

INVITED REVIEW

# Electronic Cigarettes: Harm Enhancement and Protection of Global Tobacco Interests\*

Stanton A. Glantz<sup>ID</sup>

San Francisco, CA, USA

ORCID iDs of the authors: S.A.G. 0000-0003-4620-6672.

## Main Points

- Electronic cigarettes (e-cigarettes) mimic cigarettes' delivery of a nicotine aerosol to the lungs without burning tobacco, which has led many to assume they are substantially safer than cigarettes.
- By 2023, there were nearly 10,000 scientific papers on e-cigarettes that revealed higher dangers than assumed, that e-cigarettes as consumer products do not help smokers quit, and that they have addicted millions of youth to nicotine.
- The failure of e-cigarettes as consumer products to help people stop smoking makes their relative toxicity compared to cigarettes a moot point.
- Electronic cigarettes have attracted millions of youth at low risk of initiating nicotine use of cigarettes, extending and worsening the nicotine/tobacco epidemic.
- Countries, including Turkey, which have prohibited the import and avoided the sale of e-cigarettes have done better overall at controlling the e-cigarette epidemic than countries, including the United States and England, which have adopted more laissez-faire policies toward e-cigarettes.
- Turkey should maintain and ensure effective enforcement of its current policies to continue to protect its population from e-cigarettes.

## Abstract

Electronic cigarettes mimic cigarettes' nicotine aerosol without burning tobacco. The assumption has been that electronic cigarettes are substantially safer than cigarettes because they avoid combustion. This assumption, combined with assumptions that electronic cigarettes are effective for cigarette cessation and do not appeal to youth, led many to argue electronic cigarettes are harm reduction. By 2023, evidence revealed higher risks than assumed, that electronic cigarettes as consumer products do not help smokers quit, and that electronic cigarettes have addicted millions of youth to nicotine. Dual use (using both electronic cigarettes and cigarettes) is more harmful than just smoking cigarettes. The failure of electronic cigarettes as consumer products to help people stop smoking makes their relative toxicity compared to cigarettes a moot point. Electronic cigarettes have also played a role in the multinational tobacco companies' efforts to reposition themselves as socially responsible, which helps protect their financial and political interests. Countries, including Turkey, that have prohibited the import and avoided the sale of electronic cigarettes have done better overall at controlling the electronic cigarette epidemic than countries, including the United States and England, that have adopted more laissez-faire policies toward electronic cigarettes. Turkey should maintain and ensure effective enforcement of its current policies to continue to protect its population from electronic cigarettes.

**Keywords:** E-cigarettes, electronic cigarettes, smoking cessation, youth, dual use, tobacco industry

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### Corresponding Author:

Stanton Glantz

### E-mail:

stanton.glantz@sonic.net

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## Introduction

Electronic cigarettes (e-cigarettes), devices that deliver an aerosol of ultrafine particles, nicotine, and (usually) flavorings to the lungs, are designed

to mimic the delivery of nicotine by conventional cigarettes but without burning tobacco. Unlike cigarettes, which generate the nicotine aerosol smokers inhale by burning tobacco, e-cigarettes generate the aerosol by heating a wick soaked in a liquid

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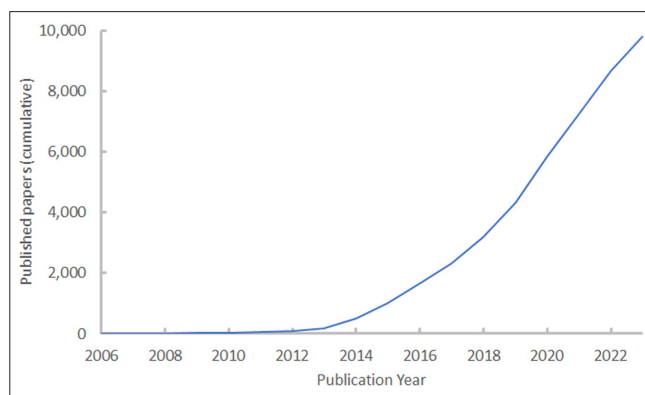


Figure 1. Peer-reviewed papers indexed in PubMed for “e-cigarette\*” as of November 3, 2023.

containing nicotine. The assumption has been that e-cigarettes are substantially safer than cigarettes because they do not generate some of the toxic combustion products produced by burning tobacco. This assumption, combined with the assumptions that e-cigarettes would be an effective way for people to stop smoking cigarettes and that they would not appeal to youth, has been widely promoted, including by some health authorities, since e-cigarettes were first marketed in 2006.

