



## SUMMARY OF THE 2018 NATIONAL ACADEMIES OF SCIENCES, ENGINEERING, AND MEDICINE (NASEM) REPORT, *THE PUBLIC HEALTH CONSEQUENCES OF E-CIGARETTES*

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In 2016, FDA commissioned the National Academies of Sciences, Engineering, and Medicine (NASEM)<sup>\*</sup> to convene a committee of scientists to review the available research on the health consequences of e-cigarette use, both at the individual and population levels. The committee included more than 800 peer-reviewed studies in the final report, which was released in January 2018. The report summarized what is currently known about the health risks and benefits of e-cigarettes, determined the strength of evidence for each of the conclusions, and identified areas in need of additional research, including the long-term health effects of e-cigarette use. Below is a summary of the report's findings and conclusions on health risks, initiation, smoking cessation, and harm reduction potential of e-cigarettes. Conclusions from the report organized by topic are also included at the end of the document.

### Brief Overview of Findings

#### Characteristics of the Product and Health Risks:

- The nicotine levels delivered by e-cigarettes are highly variable, but can be comparable to nicotine levels delivered by regular cigarettes and can result in dependence.
- E-cigarettes contain and emit numerous potentially toxic substances, although at significantly lower levels than regular cigarettes.
- The nicotine and other potentially toxic substances emitted by e-cigarettes vary considerably depending on the particular characteristics of the product and how it is operated.
- E-cigarettes are not risk-free, but current evidence suggests that e-cigarettes are likely to be far less harmful than combustible tobacco cigarettes. A smoker who completely switches to an e-cigarette is exposed to lower levels of toxic substances (other than nicotine), resulting in some reduced short-term adverse health outcomes.
- Nevertheless, little is known about the long term effects of e-cigarette use, and there is little data to assess the impact on cancer and heart disease risk. The long-term effects of e-cigarette use on morbidity and mortality are not yet clear.

#### Impact on Youth:

- Youth and young adults who use e-cigarettes are more likely to try cigarettes, and their e-cigarette use may be associated with increased frequency and intensity of subsequent cigarette smoking.

#### Smoking Cessation:

- There is limited evidence that e-cigarettes may help people stop smoking cigarettes but insufficient evidence from randomized controlled trials to assess the effectiveness of e-cigarettes as a smoking cessation aid compared to no treatment or FDA-approved smoking cessation treatments.

#### Harm Reduction:

- Completely switching from cigarettes to e-cigarettes will reduce exposure to numerous toxicants and carcinogens found in cigarettes, but there is no available evidence to indicate if using both cigarettes and e-cigarettes (dual use) lowers health risks.

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<sup>\*</sup> National Academies of Sciences, Engineering, and Medicine (NASEM), *Public Health Consequences of E-Cigarettes*, Washington, DC: The National Academies Press, 2018, <http://nationalacademies.org/hmd/Reports/2018/public-health-consequences-of-e-cigarettes.aspx>.

