after the Massachusetts restriction was enacted compared with the previous year.

Our research builds upon these previous studies but examines the effects of the menthol cigarette restriction in Massachusetts on adult smoking prevalence utilizing the

national Behavioral Risk Factor Surveillance System (BRFSS). We then utilize the menthol restriction -induced changes in smoking prevalence in Massachusetts to quantify health care cost savings related to lung cancer, myocardial infarction and stroke, pregnancy/birth complications. In addition, cost savings specifically incurred by Medicaid on smoking attributable conditions were calculated.

Methods

Data

For this study, data from the 2016-2022 national Behavioral Risk Factor Surveillance System (BRFSS) were used. The BRFSS is a health-related telephone survey that collects data on U.S. residents regarding their health-related risk behaviors, chronic health conditions, and use of preventive services. BRFSS completes more than 400,000 adult interviews each year, making it the largest continuously conducted health survey system in the world.

The dependent variable used in the regressions was a dichotomous indicator equal to one for respondents who currently used cigarettes either every day or some days and was equal to zero for respondents who did not currently use cigarettes or had never used cigarettes before. Using other items from the survey, several independent variables believed to affect cigarette use among adults were constructed. These variables include indicators for sex (male and female [reference]), indicators for age (ages 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80 +, 18-24 [reference], indicators of marital status (divorced, widowed, separated, single, couple, and married [reference]), indicators for race and ethnicity (non-Hispanic Black, non-Hispanic American Indian or Alaskan Native, non-Hispanic Asian, non-Hispanic Native Hawaiian or Pacific Islander, non-Hispanic multiple races, non-Hispanic other

race, Hispanic, and non-Hispanic White [reference]), indicators of educational attainment (less than high school, some high school, high school graduate, some college, and college graduate [reference]), indicators of employment status (unemployed, homemaker, student, retired, unable to work, employed [reference]), and inflation adjusted household income. The household income variable was a quasi-continuous variable that used the midpoints of the categorical income responses. The values and categorical responses (in parentheses) follow: $5,000 (less than $10,000), $12,500 ($10,000 to less than$15,000), $17,500 ($15,000 to less than$20,000), $22,500 ($20,000 to less than$25,000), $30,000 ($25,000 to less than$35,000) and $42,500 ($35,000 to less than$50,000), $62,500 ($50,000 to less than$75,000), $85,000 ($75,000 or more). The household income levels were adjusted for inflation using the US Bureau of Labor Statistics Consumer Price Index (in 1st quarter 2021 dollars).

We also created mutually exclusive but all-inclusive dichotomous indicators for each year of the survey and each state in the survey. The dichotomous state indicators capture all time-invariant state-level unobserved heterogeneity, and the year indicators account for overall trends in adult cigarette use over time. We also created indicators for each quarter of the year to control for seasonality of cigarette use. We performed Hausman's 1978 specification test to determine if a fixed effects or random effects model is more appropriate by testing if the differences in their estimates are statistically significant (Hausman 1978). The null hypothesis of the Hausman test is that the random effects model is the better choice (meaning the random disturbance term, which captures the unexplained variation in the dependent variable, is assumed to be independent of the regressors). The Hausman specification test rejected the null hypothesis that the random effects model is appropriate. Hence, the fixed effects regression is

utilized in the analyses. Unobserved state factors, such as sentiment toward tobacco, are very likely driving changes in both the independent and dependent variables. That is, a state with a strong anti-tobacco sentiment may be more likely to enact a new tobacco control policy and have larger reductions in smoking than a state with weak anti-tobacco sentiment. The fixed effects approach controls for all time-invariant characteristics unique to each state, effectively removing any influence characteristics such as anti-tobacco sentiment might have on the dependent variable.

The final models employ a three-way fixed-effects regression technique. The fixed effects approach amounts to including a dichotomous indicator for each state (less one), each year (less one), and each quarter (less one) as additional explanatory variables in the models.

We created a dichotomous indicator equal to one for states with policies that restrict the sale of menthol cigarettes and equal to zero otherwise. The dichotomous indicator equals one for all respondents in the state of Massachusetts after June 1, 2020, and all respondents in the state of California after December 21, 2022, and is equal to zero otherwise[1].

Using state-geocode data we merged real state cigarette excise taxes with the BRFSS data based on the day the respondents were surveyed. Nominal state level cigarette excise taxes were obtained from the annual Tax Burden on Tobacco published by Orzechoski and Walker (2021). The nominal cigarette taxes were adjusted for inflation (1st quarter 2021 dollars) using the U.S. Bureau of Labor Statistics Consumer Price Index.

[1] As part of the 2022 BRFSS wave, 11,037 respondents from California were surveyed of which 2,417 were surveyed after the menthol policy went into effect on December 21, 2022.

Using state identifiers, we also merged a dichotomous indicator equal to one for individuals who resided in states that had enacted a smoke-free air law in private worksites at the time of survey, and was equal to zero for individuals who resided in states that did not impose a smoke-free air law in private worksites at the time of the survey. The smoke-free air law data were acquired from the Centers for Disease Control and Preventions State Tobacco Activities Tracking and Evaluation System.

Statistical Analysis

We used a three-way fixed effects approach to estimate the relationship between restriction on menthol cigarettes, cigarette taxes, smoke-free air laws and adult cigarette smoking prevalence. The three-way fixed-effects regression technique controls for time-invariant unobserved state-level heterogeneity (through the use of dichotomous state indicators), changes in the distribution of cigarette consumption by adults over time (through the use of dichotomous year indicators), and seasonality (through the use of dichotomous quarterly indicators). Controlling for unobserved state-level heterogeneity is critical in attempting to estimate a causal effect of menthol policies, taxes, and smoke-free policies on adult smoking prevalence as state sentiment towards tobacco use may be simultaneously driving both changes in cigarette smoking and changes in cigarette policies and taxes. The three-way fixed-effects approach is particularly appropriate for this research given that it is impractical to randomize individuals to locations with different cigarette policies and taxes before they are adopted. Finally, all models used robust standard errors clustered at the state level.

Table 1 contains the estimates from the cigarette smoking prevalence equations. Model 1 contains a model specification that includes the following covariates: flavored cigarette restriction indicator, real income, indicators for age, marital status, gender, race and ethnicity, educational attainment, and employment status. Moreover, Model 1 includes dichotomous year indicators, dichotomous state indicators, and dichotomous quarter indicators as part of our three-way fixed effect approach. Model 2 is based on Model 1 by adding two additional covariates: the inflation adjusted tax on cigarettes and the smoke-free air indicator variable. The inclusion of the two additional policy variables in Model 2 does not have any meaningful impact on the estimated effects of the flavored cigarette smoking restriction [2]To test for collinearity, we calculated variance inflation factors (VIFs) for the 3 tobacco related policies. The VIFs for the menthol sales restrictions, cigarette tax, and private worksite smoke-free air laws were 1.01, 1.18, and 1.17, respectively. We then calculated VIFs for each variable in Model 2 (i.e., the regression that includes the full set of covariates including all three tobacco control policies). The VIF for the menthol sales restriction in Model 2 was slightly higher at 1.56 and the mean VIF across all variables in regression Model 2 was 4.94. The extremely low VIF for the menthol sales restriction indicates a very low correlation of the menthol sales restriction (the main variable of interest in our analyses) with the other included predictor variables in the full regression specification, suggesting a low likelihood of multicollinearity.