By November 2023, there were nearly 10,000 scientific papers published on e-cigarettes (Figure 1). This research revealed that e-cigarettes are more dangerous than previously assumed, that e-cigarettes as consumer products do not help smokers quit, and that they have attracted millions of youth to nicotine addiction. The net effect has been to prolong and expand the nicotine addiction epidemic to the benefit of tobacco companies.

### Electronic Cigarette Risk Compared to Cigarettes

The origin of the still-quoted “95% safer” claim was a paper by Nutt et al. (Nutt et al., 2014) that reported the results of a consensus meeting of 12 individuals, many of whom had ties to e-cigarette interests (Spencer, 2015; *The Lancet*, 2015). Nutt et al. did not cite any empirical evidence to justify their safety assessment (Eissenberg et al., 2020). Nevertheless, in 2015 Public Health England adopted this risk assessment (McNeill et al., 2015), which was still being widely promoted by pro-e-cigarette interests in 2023 (Pym & Watkinson, 2023).

In 2018, the US National Academy of Sciences, Engineering and Medicine (National Academies of Sciences Engineering and Medicine 2018) (NASEM) concluded based on a review of the available literature at the time (less than one-third of what was available as of November 2023; Figure 1) that “across a range of studies and outcomes, e-cigarettes pose less risk to an individual than combustible tobacco cigarettes.” This conclusion was based on the fact that e-cigarettes produce lower levels of many of the toxic combustion products that cigarettes produce. These combustion products are often measured in people as “biomarkers of exposure” (Wilson et al., 2021), which serve as surrogate measures (Ciani et al., 2017) of disease in the absence of epidemiological studies of actual disease associated with e-cigarette use. NASEM commented on the lack of such direct evidence of the association between e-cigarette use and disease: “Implications for long-term effects on morbidity and mortality are not yet clear.”

Since then, the epidemiological literature on actual disease effects of e-cigarette use has appeared. Meta-analyses published in 2021 and 2022 found increased odds of asthma (Chand & Hosseinzadeh, 2021; Li et al., 2022; Wills et al., 2021) and chronic obstructive pulmonary disease (Wills et al., 2021) associated with e-cigarette use independent of cigarette use. An umbrella review of literature as of July 2020 found evidence on “cardiovascular disease, cancer, development, and mental and reproductive health, is insufficient or unavailable” (Banks et al., 2023), but by June 2022 there were at least 61 population epidemiological studies of the association between e-cigarettes and disease indexed in PubMed (Glantz et al., 2022) showing statistically significant risks associated with e-cigarette use for cardiovascular, respiratory, and oral disease.

Moreover, dual use (using e-cigarettes while continuing to smoke-cigarettes) is riskier than using cigarettes or e-cigarettes alone (Glantz et al., 2022; Pisinger & Rasmussen 2022; Wang et al., 2018) This finding is important because dual use is common among adults who use e-cigarettes (Hedman et al., 2018; Kim et al., 2020; Mayer et al., 2020).

These disease risks associated with e-cigarettes in the epidemiological studies are consistent with biological studies that show a wide range of adverse pulmonary (Gotts et al., 2019; Wills et al., 2021), cardiovascular (Keith & Bhatnagar, 2021; Rao et al., 2022), and oral disease effects (Holliday et al., 2021). The risks identified in the epidemiological studies are higher than what one would predict from the biomarker studies (Wilson et al., 2021), probably because the biomarker studies focus on a small number of biomarkers that are mostly combustion products in cigarette smoke. In addition, surrogate markers often underestimate biological effects (Ciani et al., 2017). Even more importantly, e-cigarettes do not generate the same mix of toxicants as cigarettes: There are other toxicants in e-cigarette aerosol that are present at higher levels than in cigarette smoke (Gordon et al., 2022; Tehrani et al., 2021; Yan et al., 2021).

