Circulation

AHA PRESIDENTIAL ADVISORY

New and Emerging Tobacco Products and the Nicotine Endgame: The Role of Robust Regulation and Comprehensive Tobacco Control and Prevention

A Presidential Advisory From the American Heart Association

ABSTRACT: The advent of new tobacco products such as electronic cigarettes and the dramatic rise in their use, especially by adolescents and young adults, are significant public health concerns. Electronic cigarettes have become the most popular tobacco products for youth and adolescents in the United States and are attracting youth to new avenues for nicotine addiction. Although these products may have benefit by helping some smokers quit or to move to a less harmful product, the long-term health effects of these products and the net public health effect associated with their use remain unclear and widely debated. There is increasing concern that the use of newer tobacco products may catalyze transition to the use of other tobacco products or recreational drugs, particularly in young adults. Therefore, there is urgent need for robust US Food and Drug Administration regulation of all tobacco products to avoid the significant economic and population health consequences of continued tobacco use. Although the American Heart Association acknowledges that the ultimate endgame would be an end to all tobacco and nicotine addiction in the United States, it supports first minimizing the use of all combustible tobacco products while ensuring that other products do not addict the next generation of youth and adolescents. The endgame strategy needs to be coordinated with the long-standing, evidence-based tobacco control strategies that have significantly reduced tobacco use and initiation in the United States.

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In the past few decades, the rates of cigarette smoking have steadily declined in the United States and are now at historic lows. However, the burden of combustible tobacco use in the United States remains high, especially in vulnerable populations. Cigarette smoking claims ≈480 000 lives prematurely every year.[1] The advent of new tobacco products such as electronic cigarettes (e-cigarettes) and the dramatic rise in their use, especially by adolescents and young adults, are of significant concern. Although these products may benefit by helping some smokers to quit or to move to a less harmful product, the long-term health effects of these products and the net public health effect associated with their use remain unclear and widely debated. There is increasing concern that the use of these products may catalyze transition to the use of other tobacco products or recreational drugs, particularly in young adults. This trend is particularly concerning because it is unfolding at a time when the rates of cardiovascular disease mortality, which have been steadily decreasing since the 1970s, have slowed down and may even be increasing in some population groups.[2] With this background, there is urgent need for robust US Food and Drug Administration (FDA) regulation of tobacco products to avoid the significant economic and population health consequences of continued tobacco use. New tobacco products are attracting youth to different avenues for nicotine addiction.

This document describes the changing patterns of tobacco use in the United States, the latest science on e-cigarettes and other new and emerging tobacco products, and the disturbing rise in the use of and access to these new modalities of nicotine delivery by youth and other vulnerable populations. This article also describes the population health implications of tobacco regulation and control, prevention efforts, provider and patient education, and comprehensive cessation therapies. This advisory helps to position the American Heart Association (AHA) toward achieving the ultimate end to tobacco and nicotine addiction in the United States. Although the AHA acknowledges that the ultimate endgame would be an end to all tobacco and nicotine addiction in the United States, it supports first minimizing the use of all combustible tobacco products while ensuring that other products do not addict the next generation of youth and adolescents. Table 1 provides a summary of the AHA policy position described here.

CURRENT USE PATTERNS OF E-CIGARETTES AND OTHER TOBACCO PRODUCTS IN THE UNITED STATES

Table 2 summarizes the major national surveillance systems used to capture tobacco use patterns and prevalence in the United States for youth and adults.

Patterns and Prevalence of Use Among Adolescents

Nearly 90% of smokers first try a tobacco product by 18 years of age. Experimentation with combustible cigarettes by adolescents, even on an infrequent basis, is associated with an established smoking habit as an adult.[5] In the 2011 to 2018 National Youth Tobacco Survey,[6] data show a dramatic increase in e-cigarette use in adolescent initiation. Current e-cigarette use in high school students increased from 1.5% (220 000 students) in 2011 to 20.8% (3.1 million students) in 2018 ($P<0.001$). Current use of any flavored e-cigarettes increased among current e-cigarette users (from 60.9% to 67.8%; $P=0.02$); current use of menthol- or mint-flavored e-cigarettes increased among all current e-cigarette users (from 42.3% to 51.2%; $P=0.04$) and current exclusive e-cigarette users (from 21.4% to 38.1%; $P=0.002$). Middle school students' use of e-cigarettes increased from 0.6% in 2011 (60 000 students) to 4.9% (570 000 students) in 2018 ($P<0.001$). During 2017 to 2018 alone, e-cigarette use rose by 78% in high school students and 48% in middle school students.

The Monitoring the Future Survey[7] releases annual results, surveying >40 000 students in 8th, 10th, and 12th grades. In 2018, e-cigarette use nearly doubled in high school students, from 11% in the previous year to 21% in 2018; in 10th graders, the increase was from 8.2% to 16.1%. This is the largest 1-year increase seen for any substance in the history of the survey. Marijuana vaping for 12th graders increased from 9.5% in 2017 to 13.1% in 2018.

The 2011 to 2017 National Youth Tobacco Survey data[8] showed that the next most popular tobacco products among high school students were cigars (7.7%), cigarettes (7.6%), smokeless tobacco (5.5%), hookah (3.3%), pipe tobacco (0.8%), and bidis (0.7%).[8] e-Cigarettes have now become the most popular tobacco product among adolescents in the United States.

Patterns and Prevalence of Use Among Adults

Compared with e-cigarette use in adolescents, the patterns of adult use are more complex, as is the health impact assessment of these changing patterns. In particular, the frequency of dual use of traditional combustible cigarettes and e-cigarettes, as well as patterns of poly-use of multiple tobacco products, requires more nuanced interpretation. Table 3 summarizes the current patterns of tobacco product use in different subgroups based on 2014 to 2016 National Health Interview Survey data. The dominant pattern of e-cigarette use in adults is dual use (current use of both combustible cigarettes and e-cigarettes).[10] Some

Table 1. Summary of the AHA's Positions on Newer Tobacco Product Regulation and the Endgame

Issue	AHA Position
The endgame	Although the AHA acknowledges that the ultimate endgame would be an end to all tobacco and nicotine addiction in the United States, the association supports first ending the use of all combustible tobacco products while ensuring that other products do not addict the next generation of youth and adolescents and achieving a realistic goal of getting to ≤5% tobacco use prevalence.
Vulnerable populations	Tobacco control and prevention efforts and regulation should be targeted and tailored to at-risk populations, including youth and adolescents, those who live in rural areas, racial and ethnic groups with high tobacco use, those with mental health conditions, those with less education and low income, and those who identify as LGBTQ.
FDA regulation of newer tobacco products	
Nicotine reduction strategy	The AHA supports lowering nicotine concentrations in all combustible tobacco products to reduce tobacco-related mortality. Research favors doing this quickly rather than a stepwise reduction over time. This will likely be most successful if nicotine is available in noncombustible forms as nicotine replacement therapy to reduce withdrawal symptoms as smokers adjust. Any nicotine reduction strategy should consider the relationship with switching and dual use. In addition, FDA action should be taken to ensure that further changes are not made by industry to reduced-nicotine products to retain their appeal such as altering other ingredients or flavors. Over the long term, subsequent research is needed to determine whether nicotine should be reduced in noncombustible products as a strategy to end all nicotine addiction in the United States.
Flavorings	The removal of all characterizing flavors from all tobacco products is essential for reducing their appeal to youth. Controversy arises because, although there is no experimental evidence to support the view that flavors help adults switch from combustible to noncombustible tobacco products or quit tobacco altogether, individual reports suggest that for some adults flavors are appealing. However, maintaining flavors to attract adult smokers increases the risk of these products becoming available to youth and young adults. Additional research is needed to determine how best to balance the need to reduce the appeal of flavorings to youths with the potential that flavorings may facilitate smoking cessation among adult smokers. Recognizing that this is a difficult decision, the AHA's position at this time is that the FDA should ban the use of all characterizing flavors other than tobacco in all tobacco products. Emerging evidence also suggests that sweeteners in tobacco products may play a role in increasing the appeal of the product; this evidence suggests that the FDA should also consider the inclusion of high-intensity sweeteners in its definition of characterizing flavors. This should be accompanied by research aimed at studying the role of flavors in enhancing adult cessation and the toxicity of flavors. This research and surveillance will be required to determine any negative effects on the efficacy of cessation, with new approaches developed to counteract these if found.
Market review	The AHA supports restricting the marketing of JUUL and other similar e-cigarettes until their health risks to youth and adolescent users are clearly assessed and their potential benefits and harms in promoting tobacco cessation among adults are better understood. The agency should suspend internet sales of these products until adequate mechanisms and rules for age verification are established. In addition, the ban on underage sales by retailers should be effectively enforced, and the FDA should require that these products be submitted for review sooner. The FDA should reverse its 2017 decision that allows e-cigarettes that were already on the market as of August 8, 2016, to stay on the market until at least 2022 without filing applications and undergoing a public health review by the FDA.
Newer tobacco products and cessation	Further research and legal analysis are needed to facilitate e-cigarettes being regulated and sold only as FDA-approved cessation products, and the Center for Drug Evaluation and Research needs to reduce existing barriers to accomplish this work. Rigorous randomized controlled trials are critical to evaluate the effectiveness of e-cigarettes as cessation devices. Significant public health questions need to be answered about the level of nicotine in noncombustible products that optimally helps dependent smokers quit all tobacco use while developing robust regulation that protects against youth access and initiation, reinitiation by former smokers, and initiation by never smokers. The AHA encourages the Center for Drug Evaluation and Research to work in close collaboration with the Center for Tobacco Products to develop e-cigarette regulation.
Cigars, cigarillos, and little cigars	These tobacco products, including premium cigars, should continue to be subject to robust FDA regulation. Regulation for cigars, cigarillos, and little cigars should restrict flavorings and sales to minors, develop product standards and graphic warnings, and limit their marketing and advertising. These products should also be included in all tobacco excise taxes.
Marketing and advertising	The AHA supports robust FDA regulation restricting all tobacco marketing and advertising to youth and vulnerable populations, including the use of television, radio, and print ads and commercials; celebrity endorsement; movie placements; price promotions; free sampling; branded events; and nontobacco merchandise.
Warning labels	The AHA supports the FDA requiring immediate implementation of impactful, evidence-based graphic warning labels on all tobacco products in the United States.
Coordinating global efforts	The AHA supports coordinated, collaborative tobacco control and prevention efforts between dedicated global health networks, the World Health Organization, governmental agencies, individuals, and nongovernmental organizations around a unified policy framework that minimizes the devastating impact of tobacco product use in vulnerable populations around the world. Robust regulation in the United States should not increase the export of these deleterious products to other parts of the globe, especially low- and middle- income countries.
Illicit market	The FDA and other government agencies can and should develop and strengthen enforcement efforts to minimize the effects of illicit markets.
Healthcare providers and screening for and counseling on the newer tobacco products	Healthcare providers should screen for all tobacco product use and counsel cessation. Young patients should be screened for newer tobacco use and substance abuse and counseled on the dangers of these products. A previous AHA policy statement elucidated how clinicians should advise adult patients about cessation.[3] Youth substance use prevention programs should target reduction of e-cigarette and cigar use. In the intersection between the healthcare system and public health, there is a need to develop public health messages that accurately convey the scientific data on the potential harm of newer tobacco products and differentiate the absolute from the relative harm of these products compared with combustible tobacco.[4]

