Clinical Commentary Review

A Close Look at Vaping in Adolescents and Young Adults in the United States

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Vaping by adolescents and young adults is a legitimate concern as there is a risk that some may start smoking and that electronic cigarette (EC) use may have adverse effects in the developing lungs of adolescents. This commentary provides updated information on vaping patterns among adolescents and young adults in the United States, as well as the impact of EC usage on respiratory health.

EC use has surged greatly among high school students and young adults over the last decade but fortunately has declined significantly since its peak in 2019. During the same time period, smoking rates have constantly fallen to new low record levels. These trends argue against EC use as a gateway to smoking. Most EC usage is infrequent and unlikely to increase a person's risk of negative health consequences. Furthermore, the majority of EC usage has happened among those who have previously smoked. There is a dearth of data on the long-term health implications of EC usage in adolescents and young adults. We do not know whether short-term or intermittent use of EC in youth can lead to negative health outcomes in adulthood, and long-term high-quality studies in well-defined groups are needed. Although vaping has been linked to respiratory symptoms, they tend to be transient and of uncertain significance. This commentary provides up-to-date information so health care providers can give objective and responsible medical advice on EC usage.

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Key words: *E-cigarettes; Combustible cigarettes; Vaping; Smoking; Adolescents*

Electronic cigarettes (ECs) are battery-powered devices that operate by heating a metal coil that vaporizes a solution (e-liquid), mainly consisting of vegetable glycerol, propylene glycol (PG), distilled water, and flavorings, and which may or may not contain nicotine. ECs do not contain tobacco, do not create smoke, and do not rely on combustion to operate. Their design and efficiency in nicotine delivery have been modified substantially since their market introduction in early 2007. The user inhales the aerosol generated by heating the e-liquid in a process commonly referred to as "vaping." Currently, there are 3 main EC designs: (1) disposable products; (2) reusable, refillable devices that can be filled with e-liquid by the users (tank system); and (3) reusable devices that attach to prefilled e-liquid cartridges ("carts" or "pods") (Figure 1). Current EC devices are designed so that their operating temperature is electronically kept below 300°C. Because these aerosols are produced at much lower temperatures (compared with combustion, which generally starts at temperatures above 400°C), they contain less harmful and potentially harmful chemicals. They may however generate formaldehyde, acetaldehyde, and acrolein, but at much lower levels than tobacco smoke under normal condition of use.[1,2] For this reason, they have been proposed for harm reduction from cigarette smoking[3-5] and for smoking cessation,[6] although opinion remains conflicted regarding these proposals.[7-9]

There has been a surge in EC popularity among youth over the past decade. In the United States, exclusive current

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Abbreviations used
ACO- Asthma-COPD overlap syndrome
aOR- Adjusted odds ratio
CDC- Centers for Disease Control and Prevention
COPD- Chronic obstructive pulmonary disease
EC- Electronic cigarette
FDA- Food and Drug Administration
FVC- Forced vital capacity
MTF- Monitoring the Future
NHIS- National Health Interview Survey
NIDA- National Institute on Drug Abuse
NIH- National Institutes of Health
NYTS- National Youth Tobacco Survey
OD- Odds ratio
PATH- Population Assessment of Tobacco and Health
PG- Propylene glycol
QRA- Quantitative risk assessment

(past-30-day) use of ECs has risen to record levels among youth between 2011 and 2018 according to the Centers for Disease Control and Prevention (CDC),[10] with a further large increase in the period 2018-2019.[11] In terms of demographics, no gender difference has been reported, but White non-Hispanic youth have the highest vaping rates. In the United Kingdom, New Zealand, and Australia, similar high prevalence of EC use among youth has not been reported.[12-14]

Vaping by young nonsmokers is a legitimate concern. Although not studied in depth, there is a risk that some will become nicotine dependent or may take up tobacco smoking.[15-17] Although as yet there is little information regarding the long-term health effects of legally purchased combustion-free nicotine products in young people, some experts have raised concerns that EC use may have adverse effects in the developing brain and lungs of adolescents.[17] The most commonly reported adverse effects are throat/mouth irritation, headache, cough, and nausea, which dissipate with continued use.

This commentary is divided into 2 sections: (1) information on the most recent evolving patterns of vaping use among adolescents (12- to 17-year-olds) and young adults (18- to 24-year-olds), and (2) current knowledge about the impact of EC use on their behavioral and respiratory health. The goal is to provide physicians and other health care providers with updated information, so that they can be familiar with the topic and improve their counseling with patients using or intending to use ECs.

TRENDS AND PATTERNS OF E-CIGARETTE USE AMONG US YOUTH AND YOUNG ADULTS

The rising trend in vaping popularity among young nonsmokers is a valid concern. As there is little evidence of a high prevalence of regular EC use among youth in countries outside North America,[12-14] we will confine further discussion to US datasets. EC use among adolescents and young adults has become one of the most important public health concerns in the United States. Exclusive current (past-30-day) use of ECs has risen to record levels among youth between 2011 and 2019 according to the CDC[10,11] (Figure 2).