In sum, while e-cigarettes may be less toxic than cigarettes, they still pose substantial risks to users, and dual use is riskier than just smoking.

### Electronic Cigarettes and Smoking Cessation

From the beginning, e-cigarettes have been promoted as a way to stop smoking cigarettes. The idea has been that because e-cigarettes deliver an aerosol of inhaled nicotine just as cigarettes do and mimic the hand-to-mouth behavior involved in cigarette smoking, they would be a superior cigarette smoking cessation aid.

#### Randomized Controlled Trials

Systematic reviews of randomized controlled trials of e-cigarettes as smoking cessation aids delivered in a clinical context have found that nicotine e-cigarettes are effective at increasing smoking cessation compared to placebo and, in many cases, conventional nicotine replacement therapy (Hartmann-Boyce et al., 2022; Hedman et al. 2021; Lindson et al., 2023; Wang et al. 2021). While these studies suggest that e-cigarettes might pass the efficacy test when drug approval authorities assess a therapeutic intervention, they do not address the safety dimension of such an approval (The findings of positive associations between

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e-cigarette and disease discussed above raise questions about whether or not a drug authority would find a favorable benefit/risk ratio for e-cigarettes as a smoking cessation therapy). As of November 2023, no government drug authority had authorized the use of e-cigarettes as a clinical smoking cessation intervention. It is not known whether this lack of approval was the result of e-cigarette manufacturers applying for such approval and being denied or manufacturers not applying at all.

Another problem with these trials is that the outcome is “stopped smoking cigarettes” (i.e., “switched completely”) without regard to whether the smoker continued using e-cigarettes. These trials do not consider continued use of e-cigarettes an adverse effect, even though e-cigarette use alone carries substantial risks.

More importantly, these trials did not consider dual use an adverse event. It is important to consider dual use because one large randomized trial of e-cigarettes in which participants were provided free e-cigarettes through the mail (Carpenter et al., 2023) (vs. people who were not) found that at 6 months for every person who stopped smoking cigarettes (including switchers who continued using e-cigarettes and quitters who did not smoke cigarettes or use e-cigarettes), the e-cigarette group had 2.7 became dual users compared to 1.8 in the control group (Glantz, 2023). These dual users are at increased disease risk than if they had never used e-cigarettes.

The situation is even more concerning if one considers nicotine (rather than just cigarette) cessation as the outcome. A meta-analysis (Hanewinkel et al., 2022) the four randomized controlled trials that reported all product use at the end of the trial found that, while those randomized to e-cigarettes were more likely to

have stopped smoking cigarettes (risk ratio 1.58; 95% CI, 1.20 – 2.08), e-cigarette use was associated with lower nicotine abstinence than nicotine replacement therapy (risk ratio 0.50; 95% CI, 0.32 – 0.77). The authors concluded that, “the use of e-cigarettes as a therapeutic intervention for smoking cessation may lead to permanent nicotine dependence.”

### Electronic Cigarettes as They Are Actually Used

Randomized controlled trials in which e-cigarettes are provided free to people randomized to receive them and monitored as part of a research protocol represent a highly artificial environment that is not typical of the way most people use e-cigarettes: as unsupervised consumer products.

The appropriate way to assess the effect of e-cigarette use as consumer products and continued smoking behavior is population-based observational epidemiology studies. There are many more population observational studies than randomized trials, and meta-analyses of these observational studies (Hedman et al., 2021; Wang et al., 2021) find no statistically significant association between e-cigarette use and stopping cigarette smoking among the general population of smokers (Figure 2). These studies are mostly cross-sectional and the longitudinal studies follow participants for a year or less. This short follow up is important because people who stop smoking relapse over time. The two long-term (3-year) longitudinal studies found e-cigarette use is associated with significantly lower rates of cigarette smoking cessation (Chen et al., 2022; Osibogun et al., 2022).