All analyses were conducted in Stata 18 using the margins command to calculate predicted probabilities of smoking when the value of the key independent variable (menthol

flavor restriction on cigarettes) is altered from zero (no policy) to one (policy enacted) while holding all other independent variables at their actual values.

Table 1: Smoking Prevalence Equations

	Model 1 Coefficient (t statistic)	Model 2 Coefficient (t statistic)
Flavored Cigarette Restriction	-0.149*** (-4.21)	-0.157*** (-4.13)
Real Cigarette Tax		-0.0286** (-2.28)
Private Worksite Cigarette Ban		-0.00496 (-0.37)
Male	0.201*** (13.81)	0.201*** (13.81)
Age 25-29	0.683*** (35.45)	0.683*** (35.46)
Age 30-34	0.920*** (44.03)	0.920*** (44.06)
Age 35-39	1.017*** (46.49)	1.017*** (46.54)
Age 40-44	0.954*** (42.59)	0.954*** (42.62)
Age 45-49	0.855*** (40.66)	0.855*** (40.67)
Age 50-54	0.772*** (37.09)	0.772*** (37.11)
Age 55-59	0.670*** (32.08)	0.670*** (32.08)
Age 60-64	0.450*** (19.44)	0.450*** (19.44)
Age 65-69	0.160*** (6.78)	0.160*** (6.78)
Age 70-74	-0.157*** (-5.89)	-0.157*** (-5.90)
Age 75-79	-0.628*** (-22.48)	-0.628*** (-22.49)
Age 80+	-1.539*** (-45.30)	-1.539*** (-45.28)
Divorced	0.656*** (49.91)	0.656*** (49.92)
Widowed	0.538*** (38.92)	0.538*** (38.90)

Separated	0.661***	0.661***
	(43.49)	(43.48)
Single	0.381***	0.381***
	(20.09)	(20.08)
Couple	0.650***	0.650***
	(38.93)	(38.93)
Black	-0.364***	-0.364***
	(-8.83)	(-8.84)
Asian	-0.416***	-0.416***
	(-11.65)	(-11.64)
Hawaiian/Pacific Islander	-0.0167	-0.0171
	(-0.44)	(-0.45)
American Indian/Alaskan Native	0.252*	0.252*
	(1.75)	(1.75)
Other Race	0.0724	0.0718
	(1.62)	(1.60)
Multiple Races	0.220***	0.220***
	(7.08)	(7.09)
Hispanic	-0.748***	-0.748***
	(-15.44)	(-15.43)
Less Than High School	0.926***	0.926***
	(23.80)	(23.80)
Some High School	1.481***	1.481***
	(47.96)	(47.97)
High School Grad	1.048***	1.048***
	(48.71)	(48.72)
Some College	0.836***	0.836***
	(62.58)	(62.62)
Unemployed	0.331***	0.331***
	(29.06)	(29.07)
Homemaker	-0.0733***	-0.0733***
	(-2.92)	(-2.93)
Student	-0.685***	-0.685***
	(-30.56)	(-30.55)
Retired	0.0553***	0.0553***
	(6.07)	(6.07)
Unable to Work	0.363***	0.363***
	(26.48)	(26.47)
Real Income	-0.0000122***	-0.0000122***
	(-53.92)	(-53.86)
2017	-0.0107	-0.0101
	(-1.10)	(-1.02)
2018	-0.0171*	-0.0165*
	(-1.77)	(-1.69)

2019	-0.0293***	-0.0288***
	(-2.67)	(-2.63)
2020	-0.0487***	-0.0487***
	(-3.93)	(-3.89)
2021	-0.0935***	-0.0932***
	(-8.01)	(-8.82)
2022	-0.164***	-0.168***
	(-14.98)	(-14.51)
2023	-0.188***	-0.193***
	(-5.76)	(-5.79)
Quarter 2	0.0115**	0.0110**
	(2.26)	(2.16)
Quarter 3	0.00780	0.00750
	(1.14)	(1.11)
Quarter 4	0.0151**	0.0145**
	(2.23)	(2.14)
Constant	-2.552***	-2.531***
	(-65.93)	(-62.86)
Observations	2,311,108	2,311,108

All models also include state indicators. These indicators were not included in the tables to conserve space.
* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$

Results

Flavored cigarette restrictions were found to significantly decrease cigarette use prevalence in both models ($p < 0.01$). Moreover, the inflation adjusted tax on cigarettes was found to significantly decrease cigarette use prevalence in both models ($p < 0.05$). However, the prohibition of smoking in private worksites was found to have an insignificant effect on the prevalence of adult cigarette use. Both regression models produce similar results, however model 2 is inclusive of all the key independent variables, including all the tobacco control policies and therefore model 2 minimizes the probability of an omitted variables bias. We used Akaike's information criterion (AIC) to evaluate the goodness of fit of the models. Model 2

yielded a slightly lower AIC than Model 1. This suggests that Model 2, which includes the additional two tobacco control policies, fits the data better and is the preferred model.

Using the estimates from Model 2, we simulated the effects of the Massachusetts flavored cigarette restriction on adult smoking prevalence rates in the state of Massachusetts. Specifically, we estimated the predicted probabilities of smoking in Massachusetts by altering the value of the Massachusetts cigarette flavor restriction from zero to one. The models indicated that the flavored cigarette restriction reduced smoking prevalence in Massachusetts by 1.372 percentage points (or an 11.89 percent reduction) between the period when the policy went into effect and the day the last individual responded to the survey in Massachusetts on January 24, 2023. The largest effect of the policy was right after implementation with smoking prevalence declining 0.885 percentage points (or 7.85% reduction) between 2020 and 2021.

