PUBLIC HEALTH CONSEQUENCES OF E-CIGARETTES

CONCLUSIONS BY LEVEL OF EVIDENCE

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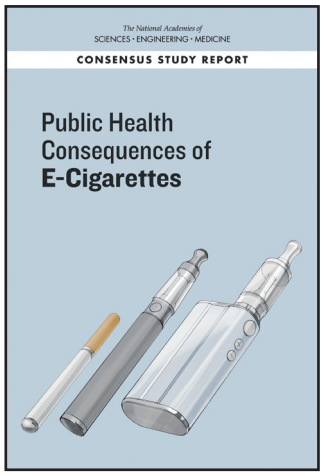

In the report *Public Health Consequences of E-Cigarettes,* an expert committee of the National Academies of Sciences, Engineering, and Medicine presents 47 conclusions related to outcomes of e-cigarettes, including their key constituents, human health effects, initiation and cessation of combustible tobacco cigarette use, and harm reduction.

The conclusions below are organized by level of evidence (with each level of evidence defined on page 2).

To see the conclusions organized by outcomes and to read the full report and related resources, please visit **nationalacademies.org/eCigHealthEffects.**

CONCLUSIVE EVIDENCE

Conclusion 3-1. There is *conclusive evidence* that e-cigarette use increases airborne concentrations of particulate matter and nicotine in indoor environments compared with background levels.

Conclusion 4-1. There is *conclusive evidence* that exposure to nicotine from e-cigarettes is highly variable and depends on product characteristics (including device and e-liquid characteristics) and how the device is operated.

Conclusion 5-1. There is *conclusive evidence* that in addition to nicotine, most e-cigarette products contain and emit numerous potentially toxic substances.

Conclusion 5-2. There is *conclusive evidence* that other than nicotine, the number, quantity, and characteristics of potentially toxic substances emitted from e-cigarettes are highly variable and depend on product characteristics (including device and e-liquid characteristics) and how the device is operated.

Conclusion 14-1. There is *conclusive evidence* that e-cigarette devices can explode and cause burns and projectile injuries. Such risk is significantly increased when batteries are of poor quality, stored improperly, or modified by users.

Conclusion 14-2. There is *conclusive evidence* that intentional or accidental exposure to e-liquids (from drinking, eye contact, or dermal contact) can result in adverse health effects including but not limited to seizures, anoxic brain injury, vomiting, and lactic acidosis.

Conclusion 14-3. There is *conclusive evidence* that intentionally or unintentionally drinking or injecting e-liquids can be fatal.

Conclusion 18-1. There is *conclusive evidence* that completely substituting e-cigarettes for combustible tobacco cigarettes reduces users' exposure to numerous toxicants and carcinogens present in combustible tobacco cigarettes.

SUBSTANTIAL EVIDENCE

Conclusion 4-2. There is *substantial evidence* that nicotine intake from e-cigarette devices among experienced adult e-cigarette users can be comparable to that from combustible tobacco cigarettes.

Conclusion 5-3. There is *substantial evidence* that except for nicotine, under typical conditions of use, exposure to potentially toxic substances from e-cigarettes is significantly lower compared with combustible tobacco cigarettes.

Conclusion 5-4. There is *substantial evidence* that e-cigarette aerosol contains metals. The origin of the metals could be the metallic coil used to heat the e-liquid, other parts of the e-cigarette device, or e-liquids. Product characteristics and use patterns may contribute to differences in the actual metals and metal concentrations measured in e-cigarette aerosol.

Conclusion 7-1. There is *substantial evidence* that e-cigarette aerosols can induce acute endothelial cell dysfunction, although the long-term consequences and outcomes on these parameters with long-term exposure to e-cigarette aerosol are uncertain.

Conclusion 7-2. There is *substantial evidence* that components of e-cigarette aerosols can promote formation of reactive oxygen species/oxidative stress. Although this supports the biological plausibility of tissue injury and disease from long-term exposure to e-cigarette aerosols, generation of reactive oxygen species and oxidative stress induction is generally lower from e-cigarettes than from combustible tobacco cigarette smoke.

Conclusion 8-1. There is *substantial evidence* that e-cigarette use results in symptoms of dependence on e-cigarettes.

Conclusion 9-2. There is *substantial evidence* that heart rate increases shortly after nicotine intake from e-cigarettes.

Conclusion 10-4. There is *substantial evidence* that some chemicals present in e-cigarette aerosols (e.g., formaldehyde, acrolein) are capable of causing DNA damage and mutagenesis. This supports the biological plausibility that long-term exposure to e-cigarette aerosols could increase risk of cancer and adverse reproductive outcomes. Whether or not the levels of exposure are high enough to contribute to human carcinogenesis remains to be determined.

Conclusion 16-1. There is *substantial evidence* that e-cigarette use increases risk of ever using combustible tobacco cigarettes among youth and young adults.

Conclusion 18-2. There is *substantial evidence* that completely switching from regular use of combustible tobacco cigarettes to e-cigarettes results in reduced short-term adverse health outcomes in several organ systems.

LEVELS OF EVIDENCE DEFINED

Conclusive evidence: There are many supportive findings from good-quality controlled studies (including randomized and non-randomized controlled trials) with no credible opposing findings. A firm conclusion can be made, and the limitations to the evidence, including chance, bias, and confounding factors, can be ruled out with reasonable confidence.

Substantial evidence: There are several supportive findings from good-quality observational studies or controlled trials with few or no credible opposing findings. A firm conclusion can be made, but minor limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.

Moderate evidence: There are several supportive findings from fair-quality studies with few or no credible opposing findings. A general conclusion can be made, but limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.

Limited evidence: There are supportive findings from fair-quality studies or mixed findings with most favoring one conclusion. A conclusion can be made, but there is significant uncertainty due to chance, bias, and confounding factors.