While not the major reason youth use e-cigarettes, many use them to try to quit using other tobacco products, such as cigarettes. Among US youth, using e-cigarettes to quit was associated with

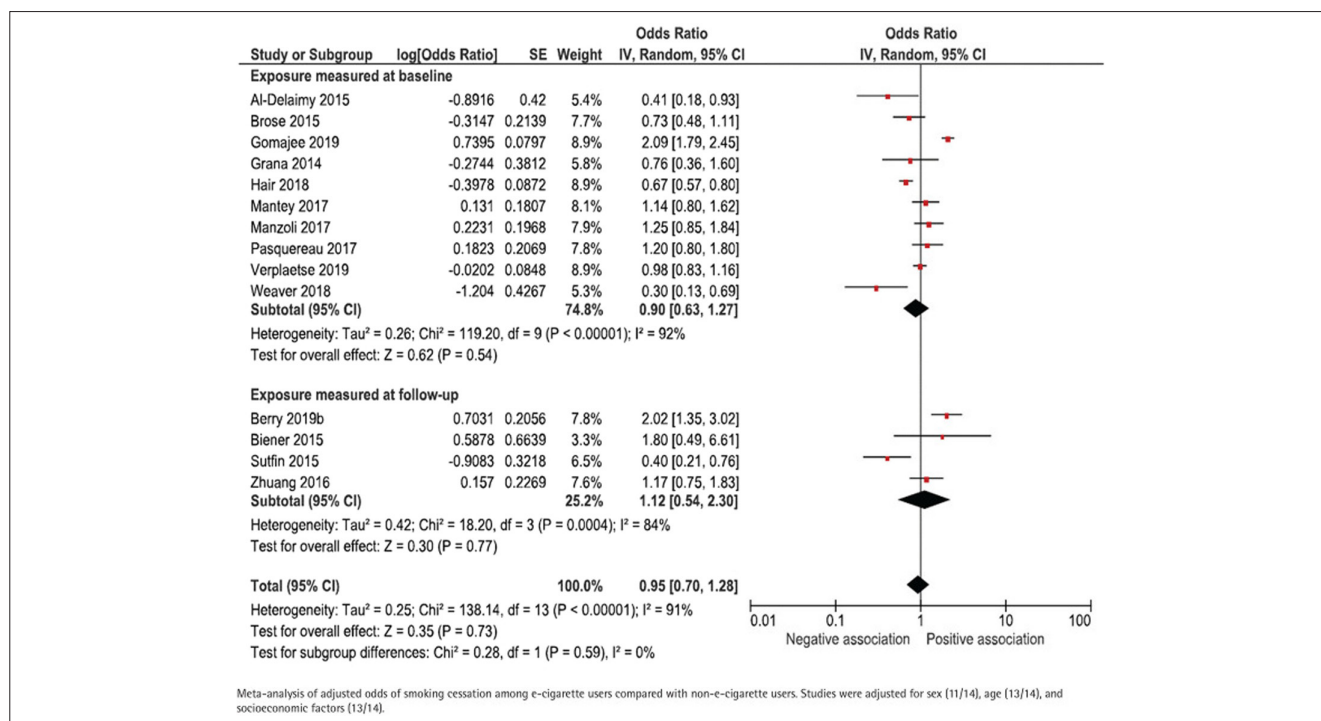


Figure 2. Electronic cigarette use is not associated with subsequent smoking cessation in cohort studies (Source: Hedman et al (2021, Figure 3) available open access distributed under the terms of the Creative Commons Attribution NonCommercial 4.0 International License).

significantly lower odds of having stopped smoking cigarettes (odds ratio, 0.62; 95% CI, 0.45 – 0.85), controlling for nicotine dependence and demographics (Glantz, 2023).

Like the randomized controlled trials, most of the observational studies assess whether or not respondents have stopped smoking cigarettes, not whether they have stopped using nicotine. In other words, someone who continues using e-cigarettes after stopping smoking cigarettes (i.e., “switches completely” to cigarettes) would be considered a “success.”

