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Public Health Consequences of e-Cigarette Use

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Source of Review:

The National Academies of Sciences, Engineering, and Medicine (NASEM) released a consensus report, *Public Health Consequences of E-cigarettes*,[1] in January 2018. The report is a comprehensive review of the health effects of electronic cigarettes (e-cigarettes). As two members of NASEM Committee on the Review of the Health Effects of Electronic Nicotine Delivery Systems (Committee) who wrote the report, including the chair (Eaton), we will summarize the key conclusions and provide our independent assessment of their implications for clinical practice.

Background:

E-cigarettes are a diverse set of battery-powered devices that deliver a nicotine-containing aerosol to the user by heating a solution (called e-liquid) of humectants (propylene glycol and/or glycerin), nicotine, and flavorants.[2] E-cigarettes entered the U.S. market in 2006 and since then, their popularity and use have increased tremendously. Millions of adults and youth use e-cigarettes.[3] Despite their popularity, little is known about the health effects of e-cigarettes. In May 2016, the Food and Drug Administration (FDA) issued a rule which extends its regulatory authority to all products that meet the statutory definition of tobacco product, including e-cigarettes.[4] To gain insight into the risks and benefits of e-cigarettes, the FDA's Center for Tobacco Products, by congressional mandate, requested and funded the NASEM to convene a committee of experts to conduct a review of the emerging

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Conflict of Interest

The authors have no conflicts to disclose.

evidence about the public health consequences of e-cigarette use, and make research recommendations.

Few topics in public health have evoked as much controversy among researchers, health practitioners, and the public over the past decade as e-cigarettes. Some argue that e-cigarettes should be used for harm reduction or as smoking cessation aids; e-cigarettes do not give off as many toxic substances as combustible cigarettes and a majority of tobacco-related diseases and death are attributed to substances in tobacco smoke other than nicotine.[5] Others contend that e-cigarettes are introducing nonsmoking youth to tobacco, renormalizing smoking, and reversing decades of progress in tobacco control. In clinical practice, smokers are asking physicians for their advice about e-cigarettes.

The NASEM Committee conducted a comprehensive review of key e-cigarette liquid and aerosol constituents, human health effects, initiation and cessation of combustible cigarette use, and harm reduction from e-cigarette use. The Committee considered the quality of studies and the totality of evidence, and categorized the evidence as conclusive, substantial, moderate, limited, insufficient, or no available evidence, in which stronger evidence implies that the observed associations between e-cigarette use and an outcome are more likely to be causal. Conclusive evidence was reached if there were many supportive findings from good-quality studies with no credible opposing findings. A firm conclusion can be made and limitations to the evidence, such as chance, bias, and confounding factors, could be ruled out with reasonable confidence. For substantial evidence, there were several supportive findings from good quality studies but minor limitations could not be ruled out with reasonable confidence. Evidence was moderate if there were several supportive findings from fair-quality studies allowing for a general conclusion to be made but limitations could not be ruled out. A conclusion of limited evidence was made if there were supportive findings from fair-quality studies or mixed findings with most favoring one conclusion, but there was significant uncertainty due to limitations. Insufficient evidence was concluded if there were mixed findings or a single poor study. Finally, no available evidence was concluded if there were no studies or a health endpoint had not been studied at all. As is the goal of all NASEM studies, in addition to the thorough review of the published literature, the Committee also received oral and written input from various stakeholders before arriving at their consensus findings on a variety of health end-points and research recommendations.

Summary of Findings:

Conclusive evidence shows that most e-cigarette products contain and emit numerous potentially toxic substances but that the number of substances and levels emitted vary depending on the products and how the products are operated. Substantial evidence shows that when e-cigarettes are used under typical conditions, exposure to these potentially toxic substances is lower compared with combustible cigarette smoking. The Committee found conclusive evidence that nicotine intake from e-cigarettes is highly variable, depending on product characteristics and how they are operated. Among experienced adult e-cigarette users, evidence is substantial that exposure to nicotine can be comparable to that from combustible cigarettes.

The Committee found no evidence whether or not e-cigarette use is associated with long-term health effects, likely due to the relatively short time period that e-cigarettes have been in use and thus the lack of long-term studies. Nevertheless, evidence on intermediate endpoints, disease symptoms, and effects of e-cigarettes on common pathophysiologic mechanisms suggests that e-cigarettes have biological effects in humans. For example, the Committee found substantial evidence that heart rate increases after nicotine intake from e-cigarettes, and moderate evidence for increased cough and wheeze in adolescents who use e-cigarettes compared to those who do not. There was substantial evidence that e-cigarette aerosol can induce acute endothelial dysfunction, and that components of e-cigarette aerosol can promote oxidative stress, both of which support the biological plausibility of tissue injury and disease from long-term e-cigarette use. There was limited evidence that some e-cigarette aerosols can be mutagenic or cause DNA damage in humans, animal models, and human cells in culture, which has implications for carcinogenic risk from long-term use e-cigarettes.