Health Care Cost Savings

Because of research and data limitations, it is not yet possible to estimate total health care cost savings in each year following the implementation of a restriction on flavored cigarette sales. Since many smoking related diseases take years to develop, smoking related health care cost savings from the implementation of a restriction on flavored cigarette sales will be relatively small at first but will grow quickly over time. We calculate lung cancer, myocardial infarction and stroke, pregnancy/birth complications cost savings overall that result from the Massachusetts restriction on flavored cigarette sales. In addition, Medicaid cost savings from the flavored cigarette restriction were calculated. All the costs estimated are direct costs. The cost savings are aggregated cost savings and were not disaggregated by payer type (private vs. public insurance etc.). We utilize the BRFSS simulated reduction in adult smoking prevalence

that were attributable to the Massachusetts restriction on flavored cigarettes sales to calculate 1-year, 5-year, and 10-year cost savings in Medicaid spending and in the following smoking-attributable conditions: lung cancer, heart attack and stroke, and pregnancy/birth complications. The estimated health care cost savings are based on an economic model that was jointly developed by researchers at Tobacconomics, the Campaign for Tobacco-free Kids, and the American Cancer Society-Cancer Action Network.

The projected savings from fewer smoking-induced heart attacks and strokes, fewer smoking affected pregnancies and related birth complications, and fewer lung cancer cases show just some of the substantial savings from the smoking reductions induced by the Massachusetts policy.

The projected lung cancer cost savings result from adult smokers who quit due to the enactment of the cigarette flavor restriction. The lung cancer cost savings take into account the relative risk of developing lung cancer among quitters and the number of lung cancer deaths attributable to smoking (Chang et al., 2004; Khuder and Mutgi, 2001). The smoking-affected pregnancy and birth savings come from reductions in smoking among pregnant women that result from the enactment of the cigarette flavor restriction and corresponding reductions in smoking-related birth complications and related health care costs for their children in their first year of life (Miller et al., 2001). The heart attack and stroke savings result from adult smokers aged 35-64 who quit smoking due to the enactment of the cigarette flavor restriction and the reduction in health care expenditures that result from fewer heart attacks and strokes following the cigarette flavor restriction (Lightwood and Glantz, 1997; Kabir et al., 2008).

The projected state savings to the Massachusetts Medicaid program are estimated based on the number of adult Medicaid recipients in Massachusetts expected to quit due to the cigarette flavor restriction and the costs averted per quitting Medicaid recipient (Miller et al., 1998). Estimates for adults enrolled in Medicaid include the additional Medicaid enrollees due to expanded Medicaid eligibility as part of the Affordable Care Act as well as adults who were eligible under existing rules prior to the expansion of Medicaid eligibility. The Medicaid cost savings are calculated using per adult enrollee health care spending data and take into account the costs of newly eligible adult Medicaid enrollees separately from the previously eligible adult Medicaid enrollees as well as future projected cost increases. The enrollment projections and costs estimates were provided by Gideon Lukens and Breanna Sharer at the Center on Budget and Policy Priorities. The fraction of the Massachusetts Medicaid program's projected cost savings that would accrue to the state government are based on the state's Federal Medical Assistance Percentage (FMAP), calculated separately for newly eligible and previously eligible enrollees. The smoking related Medicaid expenditures is calculated by multiplying the smoking attributable fraction (SAF) for publicly funded health care in the state of Massachusetts (Miller, 1998) by the total Medicaid expenditures in Massachusetts. The SAF used (14.3%) is the most recent Massachusetts estimate in the literature, which is based on a national model that uses data from the National Medical Expenditure Survey (NMES) (Miller, 1998). The state share of Medicaid savings attributable to the enactment of the menthol cigarette restriction are calculated by multiplying the decrease in the number of Medicaid smokers due to the Massachusetts menthol cigarette restriction by the smoking-related Medicaid expenditures per Medicaid smoker and by the yearly reduced risk of disease post cessation. Predicted

probabilities derived from regression analyses using the BRFSS data are used to calculate the decrease in the number of Medicaid smokers due to the menthol cigarette restriction. The estimated smoking-related Medicaid expenditures per Medicaid smoker is calculated by dividing the smoking related Medicaid expenditures by the total number of Medicaid smokers in Massachusetts. The Massachusetts specific Medicaid expenditures attributable to smoking are inclusive of all smoking attributable healthcare costs (i.e., smoking attributable medical conditions) incurred by Medicaid recipients in Massachusetts. Smoking attributable medical conditions are cancer, emphysema, arteriosclerosis, heart attack, and stroke. The total number of Medicaid smokers is calculated by multiplying the estimated prevalence of smoking by Medicaid recipients by the number of Medicaid recipients in Massachusetts. Finally, the yearly reduced risk of disease post cessation is derived using estimates from the 1990 Surgeon General's report (Samet 1990).

Only the projected cost savings to the state government are provided below (Federal Medicaid cost savings are available upon request). Note that there may be overlap between Medicaid cost savings and savings from the other listed conditions.

All projected cost savings have been adjusted to 2021 quarter 1 dollars using the Consumer Price Index for Medical Care from the United States Bureau of Labor Statistics, with the exception of the Medicaid Cost savings which were adjusted using inflations measures from the Centers for Medicare and Medicaid Services. Future forecasted costs are estimated using the average of the differences between the annual medical inflation and annual inflation for all goods that occurred between the years 2015-2020.

Table 2a and 2b contain the 1 year, 5 year, and 10 year cost savings attributable to the Massachusetts cigarette flavor restriction.

Table 2a. Estimated Health Care Cost Savings from Select Conditions Attributed to the Massachusetts Menthol Cigarette Restriction

	1 Year Cost Savings	5 Year Cost Savings	10 Year Cost Savings
Pregnancy	$775,742	$3,984,738	$8,191,116
Heart attack and stroke	$3,298,846	$45,644,111	$113,761,026
Lung Cancer	$714,588	$21,657,348	$76,015,640
Total	$4,789,176	$71,286,197	$197,967,782

Table 2b. Estimated Medicaid Cost Saving Attributed to the Massachusetts Menthol Cigarette Restriction

	1 Year Cost Savings	5 Year Cost Savings	10 Year Cost Savings
Medicaid	$1,052,343	$15,651,763	$43,244,385

As expected, the cost savings are relatively modest in the first year after the policy but increase significantly over time. The accrued five-year cost saving for pregnancy, heart attack and stroke, lung cancer are $4.0 million, $45.6 million, and $21.7 million, respectively. The accrued five-year cost saving for Medicaid is $15.7 million.

Conclusion

Our research demonstrates that the Massachusetts restriction on flavored cigarette sales has had a significant impact on reducing smoking prevalence rates in Massachusetts. The reductions in smoking, in turn, have and will continue to reduce the incidence of tobacco-related diseases leading to lower smoking attributable healthcare expenditures. In our research

we estimate lung cancer, heart attack and stroke, pregnancy, cost savings that resulted from the Massachusetts restriction on flavored cigarette sales as well as Medicaid cost savings The one-year, five-year, and ten-year costs savings associated with birth/pregnancy complications, heart attacks and strokes, and lung cancers are $4.8 million, $71.3 million, and $198 million, respectively. Moreover, we estimated that the Massachusetts restriction on flavored cigarette sales saved the state Medicaid program $1.1 million in the first year after implementation and will save the state Medicaid program $15.7 million and $43.2 million five and ten years after implementation, respectively. For comparative purposes, $19.1 billion was spent on the Massachusetts Medicaid Program in FY2021, of which $2.96 billion was spent on newly eligible adults and $2.18 billion was spent on previously eligible adults. The state of Massachusetts spent $296 million on newly eligible adults in FY 2021 and $1.09 billion on previously eligible adults in FY2021, and the federal government paid the remainder. A first-year Medicaid cost savings of $1.1 million attributed to the flavored cigarette restriction represents approximately 0.08% of what the state of Massachusetts paid for adults as part of the Medicaid program in FY2021.