(*Continued*)

Table 1. Continued

Issue	AHA Position
Public education	There is significant need for robust public education about these newer tobacco products and the harms they pose, especially for youth and adolescents.
Tobacco control and prevention strategies that need to be adapted and coordinated with the endgame strategy	
Taxation	Tobacco excise taxes should be highest for combustible products; FDA-approved modified-risk products would be taxed at a lower rate; and tobacco cessation aids would not be taxed at all.
Comprehensive smoke-free air laws	Smoke-free laws should explicitly include aerosolized, alternative nicotine delivery systems and combustible products in comprehensive smoke-free air laws to ensure that there is no passive exposure to any harmful constituent byproducts or risk of renormalizing tobacco use. Expanding existing comprehensive smoke-free air laws to include e-cigarettes should be done with caution to avoid weakening the existing statute.
Tobacco 21	The AHA advocates for Tobacco 21 laws that incorporate all tobacco products to minimize youth and adolescent initiation.
Access to comprehensive cessation therapies	Users of newer tobacco products should be offered all comprehensive tobacco cessation therapies, including counseling and pharmacotherapy. Anyone using tobacco products should have access to comprehensive cessation services with no copay.
Sales restrictions in pharmacies and health-related institutions	All tobacco products, including e-cigarettes and other newer tobacco products, should not be sold at pharmacies or other health-related institutions unless they are regulated as nicotine replacement therapy.

Additional resources on these topics may be found on the AHA's policy research website at https://www.heart.org/en/about-us/policy-research. AHA indicates American Heart Association; e-cigarette, electronic cigarette; FDA, US Food and Drug Administration; and LGBTQ, lesbian, gay, bisexual, transgender, and queer.

studies have suggested that the high prevalence of e-cigarette use in current smokers might indicate potential health benefit because these users may be using e-cigarettes in place of combustible cigarettes or as part of a smoking cessation effort.[11] However, others have claimed that dual use might make smoking cessation more difficult by providing a new nicotine delivery system that may be more socially acceptable, which could facilitate continued addiction and increased use.[12]

Table 2. Important Publicly Available Data Sets on Tobacco Use

Surveillance System	Description
National Youth Tobacco Survey (NYTS) (https://www.cdc.gov/tobacco/data_statistics/surveys/nyts/index.htm)	A nationally representative data set of students in grades 6–12. The latest version has information on tobacco from ≈17 000 individuals. The NYTS is a cross-sectional, voluntary, school-based, self-administered pencil-and-paper questionnaire survey of US middle and high school students.
Population Assessment of Tobacco and Health (PATH) (https://pathstudyinfo.nih.gov/UI/HomeMobile.aspx)	PATH has one of the most well-established cohorts with extensive phenotyping and categorization of tobacco use in youth and adults. The baseline visit was in 2013–2014, and data on 2 follow-up visits are now publicly available. PATH has an in-person visit component with blood and urine specimen collection.
Youth Risk Behavioral Surveillance System (YRBSS) (https://www.cdc.gov/healthyyouth/data/yrbs/index.htm)	This telephone survey monitors 6 categories of health-related behaviors that contribute to the leading causes of death and disability among youth and adults, including tobacco use. The national survey, conducted by the Centers for Disease Control and Prevention, provides data representative of students in grades 9–12 in public and private schools in the United States. The latest version (2017) collected data on e-cigarette use from ≈10 000 individuals.
Monitoring the Future Survey (http://monitoringthefuture.org/)	This annual survey of the behaviors, attitudes, and values of ≈50 000 students in grades 8, 10, and 12 is funded by the National Institute on Drug Abuse. The survey includes questions on adolescent tobacco use.
Behavioral Risk Factor Surveillance System (BRFSS) (https://www.cdc.gov/brfss/index.html)	The BRFSS is the most extensive telephone-based survey with 500 000 adult participants and a wide range of collected data on health behaviors and healthcare access. The Centers for Disease Control and Prevention conducts the BRFSS in collaboration with the individual US states and territories to produce state-level data on health measures. BRFSS 2016 is the iteration with questions on e-cigarette use, including ever use and intensity of use in past 30 d (daily, occasional, former).
National Health and Nutrition Examination Survey (NHANES) (https://www.cdc.gov/nchs/nhanes/index.htm)	NHANES collects data on tobacco use among both adolescents and adults, including almost 800 participants from the 2015–2016 examination cycle who were <18 y of age. The strength of NHANES, in additional to its population representation, is its in-person component with presence of laboratory results and a physical examination.
National Health Interview Survey (NHIS) (https://www.cdc.gov/nchs/nhis/index.htm)	The NHIS is an annual study conducted by the Centers for Disease Control and Prevention in which tens of thousands of adult Americans are interviewed about their health- and illness-related experiences. This is one of the first data sets to report e-cigarette use, which began in 2014, providing multiple years (from 2014–2017) of e-cigarette data. Thus, at present, this is the best data set for epidemiological trend analyses.
National Adult Tobacco Survey (NATS) (https://www.cdc.gov/tobacco/data_statistics/surveys/nats/index.htm)	One of the most extensive surveys on tobacco products in adults. Although it is not as large as BRFSS, it has more questions about other tobacco use such as cigars, nicotine replacement therapy, and pipe, in addition to questions about e-cigarette use.

e-Cigarette indicates electronic cigarette.

Table 3. Estimated Prevalence of Current Tobacco Use Among Working Adults From the NHIS, United States, 2014 to 2016[9]

Population Subgroup	Cigarettes, %	e-Cigarettes, %	Dual Use, %
Sex			
Male	16.9	4.3	6.5
Female	13.7	2.8	2.6
Age, y			
18–34	16.3	4.8	6.0
35–54	16.2	3.5	4.4
>55	12.4	1.9	2.8
Education			
Less than high school, GED	23.6	4.6	6.2
More than high school	11.7	3.2	3.9
Race			
Black, non-Hispanic	14.9	2.2	3.7
White, non-Hispanic	16.9	4.2	5.5
Hispanic	11.2	2.1	2.3
Other	11.8	3.4	3.1
Health insurance			
Not insured	27.5	5.5	7.7
Insured	13.8	3.3	4.2
Poverty index			
Poor	22.9	4.4	6.1
Near poor	22.9	5.1	6.2
Not poor	13.4	3.3	4.3
US Census region			
Northeast	14.1	2.5	3.3
Midwest	18.8	3.9	5.5
South	16.0	3.8	4.9
West	12.1	3.9	4.3

e-Cigarette indicates electronic cigarette; GED, general education diploma; and NHIS, National Health Interview Survey.

