Vaping: The Gen Z nicotine crisis

Chelsey DeGomez, MPAS, PA-C; Jennifer Feirstein, MSPAS, PA-C, DFAAPA

ABSTRACT

The topic of vaping is becoming increasingly prevalent in healthcare, especially regarding adolescents as their use of electronic cigarette products continues to increase. The many factors to consider include the safety of these products, human health and behavior, and social effects. Healthcare providers need to be aware of these issues to provide appropriate education and care to adolescent patients. **Keywords:** vaping, electronic cigarettes, adolescents

Learning objectives

- Describe the components and functionality of an e-cigarette.
- Identify factors contributing to the appeal of e-cigarettes among adolescents.
- Discuss the health implications associated with nicotine use through an e-cigarette device.
- Describe patient education and screening programs that target adolescent vaping.

E lectronic cigarettes, or e-cigarettes, are the latest among the numerous efforts to modify traditional cigarettes to minimize the harmful effects of smoking.¹ E-cigarettes were introduced in China in 2004 as a smoking cessation device or alternative cigarette; by the mid-2000s, they had been incorporated into the US marketplace.¹

E-cigarettes contain a battery that can be activated by manually turning the device on or simply by inhaling (Figure 1). A tank inside the device contains the liquid used for vaping, as this type of smoking is called.¹ E-cigarette liquid, also called *e-liquid* or *e-juice*, usually contains nicotine (although there are e-liquids without nicotine). Manufacturers also have added flavors and a humectant or solvent (usually propylene glycol and/or vegetable

DOI:10.1097/01.JAA.0000854544.26702.2e

Copyright © 2022 American Academy of PAs



glycerin).^{1,2} The battery heats an attached atomizer that vaporizes the liquid; this aerosolized liquid is inhaled by the user.

Adolescents have a number of slang terms to describe e-cigarette use.^{1,3} In addition to *vaping*, another popular term is "*JUULing*," named after one of the largest e-cigarette companies.⁴ Other popular terms among youth are e-hookah, e-pipes, mods, and tanks.^{1,3} Clinicians must be familiar with these terms; e-cigarette use by adolescents may be underreported if "e-cigarette" terminology is used in lieu of the slang terms more readily recognized among adolescents.³ Additionally, clinicians should always specifically inquire about vaping, because it is not automatically associated with smoking or tobacco use inquiries in this population.³

Use of e-cigarettes by adolescents has dramatically increased in the past decade: in 2011, just 1.5% of high school students reporting use of e-cigarettes, compared with 11.7% in 2017, 20.8% in 2018, and 27.5% in 2019.^{5,6} Similar increases have been demonstrated among middle school students, with 0.6% reporting e-cigarette use in 2011, 3.3% in 2017, 4.9% in 2018, and 10.5% in 2019.^{5,6} This translates to over 5 million youth reporting use of e-cigarettes in 2019.⁷ In contrast, the 2018 National Health Interview Survey reported that 3.2% of all adults (about 8.1 million) were current e-cigarette users, with the highest use group (7.6%) being adults ages 18 to 24 years.⁸

The significant increases in prevalence prompted Jerome Adams MD, MPH, the US Surgeon General at the time,

Chelsey DeGomez practices in obstetrics and gynecology at MomDoc Women for Women in Tempe, Ariz. **Jennifer Feirstein** is an assistant professor and director of didactic education of the PA program at Creighton University in Phoenix, Ariz. The authors have disclosed no potential conflicts of interest, financial or otherwise.

Key points

- Multiple advertising and marketing strategies contribute to the popularity of vaping among adolescents, with flavored products being one of the most significant factors.
- The long-term health implications associated with vaping are not yet fully understood.
- The effect of nicotine use on a still-developing adolescent brain may contribute to increased risk of nicotine addiction.
- Healthcare providers have a responsibility to educate patients on the risks associated with vaping, especially in adolescents.

to describe e-cigarette use as an "epidemic" among youth, saying "I 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... is a cause for great concern."⁹ With the ever-rising numbers of adolescents using e-cigarette systems, clinicians need to expand efforts to prevent traditional tobacco use to include the new health concerns that come with adolescent vaping.