Substantial evidence shows that never-smoking youth and young adults who use e-cigarettes are more likely to subsequently try smoking combustible cigarettes than those who do not use e-cigarettes. Evidence regarding risk of becoming a combustible cigarette smoker is not as strong. The strength of the evidence showing that e-cigarettes are effective smoking cessation aids is limited, mainly because few randomized controlled trials have been done and the results of longitudinal observational studies are variable. However, the Committee found moderate evidence that e-cigarettes with nicotine are more effective for smoking cessation than those without, and that more frequent use of e-cigarettes is more effective. There was insufficient evidence to assess how e-cigarettes compare as cessation aids to FDA-approved treatments. Concerning harm reduction, completely substituting e-cigarettes for combustible cigarettes conclusively reduces exposure to many toxicants and carcinogens present in combustible cigarettes, and would be expected to result in reduced adverse health outcomes. Using a range of plausible assumptions about e-cigarette effects on smoking initiation, smoking cessation, and the relative harm of e-cigarettes compared to combustible cigarettes, a population dynamic model used by the Committee suggests that, under likely scenarios, the use of e-cigarettes will result in a net public health benefit over the next 30 years (2050). The magnitude of the potential benefit is reduced if looking beyond 50 years (2070) as the potential long-term health effects of e-cigarette use, and the health impacts from the potential increase in smoking among youth, becomes more evident.

Overarching categories of research needs include: (1) addressing gaps in substantive knowledge and, (2) improving research methods and quality. Examples of specific recommendations for research include: (1) cohort studies to compare clinical and subclinical health outcomes between e-cigarette and combustible cigarette use; and (2) randomized controlled trials of the effectiveness of e-cigarettes as cessation aids, especially compared with FDA-approved treatments.

Limitations on the Evidence:

As noted above, e-cigarettes have been used for a relatively short time, limiting assessment of long-term health effects and comparisons with combustible tobacco smoking. In addition,

comparisons between studies were difficult due to the rapidly changing nature of the devices, diversity of device characteristics (flavors, nicotine content, power settings) and conditions under which users use e-cigarettes, as well as lack of standardized methods/ protocols for aerosol testing, *in vitro* studies, and measurement of e-cigarette use (frequency and intensity).

Policy Implications:

Although the report offers no clinical guidance to physicians, the findings and major conclusions have implications for clinical practice. Importantly, public health concerns about youth and young adult use of e-cigarettes is justified. The Committee found substantial evidence that youth and young adults who use e-cigarettes are at increased risk of ever trying combustible cigarettes, and moderate evidence that e-cigarette use increases the frequency and intensity of subsequent combustible cigarette smoking. Subsequent to the NASEM report, Public Health England released a report on e-cigarettes which does not support the concern that e-cigarettes can lead to smoking among youth, as smoking continues to decline among youth in the United Kingdom[6] (smoking among youth has been declining in the United States also). While it is still not clear whether e-cigarette use causes youth and young adults to progress from experimenter to smoker, experimentation with combustible cigarettes is a known risk factor for smoking in adulthood; nearly all tobacco use begins in youth and young adulthood.[7] We recommend that physicians integrate questions about nicotine and tobacco use in routine pediatric care. Biomarker screening to identify active youth users should also be considered. Physicians should seek to prevent uptake of e-cigarettes and other nicotine/tobacco products by youth and young adults, and counsel experimenters and habitual users to stop.

Current evidence suggests that e-cigarettes are less harmful than combustible cigarettes, but they are not without biological effects. The NASEM report found no evidence that e-cigarettes are, or are not, more effective smoking cessation aids than FDA-approved medication. Therefore, physicians should first recommend FDA-approved medication for smoking cessation to any smoker interested in quitting. If a smoker has failed initial treatment, has been intolerant of, or refuses to use approved medications and counseling, and wishes to use e-cigarettes to aid quitting, physicians should encourage the smoker to switch completely to e-cigarettes. We agree with Public Health England that behavioral support should be provided to smokers who want to use e-cigarettes to help them quit smoking, and that health professionals should receive education and training in use of e-cigarettes in quit attempts.[6] Physicians should also encourage patients who have quit smoking with e-cigarettes to set a quit date for e-cigarette use itself and not plan to use e-cigarette indefinitely due to uncertainty about their long-term effects.

Conclusions:

The NASEM report is the most comprehensive review of the health effects of e-cigarettes to date. While there is currently little evidence of long-term effects, e-cigarettes are not without biological effects in humans, but they are likely to pose significantly less risk to an

individual than combustible cigarettes. More research is needed to address gaps in substantive knowledge and to improve research methods and quality.

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