The prevalence of youth vaping in the United States has been monitored by many national surveys, including the following 4 federal surveys: (1) Monitoring the Future (MTF) funded by the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health (NIH), and conducted by the University of Michigan;[18] (2) the National Youth Tobacco Survey (NYTS), jointly funded by CDC and US Food and Drug Administration (FDA) and conducted by the CDC;[19] (3) the National Health Interview Survey (NHIS) conducted by the National Center for Health Statistics, which is part of the CDC;[20] and (4) the most recent Population Assessment of Tobacco and Health (PATH) study, a collaboration between the FDA Center for Tobacco Products and the NIH NIDA.[21]

When modeling the impact of EC use on public health, the frequency of EC use, concentration of nicotine in the EC, the specific EC device, vape liquid contents (eg, flavorings), and the concomitant cigarette smoking status of EC users are relevant factors to include in the models. When the 2015 NYTS revealed a significant increase in school vaping for the first time, among middle school students, only 0.6% had used an EC more than 20 times in the past 30 days (ie, frequent current users),[22,23] with 13.5% of these students having ever tried using an EC as little as once in their lifetime and 5.3% having used an EC a minimum of once in the past 30 days. Among high school students of the 2015 NYTS, these rates were 2.5%, 37.7%, and 16.0%, respectively.[22,23] According to the MTF survey,[15] past-30-day EC use was reported by 17.2% of 12th graders, but only 6.6% had used ECs for >5 days in the past month.[24,25] It is important that measures of EC use capture frequency, intensity, reasons for EC use, and concomitant cigarette smoking to provide a comprehensive framework for assessing the public health impact of ECs.[26-28] In particular, 1-time or experimental use of EC is highly unlikely to increase an individual's risk for adverse health effects.

The MTF survey also found that youths who have never smoked were much less likely to use EC than those who have smoked.[18,24] Only 1.7% and 0.7% of never smokers reported using EC for >5 days and 20 to 30 days of the past month, respectively. In contrast, 14.7% of current regular smokers and 15.0% of youth who smoked regularly in the past were using ECs frequently, suggesting that for some youth there is a predisposition to the use of nicotine containing products in general. According to the NYTS data, 87% of past-30-day EC users have ever used a combustible tobacco product, and 63% reported using a combustible tobacco product in the past 30 days.[29] In contrast, the proportion of never tobacco smokers who used EC for >10 days in the previous month was lower than 0.1%.[29] Very low rates of frequent EC use among young never smokers have also been reported in several other countries.[12-14,30,31] Concomitant cigarette smoking by EC users is likely the most important contributor to an individual's risk for developing adverse health consequences.

EC use among youth and young people in the United States peaked in the years 2018-2019. The 2019 NYTS confirmed a significant increase in vaping among high school students from previous years[10,32] (Figure 2). Exclusive current (past-30-day) use of ECs rose to record levels from 7.6% in 2017 to 15.1% in 2018 and to 22.4% in 2019.[11] In contrast, current (past-30-day) use of tobacco cigarettes declined from 7.7% in 2017 to 5.8% in 2019, mostly due to a sharp decline in exclusive use of tobacco cigarettes falling from 3.6% in 2017 to 0.8% in 2019.

According to the 2018 and 2019 NYTS data, current vaping rose from 3.1 to 4.1 million in high school students.[10,32] The number of never users of tobacco products who vaped frequently (ie, using ECs 20-30 days in the past month) more than doubled from 297,000 in 2018 to 681,000 in 2019 (Table I). However,