ADOLESCENT APPEAL

A study aiming to identify factors contributing to adolescent vaping found both protective and risk factors for the initiation of use of e-cigarettes.¹⁰ Protective factors included

cent vaping found both protective as initiation of use of e-cigarettes.¹⁰ Prot parental support and monitoring, academic involvement, and emotional self-control.¹⁰ Risk factors included peer smoking, sensation seeking, rebelliousness, parental conflict, and lower levels of parental education.¹⁰ Data analysis by Wills and colleagues suggests that health-conscious youth may use e-cigarettes because they are perceived to be safer than traditional cigarettes; youth with traditional risk factors for substance abuse may initiate vaping because of their desire for mood elevation or non-

Marketing by e-cigarette companies rapidly increased after the introduction of e-cigarettes in the US market, with advertising expenditures increasing from less than \$5 million per year (2007-2010) to \$12 million per year in 2011 and \$22 million per year in 2012.¹¹ Much of this increase in marketing and

conformity to social norms.¹⁰

advertising has targeted adolescents, with 47% of teens ages 12 to 17 years being exposed to e-cigarette magazine advertisements in 2014.¹ Additionally, advertisements in magazines with high teen readership outnumbered advertisements in magazines with high adult readership by a factor of four.¹ In the television market, adolescent exposure to e-cigarette advertising increased by 256% between 2011 and 2018; an estimated 50% of the youth population in the United States was exposed to e-cigarette advertisements on television in 2013.¹ Vaping companies also advertise on YouTube, Twitter, and other social media outlets known to be popular with adolescents, and that are disproportionally used by youth and young adults.¹²⁻¹⁶

Flavored products are listed as one of the top three reasons adolescents engage in vaping.¹⁷ This is reminiscent of traditional cigarette companies using flavors in cigarettes to target youth.¹⁸ An FDA ban on traditional cigarette flavoring was implemented to discourage use by adolescents; unfortunately, this ban does not extend to the more than 7,000 flavors available in e-cigarettes.^{17,19}

The e-cigarette device itself has been identified as being particularly appealing to adolescents.⁴ Devices may have the appearance of a flash drive, juice box, pen, cell phone case, or flashlight (**Figure 2**).^{3,14} These devices are appealing because they let adolescents discreetly use the product while in school.²

A common promotional technique used by e-cigarette companies is identifying e-cigarettes as a safe alternative to traditional smoking. Technically, this may be true smokers may assume reduced consequences if their nicotine



use is in the form of e-cigarettes rather than traditional cigarettes.²⁰ However, most adolescent e-cigarette users have never smoked traditional cigarettes.²¹ Therefore, with the onset of vaping, many adolescents assume only new risks without the concomitant mitigation of other risks that would be seen in patients who had previously used traditional cigarettes.²⁰ One major risk factor for adolescents new to vaping is the increased likelihood of transitioning to traditional cigarette use.²¹



FIGURE 2. Various e-cigarette/vaping devices. Reproduced with permission from the Minnesota Department of Health, www.health.state.mn.us/ecigarettes

SAFETY

E-cigarettes have only been in the US market for just over a decade; therefore, long-term health consequences attributed to their consumption cannot be adequately reported at this time. However, there are similarities between some of the components in e-cigarettes and traditional cigarettes, allowing for plausible extrapolations to be made about the potential health and safety effects associated with vaping. Additionally, outbreaks of severe, acute lung injury recently have been reported in association with vaping.