The idea of e-cigarettes for harm reduction is that people would “switch completely” from cigarettes to substantially less risky e-cigarettes. The fact that e-cigarettes as consumer products are not associated with increased smoking cessation and that, over a longer time, are associated with less cessation, contradicts the fundamental idea of promoting e-cigarette use for “harm reduction.” Even without getting into the precise risks of e-cigarette use compared to smoking, this result suggests that providing e-cigarettes as a cessation aid leads to harm enhancement, not harm reduction.

### Electronic Cigarettes Increase the Tobacco Epidemic by Attracting Low-Risk Youth to Nicotine Addiction

Early advocates of e-cigarettes for harm reduction focused on e-cigarettes as a potentially less dangerous form of nicotine consumption than cigarettes for adults. They argued that e-cigarettes were developed for adults and minimize the risk to youth despite aggressive marketing of e-cigarettes to youth (US Department of

Health and Human Services, 2016). In contrast, as the e-cigarette epidemic developed, use among youth and young adults (Birdsey et al., 2023) substantially exceeded that of adults (Kramarow & Elgaddal, 2023).

While some e-cigarette advocates have attempted to dismiss concerns about growing youth use on the grounds that the youth are displaced from smoking cigarettes, in the United States youth e-cigarette use increased more than the decline of cigarette smoking, reversing decades of progress in reducing nicotine addiction among youth (Creamer et al., 2021). In addition, while some youth who initiated nicotine with e-cigarettes have risk profiles similar to youth who initiated nicotine use with cigarettes, a substantial fraction of the youth who started using e-cigarettes were at low risk of initiating nicotine with cigarettes (Creamer et al., 2021; Dutra & Glantz, 2017). The introduction of e-cigarettes has increased the number of youth addicted to nicotine.

Following the innovation, pioneered by Juul e-cigarettes, of adding acid to the e-cigarette liquid to lower its alkalinity (i.e., lowering its pH) by protonating (adding a proton to) the nicotine molecule, which made nicotine easier to inhale, the age of initiation fell and levels of addiction and consumption among youth increased (Glantz et al., 2022). In addition, youth who initiate nicotine use with e-cigarettes are about three times as likely to go on and add cigarettes (Figure 3) (Khouja et al., 2020; Yoong et al., 2021). Thus, it is not surprising that after the widespread uptake of e-cigarettes, the rate of decline of cigarette smoking among youth slowed (Creamer et al., 2021).