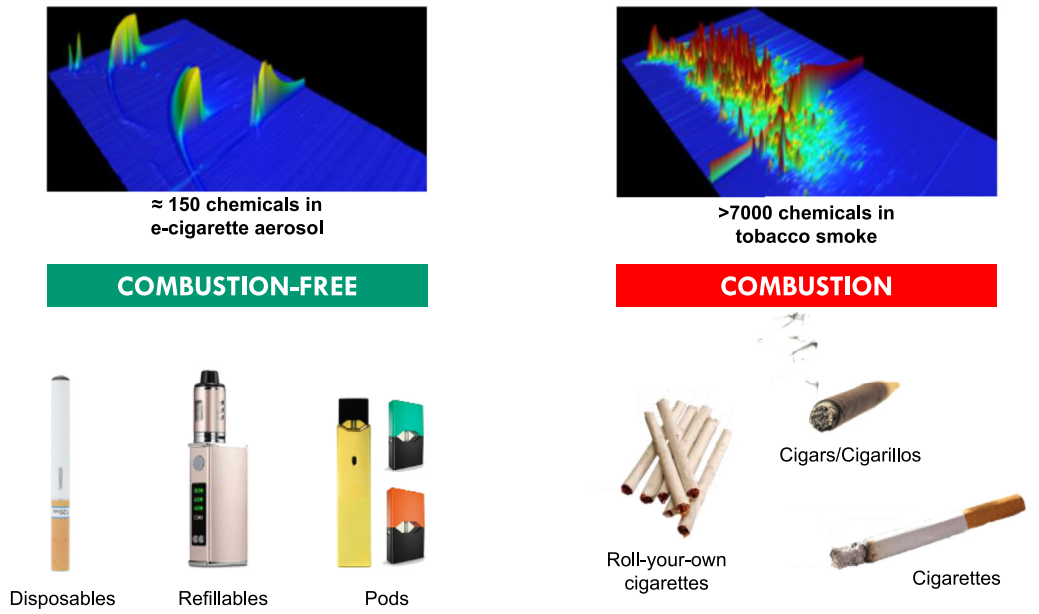

FIGURE 1. Bottom to the top: Three main e-cigarette designs: (1) disposable products; (2) reusable, refillable devices that can be filled with e-liquid by the users (tank system); and (3) reusable devices that attach to prefilled e-liquid cartridges ("carts" or "pods"). E-cigarette devices are designed to operate at much lower temperatures (below 250°C-300°C) compared with tobacco products that require combustion to operate (generally at temperatures above 400°C-450°C). For this reason, e-cigarettes emission aerosols are much less toxic than tobacco cigarettes. The untargeted analysis of cigarette smoke versus e-cigarette emission aerosol by gas chromatography with time of flight mass spectrometry (from Behrsing H, Hill E, Raabe H, Tice R, Fitzpatrick S, Devlin R, et al. In vitro exposure systems and dosimetry assessment tools for inhaled tobacco products: workshop proceedings, conclusions and paths forward for in vitro model use. Altern Lab Anim 2017;45:117-58) shows that e-cigarettes generate less toxic chemicals (and a lower levels) than tobacco cigarettes.

the most recent survey data (2021 NYTS) has shown a 58% reduction in high school vaping from a peak prevalence of 27.4% in 2019[33,34] to 11.2%. After peaking in 2019, the number of never users of tobacco products who vaped frequently has progressively declined from 681,000 to 468,000 in 2021, meaning that the percentage of American high school students with no history of previous tobacco use at risk of potentially becoming addicted to vaping nicotine is now reduced to approximately 3%. This percentage is low and does not justify the claims of a new "teen vaping epidemic." The NYTS also indicates that high school cigarette smoking is fast declining, with smoking rates falling 77%, from 8.3% (in 2018) to 1.9% (in 2021), at the time vaping rates also declined (Figure 2).

The vaping rates of both high school students based on the NYTS and young adults 18 to 24 years old from the NHIS[35] confirm the growing popularity of EC use among youth over the last 6 years, with vaping surpassing smoking for the first time in 2019 in young adults (Figure 3). Interestingly, the prevalence of vaping in young adults is substantially lower than the high prevalence in high school students reported in the NYTS. For example, in 2019, when high school vaping reached 27%, it registered only 9% among young adults.

According to NYTS data, the exclusive use of cigarettes declined substantially from 2.6% to 0.8% from 2018 to 2019 (Figure 2). Record-low levels of tobacco smoking prevalence based on the NHIS have also occurred among young adults 18 to 24 years old (Figure 3).[35] The prevalence of cigarette smoking in 2014 was 16.6%; it had fallen by over one-half by 2019 to 7.7%, a rate of decline in smoking prevalence that was even larger than that among high schoolers, which fell from 9.2% in 2014 to 5.8% in 2019.

Another important finding in the NYTS is that a large majority of high school vapers are vaping marijuana at comparatively high frequency. Approximately half of EC users in the past 30 days and 70% of frequent EC users reported ever marijuana use with EC in 2017 and 2018.[36,37] This increasing trend has been confirmed in a more recent NYTS analysis.[38] The growing popularity of marijuana vaping is of serious concern because its use during adolescence is associated with decline in memory, attention, and learning.[39] Respiratory health effects of habitual marijuana use have been recently described.[40] Moreover, the use of some marijuana vaping products contaminated with vitamin E acetate has been linked to severe lung injuries and deaths among many young Americans.[41,42] The exact biochemical interaction of vitamin E acetate with lung tissue is uncertain and is a subject of ongoing work.[43,44]

In summary, among high school students, EC use has increased substantially over the past decade, but has declined significantly since its peak in 2019. In contrast, over the same time interval, smoking rates have substantially and consistently declined to record low levels. These trends and most recent high-quality analyses[45-47] do not suggest that EC use is a gateway to smoking. The vast majority of EC use is infrequent and unlikely to increase an individual's risk for adverse health effects. Moreover, most EC use has occurred among those who have already smoked and rarely among those who have never smoked.

Among young adults (18-24 years of age), EC use has also increased over the past decade, although to a less extent than

