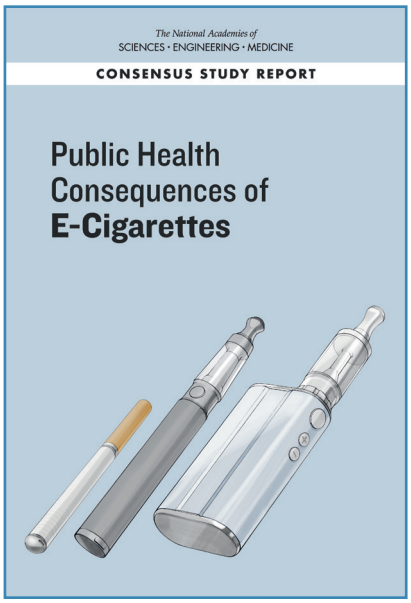
Consensus Study Report
HIGHLIGHTS
January 2018

Public Health Consequences of E-Cigarettes



Millions of Americans use electronic cigarettes (e-cigarettes). Young people especially, age 17 and under, have quickly taken up their use: Substantially more young people use e-cigarettes than any other tobacco product, including traditional combustible tobacco cigarettes.

Despite their popularity, little is known about the health effects of e-cigarettes. Perceptions of potential risks and benefits of e-cigarette use vary widely among the public, users of the products, health care providers, and the public health community.

With support from the Center for Tobacco Products of the Food and Drug Administration (FDA), the National Academies of Sciences, Engineering, and Medicine convened an expert committee to conduct a critical, objective review of the scientific evidence about e-cigarettes and health. The resulting report, *Public Health Consequences of E-Cigarettes,* provides an overview of the evidence, recommends ways to improve the research, and highlights gaps that are priority focus areas for future work.

As part of its work, the committee conducted a comprehensive, in-depth review of the scientific literature around e-cigarettes, including key constituents in e-cigarettes, human health effects, initiation and cessation of combustible tobacco cigarette use, and harm reduction. The committee considered the quality of individual studies and the totality of the evidence to provide 47 structured, consistent conclusions on the strength of the evidence (categorized as conclusive, substantial, moderate, limited, insufficient, and no evidence—all defined on the next page).

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CONSTITUENTS OF E-CIGARETTES

E-cigarettes contain liquids (called e-liquids), which typically contain nicotine, flavorings, and humectants (to retain moisture).

With respect to nicotine, conclusive evidence shows that exposure to nicotine from e-cigarettes is highly variable. It depends on characteristics of the products, including those of the device and e-liquids, as well as how the device is operated. Substantial evidence also shows that among experienced adult e-cigarette users, exposure to nicotine can be comparable to that from combustible tobacco cigarettes.

Most of the flavorings used in e-cigarettes are generally regarded as safe by the FDA, although these designations relate to oral consumption (flavorings used in food), and most have not been studied for safety when inhaled with an e-cigarette.

The primary humectants are propylene glycol and glycerol (also known as vegetable glycerin). Similar to flavorings, they are generally regarded as safe for ingestion, but less is known about their health effects when inhaled.

Overall, e-cigarette aerosol contains fewer numbers and lower levels of toxicants than smoke from combustible tobacco cigarettes. Nicotine exposure can mimic that found with use of combustible tobacco cigarettes, but it is highly variable. The exposure to nicotine and toxicants from the aerosolization of flavorings and humectants depends on device characteristics and how the device is used.

HEALTH EFFECTS OF E-CIGARETTES

Because e-cigarettes have only been on the U.S. market for a relatively brief time—first imported in 2006, most have entered the market much more recently—it is difficult to scientifically compare their health effects to those of combustible tobacco cigarettes, whose health effects were not fully apreciated until after decades of use. However, in contrast to long-term effects, research on short-term health effects of e-cigarettes is now available.

The committee evaluated the current state of knowledge on outcomes including dependence and abuse liability, cardiovascular diseases, cancers, respiratory diseases, oral diseases, reproductive and developmental effects, and injuries and poisonings.

Overall, the evidence reviewed by the committee suggests that e-cigarettes are not without biological effects in humans. For instance, use of e-cigarettes results in dependence on the devices, though with apparently less risk and severity than that of combustible tobacco cigarettes. Yet the implications for long-term effects on morbidity and mortality are not yet clear.

To see the full text of the committee's conclusions organized by levels of evidence and outcome, visit **nationalacademies.org/eCigHealthEffects.**

Levels of Evidence for Conclusions

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.

The net public health outcome of e-cigarette use depends on the balance between positive and negative consequences.