Although initial studies indicated that the prevalence of e-cigarette use among adult never smokers was negligible, these estimates have been contradicted by more recent data. Using Behavioral Risk Factor Surveillance System data, Mirbolouk et al[10] estimated that 2 million US adults without a history of smoking were current e-cigarette users in 2016, suggesting a significant uptake of e-cigarettes by never smokers. Further analysis of the 2016 survey showed that ≈60% (1.2 million) of the sole e-cigarette–using population was <25 years of age.[10] These data are consistent with the results of almost all other studies on the prevalence of e-cigarette use in adults, which showed that the prevalence of e-cigarette use was highest among younger adults (Figure). The high prevalence of e-cigarette use among young adults raises the same concerns as e-cigarette use among adolescents, that is, that they are becoming addicted to nicotine and that there may be a potential transition to combustible tobacco products with established risks and persistent dual use.

THE NEWEST TOBACCO PRODUCTS

e-Cigarettes

Several types of e-cigarettes are now available in the marketplace. The design, chemical constituents, health effects, safety, and harm of e-cigarettes were reviewed by the 2014 AHA policy statement.[3] Since that review, not only have the initiation rates of e-cigarettes continued to increase, but the devices have also been increasingly used for a number of alternative behaviors such as smoke tricks, creating novel cloud shapes, or dripping (dripping the e-liquids directly onto a heated coil)[13] and for inhaling other substances, including but not limited to marijuana.[14] A 2017 cross-sectional, case-control study of habitual e-cigarette users showed higher sympathetic predominance and oxidative stress, both of which are associated with higher cardiovascular risk.[15] A 2016 clinical study comparing smokers and exclusive e-cigarette users showed that e-cigarette vapor was associated with lower expression of a large number of immune-related genes, consistent with immune suppression in the nasal mucosa, similar to cigarette users.[16] In animal models, researchers have demonstrated impaired cardiovascular function associated with long-term exposure to e-cigarette vapor.[17] A 2018 cross-sectional study using 2014 National Health Interview Survey data showed that daily e-cigarette use was independently associated with higher odds of having a myocardial infarction compared with former or someday e-cigarette use.[18] However, the cross-sectional study design could not establish a causal relationship or determine which event occurred first (ie, heart attack or start of e-cigarette use), and the findings have been disputed.[19] Additional research is needed and is ongoing to assess the comparative effects of short- and long-term e-cigarette exposure and continued tobacco exposure on cardiovascular disease outcomes.

The popularity of e-cigarettes among youth has been attributed to their appeal[20]; however, their increasing use could also be linked to widespread marketing and advertisement as safer, cleaner products. A 2014 study showed that almost 70% of middle and high school students were exposed to e-cigarette advertisements in retail stores, on the internet, on television, in movies, in newspapers, and in magazines.[21] The use of e-cigarettes among youth seems to be nearly exclusively for recreational purposes because youth use does not seem to be associated with quit attempts or quit contemplation.[22] Recent evidence also indicates that youth

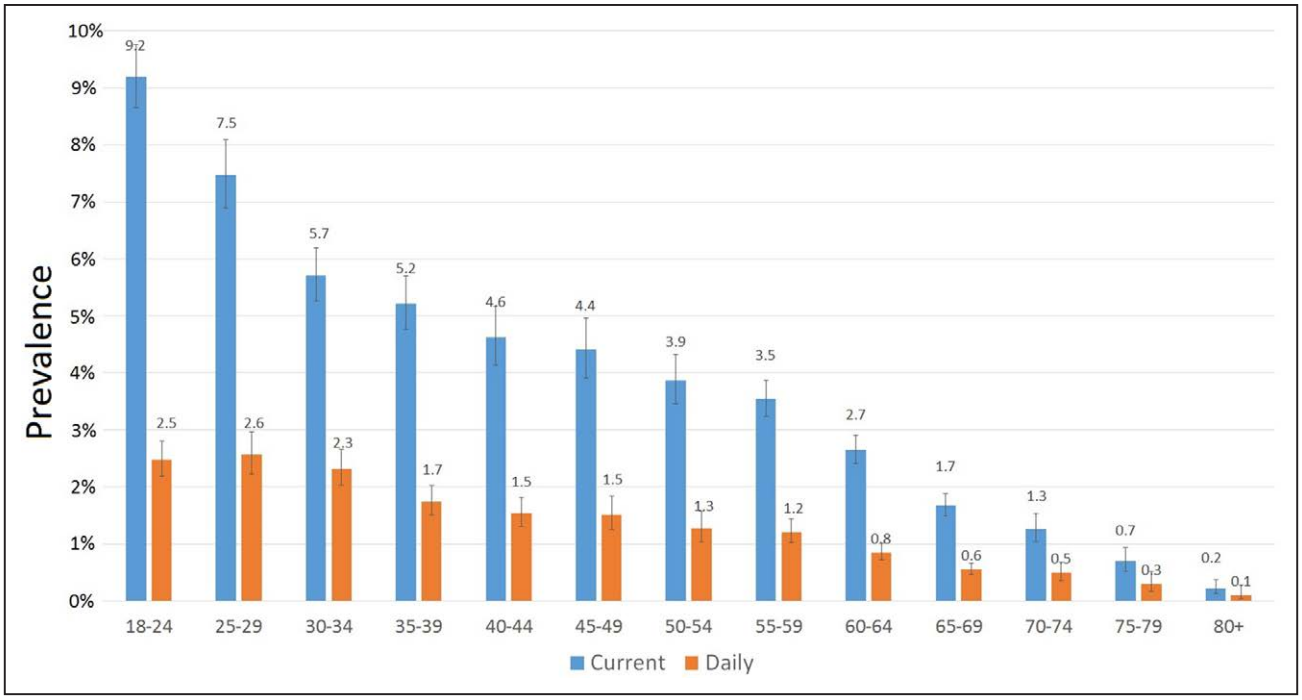

Figure. Prevalence (percent) of electronic cigarette use according to age groups (years) among US adults, Behavioral Risk Factor Surveillance Systems, 2016.

Error bars are 95% CIs. Reprinted from *Annals of Internal Medicine*, Mirbolouk et al[10] with the permission of American College of Physicians, Inc. Copyright © 2018, American College of Physicians. All rights reserved.

are using multiple devices, including the JUUL,[23] and that querying about the use of specific e-cigarette devices may be needed to get accurate measurements of e-cigarette use rates among youth.[24]

A 2018 review[25] by the National Academies of Sciences, Engineering, and Medicine summarized the latest research on e-cigarettes and considered their impact on public health. Overall, the report found that e-cigarette aerosol contains fewer numbers and lower levels of toxicants than combustible tobacco cigarettes and that exposure to nicotine and toxicants from aerosolization of e-cigarette constituents depended on the characteristics of the device and its use. On the basis of the evidence reviewed, the committee suggested that e-cigarettes are not without adverse biological effects in humans, but they are likely to pose less risk than continuing to smoke cigarettes. Nonetheless, the implications for long-term effects on morbidity and mortality are not yet clear. The report also found that there was significant evidence of e-cigarette uptake among youth. The report described that although e-cigarettes might cause youth who use them to transition to combustible tobacco products, they might also increase adult cessation of combustible cigarettes. Population dynamic modeling by the committee indicated that, assuming that the use of e-cigarettes increases the net cessation rate of combustible cigarettes among adults, the use of these products could generate a net public health benefit, despite the increased use of combustible tobacco products by young adults. This modeling happened before the recent upsurge in JUUL use. The modeling showed that in some scenarios in which e-cigarette toxicity was much higher or the gateway effects from e-cigarette use to combustible cigarette use were much stronger, the public health benefit was substantially less or e-cigarette use was even associated with net harm. Moreover, if e-cigarettes do not promote cessation of combustible tobacco products in adults, the policy model projected that there would be net public harm in both the short and long terms.[25,26] The report therefore prioritized research to determine whether e-cigarettes promote smoking cessation. The AHA believes that further research is needed on the long-term biological effects of e-cigarettes and other newer tobacco products and the effects of dual use.

JUUL

JUUL is a rapidly growing type of e-cigarette that became available in the United States in 2015. The device is particularly appealing to adolescents and young adults because it has a slim design shaped like a USB flash drive (which makes it easier to hide), it comes in different colors, and it can be consumed in different, palatable flavors.[27] Although it does not emit large smoke clouds, making it optimal for discrete use, the JUUL nicotine refills (pods) contain as much nicotine as a pack of 20 regular cigarettes.[27] Nicotine not only is high in JUUL pods but also is present in a benzoic acid salt rather than a free base.