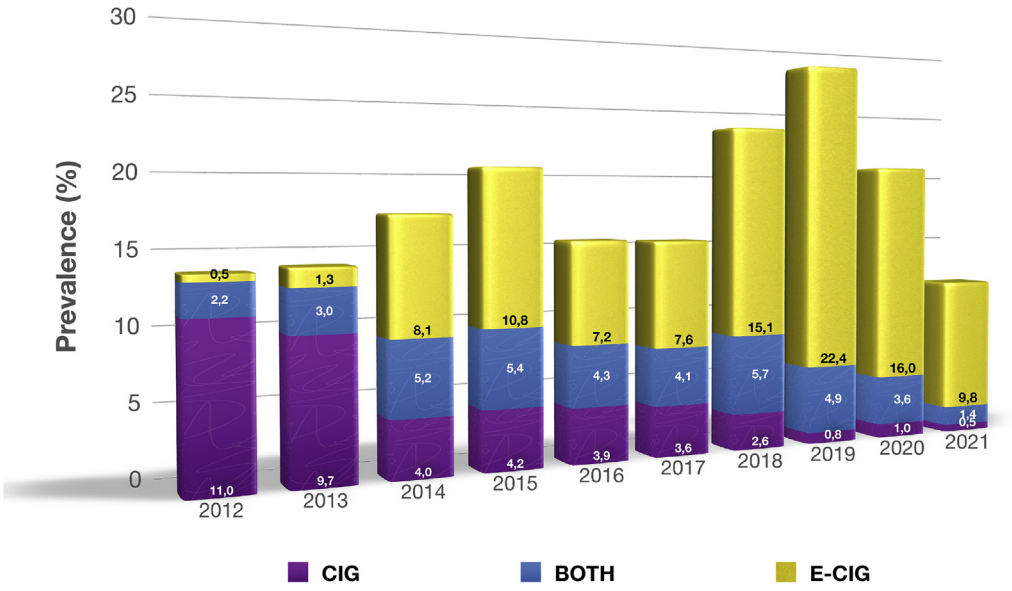

FIGURE 2. Current (past-30-day) e-cigarette and tobacco cigarette use in the United States among high school students, National Youth Tobacco Survey 2012-2021.

among high school students. Over the same time, smoking rates have markedly declined, but remain higher than the rates in high school students. As with high school students, it does not appear that EC use serves as a gateway to smoking.[45-47]

HEALTH IMPLICATIONS OF E-CIGARETTE USE AMONG US YOUTH AND YOUNG ADULTS

Youth should not vape, smoke, binge drink, or use illicit drugs, but some will take these risks anyway no matter what adults tell them. Most recent NYTS data indicate that approximately 1.2 million US high school never smokers are vaping (see Table I). There is concern that some will become nicotine dependent and/or experience adverse health effects in the developing brain and lungs,[17,48-51] but only limited information is available about the long-term health effects of legally purchased combustion-free nicotine products in adolescents and young adults.

The 2016 Surgeon General report[52] is clear that there are no existing studies regarding youth-related health outcomes of exposure to EC aerosol emissions, with the evidence for health risk being limited to studies of adults and/or findings from *in vitro* and animal studies. However, the latter studies are difficult to apply to humans because of abnormal exposure protocols that do not replicate normal conditions of use and lack appropriate experimental controls, as discussed extensively in a recent review article.[53]

To understand the actual health risks from youth vaping, it is important to consider that EC emission aerosols are produced at much lower temperatures compared with combustion (which generally starts at temperatures above 400°C) and therefore contain substantially less harmful and potentially harmful chemicals than tobacco smoke[1,2,54] and exert reduced bronchial epithelial cytotoxic and inflammatory responses under realistic conditions.[55] A number of studies supply evidence for significant reductions in exposures to toxic products in exclusive EC users, including >90% reductions in levels of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (a proxy for the cancerogenic nicotine-derived nitrosamine ketone), 1,3-butadiene and acrylonitrile (among 2 of the greatest sources of cancer risk in tobacco cigarettes), and carbon monoxide (a major risk factor for cardiovascular disease) compared with cigarette smoke exposure.[56-58]

On the other hand, EC emission aerosols do contain formaldehyde, acetaldehyde, and acrolein that can lead to adverse health effects. Although these consumer products are not risk free, a meaningful health risk evaluation of using ECs via quantitative risk assessment (QRA) provides a scientific, evidence-based analytical process that combines the chemical and biological data to quantify the probability and potential impact of some defined risks.[59] According to the US Environmental Protection Agency, QRA is essential to determine profile hazards that may pose a health risk.[60,61] When the aerosol testing data under normal condition of use are combined with QRA methodology, the potential health risks associated with EC use are thought to result in a substantially reduced level of relative health risk versus tobacco cigarettes.[1,62]

When assessing the actual health risk from youth vaping, it is also important to consider that meaningful characterization of exposure for vaping studies (eg, frequent/daily use vs ever-use) is a key factor. Moreover, studies need to be adjusted for previous or concomitant combustible cigarette smoking status, a clear confounder when assessing respiratory health effects. Only occasional or experimental vaping by nonsmokers and EC use by smokers are unlikely to have a significant impact in terms of long-term adverse health effects apart from effects of smoking itself.

Surveys investigating respiratory health effects attributable to EC use in youth have recently been published. A recent meta-analysis of 10 cross-sectional studies on vaping in adolescents showed significantly higher odds of having asthma for both current use (odds ratio [OR] = 1.36) and ever use (OR = 1.20) compared with never use.[63] Considering the cross-sectional

TABLE I. Changes in prevalence of specific profiles of tobacco product use among high school vapers from NYTS (2018-2021)

US high school population	NYTS 2018		NYTS 2019		NYTS 2020		NYTS 2021	
	14.8 million		15.0 million		15.5 million		15.4 million	
		Percentage of high school population		Percentage of high school population		Percentage of high school population		Percentage of high school population
Current vapers	3,138,000	21.2	4,114,000	27.4	3,021,000	19.5	1,722,000	11.2
	⇓		⇓		⇓		⇓	
Used other tobacco product*	1,481,000	10.0	1,474,000	9.8	1,086,000	7.0	519,000	3.4
Never used other tobacco product*	1,657,000	11.2	2,640,000	17.6	1,935,000	12.5	1,203,000	7.8
	⇓		⇓		⇓		⇓	
Less frequent vapers†	1,360,000	9.2	1,959,000	13.1	1,282,000	8.3	735,000	4.8
Frequent vapers‡	297,000	2.0	681,000	4.5	653,000	4.2	468,000	3.0

*Includes tobacco cigarettes; cigars, cigarillos, little cigars; chewing tobacco, snuff, dip, snus, or dissolvable tobacco products; smoke tobacco in a hookah or water pipe.
EC, Electronic cigarette; *NYTS*, National Youth Tobacco Survey.
†Defined as having used an EC on 1 to 19 of the past 30 days.
‡Defined as EC use on at least 20 of the past 30 days.