Caveats and Implications

In 2019, Massachusetts implemented a law prohibiting the sale of all flavored tobacco products, not just menthol cigarettes. Our estimates in this report quantify cost savings from restricting the sales of menthol cigarettes only. Additional healthcare cost savings would result from the prohibition of flavors on other tobacco and nicotine products. Unfortunately, existing research is not sufficient to calculate cost savings attributed to flavor policies for other tobacco and nicotine products.

Cigarette smoking has been causally linked to a large and ever-growing number of diseases. Substantial costs are associated with treating these diseases. We calculated lung cancer, myocardial infarction and stroke, pregnancy/ birth complications, and Medicaid cost savings that result from the Massachusetts restriction on flavored cigarette sales. We did not calculate costs savings for decreases in other conditions that may be impacted by smoking, such as asthma, and the MassHealth cost savings also do not account for all possible smoking-attributable conditions, therefore, our estimated health care cost savings are just a small fraction of the total health care cost savings that could be attributed to the policy.

The cost savings estimates assume that the effects of Massachusetts restriction of flavored cigarettes on smoking rates are the same across the different adult populations that were examined including: low-income adults (such as those on Medicaid), pregnant women, and older adults that are more likely to be impacted by lung cancer, stroke, and heart attacks as compared to young adults. To the extent that these groups respond more to menthol policies than adults in general, our cost saving estimates will be underestimates; the opposite will be true if these groups respond less to menthol policies. In addition, estimates used to calculate cost savings for the smoking attributable fraction and conditions associated with smoking (lung cancer, heart attack and stroke, and pregnancy complications) are based on national data from the literature and may differ slightly from estimates based on Massachusetts-specific claims data. Since Massachusetts has the highest healthcare spending per capita in the nation, partially due it its higher hospital (both inpatient and outpatient) utilization rate, it is likely that the cost savings included in this report are underestimates of true savings (Health Policy Commission, 2014).

Finally, our five- and ten-year cost savings estimates assume an underlying downward trend in cigarette smoking of two percent per year for adult smoking prevalence. This underlying downward trend allows for reductions in smoking in response to other tobacco control policies and in response to other tobacco control program activities. If the downward trend in smoking is steeper, then future reductions in smoking and its consequences in response to the restriction on menthol cigarettes will be smaller; the opposite will be true if the downward trend in smoking is flatter.

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Electronic cigarette use, related health outcomes and policy interventions in the USA: a call for research to fill evidence gaps

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ABSTRACT

The population-level health consequences of electronic cigarette (e-cigarette) use are heavily debated. This special communication provides updated evidence and identifies knowledge gaps across domains including: (1) health-related outcomes associated with e-cigarette use; (2) initiation and use of e-cigarettes among youth and young adults; (3) concurrent use of electronic and combustible cigarettes; (4) transitions from combustible cigarette use to exclusive e-cigarette use among adults who currently smoke cigarettes and (5) existing e-cigarette-related policy interventions. Literature was searched through PubMed and Medline for systematic reviews, scoping reviews, meta-analyses and primary research articles including emerging topics not covered in reviews published between 1 January 2017 and 1 January 2024. E-cigarette use is associated with several adverse acute health outcomes; there is currently insufficient longitudinal evidence to predict chronic health outcomes. Prevalence of e-cigarette use among youth is considerable and may be associated with subsequent combustible cigarette smoking. Evidence for the health and behavioural impact of dual use of e-cigarettes and combustible cigarettes is limited by imprecise measurement of exposure. Evidence on adults completely substituting combustible cigarettes for e-cigarettes is strong in clinical trials; observational studies do not show complete substitution. Finally, the effects of e-cigarette-related policy interventions to restrict e-cigarette consumption are currently limited in scope and too short-lived to draw causal inferences. Substantial evidence gaps related to the use, associated health impacts and regulation of e-cigarettes in the USA are identified, and we suggest key areas for future research to address that are crucial for informing the public health approach to e-cigarettes.

WHAT THIS PAPER ADDS

⇒ We synthesise published scientific reviews and selected studies published 2017–2024 on e-cigarette use on several outcomes.
⇒ We identify knowledge gaps in the specificity of exposure measurement, insufficient longitudinal follow-up to assess long-term health consequences, heterogeneity of cessation effects from clinical trials versus observational studies, and limited scope of studies assessing policy effects.
⇒ We provide several suggestions for necessary future research and call on the tobacco control community to address these gaps.

INTRODUCTION

Electronic cigarettes (e-cigarettes or e-cigs) are a diverse class of tobacco products that have increased in popularity in the USA and have continued to evolve rapidly since their introduction in 2007.[1] E-cigarettes are currently the second most popular tobacco products among US adults (18 years and older) after combustible cigarettes, with 4.5% reporting current (past-30 day) use in 2021[2]; among young adults (ages 18–24), however, the prevalence of e-cigarette use was as high as 18.3% in 2021.[2] Although rates of e-cigarette use among youth (ages 12–17) have declined from epidemic levels (in 2019, 27.5% of high school students reported using e-cigarettes[3] down to 10% of high school students in 2023),[4] youth e-cigarette use remains a concern.

Nearly a decade after e-cigarettes were introduced in the USA, the US Food and Drug Administration (FDA) extended its tobacco regulatory authorities to include e-cigarettes in 2016[5]; currently, many e-cigarettes remain on the market, pending decisions on Premarket Tobacco Product Applications (PMTAs).[6] As of June 2024, an estimated 6300 unique products existed on the consumer marketplace,[7] though this number may be even greater today. E-cigarettes vary in many ways (eg, nicotine content, flavour and other constituents, device power, and device type).[1] Salt-based nicotine e-cigarettes, for example, are often able to deliver higher concentrations of nicotine to the user as they are formulated in a way that may make them more palatable than free-base nicotine products.[1]

Identifying and addressing evidence gaps is crucial to informing robust public health and regulatory policies. Although several reviews and summaries have been published on e-cigarette use to date,[8–10] they have focused on specific topics (eg, health effects) or reported on data that are now several years old.[11] This special communication serves as a review of evidence from existing systematic reviews and additional emerging topics not covered in reviews that were published between January 2017 and January 2024. Here, we identify evidence gaps related to five broad domains: health-related

outcomes associated with e-cigarette use; initiation and use of e-cigarettes among youth and young adults; concurrent use of e-cigarettes and combustible cigarettes among youth and adults; transitions from combustible cigarette use to exclusive e-cigarette use among adults who currently smoke cigarettes; and existing e-cigarette-related policy interventions.