E-CIGARETTES AND HARM REDUCTION

FDA regulations require that tobacco products introduced to the U.S. market over the past decade must show a net public health benefit. In considering this public health effect, a product must pose less risk to users than combustible tobacco cigarettes. Additionally, if a product caused more people to start harmful tobacco use, or caused fewer people to quit tobacco use, a product would be kept off the market. So separate from the health effects of e-cigarettes, the tobacco control field must pay close attention to the effects of e-cigarettes on starting and quitting combustible tobacco products.

For youth and young adults, there is substantial evidence that e-cigarette use increases the risk of ever using combustible tobacco cigarettes. For e-cigarette users who have also ever used combustible tobacco cigarettes, there is moderate evidence that e-cigarette use increases the frequency and intensity of subsequent combustible tobacco cigarette smoking.

There is insufficient evidence from randomized controlled trials about the effectiveness of e-cigarettes as cessation aids compared to no treatment or to FDA-approved smoking cessation treatments. 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.

Overall, the evidence suggests that while e-cigarettes might cause youth who use them to transition to use of combustible tobacco products, they might also increase adult cessation of combustible tobacco cigarettes.

Completely substituting e-cigarettes for combustible tobacco cigarettes conclusively reduces a person's exposure to many toxicants and carcinogens present in combustible tobacco cigarettes and may result in reduced adverse health outcomes in several organ systems. **Across a range of studies and outcomes, e-cigarettes appear to pose less risk to an individual than combustible tobacco cigarettes.**

To examine the possible effects of e-cigarette use at the population level, the committee used population dynamic modeling. Under the assumption that using e-cigarettes increases the net cessation rate of combustible tobacco cigarettes among adults, the modeling projects that in the short run, use of these products will generate a net public health benefit, despite the increased use of combustible tobacco products by young people. Yet in the long term (for instance, 50 years out), the public health benefit is substantially less and is even negative under some scenarios. If the products do not increase combustible tobacco cessation in adults, then with the range of assumptions the committee used, the model projects that there would be net public health harm in the short and long terms.

RESEARCH RECOMMENDATIONS

There is a great need for more evidence around the new field of e-cigarettes; research with both long- and short-term horizons is required.

The committee identified gaps in the literature in every aspect in its work and provides overarching categories of research needs and specific research suggestions within the final chapters of each of the three major sections of the report. These overarching categories include: (1) addressing gaps in substantive knowledge and (2) improving research methods and quality through protocol and methods validation and development, including the use of appropriate study design.

To download a copy of the report and read the full text of the committee's recommendations, please visit **nationalacademies.org/eCigHealthEffects.**

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CONCLUSION

Although e-cigarettes are not without risk, compared to combustible tobacco cigarettes they contain fewer toxicants; can deliver nicotine in a similar manner; show significantly less biological activity in most, but not all, in vitro, animal, and human systems; and might be useful as a cessation aid in smokers who use e-cigarettes exclusively. However, young people who begin with e-cigarettes are more likely to transition to combustible cigarette use and become smokers who are at risk to suffer the known health burdens of combustible tobacco cigarettes. The net public health outcome of e-cigarette use depends on the balance between positive and negative consequences.

More and better research is needed to help clarify whether e-cigarettes will prove to reduce harm—or induce harm—at the individual and the population levels. The approach taken by the committee to evaluate the health effects of e-cigarettes in this report is anticipated to provide a generalizable template for future evaluations of the evidence.

To read the full report, please visit
nationalacademies.org/eCigHealthEffects

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Surgeon General's Advisory on E-cigarette Use Among Youth

I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of protecting our children from a lifetime of nicotine addiction and associated health risks by immediately addressing the epidemic of youth e-cigarette use. The recent surge in e-cigarette use among youth, which has been fueled by new types of e-cigarettes that have recently entered the market, is a cause for great concern. ***We must take action now to protect the health of our nation's young people.***

KNOW THE RISKS. TAKE ACTION. PROTECT OUR KIDS.

The E-cigarette Epidemic Among Youth

Considerable progress has been made in reducing cigarette smoking among our nation's youth.[1] However, the tobacco product landscape continues to evolve to include a variety of tobacco products, including smoked, smokeless, and electronic products, such as e-cigarettes.[2] E-cigarettes are designed to deliver nicotine, flavorings, and other additives to the user via an inhaled aerosol.[2]

E-cigarettes entered the U.S. marketplace around 2007, and since 2014, they have been the most commonly used tobacco product among U.S. youth.[2] E-cigarette use among U.S. middle and high school students increased 900% during 2011-2015, before declining for the first time during 2015-2017.[3] However, current e-cigarette use increased 78% among high school students during the past year, from 11.7% in 2017 to 20.8% in 2018.[4] In 2018, more than 3.6 million U.S. youth, including 1 in 5 high school students and 1 in 20 middle school students, currently use e-cigarettes.[4]