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This formulation increases the rate of nicotine delivery and decreases the harsh sensation in the oropharynx. Pharmacokinetic studies show that the nicotine delivery by JUUL approximates that of conventional combustible cigarettes.[27] Likely as a result of these features, JUUL has rapidly become the most popular e-cigarette sold in the United States. The sale of JUUL e-cigarettes has increased 641% in a year, and JUUL accounts for nearly 1 of every 3 e-cigarettes sold in the United States.[28] Inspired by this success, other manufacturers have developed several other USB-shaped devices containing e-liquids in pods. These devices can be used to deliver both nicotine and other drugs.[27] Alarmed by the high popularity of JUUL among youth, the FDA sent a letter to JUUL Labs in the spring of 2018 requesting specific documents that would elucidate the reportedly high rates of use and appeal of this product among youth. This inquiry was followed by a letter from the FDA to manufacturers of 5 leading e-cigarette brands—JUUL, Vuse, Mark Ten, Blu, and Logic—requesting a response detailing their plans to address sales to minors, with the threat that an inadequate response may lead the FDA to remove certain flavored e-cigarettes from the market.[29] Subsequently, the FDA seized documents from JUUL headquarters on the company's sales and marketing practices because of concern that adolescent use of these products has reached epidemic proportions.[29] In September 2018, the FDA issued >1300 warning letters and civil money penalty fines to retailers who illegally sold e-cigarette products to minors, which was the largest coordinated enforcement effort in the FDA's history.[30] Subsequently, in November 2018, the agency proposed several new steps to curb youth access to and use of flavored tobacco products, including limiting the sale of many flavored e-cigarettes to age-restricted retail stores, developing heightened age verification for online sales, banning flavors in cigars, and banning menthol in combustible cigarettes and cigars. However, the FDA has not yet taken formal action to implement these proposals.[31]

The AHA supports restricting the marketing of JUUL and other similar e-cigarettes until their health risks to youth and adolescent users are clearly assessed and their potential benefits and harms in promoting tobacco cessation among adults are better understood. The agency should suspend internet sales of these products until adequate mechanisms and rules for age verification are established. In addition, the ban on underage sales by retailers should be effectively enforced, and the FDA should require these products to be submitted for review sooner. The FDA should reverse its 2017 decision that allows e-cigarettes that were already on the market as of August 8, 2016, to stay on the market until at least 2022 without filing applications and undergoing a public health review by the FDA.

Heat-Not-Burn Products

The tobacco industry's most recent products include heat-not-burn tobacco cigarettes, also called heated tobacco products.[32] These devices typically contain nicotine, flavorings, propylene glycol, and other tobacco constituents, and these devices heat tobacco at ≈500°F to generate an inhalable aerosol rather than burning.[32,33] These products usually contain nicotine at concentrations similar to those in combustible tobacco cigarettes, but the levels of nicotine in the aerosols of the heat-not-burn product are usually lower than those in a combustible cigarette.[34] They deliver higher levels of nicotine than e-cigarettes at low puff duration; however, the delivery is lower compared with high-powered e-cigarettes used with longer puff durations.[34] Heat-not-burn products, such as iQOS and Ploom, are being sold by tobacco companies like Philip Morris International and Pax Labs in countries such as Japan and Italy.[35] However, interest in these products is growing worldwide, which has led to their planned introduction in new markets. Although these products are not currently available in the United States, Philip Morris has applied to the FDA to sell iQOS in the United States, as both a conventional tobacco product and a modified-risk tobacco product. An early 2018 meeting of the Tobacco Products Scientific Advisory Committee voted against granting modified-risk tobacco product status. Meanwhile, public health practitioners should include heat-not-burn products in surveillance, incorporate them into tobacco control strategies, and continue to research not only their health risks but also their advertising and marketing and impact on dual use/switching.[33] Additional work is also needed to assess their secondhand exposure.

In the United States, smoke-free laws in many states include only combustible tobacco products. With newer tobacco products either on or potentially coming on the market, smoke-free laws should explicitly include alternative nicotine delivery systems in comprehensive smoke-free air laws to ensure no passive exposure to any harmful constituent byproducts and no risk of renormalizing tobacco use.[32] Although in devices such as iQOS tobacco is heated and not burned, these products generate detectable levels of harmful and potentially harmful constituents such as volatile organic compounds, polycyclic aromatic hydrocarbons, and carbon monoxide, albeit at levels lower than cigarette smoke.[32] Because there is no safe threshold of exposure to these harmful and potentially harmful constituents, heat-not-burn products should be included in all comprehensive smoke-free air laws and other tobacco control strategies.[32]

Hookah/Water Pipes

Water pipe smoking is prevalent worldwide, especially among young adults.[36] Although most users in Western countries smoke water pipe intermittently, they often use other tobacco products concurrently. The spread of water pipe tobacco smoking is promoted by the use of sweetened and flavored tobacco, social media that promotes water pipes, social acceptance, and misperceptions about the addictive potential and adverse health effects of water pipe smoking and presumed lack of addiction.[37] Most users believe that water pipe tobacco smoking is less harmful than cigarette smoking,[38] that the probability of addiction is low, and that quitting water pipe tobacco smoking is not difficult.[39] However, the risk of initiation of cigarette smoking is higher among water pipe smokers than among never smokers, and the level of nicotine to which water pipe tobacco smokers are exposed can produce dependence with repeated exposure.[40] Although direct comparisons are difficult to interpret, compared with a single cigarette, a single session of water pipe typically results in greater exposure to carbon monoxide and particulate matter.[41] Water pipe exposes smokers to significantly higher levels of heavier and more toxic polycyclic aromatic hydrocarbons, volatile organic chemicals, heavy metals, and cadmium, all of which have been associated with cardiorespiratory injury.[42] Although the evidence for water pipe–attributable disease is not as robust as the evidence for cigarette smoking, a growing number of studies suggest that water pipe tobacco smoking is a potential risk factor for pulmonary and cardiovascular disease.[42] Given the high popularity of water pipe use, healthcare providers should ask users about hookah use, advise users to quit, assist them in their efforts, and refer water pipe smokers to credible sources of information on the addictiveness and health consequences of water pipe use.

Cigars/Cigarillos

Definitions of and data on the use of premium cigars and cigarillos, including use patterns, advertising, and toxicant exposure, are limited.[43] Primary cigar smoking has been associated with higher risks for all-cause mortality, several cancers, coronary heart disease, and aortic aneurysms.[44] In view of this evidence, all cigars, including premium cigars, should continue to be included in robust FDA regulation of tobacco products. Continued research is needed to understand the long-term public health impact of cigar and cigarillo use over the life course. The main reasons why adolescents try cigars or cigarillos include curiosity, appealing flavors, peer influence, and low cost.[45] Like hookah smoking, adolescents do not consider cigarillos to be as dangerous for their health as cigarettes.[46] In a 2017 study, >40% of adolescent cigarillo users either replaced or supplemented tobacco in the cigarillo with marijuana to create a blunt.[45] Cigar regulation should focus on the elimination of all flavorings, use of warning labels, product standards, higher costs, sales restrictions to minors, and advertising limits as part of comprehensive tobacco prevention and control strategies.[45]

Smokeless Tobacco

There is consistent evidence that cardiovascular risks are lower with the use of smokeless tobacco products compared with cigarette smoking[47] yet higher than the risks for nonusers of tobacco.[48] However smokeless tobacco products are not without harm, and there is evidence that long-term use of these products may be associated with a modest risk of fatal myocardial infarction and fatal stroke, suggesting that smokeless tobacco use may complicate or reduce the chance of surviving both of these events.[47] In addition, there is inadequate evidence to support the use of smokeless tobacco products as an effective cessation strategy.[47] In a 2018 randomized trial, smoking cessation rates were comparable between snus and nicotine lozenges,[49] suggesting that smokeless tobacco products may not aid smoking cessation more than FDA-approved cessation aids with higher risks for long-term adverse events.

Summary

The use of any tobacco product, including e-cigarettes, hookah, noncigarette combustible tobacco, or smokeless tobacco, has adverse effects on biological systems, although each product may differ in the extent of exposure to harmful and potentially harmful constituents and therefore the extent of cardiovascular risk imposed by use. There is significant need for longitudinal research on the impact of e-cigarette use on cardiovascular disease. Because these products contain nicotine, they can lead to dependence. The use of 1 tobacco product is often associated with the use of other tobacco products, although the prevalence of dual use and poly use remains incompletely understood. For e-cigarettes and hookah, their use is associated with initiation of cigarette smoking.[5]

INCREASING USE OF NEWER TOBACCO PRODUCTS

Youth

Since 2016, youth use of e-cigarettes has been increasing dramatically. Because of the staggering variety of these new devices, varying nomenclature, and misunderstanding of the nature of these products, these trends may be underestimates of the true prevalence

of current youth use of alternative nicotine delivery systems. For instance, a 2018 report suggests that some youth self-report that they are not using e-cigarettes when they are using electronic hookah, JUUL, and other similar products.[50] Thus, youth use of e-cigarettes may be underestimated if the product names and descriptions are not used explicitly in surveys. Nonetheless, current evidence is consistent with the view that newer tobacco products may be increasing nicotine addiction and risk for combustible tobacco or illicit drug use.[5,51] The AHA aims to decrease all tobacco use in the United States and to eliminate youth use of all tobacco products to prevent nicotine and tobacco addiction in the next generation.