## Additional Details from the NASEM Report

### ***Characteristics of the Product and Health Risks:***

- E-cigarette liquid and aerosol:
  - Nicotine levels within e-cigarettes (e-liquid) are highly variable. Nicotine delivery can vary depending on the device (electrical power) and user behavior (puff duration), but can be comparable to nicotine levels delivered by regular cigarettes. Use of e-cigarettes can result in dependence, though the risk and severity may be lower than combustible cigarettes and may depend on product characteristics.
  - E-cigarettes contain and emit numerous potentially toxic substances at various levels depending on the device and how it is used. However, those levels are typically significantly lower than the levels found in combustible cigarettes.
  - The committee stated that flavoring compounds in e-liquids are “of greater concern” than the hazardous compounds in e-cigarette aerosol because they “have not been widely tested for sensitizing, toxic, or irritating potency.” Moderate evidence indicated that flavorings can enhance abuse liability of e-cigarettes, but there were some limitations to the studies referenced. The committee suggested that more studies are needed to determine how flavors in e-liquids can affect nicotine absorption and exposure in users.
  - Studies have shown the presence of compounds in e-liquids that were not listed on product labels.
  - A variety of metals are present in e-cigarette aerosol, the types and concentration of which depend on the device and how it is used. It is possible that more types of metals are present in e-cigarette aerosol than in combustible cigarettes, except for cadmium, which is lower in e-cigarettes compared to combustible cigarettes.
  - E-cigarette aerosols can affect the body at the cellular level, including inducing acute endothelial cell dysfunction and promoting formation of reactive oxygen species/oxidative stress, though at lower levels than for combustible cigarettes.
- Overall health impact:
  - E-cigarettes are not risk-free, but current evidence suggests that e-cigarettes are likely to be far less harmful than combustible tobacco cigarettes. A smoker who completely switches to an e-cigarette is exposed to lower levels of toxic substances (other than nicotine), resulting in some reduced short-term adverse health outcomes.
  - Nevertheless, little is known about the long term effects of e-cigarette use, and there is little data to assess the impact on cancer and heart disease risk. The long-term effects of e-cigarette use on morbidity and mortality are not yet clear.
- Cardiovascular effects:
  - Though the nicotine in e-cigarettes has been found to increase heart rate and diastolic blood pressure shortly after use, there is no available evidence to assess whether or not e-cigarette use is associated with other cardiovascular outcomes, such as heart disease or stroke.
  - Based on known cardiovascular effects of nicotine, exposure to nicotine from e-cigarettes likely elevates cardiovascular disease risk in people with pre-existing cardiovascular disease, but the cardiovascular risks in people without cardiovascular disease is uncertain.
- Cancer outcomes:
  - There is no evidence to indicate that nicotine alone is a carcinogen.
  - There is not enough evidence to make any conclusions about cancer or intermediate markers for cancer in humans from e-cigarette use.
  - While there is limited evidence that e-cigarette aerosol can be mutagenic or cause damage to human DNA, some cancer-causing chemicals, including formaldehyde and acrolein, are present in e-cigarette aerosols. It is yet unknown if the levels of

- exposure to those chemicals are high enough to increase the risk of cancer and adverse reproductive outcomes.
- Respiratory system:
    - There is no available evidence to determine whether or not e-cigarettes cause respiratory diseases.
    - There is some evidence for increased coughing, wheezing, and asthma exacerbations among adolescents after e-cigarette use.
    - When aerosolized, humectants (mostly propylene glycol and glycerol) in e-cigarettes emit extremely high levels of fine particles into the respiratory system, though the long-term effects of such exposure are still unknown.
    - There is limited evidence that use of e-cigarettes can improve lung function and respiratory symptoms among adult smokers with asthma, or reduce COPD exacerbations among adult smokers with COPD for those who dual use or switch completely. The committee mentioned that e-cigarettes could also increase harm for smokers with COPD if their use prevented cessation or further damaged lungs.
    - The nicotine in e-cigarettes could exacerbate respiratory symptoms in cystic fibrosis carriers.
  - Pregnancy/fetal development:
    - There is currently no evidence on the effect of e-cigarette use on pregnancy outcomes and not enough evidence on the effect of e-cigarette use on fetal development, leading the committee to state that “further studies are needed before recommendations can be made regarding...if e-cigarette use [during pregnancy] as a substitute for combustible tobacco products is a safer alternative compared with NRT.”
    - The committee also noted that the nicotine could have adverse effects on the lung function of pre-term infants and that it is “unknown whether the particle size of emissions or flavoring contained in some e-cigarette emissions can adversely affect fetal development.”
  - Oral health:
    - Though there is limited evidence that smokers switching to e-cigarettes can improve periodontal disease, the e-cigarette aerosol can damage cells in the oral tissue of non-smokers.
    - The committee also noted studies suggesting that e-cigarette aerosols can induce gingival inflammation to harm oral health.
  - Injury/poisoning:
    - E-cigarette devices can explode and cause burns and injuries from resulting projectiles.
    - Drinking and contact of the e-liquid through eyes or skin can cause adverse health effects, and drinking and injecting oneself with e-liquid can be fatal.
  - Secondhand exposure:
    - Use of e-cigarettes indoors increases airborne concentrations of particulate matter and nicotine, though secondhand exposure is lower compared to combustible cigarettes.

***Impact on Youth:***

- There is substantial evidence that e-cigarette use among youth and young adults increases the risk of ever using combustible tobacco cigarettes.
- For youth and young adult e-cigarette users who ever smoke cigarettes, e-cigarette use may increase the frequency and intensity of subsequent cigarette smoking. E-cigarette use by youth and young adults may increase how long they smoke combustible cigarettes in the near term.