E-cigarette aerosol is not harmless.[2] Most e-cigarettes contain nicotine – the addictive drug in regular cigarettes, cigars, and other tobacco products.[2] Nicotine exposure during adolescence can harm the developing brain – which continues to develop until about age 25.[2] Nicotine exposure during adolescence can impact learning, memory, and attention.[1,2] Using nicotine in adolescence can also increase risk for future addiction to other drugs.[1,2] In addition to nicotine, the aerosol that users inhale and exhale from e-cigarettes can potentially expose both themselves and bystanders to other harmful substances, including heavy metals, volatile organic compounds, and ultrafine particles that can be inhaled deeply into the lungs.[2]

Many e-cigarettes also come in kid-friendly flavors. In addition to making e-cigarettes more appealing to young people,[5] some of the chemicals used to make certain flavors may also have health risks.[2] E-cigarettes can also be used to deliver other drugs, including marijuana.[2] In 2016, one-third of U.S. middle and high school students who ever used e-cigarettes had used marijuana in e-cigarettes.[6]

For adults, e-cigarettes may have the potential to reduce risk for current smokers if they completely transition from cigarettes to e-cigarettes; however, a majority of adults who use e-cigarettes also smoke cigarettes.[7] For youth, the use of multiple tobacco products puts youth at even greater risk for addiction and tobacco-related harms.[1,2] Moreover, a 2018 National Academy of Sciences, Engineering, and Medicine report concluded that there was moderate evidence that e-cigarette use increases the frequency and intensity of cigarette smoking in the future.[7] But any e-cigarette use among young people is unsafe, even if they do not progress to future cigarette smoking.[2]

E-cigarettes Come in Many Shapes and Sizes

E-cigarettes are a rapidly changing product class, and are known by many different names, including "e-cigs," "e-hookahs," "mods," and "vape pens."[2] Recently, a new type of e-cigarette has become increasingly popular among our nation's youth due to its minimal exhaled aerosol, reduced odor, and small size, making it easy to conceal.[8] Many of these new e-cigarettes look like a USB flash drive, among other shapes. One of the most commonly sold

USB flash drive shaped e-cigarettes is JUUL, which experienced a 600% surge in sales during 2016-2017, giving it the greatest market share of any e-cigarette in the U.S. by the end of 2017.[9] Other companies are now also starting to sell e-cigarettes that look like USB flash drives.

All JUUL e-cigarettes have a high level of nicotine. A typical JUUL cartridge, or "pod," contains about as much nicotine as a pack of 20 regular cigarettes.[10] These products also use nicotine salts, which allow particularly high levels of nicotine to be inhaled more easily and with less irritation than the free-base nicotine that has traditionally been used in tobacco products, including e-cigarettes. This is of particular concern for young people, because it could make it easier for them to initiate the use of nicotine through these products and also could make it easier to progress to regular e-cigarette use and nicotine dependence. However, despite these risks, approximately two-thirds of JUUL users aged 15-24 do not know that JUUL always contains nicotine.[11]

You Can Take Action

We must take aggressive steps to protect our children from these highly potent products that risk exposing a new generation of young people to nicotine.[2,7] The bad news is that e-cigarette use has become an epidemic among our nation's young people. However, the good news is that we know what works to effectively protect our kids from all forms of tobacco product use, including e-cigarettes.[1,2,12] We must now apply these strategies to e-cigarettes, including USB flash drive shaped products such as JUUL. To achieve success, we must work together, aligning and coordinating efforts across both old and new partners at the national, state, and local levels. Everyone can play an important role in protecting our nation's young people from the risks of e-cigarettes.

Information for Parents

- **You have an important role to play in addressing this public health epidemic.**
- Learn about the different shapes and types of e-cigarettes and the risks of all forms of e-cigarette use for young people at https://e-cigarettes.surgeongeneral.gov/.
- Set a good example by being tobacco-free. If you use tobacco products, it's never too late to quit. Talk to a healthcare professional about quitting all forms of tobacco product use. For free help, visit smokefree.gov or call 1-800-QUIT-NOW.
- Adopt tobacco-free rules, including e-cigarettes, in your home and vehicle.
- Talk to your child or teen about why e-cigarettes are harmful for them. It's never too late.
- Get the Surgeon General's tip sheet for parents, Talk With Your Teen About E-cigarettes, at https://e-cigarettes.surgeongeneral.gov/. Start the conversation early with children about why e-cigarettes, including JUUL, are harmful for them.
- Let your child know that you want them to stay away from all tobacco products, including e-cigarettes, because they are not safe for them. Seek help and get involved.
    - Set up an appointment with your child's health care provider so that they can hear from a medical professional about the health risks of tobacco products, including e-cigarettes.
    - Speak with your child's teacher and school administrator about enforcement of tobacco-free school policies and tobacco prevention curriculum.
    - Encourage your child to learn the facts and get tips for quitting tobacco products at Teen.smokefree.gov.