Transition From e-Cigarettes to Combustible Products and Association of e-Cigarette Use With Other Substance Abuse

Youth who use e-cigarettes, particularly those with higher nicotine content, are more likely than those not using these products to try and to continue cigarette smoking.[25,51–57] The use of e-cigarettes has been associated with known behavioral predictors of substance use behaviors, including susceptibility to future use[51] and impulsivity.[51] e-Cigarette use also clusters with other risky behaviors,[58] suggesting that the use of these devices may be associated with risk-seeking behavior and that initiation of cigarette smoking may be related to a cluster of personality traits rather than the use of e-cigarettes per se. Compared with no use of e-cigarettes, use of e-cigarettes has been positively correlated with a higher prevalence of substance use, including alcohol, cocaine, amphetamines, inhalants, hallucinogens, and ecstasy, as well as the misuse of over-the-counter and prescription medications.[20]

Reinitiation and Dual Use of e-Cigarettes and Combustible Products

There is concern that the newer tobacco products may entice former smokers to reinitiate tobacco use and to sustain nicotine addiction, although robust evidence to demonstrate this is lacking. More research is needed to assess the prevalence of reinitiation. Additional evidence is also needed on the role of e-cigarettes and other new tobacco products in supporting and sustaining dual use, in which smokers do not switch entirely but maintain some level of smoking while using these new products. The dose-response relationship between smoking and cardiovascular mortality is strikingly nonlinear, such that smoking only 3 cigarettes per day imparts 80% of the risk associated with smoking 20 cigarette per day.[59] Thus, exposure to smoking or secondhand smoke, even very low levels, has serious health consequences,[60] and reduction in exposure does not necessarily translate to a proportional reduction in harm.

Whether dual use of e-cigarettes is sustained as a long-term habit or is an intermediate step leading to complete smoking cessation remains unclear. One population-based, prospective cohort study found no evidence that e-cigarette use helps adult smokers quit at rates higher than when these products are not used.[61] Dual users may smoke fewer cigarettes but compensate with more e-cigarette use, increasing their overall exposure to nicotine.[62] Therefore, even though e-cigarettes might help maintain smoking reduction and lower withdrawal symptoms, the long-term health impact of dual use remains largely unknown.[62] The long-term health effects of completely switching to e-cigarettes are also unclear, although the use of e-cigarettes is likely to be less harmful than continuing to smoke combustible cigarettes.

INEQUITY OF TOBACCO USE IN VULNERABLE POPULATIONS

Tobacco use is disproportionately concentrated in certain racial/ethnic groups, rural areas, those with low income and less education, those with mental health issues, and the lesbian, bisexual, gay, transgender, and queer (LGBTQ) community.

Racial/Ethnic Disparities

A 2016 survey showed that compared with whites and Hispanics, blacks were less likely to report ever using e-cigarettes.[63] However, blacks were more likely to use e-cigarettes as a cessation aid.[63] Moreover, compared with whites, Native Hawaiians and Filipinos have reported more perceived improved heath resulting from e-cigarette use.[64] A 2016 study in California showed that e-cigarette use was higher among ever smokers of conventional cigarettes, individuals at >200% of the Federal Poverty Level, US citizens, and those who spoke English only at home.[65] However, e-cigarette marketing appears to be increasingly targeting and influencing blacks, with particular exposure from radio and television, and this may increase e-cigarette use.[66]

Geographic Disparities

In the United States, there is a higher prevalence of diabetes mellitus and coronary heart disease in rural populations, and this is driven, at least in part, by the higher prevalence of tobacco use.[67] A 2016 study assessed rural and urban tobacco use across the United States and found that the use of cigarettes, chew, and snuff was higher in rural than in urban areas.[68]

Across all tobacco products, urban and rural differences were more pronounced in certain regions of the country, especially in the South Atlantic, and were not fully explained by differences in poverty.[68] These disparities in rural tobacco use may be the result of disproportionately more tobacco control and prevention policies in urban areas and greater enforcement of regulations around the sale and marketing of tobacco products.[69]

There are worrisome issues in urban areas as well. There is a higher tobacco outlet density in urban compared with rural locations, as well as a higher tobacco outlet density where larger proportions of blacks, Hispanics, and people with lower levels of education reside.[70] This means that tobacco outlets are most concentrated in areas where people with higher risk for negative health outcomes live.[70] Hence, geographic disparity should be considered in regulatory efforts, and tobacco control and prevention strategies should be targeted and tailored to vulnerable populations, including individuals living in rural areas.

Individuals With Mental Health Conditions

Individuals with mental health conditions have a disproportionately higher use of tobacco products; thus, they experience higher rates of tobacco-related morbidity and mortality compared with individuals without mental health conditions.[71] Nicotine has an antidepressant effect[72]; therefore, those with mental health conditions may have lower rates of tobacco cessation at similar quit attempts. Broader or more intensive assistance may be needed to increase quit rates in those with mental health issues. More innovative and integrated approaches could be developed to support tobacco cessation in this population, which could involve temporary use of reduced-harm tobacco products with the ultimate goal of quitting tobacco products all together.

Socioeconomic Position and Education

Low socioeconomic position and lower education levels are associated with the use of multiple types of tobacco and greater tobacco use.[73] Concurrently, there is lower perceived harm of tobacco products, especially smokeless products, in those with less education and income.[74]

The LGBTQ Community

The use of all tobacco products is higher in the LGBTQ community than in the general population.[75] In some areas of the country, despite robust tobacco control and prevention policies, current smoking prevalence for LGBTQ individuals remains 2-fold higher than in the general population.[76] A 2018 cross-sectional study also revealed that the standardized prevalence of e-cigarette use was highest among men and LGBTQ individuals.[10] There is a significant gap in the area of prevention and cessation interventions for LGBTQ youth and young adults, and more research is needed to develop effective, tailored interventions for tobacco cessation and prevention within the LGBTQ community.[77,78]

Summary

For all vulnerable populations, it is important to consider the disproportionate use and whether the larger social conditions such as poverty, discrimination, marginalization, lack of access to care, and targeted tobacco product marketing can be addressed to reduce the overwhelming burden of tobacco use in these groups. Robust tobacco control and prevention efforts and comprehensive cessation strategies should be tailored and targeted to assist those with mental health conditions, people living in rural communities, certain racial/ethnic groups, those with less education and income, and the LGBTQ community to overcome their nicotine addiction.

SAFETY/HARM

Although most of tobacco-related morbidity and mortality are attributable to other chemicals, nicotine is the main addictive substance in tobacco products that keeps individuals using tobacco and at risk for suffering tobacco-related harms. In general, people do not fully understand nicotine addiction and underestimate its power. Moreover, from a regulatory perspective, the concept of nicotine addiction and its consequences in terms of harmful tobacco product use have not been communicated well to the public. Nicotine is a strong reinforcer that leads to release of dopamine in the brain. It has been proposed that individual differences in the addictive potential of nicotine may be related to a balance between the desensitization and stimulation of the nicotinic acetylcholine receptors and subsequent effects on dopamine and other neurotransmitter pathways.[79] Therefore, it may be important to understand that there are variations in individual susceptibility and in population vulnerability, as well as the larger social context that supports and promotes addiction. Current tobacco users who use newer tobacco products or have distinct use patterns may or may not need different strategies for quitting from those that have proved effective in the past. Further work is required to assess the efficacy of conventional cessation approaches for a new generation of smokers and, if necessary, to develop new interventions for those addicted to new tobacco products such as e-cigarettes.

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Changing the Social Construct

The transformational rise in the popularity of products such as JUUL and the results of recent national surveillance indicate that youth, adolescents, and young adults have particularly high acceptance of emerging tobacco products over combustible products.[8] This attraction to new tobacco products may be related to flavors, social cues, peer influence, beliefs about addiction, and cognitive risk perception specific to youth, adolescents, and young adults.[80] Therefore, it is important to educate these groups about the potential dangers associated with the use of these products,[81] although this may be challenging and require a nuanced approach. Research has shown that users do not understand the relative versus absolute risks of e-cigarette use versus combustible tobacco use or dual use.[4] This gap in consumer understanding reinforces the importance of regulating the marketing, advertising, and modified-risk claims of all tobacco products to ensure that there are no misperceptions about their safety and that risks are accurately portrayed and based on the best available evidence.[4,82]

EFFICACY OF NEWER TOBACCO PRODUCTS FOR CESSATION

As the National Academies of Sciences, Engineering, and Medicine report concludes,[25] there is limited evidence that e-cigarettes may help smokers quit using combustible tobacco because of the small number of clinical trials conducted to date. The results of longitudinal observational studies are mixed. A 2018 nonrandomized observational study found no evidence that use of electronic nicotine delivery systems helped adult smokers quit at rates higher than not using these products.[61] There is also a significant genetic link to nicotine addiction,[83,84] which is important to consider when positioning these newer products for cessation and indicates a potential role for precision medicine in cessation treatment and tobacco use prevention.