Contents Although some e-cigarettes do not contain nicotine, most (67%) adolescents ages 15 to 17 years who reported using e-cigarettes use products containing nicotine.²⁰ Assessing how much nicotine adolescents are vaping is challenging, because e-cigarettes are available with nicotine concentrations ranging from zero to more than 25 mg/mL.²² Among adolescents who use high-nicotine concentration e-cigarettes (18 mg/mL or greater), typical use is 8.6 episodes of vaping daily and 10.3 puffs per episode.²² Applying this typical use data to the *JUUL* brand of e-cigarettes, a patient using high-nicotine concentration e-cigarettes are available and 10.3 puffs per episode.²⁴ Applying this typical use data to the *JUUL* brand of e-cigarettes inhales an amount of nicotine per day equivalent to a half-pack of cigarettes.^{22,23}

Accidental or intentional ingestion of liquid nicotine can cause serious cardiovascular problems from nicotine toxicity. The two concentrations available for a single *JUUL* pod are 5% (59 mg/mL) and 3% (35 mg/mL), and the pod volume is 0.7 mL.^{2,23} Thus, the amount of nicotine in a single *JUUL* pod ranges from 24.5 to 41.3 mg. The estimated lethal dose of nicotine ranges from 0.5 to 1 mg/kg body weight, with the commonly reported lethal dose in children being 10 mg.^{24,25} According to poison control centers, calls regarding e-cigarettes have increased dramatically since 2011, and the most common symptoms related to nicotine overdose are nausea and vomiting.²⁶

A study of habitual e-cigarette use found that the negative cardiovascular effects associated with use of traditional cigarettes also are seen with nicotine use in the form of e-cigarettes.²⁷ These effects include increased sympathetic tone, which is associated with tachycardia, and increased oxidative stress, which is associated with free radical formation.²⁷ These factors may put patients at risk for coronary artery disease leading to myocardial infarction and stroke.²⁷

Inhalation of components of the aerosol produced by e-cigarettes has been linked to symptoms of chronic bronchitis, such as coughing, congestion, phlegm, and wheezing.²⁸ These symptoms likely are the result of the inflammatory effects and oxidative stress created by the aerosol components, which include metals and toxins.²⁸ The flavors added to the liquid in the cartridge also may contribute to the respiratory risks. Cherry flavors contain benzaldehyde, and diacetyl is found in other sweet flavors.²⁹ Both benzaldehyde and diacetyl are known respiratory irritants; diacetyl, in particular, is a known causative factor in acute-onset bronchiolitis obliterans.²⁹

Propylene glycol is the main constituent of the cartridge liquid.³⁰ In children, chronic exposure to propylene glycol has been associated with rhinitis, asthma, and dry throat and mouth.³⁰ Additionally, when heated, propylene glycol forms propylene oxide, a known carcinogen.³⁰ Propylene glycol decomposes to form formaldehyde and acetaldehyde; the toxin, acrolein, is a byproduct of this degradation that is associated with mucosal irritation.³¹ All of these byproducts are either toxic or carcinogenic.³¹

Although the tar and carbon monoxide exposure associated with traditional smoking does not exist with vaping, patients who vape are exposed to other tobacco-specific carcinogens, specifically, nitrosamines, carbonyl compounds, metals, volatile organic compounds, and phenolic compounds.³¹ Although these carcinogenic and toxic compounds are found in small quantities compared with traditional cigarettes, their presence at any level is concerning.³⁰

E-cigarette, or vaping, product use-associated lung injury (**EVALI**) An example of an additional health implication associated with vaping is the EVALI outbreak that began in June 2019. During the time of EVALI data collection by the CDC (August 2019 to February 2020), 2,807 hospitalizations for EVALI were reported, with 68 confirmed deaths.³² A full discussion of EVALI is beyond the scope of this article, but clinicians should have a basic understanding in order to facilitate early recognition.