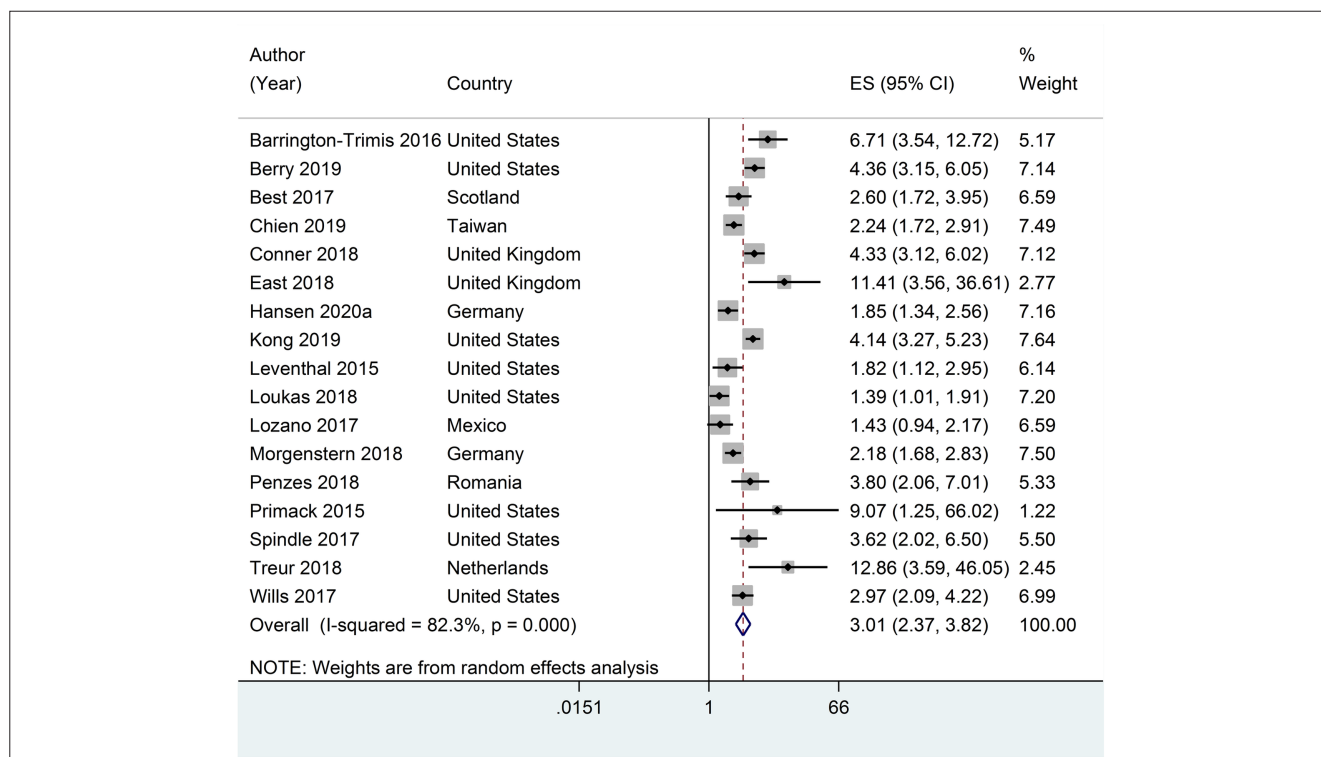


Figure 3. Longitudinal studies show that among youth who had never smoked a cigarette at baseline, e-cigarette use elevated the relative risk of smoking at follow-up. Combining all the studies the adjusted risk ratios for cigarette smoking were about tripled (ever smoking: OR=3.01, 95% CI 2.37 to 3.82; p<0.001; current smoking: OR=2.56, 95% CI 1.61 to 4.07; p<0.001, not shown) at follow-up. (Source: Yoong et al (2021) available open access under the terms of the Creative Commons Attribution License.)

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The rapid penetration and expansion of the youth market in countries that permit legal sale of e-cigarettes is another way that the introduction of e-cigarettes has enhanced harm.

### Electronic Cigarettes and the Tobacco Industry

The first commercial e-cigarettes marketed in 2006 were developed independent of the multinational tobacco companies. As a result, supporters of e-cigarettes within the health and medical communities saw them as a disruptive technology that would compete with Big Tobacco's cigarettes to the benefit of public health. While the first commercialized e-cigarettes did come from outside the major tobacco companies, by the late 1980s, the multinational tobacco companies had identified the need for an alternative tobacco product that would appeal to health-concerned smokers who would otherwise stop using all tobacco (Dutra et al., 2017). By the mid-1990s, Philip Morris had a functional e-cigarette but decided not to take it to market for political and legal reasons (Dutra et al., 2017). By 2022, all the major multinational tobacco companies had entered the e-cigarette business and controlled much of the market.

In addition, promotion of e-cigarettes and other nominally "reduced harm" products became central to the multinational tobacco companies' efforts to present themselves as socially responsible players who could partner with public health agencies and governments rather than companies who were profiting at the expense of public health (Legg et al., 2023; Matthes et al., 2023; Peeters & Gilmore, 2015). This positioning is in direct contradiction to Article 5.3 of the WHO (World Health Organization) Framework Convention on Tobacco Control, which commits parties to the treaty to avoid such partnerships and insulate the policymaking process from tobacco companies (WHO Framework Convention on Tobacco Control, 2013).