Preliminary research has shown some beneficial effects of short-term switching to e-cigarettes, including reduced smoke toxicant exposure and cigarette dependence and increased motivation to quit.[85,86] A 2015 cross-sectional study found that there was higher interest in using electronic nicotine delivery systems for cessation and harm reduction versus smokeless tobacco.[87] Other research has shown that electronic nicotine delivery system users also continue to smoke cigarettes.[88] Dual users often have higher levels of overall tobacco use and lower intention of quitting over the long term.[89,90]

In general, noncombustible products with higher nicotine levels lead to a more significant reduction in tobacco cravings than those with lower nicotine levels.[91] A stronger effect on craving helps increase satisfaction with noncombustible products and subsequent reporting that they help with quitting tobacco use.[91] More research is needed to understand the efficacy of e-cigarettes in promoting quitting relative to other FDA-approved cessation therapies. Additional work is required to assess the prevalence and impact of dual use and whether the use of newer tobacco products leads to completely quitting combustible tobacco or simply adding the use of tobacco products without reducing health risks. Many current cohort and observational studies lack methodological rigor, statistical power, and adequate analytical approaches to ensure validity.[92,93] Future research should use better measures of patterns of e-cigarette use and reasons for use, use frequency, and the concurrent use of cessation aids.[92] There are also urgent needs to address significant public health questions about the level of nicotine in noncombustible products that optimally helps dependent smokers quit all tobacco use and to develop robust regulation that protects against youth access and initiation, reinitiation by former smokers, and initiation by never smokers.

ROLE OF FDA REGULATION

In 2009, the Family Smoking Prevention and Tobacco Control Act gave the FDA the authority to regulate the manufacture, distribution, and marketing of tobacco products. As a result of this legislation, the FDA's Center for Tobacco Products was established to implement and enforce the law. Subsequently, in 2010, the Tobacco Products Scientific Advisory Committee was organized to provide advice, information, and recommendations to the FDA commissioner on matters related to the regulation of tobacco products. In 2016, the FDA finalized its deeming rule to regulate all tobacco products, including e-cigarettes. The AHA supports effective FDA regulation of tobacco products that addresses manufacturing and design of tobacco products, as well as marketing, youth access, labeling, quality control, free sampling, and standards for contaminants.[3] Most smokers support robust regulation of tobacco products in the marketplace.[94]

Regulating Nicotine

In 2014, the surgeon general called for implementing new strategies, including eliminating the use of combustible tobacco products that would bring an end to the most preventable cause of death in the United States.[95] In July 2017, acknowledging the link between smoking-related death and disease and the addictive nature of nicotine, the FDA announced a new plan to place "nicotine, and the issue of addiction, at the center of the agency's tobacco regulation efforts."[96] Nicotine addiction is the leading cause of continued tobacco use. Building on this announcement, the FDA

released an Advance Notice of Proposed Rulemaking in March 2018, focused on reducing the level of nicotine in combustible cigarettes. In the Advance Notice of Proposed Rulemaking, the FDA asked important questions, including whether nicotine should be reduced only in cigarettes or in other combustible products, the maximum allowable nicotine level, the method of implementation, technical achievability, and the countervailing effects and potential unintended consequences (illicit tobacco market, dual use, deeper inhalation, or increase in number of cigarettes smoked). Research has attempted to answer these questions.

To assess the impact of nicotine reduction, a 2018 modeling study showed that lowering nicotine in cigarettes to minimally addictive levels would lead to a substantial reduction in tobacco-related mortality, most likely as a result of increased rates of smoking cessation and attempts to quit, which would create a substantial population health impact.[97] When tested in a 1250-participant, double-blind, randomized controlled trial comparing immediate reduction to 0.4 mg nicotine per 1 g tobacco with gradual reduction or no change, participants randomized to the immediate reduction group had a significantly larger decrease in biomarkers of smoking exposure compared with individuals randomized to either the gradual reduction or the control group.[98] Reducing nicotine to 0.4, 2.3, and 5.2 mg nicotine/g from the typical tobacco product with 15.8 mg nicotine/g tobacco was also found to lower addiction potential from cigarettes in a double-blind, within-participant study in 3 vulnerable populations: individuals with psychiatric disorders, those with opioid dependence, and low-income women.[99] The study also found that withdrawal symptoms lasted longer with the higher-dose nicotine cigarettes and that smokers with psychiatric conditions and lower socioeconomic status were more addicted, were less likely to quit, and had more withdrawal symptoms.[99]

More longitudinal studies with more diverse populations are required to assess the impact of lowering nicotine levels in noncombustible products in the context of other lowered-nicotine combustible products.[100] Longer-term e-cigarette–only use and longer-term nicotine replacement therapy only are associated with substantially reduced levels of measured toxins and carcinogens,[101] but this is not true in many cases of dual use with combustible tobacco products. The major reason for reducing nicotine is to reduce addiction, and at least theoretically, the potential individual-level gains seem to outweigh the risk of compensatory smoking, especially in youth. At least in 1 study, compensatory smoking of the reduced-nicotine products that were provided seems to have been minimal.[102] However, recent data suggest that these individuals may get the additional nicotine they crave from other sources, especially electronic nicotine delivery systems.[98] Further studies are required to assess the true extent of compensatory smoking or use of other nicotine sources, whether nicotine reduction leads to harmful and potentially harmful constituents reduction, and whether nicotine reduction leads to reduction in youth use of tobacco products. Nevertheless, currently available data suggest that reducing the nicotine content in combustible products decreases nicotine exposure in smokers, reduces the number of cigarettes smoked per day, and increases the likelihood of contemplating, making, or succeeding in a quit attempt.[103] Therefore, to minimize youth uptake and to promote adult cessation, nicotine should be reduced in all combustible tobacco products to prevent users from switching from 1 combustible product to another. The FDA should require that the nicotine concentration be labeled on all tobacco products. Because many who use combustible products switch to noncombustible products, it is important for any nicotine reduction strategy to consider the relationship between switching and dual use and how this is affected by lower nicotine concentration in combustible products. Action should also be taken to ensure that further changes are not made by the tobacco industry to reduced-nicotine products to retain their appeal such as altering other ingredients or flavors that could retain the appeal and addictive potential of these products.

Little is known about how nicotine reduction in combustible products would affect the use of noncombustible products and what might happen if nicotine also is reduced in noncombustible products. One likely scenario is that reduction in nicotine in combustible products may lead to increased use of noncombustible products. This may lead smokers to switch from combustibles. This transition, accompanied by careful regulation of other tobacco products, in the context of a nicotine replacement strategy could help accomplish the long-term goal of greater cessation. Another approach could be to make noncombustible tobacco products available as regulated cessation aids. The AHA will support this approach if future high-quality research demonstrates that e-cigarettes are safe and effective in cessation. Having noncombustible tobacco products regulated and sold as cessation products would reduce youth access in retail environments and would focus marketing to adults for cessation purposes only. Characterization of e-cigarettes as cessation devices could decrease their allure to youth, which may help achieve the ultimate goal of ending all tobacco and nicotine addiction in the United States.

Illicit Market

Little research exists on the illicit tobacco market.[104] Nevertheless, there is concern that lowering nicotine in tobacco products might trigger the rise of a black market for high-nicotine products.[105] Illicit markets can offset

robust public health measures if they provide consumers with access to prohibited products. However, this scenario is not supported by most available data, and such activities are likely to be offset by the overall public health benefit from reducing nicotine exposure.[103,106] A 2015 Institute of Medicine report found that "a market in banned product would necessarily involve large-scale smuggling from outside the country or illegal domestic manufacturing."[106] The report concluded that neither of these conditions has prevailed in the United States and neither is likely to occur as a consequence of the promulgation and enforcement of product standards.[106] The FDA and other governmental agencies can and should develop and strengthen enforcement efforts to minimize the effects of illicit markets.

Menthol and Other Flavorings

The Family Smoking Prevention and Tobacco Control Act of 2009 banned characterizing flavors in cigarettes, except for menthol, but did not address flavors in other tobacco products.[107] The number of flavors in newer tobacco products has increased substantially in recent years, with industry marketing thousands of youth-enticing flavors such as fruit-, candy-, vanilla-, unicorn-, and mint-flavored products.[108] This has led to a dramatic increase in youth initiation of these products.[107] There is overwhelming evidence showing that flavors attract youth. For example, in the 2013 to 2014 PATH study (Population Assessment of Tobacco and Health), the first tobacco product used by 81% of youth 12 to 17 years of age was a flavored tobacco product.[107] Flavors not only promote youth initiation and use but also could increase the potential toxic effects of the product. Recent evidence suggests that short-term exposure to the flavorings used in certain tobacco products could have adverse effects on the regulation of blood vessel function because of their effects on endothelial cells. Such endothelial injury and dysfunction in individuals using flavored products could contribute to potential cardiovascular toxicity and elevate the risk for heart disease.[109]

Although characterizing flavors have been banned in combustible cigarettes, the sale of mentholated cigarettes is legal. Menthol is widely used in combustible tobacco products because it reduces their harshness. It also facilitates and prolongs nicotine exposure, increases dependence, allows easier experimenting, and attracts youth.[107,110] Menthol has also been shown to enhance the appeal of e-cigarettes containing nicotine.[111] Tobacco products with menthol have been specifically marketed to communities of color, especially blacks.[112] Thus, to reduce inequities and to prevent youth initiation and experimentation, it is important to close this regulatory loophole and to ban the use of menthol in all tobacco products.