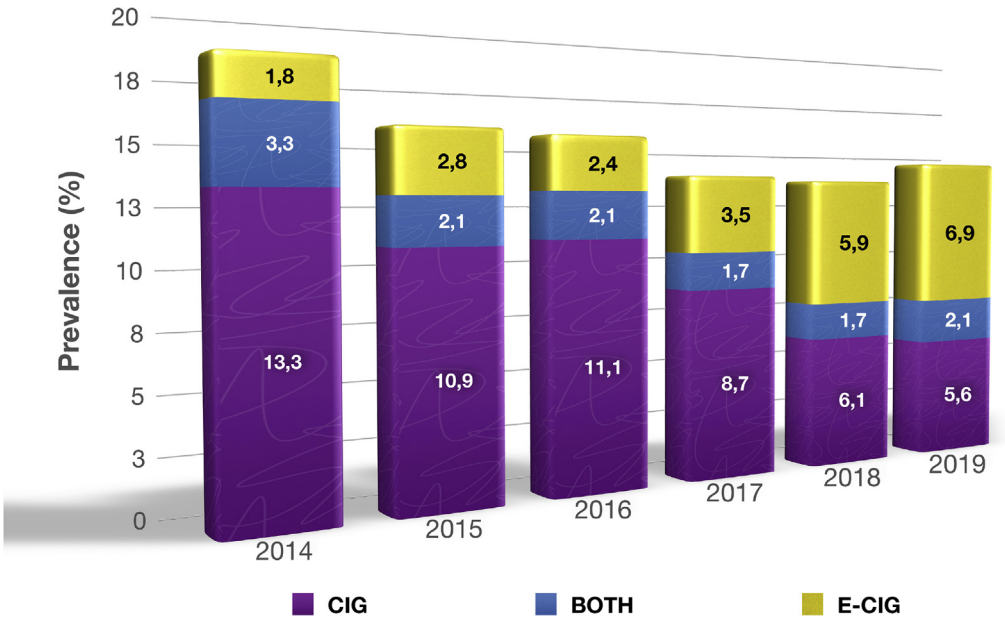

FIGURE 3. Current (every or some days) e-cigarette and tobacco cigarette use in the United States among 18- to 24-year-olds, National Health Interview Survey 2014-2019.

nature of all selected studies and the lack of information about the temporal sequence between cause (ie, EC use initiation) and effect (ie, self-reported asthma), no conclusions about causality can be reached with certainty. This is particularly true when considering that asthma prevalence is higher predominantly during childhood, and that vaping may have started after asthma diagnosis, therefore ruling out causality. Young participants' self-reporting whether they had asthma diagnosed by a doctor within the past year is an imprecise measure of asthma, and the diagnosis of asthma could have been already present many years before any EC use. Current users were defined by any EC use in the past 30 days, and all selected studies lacked more detailed quantitation of exposure frequency. As discussed in the previous section of this commentary, frequent/daily use among adolescents is not highly prevalent with the largest portion of EC users reporting use only 1 to 2 times during the past 30 days. It is unlikely that such low-level exposure is causative for the reported increase in the risk of a doctor's diagnosis of asthma. Alternative factors should be considered. The selected studies do not adequately adjust for the residual confounding from tobacco

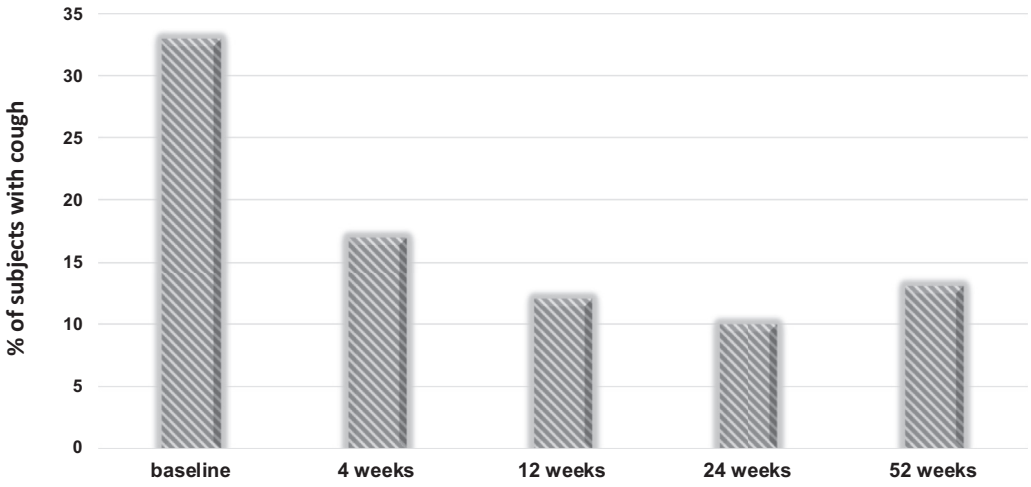

FIGURE 4. Reduction in dry cough reported by regular e-cigarette users who managed to abstain completely from tobacco smoking after switching at baseline.[56,70]

smoking, which itself is an important risk factor for both incident asthma and asthma exacerbation.[64]

