Introduction

On September 12, 2018, U.S. Food and Drug Administration (FDA) Commissioner Scott Gottlieb, M.D., said the use of e-cigarettes by U.S. teenagers had reached epidemic proportions. The first of a two-part series highlighted the increased use among teens and adults as well as regulatory action at the federal and state levels, bit.ly/ECigUseInKansas. This issue brief, the second in the series, examines the latest research concerning the health effects of e-cigarettes.

E-Cigarette Basics

Electronic cigarettes, commonly known as e-cigarettes, are battery-powered devices that provide nicotine and other additives to the user in the form of an aerosol. Using an e-cigarette also is referred to as “vaping.” E-cigarettes entered the U.S. market in 2007 and initially were marketed as a smoking cessation tool for adults and a “safer” alternative to conventional cigarettes. Within five years, policymakers at the federal, state and local levels began enacting laws and ordinances to ban the sale and use of e-cigarettes to minors, limit their use in public places, and impose taxes similar to those on conventional cigarettes.

The e-cigarette industry has grown in size and organizational complexity in recent years, most notably with the entry of major tobacco companies and the proliferation of vape shops. JUUL, an e-cigarette device launched in 2015 that resembles a USB drive, has become especially popular among teens and young adults as it can be used discreetly, has a high nicotine content, and comes in flavors such as mint, mango and fruit. Juul pods, as advertised, are manufactured in 5 percent (59 milligrams of nicotine per milliliter of liquid) and 3 percent (35 milligrams of nicotine per milliliter of liquid) formulations. However, it’s the presumed rate of absorption reported by JUUL that sets it apart — the company suggests the pattern of nicotine levels in the blood over time mimics that of

The NASEM report also found:

- Moderate evidence that more frequent use of e-cigarettes is associated with an increased likelihood of cessation of conventional cigarettes,
- Limited evidence that e-cigarettes may be effective aids to promote smoking cessation,
- Conclusive evidence that e-cigarette use increases airborne concentrations of particulate matter and nicotine in indoor environments compared with background levels,
- Conclusive evidence that most e-cigarette products, in addition to nicotine, contain and emit numerous potentially toxic substances, and
- Evidence on short-term exposure to e-cigarettes and health effects exists, but is not conclusive.
cigarette smoking due to the use of nicotine salts in their formulation. A 2-pack of JUUL pods costs about $10. JUUL Labs holds nearly three-quarters (72.8 percent) of the e-cigarette retail market in the U.S. as of September 2018 and sold over $1.29 billion in vape kits and nicotine pods during the 12 months ending August 2018.

**Health Effects of E-Cigarette Use**

In early 2016, published research on the safety or long-term health effects of e-cigarette use was very limited. Back then, there were studies indicating that the vapor emitted by e-cigarettes was less harmful than conventional cigarette smoke but evidence suggesting that e-cigarettes were an effective smoking cessation tool was lacking. Public health officials also were starting to suspect that teen e-cigarette use was associated with higher intention to smoke and one study had concluded that teens who try e-cigarettes are more likely to try other tobacco products, including conventional cigarettes.

At the request of the FDA Center for Tobacco Products, which regulates e-cigarettes as tobacco products, the National Academies of Sciences, Engineering, and Medicine (NASEM) convened a committee of experts to conduct a review of the emerging evidence about the health effects of e-cigarettes. The committee conducted a comprehensive review of the scientific literature about e-cigarettes regarding the key constituents (chemical components), human health consequences, effects on initiation and cessation of conventional tobacco cigarette use, and harm reduction. In 2018, the committee released a report, bit.ly/NASEMReport, providing a comprehensive analysis of 800 peer-reviewed studies about the health effects of e-cigarettes. The results of the NASEM study were released as a set of conclusions on each topic.

**Chemical Components**

E-cigarettes contain liquids (referred to as e-liquids or vape juice) that are converted to an aerosol when the device is used. The e-liquids burned in e-cigarettes typically contain nicotine (although some users prefer e-liquids without nicotine), flavorings and humectants (for moisture retention). It is well-established that nicotine causes dependence and addiction.

While most flavorings in e-liquids are designated as generally safe by the FDA for oral consumption in food, those designations do not apply to flavorings used in e-cigarettes as most have not been studied for toxicity when inhaled. The primary humectants — propylene glycol and glycerol — are widely used for other purposes and have been the subject of significant scientific study.