Recognizing the risks associated with their use, several countries have banned menthol cigarettes. The effort was led by Brazil, where menthol cigarettes were banned in 2013. This was followed by bans in Canada, the European Union, Ethiopia, Moldova, and Turkey, among other nations. As of this writing, ≈10 cities in California and the city of Minneapolis have banned the sale of menthol cigarettes. In 2017, San Francisco passed the most stringent flavored tobacco product ban in the United States, eliminating all flavored e-cigarette liquids, cigars, and hookah. A referendum promoted by RJ Reynolds to overturn the legislation was unsuccessful, and neighboring cities in the San Francisco Bay Area subsequently adopted legislation modeled after the San Francisco ban. The state of California has now introduced legislation that would ban flavored tobacco products, and New York may be doing so through a proposed rule.

Restricting flavorings in all tobacco products may be 1 key to achieving the tobacco endgame. In their original conception, e-cigarettes were intended to deliver aerosolized nicotine without the addition of a complex mixture of multiple flavoring chemicals that might carry their own inherent health hazards. Although most of these flavoring chemicals are on the FDA's list of compounds generally regarded as safe, this designation is based on their safety when used as food additives for ingestion. The designation of generally regarded as safe does not provide assurance about their safety when aerosolized and inhaled, and several flavoring chemicals have been withdrawn from use because of their association with serious pulmonary disorders such as bronchiolitis obliterans. Users of e-cigarettes inhale large quantities of flavoring chemicals over long periods of time, and these chemicals cannot be considered safe without a thorough investigation of their inhalation toxicity. There are >15 000 different flavors on the market, but studies of several classes of these compounds are underway.[113]

Restrictions on flavored tobacco may be facilitated by achieving uniformity in the laws that are being passed in different US cities or in a federal ban. Currently, such laws are heterogeneous. Some focus on menthol, whereas others focus on e-cigarettes. Moreover, once a city has passed a ban including one or the other, it is difficult to return and to try to convince voters or legislators to revisit the topic and ban other items that have heretofore been legal.

The removal of all characterizing flavors from all tobacco products is essential for reducing their appeal to youth. Controversy arises because, although there is no experimental evidence to support the view that flavors help adults to switch from combustible to noncombustible tobacco products or to quit tobacco altogether, individual reports suggest that, for some adults, flavors are appealing. However, maintaining flavors to attract adult

smokers increases the risk of these products becoming available for youth and young adults. Additional research is needed to determine how best to balance the need to reduce the appeal of flavorings to youths with the potential that flavorings may facilitate smoking cessation among adult smokers. Recognizing that this is a difficult decision, the AHA's position at this time is that the FDA should ban the use of all characterizing flavors other than tobacco in all tobacco products. Emerging evidence also suggests that sweeteners in tobacco products may play a role in increasing the appeal of the product. For example, high-intensity sweeteners were found in a number of alternative tobacco products, including e-cigarettes,[114] and were also commonly found in the mouth side of many cigarillos.[115] Although further research is needed in this area, this evidence suggests that the FDA should also consider the inclusion of high-intensity sweeteners in its definition of characterizing flavors. This should be accompanied by research aimed at studying the role of flavors in enhancing adult cessation and the toxicity of flavors. Such research and surveillance will be required to determine any negative effects on the efficacy of cessation, with new approaches developed to counteract these negative effects, if found.

Marketing/Advertising

To lure users to their products, the tobacco industry has historically used celebrities, movie placements, and price promotions that include coupons, rebates, and discount codes. For combustible cigarettes and smokeless tobacco products, the FDA has banned some marketing practices (eg, free samples, vending machine sales, brand-name sponsorship of events, and branding nontobacco merchandise). The marketing and advertising for the newer tobacco products continue to proliferate. Nearly 1 in 7 US adult users of electronic products reports seeing and using price promotions in purchases,[116] and almost 70% of middle and high school students are exposed to e-cigarette advertisements in retail stores, as well as on the internet and in television, movies, newspapers, and magazines.[21] Such rampant advertising and aggressive marketing have likely fueled youth initiation.[21] Of particular concern is aggressive marketing targeted to racial and ethnic minority groups who have a lower prevalence of tobacco use than white youth because such marketing puts these groups at a higher risk of sustaining and increasing their tobacco use behavior.[117] The AHA supports robust FDA regulation restricting all marketing and advertising of all tobacco products, including noncombustible products, especially to youth, adolescents, and vulnerable populations, including through online, television, radio, and print ads; commercials; celebrity endorsements; movie placements; price promotions; brand-name event sponsorships; and branding of nontobacco merchandise.

Warning Labels

In the final deeming rule of May 2016, the FDA declared that warning labels on e-cigarettes and other newer tobacco products were under the purview of the agency and therefore could be instituted. For now, they will be text labels. US cigarette warning labels have not been updated since 1984. However, in September 2018, Judge Indira Talwani of the US District Court in the District of Massachusetts concluded that the FDA had both "unlawfully withheld" and "unreasonably delayed" agency action on a requirement in the 2009 Tobacco Control Act that graphic warning labels should be included on cigarette packaging and advertising. The FDA issued an initial rule on graphic warning labels in 2011, but the rule was struck down by judges on the US Court of Appeals for the District of Columbia Circuit who found that the specific graphic warnings proposed by FDA, not the law itself, violated the First Amendment. At the time, the FDA committed to developing new graphic warnings, but years have passed with little action. However, with the 2018 ruling, the FDA is now required to move forward with graphic warning labels for cigarettes in an expedited manner. Research shows that graphic warning labels are a low-cost and cost-effective measure to reduce tobacco use compared with text-only warning labels, even in diverse socioeconomic and racial/ethnic populations.[118–120] Some countries such as Australia, Canada, and Uruguay have implemented standardized, plain packaging on tobacco products, which has contributed to reducing tobacco consumption.[121] The tobacco industry has been successful in delaying the implementation of graphic warning labels on combustible cigarettes in the United States for nearly a decade, but this needs to change. The AHA supports rapid implementation of impactful, evidence-based, product-specific graphic warning labels on all tobacco products in the United States.

GLOBAL COORDINATION OF REGULATORY EFFORTS AROUND TOBACCO CONTROL AND PREVENTION

Between 0.8 and 1 billion people use tobacco products worldwide.[122] Tobacco remains the leading cause of preventable death, and it has been estimated that nearly 6 million people die of tobacco-related diseases per year.[123] To date, tobacco use has been linked to >100 million deaths, and if the current use pattern persists, >1 billion people will die of tobacco use in the 21st century.[124] Robust regulation of tobacco products in the United States should not exacerbate tobacco use prevalence in other regions of the world by incentivizing the ongoing efforts of the tobacco industry to export its products to vulnerable populations in other countries.

With regard to e-cigarettes, there is wide variability in terms of how e-cigarettes are classified in various countries, which has led to large differences in regulations on these products and in their inclusion in policies that have been standardly applied to combustible tobacco products such as minimum age of purchase; restrictions on sales, marketing, and packaging; product regulation; and inclusion in clean air and taxation laws.[125]

In a positive development in 2017, the FDA announced its intention to accept and consider a single-source application for an award to the World Health Organization for building research capacity in global tobacco regulatory efforts.[126] The purpose of this work is to support, develop, conduct, and coordinate research efforts relating to tobacco control laws and rules in foreign countries that will directly inform and support the FDA's regulatory efforts around the manufacture, distribution, marketing, and sale of tobacco products in the United States. The FDA will likely benefit from the expertise of the World Health Organization member states and their extensive international contacts in the area of global tobacco control, as well as the programmatic expertise within the World Health Organization, to inform and support adequate manufacture, distribution, and market regulations of tobacco products for the protection of public health in the United States. Importantly, this collaboration could provide universal public health benefit by creating opportunities for collaboration and research development globally. This could result not only in better informed and more effective global tobacco product regulation but also in a global increase in public knowledge about tobacco use and its harms. The AHA supports these coordinated global efforts. Comprehensive tobacco control and prevention efforts worldwide require the World Health Organization's leadership, a consensus policy framework, dedicated global health networks, and coordination and collaboration among individuals, organizations, nongovernmental organizations, and governmental agencies to minimize the devastating impact of tobacco products in vulnerable populations worldwide.[127]

POSITIONING THE AHA ON THE TOBACCO ENDGAME

The 50th Anniversary Report[95] by the surgeon general began to frame the idea of a tobacco endgame, which is, in the United States, that there could be an end to the use of combustible tobacco. However, a clear and consistent definition of the tobacco endgame is lacking. Some define it as eliminating all tobacco or nicotine addiction; others define it as ending all combustible tobacco use; and others consider the endgame to be a ≤5% tobacco use prevalence.[128] Reaching 0% tobacco use prevalence may be considered ideal, but this would likely require a disproportionate amount of resources and a comprehensive ban on all tobacco products, which is not an option under current US federal law. Although the AHA acknowledges that the ultimate endgame would be an end to all tobacco and nicotine addiction in the United States, the AHA supports first minimizing the use of all combustible tobacco products while ensuring that other products do not addict the next generation of youth and adolescents to achieve a more realistic goal of reaching a tobacco use prevalence of ≤5%. However, current trends seem to be moving in the opposite direction. In 2014, combined cigarette and e-cigarette use in adolescents was higher than cigarette use in 2009, creating increased nicotine dependence with the use of different products.[129] Youth who try e-cigarettes might not have tried combustible products, but once dependent on nicotine, they might switch to combustible products and use other psychoactive substances. Most adults using noncombustible products are not quitting combustibles but remain dual users. If combustible tobacco use is substantially decreased with nicotine reduction and then elimination from the marketplace, then dual use and transition to combustible products would be far less common.