The syndromic appearance of EVALI includes respiratory symptoms (shortness of breath and cough) associated with gastrointestinal (nausea, vomiting) and constitutional (fever, chills) symptoms; these symptoms progressively worsen over several days to weeks and about half of patients require ICU admission.³³⁻³⁵ The most common findings on pulmonary imaging include patchy, bilateral, ground-glass opacities on CT; however, variable patterns are possible.³⁵ Laboratory analysis for respiratory infectious diseases usually is negative.³³⁻³⁵ Patients with EVALI, by definition, report having used e-cigarettes in the 90 days before symptom onset, most frequently with products containing tetrahydrocannabinol (THC).^{33,34} Vitamin E acetate has been strongly linked to the EVALI outbreak because it was detected in the bronchoalveolar lavage fluid of 94% of patients with EVALI and outbreaks corresponded temporally with the introduction of vitamin E acetate to THCcontaining products.³⁴ EVALI cases declined after identification of vitamin E as the probable cause; however, clinicians should be vigilant about monitoring for similar future outbreaks due to the potential for e-cigarettes to be used with nonregulated products.³²

Secondhand exposure No long-term studies of the effects of secondhand vapor exposure have been completed. As with traditional cigarettes, the risks associated with secondhand exposure are assumed to be far less than the risks to the person vaping.³¹ However, theoretically any risks or consequences associated with being a primary user may translate to those exposed secondhand. As vaping becomes more widespread, healthcare providers may need to consider asking patients about secondhand vapor exposure, and healthcare advocates may need to explore policies on public exposure to e-cigarette vapor.

Devices The e-cigarette device itself can be associated with negative health effects, as demonstrated by the increase in ED visits due to burns related to device overheating.³⁶ The batteries required to operate the device also can explode. Most of these injuries occur with the device in the user's front pants pocket, resulting in burns to the thigh and groin.³⁶ Men are more frequently affected than women, with the typical injury involving a second-degree burn; half of injured patients have an average hospital stay of 4 days.³⁶

Neuropsychiatric development Although the effects of nicotine are not specific to vaping, the increased popularity of vaping among youth is particularly concerning because of the potential long-term effects of nicotine on adolescents' developing brains.³⁷ The prefrontal cortex is responsible for executive functions such as judgment, planning, and decision-making. Because the brain is not fully developed until age 25 years, early exposure to nicotine through e-cigarettes may interfere with development of these executive functions, and can cause poor concentra-

tion, depression, anxiety, and increased engagement in reckless behaviors. $^{\rm 37}$

Adolescent use of e-cigarettes may eventually contribute to nicotine dependence and addiction secondary to the "high," or sense of pleasure, associated with nicotine.³⁷ Specifically, in undeveloped brains, activation of nicotine receptors causes upregulation of these receptors, eventually requiring increasing amounts of nicotine exposure to induce the same pleasure response.³⁷

SOCIAL EFFECTS

Normalization of nicotine use Many laws and regulations have been enacted in an effort to discourage traditional cigarette smoking; however, these same tactics have not been used with e-cigarettes. This may normalize nicotine use, potentially leading to reduced attempts at quitting, relapse from nicotine cessation, and increased nicotine initiation in youth.³⁰ Additionally, patients who use e-cigarettes may transition into using traditional cigarettes: Primack and colleagues found that 68.8% of adolescents and young adults ages 16 to 26 years whose nicotine use began with e-cigarettes were using traditional cigarettes within 1 year, but only 18.9% of e-cigarette nonusers initiated use of traditional cigarettes within the 1-year study period.³⁸

Alcohol use Oh and colleagues found that adolescents who had used e-cigarettes drank alcohol more frequently than adolescents who did not use e-cigarettes.³⁹ The frequency of vaping also was found to correlate positively with frequency of alcohol use, with daily e-cigarette use associated with a higher likelihood to drink alcohol than in those who only intermittently vaped.³⁹

Other substance use E-cigarettes may be a gateway to use of other substances, such as alcohol and marijuana.² E-cigarette or hookah use has been shown to increase the likelihood of adolescents to use marijuana.⁴⁰ Additionally, it may lead to more frequent or regular marijuana use; nicotine exposure has been shown to prime the brain's reward system so that subsequent exposure to drugs is associated with a more significant pleasure response.⁴⁰