In a recent paper that was not included in the meta-analysis discussed above, Bircan et al[65] investigated the association between EC use and a self-reported diagnosis of asthma, chronic obstructive pulmonary disease (COPD), and asthma-COPD overlap syndrome (ACO) using a large representative sample of persons from the Behavioral Risk Factor Surveillance System with a particular focus on those 18 to 24 years old. The authors excluded people with a previous and current smoking history from their study sample, thus limiting the impact of a major confounder on respiratory disease outcomes. Although they reported significant associations of exclusive EC use with self-reported asthma, COPD, and ACO, they did point out that the study could not demonstrate a causal effect because of its cross-sectional design. Besides the real possibility of diagnostic mislabeling, the reported associations with asthma rest on a relatively small number of cases, namely, 430 and 314 cases of asthma among EC users and nonusers, respectively. The reported data on self-reported COPD and asthma are likely unreliable because COPD is rarely diagnosed before the age of 40 years and the total number of asthma cases (744, combining EC users and nonusers) is much smaller than expected (approximately 1.5%) in the population of 469,077 persons surveyed. Moreover, the reported associations do not consider key predictors for asthma diagnosis (such as family history of asthma and other allergic diseases), and their propensity score only matches demographic conditions. Finally, given the significant associations found with self-reported asthma in this study, the possibility of reverse causation should be considered. For example, young adults with respiratory symptoms may try vaping because they have heard that it might provide some relief from the aggravating effects of smoking.

Cross-sectional analyses of population-based data are inconclusive with respect to health effect outcomes. Recently, a longitudinal study has investigated the respiratory health effects of EC use in a nationally representative cohort of US young adults. Using data derived from PATH waves 2, 3, 4, and 5 for young adults aged 18 to 24 years, Xie et al[66] showed that both former and current EC use were associated with higher odds of developing any respiratory symptom (adjusted OR [aOR] = 1.20 and 1.32 for former and current EC use, respectively) and wheezing (aOR = 1.41 and 1.51 for former and current EC use, respectively). Like most previous studies, cigarette smoking history was either not considered or insufficiently adjusted for in the analysis. Although this paper did consider different types of tobacco use history (eg, having a separate group of never smokers who use ECs is a strength of the paper), using cigarette smoking as a binary covariate (ie, yes/no) in an adjusted model is insufficient. A much stronger analytical approach is to adjust for cumulative amount of cigarette smoked (ie, pack-years) as used in the recent study by Sargent et al[67] based on data derived from PATH. When these authors adjusted for pack-years of smoking history, the significant association became nonsignificant—illustrating how much residual confounding there is when using "crude" binary measures. Interestingly, Xie et al[66] found that current EC-only use was associated with significantly lower odds of developing wheezing in the chest (aOR = 0.62; 95% confidence interval: 0.39, 0.99) in comparison with current combustible cigarette smoking only. Although associations of EC use with any respiratory symptoms were also lower in current EC-only users than in current cigarette-only smokers, these differences were not statistically significant in the fully adjusted models.

The limitations of the study of Xie et al[66] and other similar surveys are not acknowledged and as a result many researchers are led to believe that EC use harms the lungs.[68] Because most current EC research is poorly designed, conducted, and interpreted, producing fair and reliable information for the adoption of more effective tobacco control policies and healthier lifestyles has become very challenging. Public mistrust about ECs is exacerbated by the spread of misinformation and distortion of scientific truth. Propagation of common mistakes in epidemiological surveys requires urgent critical review and reform. Common flaws in the methodology of epidemiology research have been critically analyzed, including lack of a clear hypothesis statement, methods that were not tailored to address the question of interest, poor characterization of outcome measures, failure to control for

TABLE II. Common misconceptions about electronic cigarettes (ECs)