The US federal government and individual states could adopt an integrated endgame strategy approach in which traditional tobacco control policies are synergistically implemented in the context of several endgame strategies (Table 4). A combination of approaches adopted concurrently would be ideal for reducing nicotine and tobacco addiction. However, public support for endgame strategies is unclear, and many ideas have not yet been implemented, let alone have been upheld after legal challenges.[128] Such uncertainties notwithstanding, continued change in social norms around all tobacco use, effective regulation of all tobacco products, promotion of robust cessation efforts, reduction in barriers to treatment of tobacco dependence, and elimination of youth access and initiation would allow the United States to embrace a tobacco-free future.

Other Comprehensive Tobacco Control and Prevention Efforts That Complement the Tobacco Endgame

While pursuing the endgame, the AHA and its partners need to continue to implement evidence-based tobacco control strategies that have significantly reduced tobacco use and initiation in the United State such as tobacco excise taxes, comprehensive clean indoor air laws, comprehensive coverage of evidence-based tobacco cessation therapies, elimination of the sale of tobacco in pharmacies and other health-related outlets, an increase in tobacco sales age to 21 years (ie, Tobacco 21), advertising restrictions, and denormalization of tobacco use. These strategies need to be refined to achieve the tobacco endgame in the context

Table 4. Potential Tobacco and Nicotine Endgame Strategies[128]

Strategies	Feasible, Especially in the Regulatory Environment	Constitutional
Product focused		
Regulate and reduce nicotine in combustible products to make them nonaddictive or less addictive	Yes	Yes
Redesign cigarettes and other combustible products to make them less appealing (raise pH, ban flavors in all tobacco products, including menthol in cigarettes, ban particular ingredients that enhance addiction and appeal)	Yes	Yes
Potential modified-risk products (regulate, market, sell, tax less, continue research on long-term health impact)	Yes	Yes
User focused		
Smoker's license that is renewable annually with purchase limits established by the user and purchasing age increased	Maybe, but costly to implement for smokers and retailers; could also be stigmatizing; would send a message about the dangers of smoking	Yes Seems highly unlikely; it is a legal product that can be sold to individuals >18 y of age according to federal law
Prescription to purchase noncombustible tobacco (given only after cessation efforts have failed)	Maybe, but clinicians would likely be unwilling to write prescriptions for products that are dangerous for their patients; would conflict with policies designed to eliminate all tobacco sales from pharmacies; would have regulatory/legal hurdles	Yes
Restrict sales by year born to create tobacco-free generations to phase out the sale of tobacco use	Maybe, an incremental approach; achieving an end point would take decades, and there would be regulatory/legal hurdles	May be challenged because adults have the right to take informed risks
Market/supply focused		
Licensing tobacco retailers; could be designed to discourage adult use (restricted hours, lower number of licensed outlets, etc) or limited to adult-only stores	Yes	Yes, but may be challenged by industry
Set minimum prices	Yes, and already happening in many states and the District of Columbia	Yes
Point of sale/advertising bans	Yes, but may not lead to significant reductions	May be challenged by industry on First Amendment grounds
Ban commercial sales of combustible products	May be possible in local jurisdictions, but there are significant political barriers; FDA is forbidden by federal law from banning sale of cigarettes, cigars, pipe tobacco, and roll-your-own products	May be challenged because it is a currently a legal product for sale in the United States
Market disadvantage for combustible products compared with modified-risk products (higher taxes, restricted availability, etc)	Yes	Yes
A quota on tobacco manufacture and imports to be regularly reduced under a "sinking lid"; quotas are reduced, and prices for tobacco products would rise until demand shrinks, like a cap-and-trade system	Maybe, but very complex	Maybe
Price caps; a regulatory body would set maximum wholesale price for cigarettes, reducing industry profits	Maybe, and would reduce price differentials between products	May be challenged in a free-market system
Institutional structure focused		
Regulate the market in which a regulator is the sole purchaser of tobacco from manufacturers and importers, controlling price, packaging, ingredients, advertising, and promotion	Maybe, but challenging in the United States	May be challenged in a free-market system
State takeover of tobacco companies	Could be challenged in the United States	May be challenged in a free-market system
Performance-based regulation	Yes	Yes

FDA indicates US Food and Drug Administration.

of newer products. For example, tobacco excise taxes should be highest for combustible products, whereas FDA-approved modified-risk products should be taxed at a lower rate. Raising the price of tobacco is one of the most effective ways to reduce tobacco product use,[130] but there is concern that tobacco excise taxes are regressive. However, according to the 2018 *Lancet* Taskforce on Non-Communicable Diseases and Economics,[131] tobacco tax increases are progressive because health benefits exceed increases in tax liability,

and these benefits accrue disproportionately in lower-income households.[132]

All combustible tobacco products and those that generate aerosols should be included in comprehensive clean indoor air laws. Those who use tobacco products should have coverage and access to comprehensive tobacco cessation therapies that include counseling and pharmacotherapy and are expanded to incorporate smokeless tobacco and newer products such as e-cigarettes and hookah. The highest priorities in our policy work are to promote cessation and to prevent youth initiation.

IMPLICATIONS FOR HEALTHCARE PRACTITIONERS

The rapid increase in the use of newer tobacco products needs immediate attention by all healthcare providers, who should receive adequate professional development about how these products are regulated and used and about issues related to youth access and initiation, potential health impacts, and the role of these products in switching and cessation. Practitioners will need to stay abreast of this emerging area to provide the most appropriate tobacco cessation counseling to their patients.[133] Specific guidance to practitioners has been included in an AHA statement on e-cigarettes.[3]

In general, providers should screen for all tobacco use in all patients, with the understanding that current tobacco use is not restricted to the use of cigarettes or smokeless tobacco and may involve a variety of different use patterns, devices, and modalities. They should encourage patients to first consider established pharmacological and behavioral smoking cessation therapies and should be prepared specially to counsel their youth and adolescent patients to avoid or quit the use of all tobacco products, including e-cigarettes, hookah, cigarillos, cigars, smokeless tobacco, and combustible cigarettes. Youth substance use prevention programs should target reduction of e-cigarette use.

For adults, there is not enough evidence yet for clinicians to counsel their patients using combustible tobacco products to use e-cigarettes as a primary cessation aid. However, should a patient fail initial treatment, be unable or unwilling to use conventional smoking cessation medications, and wish to use e-cigarettes to aid quitting, it may be reasonable to support the attempt. Nevertheless, patients should be informed that although e-cigarettes may be less toxic than cigarette smoking, these products might have adverse effects on their cardiovascular system and overall health if used long term. Providers should advise their patients not to plan to use them indefinitely but to quit e-cigarette use eventually. The provider should advise patients that the use of e-cigarettes should not endanger their abstinence from combustible tobacco products. It is important to stress that patients should quit smoking cigarettes entirely as soon as possible because continued cigarette smoking, even at reduced levels, imposes significant health risks.

CONCLUSIONS

Continued, robust regulation of newer tobacco products is urgently needed not only to strengthen ongoing tobacco prevention and control efforts but also to achieve a tobacco endgame strategy. Although e-cigarettes may have the potential to serve as cessation aids or as reduced-harm products, there are also substantial concerns about the dramatic increase in youth initiation and use of these products with major public health consequences as a result. There is also a need for independent research to evaluate the impact of long-term use and dual use on population health. The FDA and other independent research must assess the quality and strength of evidence that new products are reduced-harm products or effective cessation aids. The AHA calls for a broad policy dialogue for policy development, implementation, and enforcement with surveillance and monitoring on the impact of implementing these policies with special focus on vulnerable populations. Ultimately, the AHA wants to ensure equitable, effective regulation for tobacco prevention and control to achieve a tobacco endgame for the entire population of the United States.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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*Modest.

†Significant.

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