Tobacco industry-supported and affiliated research also continues to appear; these studies are significantly more likely to support the value of e-cigarettes for harm reduction than the literature in general (Hendlin et al., 2019; Pisinger et al., 2019; Suzuki et al., 2023; Vidana-Perez et al., 2022). This bias (which is also present in studies from England (Vidana-Perez et al., 2022)) needs to be considered when assessing the literature.

### Implications for Turkey

As of 2020, Presidential Decree No. 2149 banned the import of e-cigarettes and similar tobacco products regardless of whether they contain nicotine. While the manufacture, marketing, and sale of e-cigarettes is not banned in Turkey, as of July 2021 no e-cigarette had been licensed for sale in Turkey (Global Tobacco Control, 2023). While not keeping all e-cigarettes out of Turkey, in 2016 e-cigarette use among people aged 15+ was only 1.1% (Pan et al., 2022) compared with 4.5% for people aged 18+ in the United States (Obisesan et al., 2020). This low use of e-cigarettes is consistent with experience in Brazil (Instituto Nacional de Cancer [Brasil], 2019) and Thailand (Patanavanich et al., 2021), which also prohibit the import and sale of e-cigarettes.

### Conclusion

In the 17 years between 2006 when e-cigarettes entered the commercial market and 2023, the scientific evidence on the health and

behavioral effects of e-cigarettes has grown substantially. While the idea that e-cigarettes would contribute to harm reduction by being a substantially less dangerous replacement for combusted cigarettes for established smokers was initially plausible owing to lack of evidence, the evidence that has accumulated shows that this optimistic hypothesis was incorrect. Instead, while probably not quite as high as cigarettes, e-cigarettes still carry substantial health risks. Dual use, which is common among adults, is riskier than smoking cigarettes alone. Moreover, e-cigarettes as consumer products are not associated with "switching completely" from cigarettes in the short term and, over the long term, are likely to keep people smoking cigarettes. Indeed, the failure of e-cigarettes as consumer products to help people stop smoking makes their relative toxicity compared to cigarettes a moot point, particularly in light of evidence that providing smokers e-cigarettes is more likely to lead them to become dual users than to switch completely from cigarettes. As a result, the availability of e-cigarettes has probably enhanced rather than reduced harm.

In addition to not realizing the hopeful predictions for adult use of e-cigarettes that existed in 2006, e-cigarettes, as actually marketed, have attracted millions of youth at low risk of initiating nicotine use of cigarettes, extending and worsening the nicotine/tobacco epidemic.

In short, e-cigarettes have played exactly the role that tobacco companies hoped they would when they started developing e-cigarettes and similar "new" tobacco products in the late 1980s to hold on to health-concerned smokers who would otherwise stop purchasing tobacco products (Dutra et al., 2017; Elias et al., 2018). E-cigarettes have also played a role in the multinational tobacco companies' efforts to reposition themselves as socially responsible companies worthy of partnership with public health agencies and governments, which creates a situation that makes it easier for the industry to protect its financial and political interests.

Countries, including Turkey, which have prohibited the import and avoided the sale of e-cigarettes have done better overall at controlling the e-cigarette epidemic than countries, including the United States and England, which have adopted laissez-faire policies toward e-cigarettes. Turkey should maintain and ensure effective enforcement of its current policies to continue to protect its population from e-cigarettes.

### Limitations of the Study and Future Directions

The primary limitation of this paper is that it is based on an overview plenary lecture at a meeting; it is not a systematic review of the entire literature on e-cigarettes.

There is a need for future research on the health effects and underlying pathophysiology of e-cigarettes, particularly on disease endpoints (rather than surrogate measures, particularly biomarkers of exposure) and how these outcomes are similar to and differ from cigarettes. Studies of the association between e-cigarette use and cigarette smoking should define "cessation" as cessation of all nicotine products. Even if they do not, investigators in future studies should report what fraction of people continue using e-cigarettes or become dual users. Studies of youth use should extend into adulthood and examine determinants of initiation, cessation, and transitions between different use

patterns and tobacco and non-tobacco products (e.g., cannabis). The tobacco industry's influence on science and public health policy making should also be evaluated, as well as how public health and governments respond to the industry's pressures.

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