Information for Teachers

- **You have an important role to play in addressing this public health epidemic.**
- Learn about the different shapes and types of e-cigarettes and the risks of all forms of e-cigarette use, including JUUL, for young people at https://e-cigarettes.surgeongeneral.gov/.
- Develop, implement, and enforce tobacco-free school policies and prevention programs that are free from tobacco industry influence, and that address all types of tobacco products, including e-cigarettes.

- Engage your students in discussions about the dangers of e-cigarette use. To help you, the Food and Drug Administration (FDA), and Scholastic, developed free resources for teachers. These materials can be found at www.scholastic.com/youthvapingrisks.

Information for Health Professionals

- **You have an important role to play in addressing this public health epidemic.**
- Learn about the different shapes and types of e-cigarettes and the risks of all forms of e-cigarette use, including JUUL, for young people at https://e-cigarettes.surgeongeneral.gov/.
- Ask about e-cigarettes, including small, discreet devices such as JUUL, when screening patients for the use of any tobacco products.
- Educate patients about the risks of all forms of tobacco product use, including e-cigarettes, for young people.
- Encourage patients to quit. For free help, patients can visit smokefree.gov or call 1-800-QUIT-NOW.

Information for States, Communities, Tribes, and Territories

- **You have an important role to play in addressing this public health epidemic.**
- Implement evidence-based population-level strategies to reduce e-cigarette use among young people, such as including e-cigarettes in smoke-free indoor air policies, restricting young peoples' access to e-cigarettes in retail settings, licensing retailers, implementing price policies, and developing educational initiatives targeting young people.
- Implement strategies to curb e-cigarette advertising and marketing that are appealing to young people.
- Implement strategies to reduce access to flavored tobacco products by young people.

KNOW THE RISKS. TAKE ACTION. PROTECT OUR KIDS.

References

1. Office of the Surgeon General. *The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General.* Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention (US), National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014. https://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf.
2. Office of the Surgeon General. *E-cigarette Use among Youth and Young Adults: A Report of the Surgeon General.* Washington, DC: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2016. https://www.cdc.gov/tobacco/data_statistics/sgr/e-cigarettes/pdfs/2016_sgr_entire_report_508.pdf.
3. Wang TW, Gentzke A, Sharapova S, et al. Tobacco Use Among Middle and High School Students - United States, 2011-2017. *MMWR Morbidity and Mortality Weekly Report.* 2018;67(22):629-633.
4. Cullen KA, Ambrose BK, Gentzke AS, Apelberg BJ, Jamal A, King BA. Notes from the Field: Increase in use of electronic cigarettes and any tobacco product among middle and high school students – United States, 2011-2018. *MMWR Morbidity & Mortality Weekly Report* 2018; 67(45):1276-1277.
5. Ambrose BK, Day HR, Rostron B, et al. Flavored Tobacco Product Use Among US Youth Aged 12-17 Years, 2013-2014. *Jama.* 2015;314(17):1871-1873.
6. Trivers KF, Phillips E, Gentzke AS, Tynan MA, Neff LJ. Prevalence of Cannabis Use in Electronic Cigarettes Among US Youth. *JAMA pediatrics.* 2018;172(11):1097-1099.
7. National Academies of Sciences, Engineering, and Medicine. 2018. Public Health Consequences of E-Cigarettes. Washington, DC: The National Academies Press. https://doi.org/10.17226/24952.
8. Ramamurthi D, Chau C, Jackler RK. JUUL and other stealth vaporisers: hiding the habit from parents and teachers. *Tob Control.* 2018. Epub ahead of print. doi: 10.1136/tobaccocontrol-2018-054455.
9. King BA, Gammon DG, Marynak KL, Rogers T. Electronic Cigarette Sales in the United States, 2013-2017. *Jama.* 2018;320(13):1379-1380.

10. Willett JG, Bennett M, Hair EC, et al. Recognition, use and perceptions of JUUL among youth and young adults. *Tob Control.* 2018. Epub ahead of print. doi: 10.1136/tobaccocontrol-2018-054273.
11. Truth Initiative. JUUL e-cigarettes gain popularity among youth, but awareness of nicotine presence remains low. https://truthinitiative.org/news/juul-e-cigarettes-gain-popularity-among-youth.
12. US Department of Health and Human Services. *Preventing tobacco use among youth and young adults.* Atlanta, GA: US Department of Health and Human Services, CDC;2012. https://www.cdc.gov/tobacco/data_statistics/sgr/2012/index.htm.