Common misconceptions	Countering misconceptions	Key evidence (see the list below)
ECs do not help smokers quit	Evidence from randomized controlled trials, observational studies, and population data converge on showing that vaping is an effective approach to smoking cessation. Daily vaping delivers better nicotine replacement and is far more effective than less frequent use. Those who vape daily are 2 to 8 times more likely to quit smoking than smokers who do not vape. Many studies that claim to show no effect suffer a range of shortcomings and biases.	References[6,28,81-88]
ECs and tobacco cigarettes are similarly harmful	ECs are much less harmful beyond any reasonable doubt. This is because vaping products do not involve combustion and the chemical composition of EC emission aerosols contains substantially less harmful and potentially harmful chemicals than the smoke from burning tobacco in cigarettes. The evidence for "less harmful" comes not only from EC emission aerosols toxicology but also from human biomarker studies with substantial reductions in exposures to toxic chemicals occurring in exclusive EC users compared with cigarette smokers. Comparisons of EC emission aerosols and cigarette smoke toxicity suggest that nicotine vaping is likely to have at least 95% lower risk than cigarette smoking.	References[1,2,55,57,77,78,89]
Nicotine is harmful	Nicotine does not cause cancer, heart, or lung disease. It does not cause cancer in humans according to leading health authorities including the US Surgeon General and the International Agency for Research on Cancer. Nicotine is not the main cause of heart disease from cigarette smoking. Although people with established cardiovascular disease might incur some increased risk from EC use, the risk is certainly much less than that of cigarette smoking and may be similar to risks from drinking coffee (people with severe heart conditions are commonly advised not to drink coffee or use caffeine). When switching to ECs, the harms from smoking would be substantially reduced and there would likely be a substantial net benefit for cardiovascular health. There is also no evidence that nicotine itself causes lung damage or disease as shown by decades of postmarketing surveillance for nicotine patches and nicotine gum.	References[4,90-94]
Nicotine harms adolescent brains	Concerns of harm to brain development from nicotine are based on rat and mouse studies. The validity of extrapolation of brain "changes" in young rodents exposed to nicotine levels that are not relevant to human exposure is highly speculative. Similar brain changes are seen when young rodents are exposed to caffeine. Research has yet to elucidate whether nicotine use in the human adolescent years results in later sequelae. Concerns about brain function effects of nicotine exposure through vaping deserve serious examination.	Reference[52]
Vaping causes cancer, and heart and lung disease	There is no evidence that these products present a material risk of disease at this stage. Studies that claim vaping harms have ignored the fact that most adult vapers are former smokers and have lingering harms caused by that behavior. Improvement in endothelial function, vascular stiffness, flow-mediated dilation, and blood pressure is reported in smokers after switching from tobacco cigarettes to ECs. Likewise, improvement in subjective and objective respiratory outcomes is reported in smokers switching to ECs.	References[2,28,52,76,94-101]
ECs can cause EVALI	Nicotine vaping was not the cause of the EVALI outbreak (EC, or vaping product use −associated lung injury) in the United States in 2019. This condition was strongly linked to vitamin E acetate (VEA) that was added to black-market THC vaping oils. It disappeared after VEA was removed from the illicit supply chain.	References[41,42]
There is a "teen nicotine vaping epidemic" in the United States	Current federal dataset do not show a "teen nicotine vaping epidemic." A close look at NYTS figures of frequent and daily use does not provide support for claims of a new "epidemic" of nicotine addiction, because only approximately 3% of American high school students with no history of previous tobacco use are at risk of potentially becoming addicted to vaping nicotine. In addition, the CDC has acknowledged that the so-called epidemic had subsided in 2020, and that teen vaping rates plummeted in 2020-2021.	References[102-105]
Youth vaping is a gateway to smoking	US high school smoking has dropped 90% over the past 10 years (2012-2021). Further, among all US adults, the age group with the steepest rate of smoking decline over the past decade is young adults, followed by the next age cohort (25-34 years old). Ten years of EC use shows no hint of the claimed gateway-to-smoking effect. These trends and most recent rigorous prospective studies that adjust for a wide range of common risk factors for smoking and vaping (confounders) do not suggest that EC use is a gateway to smoking. Moreover, evidence from population studies also suggests that vaping more likely diverts young people from smoking than encourages them to smoke.	References[45-47,106-108]

(continued)

TABLE II. *(Continued)*

Common misconceptions	Countering misconceptions	Key evidence (see the list below)
ECs more addictive than cigarettes	Statements about the risk of addiction from nicotine vaping draw from the existing literature on cigarette smoking—and not nicotine vaping. By equating findings obtained from conventional cigarette smoking to EC vaping, a comparable risk is ultimately portrayed. The sharp decline in nicotine vaping among youth does not support the notion that nicotine vaping is as addictive as cigarette smoking. Moreover, youth exclusive EC use (in never smokers) is not stable over time and there are very few regular every day users. Although ECs have been shown to perpetuate the already existing addiction in former or current smokers concurrently using these combustion-free products, the current consensus is that ECs are less addictive than cigarettes. Smoke contains other chemicals that enhance the addictiveness of smoke and these are absent from EC emission aerosols. No data are available in exclusive EC users who never smoked before (people without previous nicotine addiction as in former cigarette smokers).	References[19,20,52,105,109-113]
Most vaping is "dual-use" of ECs and tobacco cigarettes	Many vapers do use both ECs and cigarettes together for variable periods. However, the proportion of dual users has been falling in the United Kingdom and the United States, and is now well below half (US NHIS 2020 27%; UK ASH 2021 30.5%). Higher declines in dual usage rate have been reported for youth in NYTS and NHIS (NHIS 2019 23%; NYTS 2021 12.5%). This is probably due to several factors: many dual users are in transition from smoking to vaping over a period of months or years. Also, as the technologies improve over time, it is likely that more of the users will find exclusive vaping a satisfactory alternative to smoking. Dual use should be properly understood as part of a behavioral pathway that evolves over time, not something that is static and fixed. Vaping may start with no intention to quit smoking, but as the user becomes more familiar and finds the product they like, they gradually make more use of the product in more situations. Although dual users are more heavily dependent, most studies show substantial reductions in cigarette consumption and reduced biomarker levels. They are also more likely to quit than exclusive smokers.	References[19,20,105,114-117]

ASH, Action on Smoking and Health; *CDC*, Centers for Disease Control and Prevention; *NYTS*, National Youth Tobacco Survey; *NHIS*, National Health Interview Survey; *THC*, tetrahydrocannabinol.

relevant confounding factors, and claim of causal association unsupported by the data.[28]

Cough has been repeatedly noted to be commonly associated with inhalation of respiratory irritants in EC emission aerosols (eg, PG, some flavorings, formaldehyde, acetaldehyde, and acrolein).[53,69] This triggering of the (physiological) reflex of the cough has been shown to be transitory[56,70] (Figure 4) and is of uncertain prognostic value with regard to the development of actual respiratory illnesses.