In reviewing the literature about the chemical components in and exposures from e-cigarettes, the committee found:

- Conclusive evidence that e-cigarette use increases airborne concentrations of particulate matter and nicotine in indoor environments compared with background levels;
- Conclusive evidence that exposure to nicotine from e-cigarettes is highly variable and depends on the characteristics of the device, the e-liquid used and how the device is operated;
- Conclusive evidence that in addition to nicotine, most e-cigarette products contain and emit numerous potentially toxic substances;
- 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 the characteristics of the device, the e-liquid used and how the device is operated;
- Substantial evidence that nicotine intake from e-cigarette devices among experienced adult users can be comparable to that from conventional cigarettes;
- Substantial evidence that under typical conditions of use, exposure to potentially toxic substances from e-cigarettes, except for nicotine, is significantly lower compared with conventional cigarettes; and
- 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 the e-liquids.
Human Health Effects From Short-Term Exposure to E-Cigarettes

While the serious health risks posed by the use of conventional cigarettes are well-documented, the relatively short history of e-cigarette use makes comparisons to those risks very difficult. However, some evidence on short-term exposure to e-cigarettes and the effects on disease symptoms does exist. The National Academies of Sciences, Engineering, and Medicine (NASEM) committee reviewed this evidence, bit.ly/NASEMReport, and found:

- Substantial evidence that e-cigarette use results in symptoms of dependence on e-cigarettes;
- Moderate evidence that the risk and severity of dependence are lower for e-cigarettes than conventional cigarettes;
- 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;
- Conclusive evidence that intentional or accidental exposure to e-liquids (from drinking, eye contact, or skin contact) can result in adverse health effects including but not limited to seizures, anoxic brain injury, vomiting and lactic acidosis;
- Conclusive evidence that intentionally or unintentionally drinking or injecting e-liquids can be fatal;
- Moderate evidence for increased cough and wheezing in adolescents who use e-cigarettes and an association with e-cigarette use and an increase in shortness of breath, coughing, wheezing and chest tightness associated with asthma;
- Insufficient evidence that e-cigarette use is associated with long-term changes in heart rate, blood pressure and cardiac function;
- No available evidence whether or not e-cigarettes cause respiratory diseases in humans;
- Insufficient evidence whether or not maternal e-cigarette use affects fetal development;
- No available evidence whether or not e-cigarettes affect pregnancy outcomes;
- 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;
- Substantial evidence that some chemicals present in e-cigarette aerosols (e.g., formaldehyde, acrolein) are capable of causing DNA damage, suggesting that long-term exposure to e-cigarette aerosols could increase risk of cancer and adverse reproductive outcomes; and
- Limited evidence that long-term e-cigarette use could increase the risk of cancer and no available evidence from adequate long-term animal studies to inform cancer risk.

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Initiation and Cessation

On the effects of e-cigarette use on initiation and cessation of conventional cigarette use, the NASEM found:

- Substantial evidence that e-cigarette use increases risk of ever using conventional cigarettes among youth and young adults;
- Moderate evidence that e-cigarette use increases the frequency and intensity of subsequent conventional cigarette smoking among youth and young adult e-cigarette users who ever use conventional tobacco cigarettes;
- Moderate evidence that more frequent use of e-cigarettes is associated with an increased likelihood of cessation of conventional cigarettes;
- Limited evidence that e-cigarettes might be effective aids to promote smoking cessation; and
- Insufficient evidence about the effectiveness of e-cigarettes as cessation aids compared with no treatment or to other FDA-approved smoking cessation treatments.

Harm Reduction

When reviewing the evidence on what is known about e-cigarette exposure and health effects compared with conventional tobacco cigarettes, the committee found:

- Conclusive evidence that completely substituting e-cigarettes for conventional cigarettes reduces user exposure to numerous toxic substances and carcinogens present in conventional cigarettes; and
- Moderate evidence that secondhand exposure to nicotine and particulates is lower from e-cigarettes than conventional cigarettes.

Conclusion

With the rising use of e-cigarettes, especially among youth, research is expanding rapidly as researchers gain new insights and access to data about the long-term use of this product. It will be critical for policymakers, public health officials and health policy advocates to remain up-to-date as additional studies emerge detailing how these products affect health.

ABOUT THE ISSUE BRIEF

This brief is based on work done by Linda J. Sheppard, J.D., and Hina B. Shah, M.P.H. It is available online at khi.org/policy/article/19-15.

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