We acknowledge that the large heterogeneity in e-cigarettes within the USA presents a challenge in summarising the literature in a systematic way. Therefore, despite the potential usefulness of studies from other countries, given the considerable global variability in e-cigarette characteristics, heterogeneity in populations, and different regulatory environments, we focus here on studies conducted in the USA to limit other sources of variability.

METHODS

Literature was searched through PubMed and Medline for systematic reviews, scoping reviews, meta-analyses and select primary research articles on emerging topics not covered in reviews published starting 1 January 2017 (indicative of the maturing of e-cigarette uptake in the USA over 2011–2016 and the introduction of salt-based nicotine e-cigarettes) to 1 January 2024. We included human studies of various designs and outcomes, though preclinical evidence presented as part of systematic reviews involving humans was also reviewed to supplement the evidence on clinical health outcomes. Given this was not a meta-analysis or systematic review and the many different study designs and outcomes, we did not formally assess the risk of biases nor quality of the evidence (see online supplemental appendices A and B for more on methods).

RESULTS

Although several self-reported measures of e-cigarette use exist (eg, number of days used per month),[12] our review found that these largely capture frequency but do not adequately capture intensity. Intensity is influenced by device/e-liquid characteristics and user behaviour, is often difficult to measure in observational studies, and there is considerable evidence that individuals have difficulty recalling or estimating these aspects.[12] These measurement challenges are even more evident for 'open-system' e-cigarettes which allow the user to modify virtually every component part and/or fill them with any liquid.[13] Therefore, the following findings should be interpreted with these fundamental measurement limitations in mind.

Health outcomes associated with e-cigarette use

E-cigarette use is associated with adverse effects on organ and cellular health in humans, animals and in vitro.[14] Overall, e-cigarette use is associated with several acute adverse health outcomes, including acute respiratory effects (eg, increased shortness of breath, lung inflammation, respiratory infections, throat and mouth irritation, and asthma), cardiovascular conditions (eg, increased heart rate and blood pressure, arterial stiffness, impaired endothelial function, increased risk of myocardial infarction) and various other outcomes (eg, poisonings, risk of burns).[15–18] The association between e-cigarette use and stroke is largely confounded by prior combustible tobacco use.[19] Because the brain is not yet fully developed in youth and young adults, establishing nicotine dependence earlier in life may result in poorer mental health outcomes (eg, anxiety, depression) and neurological changes that result in greater nicotine dependence and escalation in substance use later in life.[3]

Decades of chronic e-cigarette use are needed to observe the lagged effects on several disease endpoints, so the long-term population effects of e-cigarette use are currently unclear. The long incubation period of many cancer types makes it difficult to connect e-cigarette exposure to cancer outcomes without long observation periods allowing follow-up (eg, following youth and young adults who use e-cigarettes into older adulthood). Biomarkers of exposure, collected through biological samples (eg, blood or urine), are currently being used to predict potential chronic health conditions and disease endpoints.[20 21] Based on the findings from observational studies on biomarkers,[20 21] two major conclusions can be drawn. First, concentrations of several tobacco exposure biomarkers, including tobacco specific nitrosamines, volatile organic compounds and metals, were higher in persons using e-cigarettes exclusively compared with non-users, which may translate to long-term risk of cancer, respiratory, developmental, and reproductive diseases. Second, most biomarkers were significantly lower among persons using e-cigarettes exclusively than among individuals who currently smoked cigarettes. Together, these findings suggest that use of e-cigarettes presents health risks, but the known risks for exclusive e-cigarette use among those who have formerly smoked cigarettes may be lower compared with those continuing to smoke cigarettes.[20–22]

The literature on evaluating health outcomes associated with e-cigarette use is limited in several ways. First, there is conclusive evidence that toxins emitted from e-cigarettes are highly variable and depend on device and e-liquid characteristics and user behaviour,[23] but these aspects are often inadequately captured in many of the data sources of studies reviewed here. Second, associations between e-cigarettes and health outcomes were often confounded by the strong influence of concurrent or prior combustible tobacco use. Third, existing studies are based on relatively short-term observations that preclude documenting actual endpoints for chronic diseases; no long-term toxicological/safety studies of e-cigarette use have been documented yet in humans. Fourth, given the variety of ingredients in the thousands of different products on the market, this research is exceptionally difficult to pursue in a systematic fashion; findings from various studies may not be comparable and generalisable, and compounds that are not listed on e-liquid labels have also been discovered in e-liquids.[24] Fifth, there are currently no e-cigarette-specific biomarkers of exposure and much remains unknown about the long-term health effects of inhaling other compounds found in e-liquids (eg, flavourants). Many e-cigarette flavours are also food additives and scents used in cosmetics; however, the health impact of inhaling these compounds at the levels found in e-cigarettes over time is uncertain, though there is initial evidence of pulmonary toxicological effects[14] and endothelial dysfunction.[25] Still, e-cigarette liquids involve many different combinations of chemically unstable compounds that may have novel toxicological effects.[24] Finally, most clinical biomarker studies are manufacturer funded, which could lead to publication bias.[21]

Risks of e-cigarette initiation and use among youth and young adults

Most tobacco initiation and nicotine dependence are established in adolescence, [26 27]and therefore, the vast majority of studies on initiation have focused on youth. Initiation is often motivated by curiosity and peer influence, social media marketing, perception of e-cigarettes as a less harmful and less addictive alternative to cigarettes, industry marketing targeting youth and the emergence of new and more efficient nicotine delivery systems.[28] Most relevant to youth initiation is the availability of appealing

e-cigarette flavours,[29] such as candy and dessert flavours, fruit and mint/menthol, flavours also associated with decreased harm perceptions as compared with tobacco flavours.[30] Several other e-cigarette characteristics may appeal to youth and young adults (eg, attractive colours, sleek designs, low odour/vapour levels).[28]