This is in agreement with several acute clinical studies consistently showing no changes in lung function or signs of airway inflammation in response to EC use (both subjects with pre-existing respiratory condition and matched healthy controls) (reviewed in the paper by Polosa et al[53]) and also consistent with results from a large internet survey reporting transient throat irritation, dry cough, and other symptoms of respiratory irritation in some smokers when switching to ECs.[71]

Further investigations of the respiratory health impact of long-term EC use face the challenge that previous smoking is likely to cloud any vaping health effects.[72] Such studies would require precise information about former smoking intensity (duration, quantity, intensity of puffing behavior, etc) and a very large sample size to "control for" the effects of former smoking. Because all plausible hypotheses about the health risks from vaping are confounded by former smoking, only studies of people who vape but have had very limited smoking history will allow us to detect long-term health risks from vaping. Prospective studies in young vapers may present an opportunity for evaluating these risks. In a small prospective study of relatively young daily EC users (mean age of 29.7 years) who had never smoked, no noticeable changes from baseline were observed over the 3.5-year observation period.[73] Because the EC users in this study were never smokers, potential confounding by inhalation of combustion products of tobacco was obviated. Daily exposure to EC aerosol emissions caused no significant changes in any of the health outcomes investigated, including the measures of lung function and lung inflammation. Moreover, no significant structural abnormalities could be identified on High Resolution Computed Tomography of the lungs, and no respiratory symptoms were consistently reported. However, the sample size was small and the follow-up interval short. Prospective high-quality studies over long time intervals in large cohorts of young EC users are clearly warranted to accurately advance the current understanding of ECs' impact on human health. These recommendations have been discussed in a recent commentary.[74]

A few clinical studies have been conducted on asthma, but none in youth asthma. Findings in a small ambulatory population of regular EC users with mild-to-moderate asthma did not show any deterioration in lung function, asthma symptoms, and exacerbation rates, but exhibited progressive significant improvement in the Juniper's Asthma Control Questionnaire, forced expiratory volume in 1 second, forced vital capacity (FVC), and forced expiratory flow between 25% and 75% of the FVC, as well as airway hyper-responsiveness to inhaled methacholine.[75] A 2-year follow-up study of this small cohort confirmed that EC use ameliorated objective and subjective adverse asthma outcomes and suggests that these beneficial effects may persist in the long term.[76]

The possibility that exposure to EC emission aerosols can trigger asthma attacks or cough cannot be discounted. However, cough is commonly reported in EC users (particularly soon after switching), and this is independent from the presence of asthma.[6,56,70] The vapers' cough is a physiologic response to the inhalation of nonspecific respiratory irritants (eg, propylene glycol, freebase nicotine) in vaping products and has been shown to be transitory.[6,56,70]

CONCLUSIONS

The current trends of decreasing combustible cigarette smoking and EC use are encouraging. Nonetheless, we must remain vigilant to ensure that excessive levels of vaping among youths are promptly detected and reversed as soon as possible. In the meanwhile, authorities must enforce current regulations addressing illicit sales to minors to limit the access to tobacco and nicotine products.

When compared with tobacco cigarettes, ECs have been shown to emit far fewer toxicants and carcinogens. Despite existing knowledge about the potential adverse effects of the chemicals in EC emission aerosols—based on analytic chemistry, and the toxicology and epidemiology of those exposures—we do not know whether short-term or intermittent use of EC in youth can lead to adverse health consequences in adulthood, and clearly long-term high-quality studies in well-characterized populations (that consider important factors such as user characteristics, frequency of use, device used, and e-liquid type consumed) are needed.

Although the US FDA's strict regulatory requirements will ensure that ECs on the market for US smokers are "appropriate for the protection of public health," robust postmarket surveillance will be required to identify any unanticipated health issues that may arise from any harmful chemicals emitted by ECs. On the basis of the review of the scientific data, the US FDA has recently granted market authorization of several vaping products.[77,78]

Concerns that ECs may provide a risk are valid, but this risk might be reduced by a mix of technological innovation and vaping product regulation that prioritizes quality and safety checks. For example, to avoid overheating and excessive carbonyl buildup, newer devices have improved wicking designs and introduced automatic temperature control functions. Vaping product standards now address concerns regarding product quality and safety,[79,80] but a regular review of these regulations is valued.

Although EC use by young nonsmokers is a legitimate concern, known risks from vaping are often greatly exaggerated; common misconceptions about EC use and the evidence to refute these misconceptions are summarized in Table II.

This commentary gives updated information to physicians and other health care providers so that they can be knowledgeable about the topic and provide objective and responsible medical advice concerning EC use. The general public has a right to accurate information regarding the potential hazards of using EC as well as their favorable safety profile versus combustible cigarettes.

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