**Smoking Cessation:**

The primary questions considered by the committee were whether or not e-cigarettes helped people quit, and how effective e-cigarettes were, relative to FDA-proven cessation aids, at helping motivated people to quit. The committee prioritized findings from the gold-standard, randomized control trials (RCTs), and included findings from some related observational studies to determine their conclusions.

- There is limited evidence that e-cigarettes may help people stop smoking cigarettes. However, the few RCTs available provide insufficient evidence to assess the effectiveness of e-cigarettes as a smoking cessation aid compared to no treatment or FDA-approved smoking cessation treatments.
- Some evidence indicates that using e-cigarettes more frequently increases the likelihood of cessation, and e-cigarettes with nicotine are more effective for cessation than non-nicotine e-cigarettes.

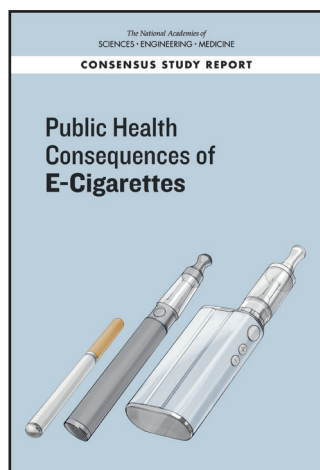
**Potential for Harm Reduction:**

- Switching completely to e-cigarettes reduces smokers' exposure to numerous toxicants and carcinogens in combustible cigarettes and reduces their short-term adverse health outcomes in some organ systems.
  - The committee stated, "E-cigarettes might be considered as a harm reduction tool for tobacco smokers if their efficacy in reducing health risk is supported by epidemiological studies and proven in well-performed epidemiological studies and RCTs."
- While the health effects of using e-cigarettes are "still not well understood," the report did state that "current evidence points to e-cigarettes being less harmful than combustible tobacco cigarettes." However, based on the available evidence, the committee also noted that "the absolute risks of the products cannot be unambiguously determined at this time."
- There is no available evidence to determine if long-term use of e-cigarettes changes morbidity or mortality among those who use e-cigarettes and cigarettes (dual users) compared to exclusive combustible cigarette smokers, and insufficient evidence to determine if using e-cigarettes changes short-term adverse health outcomes in various organ systems among dual users.
  - The committee found that dual use "is highly prevalent among adults and youth" and recognized that more information on patterns of use, quit attempts, and contexts of use among dual users is needed.
  - The committee stated, "reduction in rate of smoking does not ensure reduction in tobacco-related harm."
  - "It is very unlikely that those smokers who do not reduce smoking after initiating e-cigarette use will reduce health risk of smoking and they may as well be also exposed to additional adverse health effects of e-cigarettes."

**Research Needs:**

The committee identified several areas where additional research is needed. The actual recommendations went into more detail, but in general, they recommended:

- Research on the long- and short-term health effects of e-cigarettes on individuals.
- Research to improve the quality of e-cigarette research on health outcomes, such as methodologies and appropriate study designs.



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 outcome. To see the conclusions organized by level of evidence and to read the full report and related resources, please visit [nationalacademies.org/eCigHealthEffects](http://nationalacademies.org/eCigHealthEffects).

### CONSTITUENTS OF E-CIGARETTES

**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 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 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 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 5-1.** 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 is highly variable and depends on product characteristics (including device and e-liquid characteristics) and how the device is operated.

**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 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.

## HEALTH EFFECTS OF E-CIGARETTES

**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 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 9-1.** 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 9-2.** There is *substantial evidence* that heart rate increases after nicotine intake from e-cigarettes.

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

## 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.

## HEALTH EFFECTS OF E-CIGARETTES (CONTINUED)

**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 comparisons of e-cigarette use compared with combustible tobacco cigarettes and e-cigarette use compared with no use of tobacco products.

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

**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).

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

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

**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 are being 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.

## INITIATION AND CESSATION

**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 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 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.

**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 17-3.** 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 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 increased likelihood of cessation.

## HARM REDUCTION

**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.

**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.

**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.

**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).

**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.

TO READ THE FULL REPORT AND VIEW RELATED RESOURCES, PLEASE VISIT  
[NATIONALACADEMIES.ORG/ECIGHEALTHEFFECTS](https://www.nationalacademies.org/ecighealtheffects)