Youth using newer generation e-cigarettes are more likely to vape daily and show greater nicotine dependence symptoms than youth using earlier generation e-cigarettes.[31] Even low-level e-cigarette use in early adolescence may increase the risk of escalated use later, with a younger age of initiation of e-cigarette use predicting greater e-cigarette use intensity.[32] There is also emerging evidence that e-cigarette use by youth who do not currently smoke is associated with increased odds of subsequent combustible cigarette smoking initiation later in life and dual use of e-cigarettes and cigarettes.[23 33–35] Several longitudinal studies have reported associations between e-cigarette use and subsequent cigarette smoking initiation among youth who would not have initiated cigarette smoking otherwise.[35 36] However, at the same time, trends in population data do not show increases in cigarette use among youth or young adults,[37 38] and evidence suggests continued declines in combustible cigarette use are independent from the uptake of e-cigarettes among youth.[39] More methodologically rigorous studies are needed to disentangle whether the observed associations between e-cigarette uptake and changes in cigarette use at the population level are related or independent. If related, there is a need to identify whether the relationship supports replacement or substitution of e-cigarettes for combustible cigarettes among youth, a gateway hypothesis (ie, e-cigarettes lead to progression to combustible cigarette use), and/or a common liability that predicts tobacco use generally.[40]

The literature on determining the risks of e-cigarette initiation and use among youth and young adults is limited in several ways. There is currently limited evidence on whether youth who initiate e-cigarettes continue use into young adulthood. More evidence on the longitudinal trajectory of e-cigarette use, as well as the frequency and intensity of e-cigarette use (eg, escalation in use), and if and/or how youth and young adults become established dual users of e-cigarettes and other tobacco products is necessary. Finally, there is emerging evidence of increased e-cigarette initiation among young adults without a prior history of tobacco use,[41 42] but it is unclear whether youth who started e-cigarettes are continuing using in young adulthood (cohort effect) and/or whether young adults who used tobacco are starting at later ages.

Concurrent use of e-cigarettes and combustible cigarettes

There are varying definitions of concurrent use (encompassing dual/poly/multiple tobacco product use) across studies, likely contributing to heterogeneity in the measures of concurrent use and its derived variables in the existing literature.[12 43] This lack of uniform and comparable measures also makes it challenging to make strong conclusions on outcomes related to concurrent use. In the USA, approximately 3.4% of adults, 4.8% of young adults and 3.4% of youth reported currently using multiple tobacco products.[4 44] This mostly reflects the use of e-cigarettes with cigarettes or cigarillos, with nearly one-third of individuals who reported current use of tobacco products reporting use of both e-cigarettes and cigarettes, a trend increasing over time.[45]

There are a limited number of systematic reviews on this topic. Emerging evidence suggests roughly half of adults concurrently using e-cigarettes and combustible cigarettes continue doing so after a year's follow-up,[46] and another study found persistent dual use of e-cigarettes and cigarettes for multiple years.[47] While some research shows dual use may transition to exclusive e-cigarette use,[48] other evidence suggests that e-cigarette use may lead to overall greater tobacco use and an increased likelihood of sustained dual use.[46] In addition, individuals without prior tobacco product use who use e-cigarettes are more likely to initiate cigarette smoking than those individuals who do not use e-cigarettes, and individuals who formerly smoked cigarettes and currently use e-cigarettes are twice as likely to relapse to cigarette smoking than those who do not use e-cigarettes.[9 33 49–51] People concurrently using e-cigarettes and combustible cigarettes may also be exposed to more toxicants than individuals reporting exclusive cigarette use.[22]

The literature on the concurrent use of e-cigarettes and combustible cigarettes is limited in several ways. Importantly, measurement of concurrent use is limited by current measures of e-cigarette use[12] and often lacks information on how frequently individuals use each product (eg, ratio of e-cigarette consumption to cigarettes) and for how long individuals continue to use both products. Furthermore, concurrent use remains largely understudied among all populations, including the identification of demographic and other relevant characteristics (eg, situational contexts) that predict multiple tobacco product use.[45]

Transitions from combustible cigarette use to exclusive e-cigarette use among adults who currently smoke

A review of observational studies in 'real-world' population-based samples found that use of e-cigarettes as consumer products is not associated with substitution of e-cigarettes for combustible cigarette smoking.[52] These findings were consistent even among those who reported they were motivated to quit smoking combustible cigarettes. However, daily e-cigarette use was associated more with quitting combustible cigarettes than less-than-daily use.[52]

Research in clinical trials shows high-certainty evidence that providing nicotine-containing e-cigarettes was as effective in promoting cessation from combustible cigarettes as some FDA-approved cessation medications.[53] Furthermore, prescribed e-cigarette use was associated with greater combustible cigarette cessation than nicotine replacement therapies and non-nicotine e-cigarettes, with estimates of 5–8 additional quitters per 100 persons[53] (see also Ashour and Wang*et al*[10 52] for review). There is, however, evidence that individuals who used e-cigarettes compared with FDA-approved cessation medications to quit smoking combustible cigarettes often did not discontinue using all tobacco products completely; further, individuals may be more prone to cigarette smoking relapse than if they had used FDA-approved cessation medications, given their continued dependence on nicotine.[53]

The literature on transitions from combustible cigarette use to exclusive e-cigarette use among adults is limited in several ways. Differences in study designs and contexts between observational and clinical studies limit comparability and generalisability of the results from these two types of studies. For example, clinical trials often test specific e-cigarette product(s), whereas observational studies involve collapsing outcomes across many different e-cigarette products. In addition, data from clinical trials can be claimed as causal, whereas observational studies are primarily associational.

Existing e-cigarette-related policy interventions

Comprehensive tobacco control policies (eg, combinations of taxation/price increases and social programmes) have proven effective in reducing the prevalence of tobacco use worldwide.[54] Approaches for regulating e-cigarettes in the USA to date have

been mostly at the state and local level; many of these have been relatively narrow in scope, resulting in a negligible impact on reducing e-cigarette use among the younger population and accompanied by some unintended consequences (see O'Connell and Kephart and Reiter *et al*,[55 56] for further discussion). As a result, much of the evaluation of US policies regulating e-cigarettes is ongoing and there are few systematic reviews.

Though perhaps the most widespread intervention, there is currently insufficient evidence that minimum legal sales age (MLSA) laws alone have reduced youth e-cigarette use.[56] Some studies found decreases in youth e-cigarette use,[57 58] while others reported that these laws were associated with increases in e-cigarette use[59] and initial increases in cigarette smoking[58] among youth. Flavour restrictions have been implemented at the federal, state and local levels with some success in reducing youth e-cigarette use.[56] At the federal level, the US FDA announced in February 2020 increased enforcement action against certain unauthorised flavoured cartridge-based e-cigarettes. This action was associated with increased e-cigarette quit intentions and cessation among youth in particular,[60 61] and initial decreased flavoured e-cigarette sales,[61 62] but also switching to other exempt e-cigarettes (eg, disposable e-cigarettes), other flavours (eg, from mint to menthol), and temporarily to combustible tobacco products.[60 63 64] A number of states (eg, California, Massachusetts) and local jurisdictions have also adopted restrictions on the sale of flavoured e-cigarettes[65]; these have been associated with reductions in e-cigarette sales at varying degrees depending on retailer compliance and enforcement.[66 67]

In September 2020, the FDA initiated a substantive review of e-cigarette PMTAs, a regulatory pathway required to market new tobacco products as consumer products. As of August 2024, 34 e-cigarette products have been authorised for legal marketing and hundreds of e-cigarettes have been issued marketing denial orders; still, the market includes thousands of products that are being sold illegally.[68 69]

Limitations to the e-cigarette-related policy interventions literature have been that most efforts are piecemeal; several unintended consequences are likely a result of isolated policy initiatives that did not account for the tobacco landscape and compensatory behaviours. Furthermore, while policies have been developing or considered, e-cigarettes have continued to evolve rapidly.