Insufficient evidence: There are mixed findings or a single poor study. No conclusion can be made because of substantial uncertainty due to chance, bias, and confounding factors.

No available evidence: There are no available studies; health endpoint has not been studied at all. No conclusion can be made.

MODERATE EVIDENCE

Conclusion 8-2. There is *moderate evidence* that risk and severity of dependence are lower for e-cigarettes than combustible tobacco cigarettes.

Conclusion 8-3. There is *moderate evidence* that variability in e-cigarette product characteristics (nicotine concentration, flavoring, device type, and brand) is an important determinant of risk and severity of e-cigarette dependence.

Conclusion 9-3. There is *moderate evidence* that diastolic blood pressure increases shortly after nicotine intake from e-cigarettes.

Conclusion 11-4. There is *moderate evidence* for increased cough and wheeze in adolescents who use e-cigarettes and an association with e-cigarette use and an increase in asthma exacerbations.

Conclusion 16-2. Among youth and young adult e-cigarette users who ever use combustible tobacco cigarettes, there is *moderate evidence* that e-cigarette use increases the frequency and intensity of subsequent combustible tobacco cigarette smoking.

Conclusion 17-2. There is *moderate evidence* from randomized controlled trials that e-cigarettes with nicotine are more effective than e-cigarettes without nicotine for smoking cessation.

Conclusion 17-4. While the overall evidence from observational trials is mixed, there is *moderate evidence* from observational studies that more frequent use of e-cigarettes is associated with an increased likelihood of cessation.

Conclusion 18-5. There is *moderate evidence* that second-hand exposure to nicotine and particulates is lower from e-cigarettes compared with combustible tobacco cigarettes.

LIMITED EVIDENCE

Conclusion 3-2. There is *limited evidence* that e-cigarette use increases levels of nicotine and other e-cigarette constituents on a variety of indoor surfaces compared with background levels.

Conclusion 5-5. There is *limited evidence* that the number of metals in e-cigarette aerosol could be greater than the number of metals in combustible tobacco cigarettes, except for cadmium, which is markedly lower in e-cigarettes compared with combustible tobacco cigarettes.

Conclusion 9-4. There is *limited evidence* that e-cigarette use is associated with a short-term increase in systolic blood pressure, changes in biomarkers of oxidative stress, increased endothelial dysfunction and arterial stiffness, and autonomic control.

Conclusion 10-2. There is *limited evidence* from in vivo animal studies using intermediate biomarkers of cancer to support the hypothesis that long-term e-cigarette use could increase the risk of cancer; there is no available evidence from adequate long-term animal bioassays of e-cigarette aerosol exposures to inform cancer risk.

Conclusion 10-3. There is *limited evidence* that e-cigarette aerosol can be mutagenic or cause DNA damage in humans, animal models, and human cells in culture.

Conclusion 11-2. There is *limited evidence* for improvement in lung function and respiratory symptoms among adult smokers with asthma who switch to e-cigarettes completely or in part (dual use).

Conclusion 11-3. There is *limited evidence* for reduction of chronic obstructive pulmonary disease (COPD) exacerbations among adult smokers with COPD who switch to e-cigarettes completely or in part (dual use).

LIMITED EVIDENCE (CONTINUED)

Conclusion 11-5. There is *limited evidence* of adverse effects of e-cigarette exposure on the respiratory system from animal and in vitro studies.

Conclusion 12-1. There is *limited evidence* suggesting that switching to e-cigarettes will improve periodontal disease in smokers.

Conclusion 12-2. There is *limited evidence* suggesting that nicotine- and non-nicotine–containing e-cigarette aerosol can adversely affect cell viability and cause cell damage of oral tissue in non-smokers.

Conclusion 16-3. Among youth and young adult e-cigarette users who ever use combustible tobacco cigarettes, there is *limited evidence* that e-cigarette use increases, in the near term, the duration of subsequent combustible tobacco cigarette smoking.

Conclusion 17-1. Overall, there is *limited evidence* that e-cigarettes may be effective aids to promote smoking cessation.

INSUFFICIENT EVIDENCE

Conclusion 9-5. There is *insufficient evidence* that e-cigarette use is associated with long-term changes in heart rate, blood pressure, and cardiac geometry and function.

Conclusion 13-2. There is *insufficient evidence* whether or not maternal e-cigarette use affects fetal development.

Conclusion 17-3. There is *insufficient evidence* from randomized controlled trials about the effectiveness of e-cigarettes as cessation aids compared with no treatment or to Food and Drug Administration–approved smoking cessation treatments.

Conclusion 18-4. There is *insufficient evidence* that e-cigarette use changes short-term adverse health outcomes in several organ systems in smokers who continue to smoke combustible tobacco cigarettes (dual users).

NO AVAILABLE EVIDENCE

Conclusion 9-1. There is *no available evidence* whether or not e-cigarette use is associated with clinical cardiovascular outcomes (coronary heart disease, stroke, and peripheral artery disease) and subclinical atherosclerosis (carotid intima-media thickness and coronary artery calcification).

Conclusion 10-1. There is *no available evidence* whether or not e-cigarette use is associated with intermediate cancer endpoints in humans. This holds true for e-cigarette use compared with use of combustible tobacco cigarettes and e-cigarette use compared with no use of tobacco products.

Conclusion 11-1. There is *no available evidence* whether or not e-cigarettes cause respiratory diseases in humans.

Conclusion 13-1. There is *no available evidence* whether or not e-cigarettes affect pregnancy outcomes.

Conclusion 18-3. There is *no available evidence* whether or not long-term e-cigarette use among smokers (dual use) changes morbidity or mortality compared with those who only smoke combustible tobacco cigarettes.

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