Conclusions and recommendations for future research

Based on the status of the current scientific literature on e-cigarettes, we have made several observations. First, current measures of e-cigarette use vary widely and lack specificity across studies reviewed here. E-cigarette products are most often treated as a homogenous class, and product specifics (eg, device model/type, nicotine concentration) and use intensity are often not characterised. This impacts the generalisability and time sensitivity of conclusions in every area. Second, the long-term health consequences of e-cigarette use, trajectories of initiation, dual-use and transitions away from combustible cigarettes, and the impact of e-cigarette policy interventions and regulations on e-cigarette use at the population level all have large knowledge gaps that present significant challenges for the public health community, including substantial regulation lag.

Given these many unknowns, we make the following set of recommendations for future research:

1. E-cigarettes are a very polarising topic within the tobacco control community, and continued efforts must be made to identify and reduce bias in scientific research and conclusions. One of the most obvious is commercial interest in the outcomes of studies. For example, we noted that most clinical biomarker studies were manufacturer funded.[21] Still, strong ideological differences between research groups too may bias studies and conclusions. There is an urgent need to encourage more collaborative research from those holding different views on the potential public health impacts of e-cigarettes. For example, resolving disputed research questions via an adversarial collaborative approach, rooted in an open science framework, can encourage researchers to agree on critical research questions and the data and statistical analyses required to address them.[70]
2. Continued efforts should be made to characterise e-cigarette use intensity in studies. This is especially challenging given the substantial heterogeneity of e-cigarettes as products and how e-cigarette use tends to occur intermittently in many 'sessions' throughout a day.[12] One possibility is for surveys to ask individuals to upload images of the products they use and/or provide videos of themselves using the products to allow researchers to estimate aspects of user behaviour (eg, puff duration), as well as use methods like ecological momentary assessment to reduce recall bias.[71]
3. The extreme heterogeneity of e-cigarette products and user behaviour (including current or former multiple tobacco product use) presents significant challenges in understanding chronic health and disease risks of e-cigarette use. The health impact of inhaling flavourants and other e-liquid compounds at the levels found in e-cigarettes over time is unknown, and the many different compounds in different e-cigarettes may have novel toxicological effects. Continued exposure studies (including preclinical) and identifying biomarkers unique to e-cigarette use are necessary steps to address these gaps.
4. Many measures of concurrent use do not precisely capture the ratio of cigarette to e-cigarette use. Future research should more precisely quantify dual and poly tobacco use, as understanding these use patterns has health and regulatory implications. Finally, more longitudinal research is necessary to understand the persistence of dual use status, as well as sociodemographic and environmental/economic factors underlying dual (and poly) use.
5. Although it appears that the findings from observational studies and clinical trials are conflicting, each study type could inform different regulatory pathways (ie, the FDA's Center for Tobacco Products (CTP) regulates e-cigarettes as consumer products whereas the FDA's Center for Drug Evaluation and Research regulates cessation medications) and which route(s) may have the most optimal public health benefit. Pragmatic trials testing if interventions in clinical trials can translate into clinical practice and/or what components of clinical interventions are crucial in the natural environment to obtain similar results are needed. Similarly, e-cigarettes and their role in transitioning people from combustible cigarettes when used as consumer products, without prescription and professional supervision, should continue to be studied through carefully controlled observations.
6. Flavour restrictions have been associated with some reductions in e-cigarette sales at the state and local level; however, many stand-alone policy interventions have thus far proven ineffective. Perhaps the most widespread intervention, minimum age restrictions, have alone failed to reduce youth e-cigarette use[56] but may be more effective if combined with other initiatives. Comprehensive policies (eg, involving taxation, price increases and social programmes) have historically done more to reduce tobacco consumption than any strategy

alone. Such policies applied to e-cigarettes may be explored via population-level simulation models to aid in instilling synergy in tobacco control policies that address the current tobacco marketplace as a whole. Finally, it may also be beneficial to consider the successes and failures of countries outside of the USA in regulating e-cigarettes; though many differences exist in the regulatory environments and populations, considering the approaches of other countries may be at least somewhat instructive. For example, Australia's experiment with prescription e-cigarettes may provide lessons on intended and unintended consequences.[72] Similarly, considering research on the effectiveness of different policies towards illicit drugs may also prove instructive, especially regarding e-cigarette restrictions.[73]

There are several limitations to our analyses that are worth noting here. First, there is substantial heterogeneity in e-cigarette products and user behaviour. Treating these products as a single class of products, as most of the literature reviewed does, is suboptimal and results in an absence of product-specific outcomes. Second, although we tried to acknowledge limitations of the reviewed studies, there were many different measures, outcomes and study designs, all of which can be biased by poor measurement of exposures and unmeasured confounders. Third, the conclusions drawn from published research may correspond to products that are outdated, especially given the ever-changing nature of these products and the market.

CONCLUSIONS

Substantial knowledge gaps exist regarding fundamental aspects of e-cigarette use, including precise measurement of e-cigarette product characteristics and behavioural use patterns and remaining unknowns regarding the long-term health consequences associated with e-cigarette use. It is, therefore, crucial that the tobacco research community addresses these gaps with scientific evidence free from biases to inform policy and advise the public on how to make informed decisions about e-cigarette use.

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Invalidity of an Oft-Cited Estimate of the Relative Harms of Electronic Cigarettes

In July 2013, a group of 12 experts in decision science, medicine, pharmacology, psychology, public health policy, and toxicology rated the relative harm of 12 nicotine-containing products by using 14 criteria addressing harms to self and others.[1] The group concluded that combustible cigarettes were the most harmful and that electronic nicotine delivery systems (electronic cigarettes or e-cigarettes) were substantially less harmful than combustible cigarettes. These results have been characterized and repeated in the popular media as e-cigarettes are "95% less risky" or "95% less harmful" than combustible cigarettes. However, as the authors noted in a sweeping statement regarding the shortcomings of their own work, "A limitation of this study is the lack of hard evidence for the harms of most products on most of the criteria."[1(p224)]

Despite this lack of hard evidence, Public Health England and the Royal College of Physicians endorsed and publicized the "95% less harmful" assertion.[2,3] Senior Public Health England staff emphasized the "evidence" underlying the 95% figure, despite the evidence being lacking. Much has been written about the dubious validity of the "95% less harmful" estimate in 2014 to 2016, especially about the paucity of research on the health effects of e-cigarettes available in 2013. After six years of e-cigarette–focused research, which has yielded a growing body of hard evidence regarding harm (see Appendix A, available as a supplement to the online version of this article at http://www.ajph.org, for a nonexhaustive list), the time has come to re-examine that estimate.

TODAY'S ELECTRONIC CIGARETTES ARE DIFFERENT

There is ample evidence that the range of e-cigarette products available today is very different from that in July 2013. The differences are such that, even if the 2013 estimate was valid then, it can no longer apply today. For example, in addition to using different materials and more numerous heating coils, many e-cigarettes today can attain power output that exceeds that of most over-the-counter 2013 models by 10 to 20 times (i.e., up to and sometimes exceeding 200 watts). Greater power increases the potential harms of e-cigarette use because more aerosol is produced that exposes users to increased levels of nicotine and other toxicants. It also increases bystander exposure to any harmful aerosol constituents because users exhale more aerosol. In addition, greater power increases the potential for malfunction (e.g., the device exploding), which could harm users and bystanders.

Also, e-cigarette liquids have changed considerably from 2013, with widespread availability of thousands of flavors that use chemicals "generally recognized as safe" to eat but with unknown pulmonary toxicity. Perhaps the most striking change has been the pervasive marketing of liquids with protonated nicotine.[4] Protonated nicotine ("nicotine salt") is made by adding an acid to free-base nicotine, thus introducing another potential toxicant that was rare in 2013. Relative to free-base nicotine, aerosolized protonated liquid is less aversive to inhale, allowing users to increase the nicotine concentration of the liquid and likely increase their own nicotine dependence. Protonated nicotine e-cigarette liquids are available today in concentrations greater than 60 milligrams per milliliter, and these liquids have become very popular, sparking a "nicotine arms race."[4]

ELECTRONIC CIGARETTES CAUSE HARM TO CELLS

There is ample evidence, unavailable in 2013, that e-cigarette aerosols contain toxicants and that these aerosols are harmful to living cells in vitro and in vivo. For example, thermal degradation of e-cigarette liquid constituents can produce volatile aldehydes, which, at concentrations generated by e-cigarettes, display a variety of cardiorespiratory toxic effects. E-cigarettes can produce carcinogenic furans in addition to other toxicants such as chloropropanols. Even at room temperature, e-cigarette liquids can be unstable, producing irritating acetal compounds carried over into the aerosol. Numerous studies demonstrate that cell function is compromised following exposure to e-cigarette

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aerosol. Similarly, animals that are exposed to e-cigarette aerosols show clear indication of adverse consequences, including in models related to cardiovascular disease.

ELECTRONIC CIGARETTES HARM USERS

Recent evidence reveals that e-cigarette users show evidence of harm. For example, in a sample of healthy young occasional cigarette smokers who used an e-cigarette with or without nicotine, airway epithelial injury was observed in both conditions, with the authors concluding, "Thus, [e-cigarette] aerosol constituents could injure the respiratory system or worsen preexisting lung disease through a variety of mechanisms."[5(pL716)] Consistent with this report, wheezing, a symptom of potential respiratory disease, has been associated with e-cigarette use. E-cigarette use increases heart rate, blood pressure, and platelet activation, and decreases flow-mediated dilation and heart rate variability, effects that are prognostic of long-term cardiovascular risk. Indeed, a preliminary report indicates that e-cigarette users may be at increased risk for myocardial infarction and coronary artery disease.[6]

ELECTRONIC CIGARETTES INCREASE SMOKING RISK

Since 2013, numerous surveys have demonstrated that e-cigarette use is increasing among individuals who previously were naïve to nicotine and that these individuals are at increased risk for initiation of combustible cigarette smoking. As the US National Academies of Sciences, Engineering, and Medicine concluded, "There is substantial evidence that [e-cigarette] use increases risk of ever using combustible tobacco cigarettes among youth and young adults."[7(p532)] To the extent that initial e-cigarette use is a causal factor in subsequent combustible tobacco smoking for an individual who would have otherwise never initiated smoking, e-cigarette use could be considered to be as harmful as tobacco smoking for that individual.

ELECTRONIC CIGARETTE AEROSOL IS NOT HARMLESS

Differences in toxicant content between e-cigarette aerosol and cigarette smoke, by themselves, cannot convey lesser lethality because toxicity depends upon both the extent and mode of use. For example, propylene glycol (PG) is one of the primary constituents of e-cigarette aerosol and is generally recognized as safe when eaten but, when injected intravenously over a period of days, is toxic. E-cigarette aerosols containing propylene glycol and vegetable glycerin, another common constituent, cause inflammation in human lungs, suggesting differing safety profiles for inhaled versus ingested propylene glycol and vegetable glycerin. Furthermore, as the toxicants in e-cigarette aerosol sometimes differ from cigarette smoke, so might any resulting e-cigarette–caused disease states. There is little doubt that exclusive e-cigarette users are unlikely to die from lung cancer that is caused by carcinogenic tobacco-specific nitrosamines or polycyclic aromatic hydrocarbons, toxicants largely absent from e-cigarette aerosols. What diseases they may die of—and if their deaths are hastened by their e-cigarette use—will be part of the much-needed evidence base upon which valid risk estimates can be built.

CONCLUSIONS

In sum, a 2013 evidence-lacking estimate of the harm of e-cigarettes relative to combustible cigarettes has been cited often. However, since 2013, e-cigarette devices and liquids have changed. Evidence of potential harm has accumulated. Therefore, the evidence-lacking estimate derived in 2013 cannot be valid today and should not be relied upon further. Future estimates of the harm of e-cigarettes should be based on the evidence that is now available and revised accordingly as more evidence accrues.

CALL TO ACTION

The "95% safer" estimate is a "factoid": unreliable information repeated so often that it becomes accepted as fact. Public health practitioners, scientists, and physicians should expose the fragile status of the factoid emphatically by highlighting its unreliable provenance and its lack of validity today, noting the many changes in e-cigarette devices and liquids, the accumulation of evidence of potential harm, the increased prevalence of use, and the growing evidence that e-cigarette use is associated with subsequent cigarette smoking. AJPH

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CONFLICTS OF INTERESTS
T. Eissenberg and A. Shihadeh are paid consultants in litigation against the tobacco industry and are named on a patent for a device that measures the puffing behavior of electronic cigarette users. In addition, as of September 2019, T. Eissenberg is a consultant in litigation against the electronic cigarette industry. S. Jordt reports receiving personal fees from Hydra Biosciences LLC and Sanofi SA and nonfinancial support from GlaxoSmithKline Pharmaceuticals outside the submitted work.

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