Some e-cigarette devices can be used with marijuana, and it has been shown that 1 in 11 middle and high school students have used e-cigarettes containing marijuana.⁴¹ Vaporized cannabis has been shown to have a more significant subjective drug effect compared with smoked cannabis and causes greater impairment of cognition and psychomotor skills; blood THC concentrations also are higher.⁴² Serious lung injury also is a concern with vaping THC as was demonstrated in the EVALI cases discussed earlier. THC-containing products for vaping are illegal in many states, yet remain widely available; this raises concern for substances that may be in these unregulated products and may cause significant health effects.³³ This is an emerging field of study, and more research is needed to fully understand the health effects of vaping THC-containing products.

NEXT STEPS

Research Additional research is needed because of the constant influx of information regarding e-cigarette use. For example, in April 2019, the FDA made a special announcement informing the public of a possible link between vaping and seizures, especially in adolescents and young adults.⁴³ Although seizures are a known symptom of nicotine toxicity, the seizures referenced in this special report are occurring in e-cigarette users without coexistent nicotine toxicity.⁴³ Since this 2019 announcement by the FDA, case reports have been published linking seizure activity with vaping; however, causality has not been demonstrated.44-46 More long-term studies are needed to fully understand the harms associated with vaping. In the interim, regulatory organizations must protect the public based on the limited evidence-based studies and information that exists, and healthcare providers should continue to assume the role of educating patients about the potential harmful effects of vaping.

Regulation Since the initial introduction of e-cigarettes when there were no FDA regulations in place, progress has been made in regulating this industry. Manufacturers are now required to include a statement on their packaging informing buyers that the product contains nicotine. Other improvements include restricted sales to those under age 18 years in an effort to mitigate adolescent use, and restrictions in advertising.⁴⁷

In June 2022, the FDA issued a marketing denial order to JUUL Labs Inc., which would have required JUUL products to be removed from the US market; however, this was promptly followed the next day with a temporary administrative stay by the US Court of Appeals for the DC Circuit, and an FDA administrative stay in early July 2022.⁴⁸ Although the viability of JUUL in the United States is undetermined at press time, clinicians must remember that the elimination of JUUL products from the US market would not eliminate the adolescent vaping problem, because many alternatives to JUUL are available for e-cigarette use.

Additionally, despite measures to progressively increase regulation of e-cigarettes by the FDA, they only pertain to products that contain nicotine.⁴⁷ Products without nicotine are not regulated, the rationale being that flavors determined safe for ingestion in foods should be safe for inhalation. However, the gastrointestinal tract can safely digest substances that, in the lungs, are associated with respiratory toxicity.²⁹ Testing and FDA regulation should be adopted for nonnicotine e-cigarettes, because using these substances may pose unique risks.

As previously discussed, flavoring used in nicotine and nonnicotine e-cigarettes is a significant temptation toward adolescent use of the products. Flavorings have been banned from use in traditional cigarettes for this very reason; however, similar bans have yet to be implemented with e-cigarettes.

Another strategy employed by the FDA in an attempt to reduce traditional cigarette use is the implementation of a

federal tax; however, no federal tax has been adopted for vaping products. Additionally, only 60% of states have implemented a state tax on e-cigarette products; 22 of those states have enacted their e-cigarette tax in the past 3 years.⁴⁹ Increasing the expense of using e-cigarettes through the adoption of a vaping tax may be an effective method for reducing adolescent use. Overall, the FDA has the power to help mitigate adolescent use by implementing regulations that discourage use of e-cigarettes, as has been done for traditional cigarettes.

CONCLUSION

Healthcare providers have a significant role to play in protecting adolescents from the harmful effects of vaping. Clinicians must be aware of the prevalence of vaping among adolescents, and recognize the trend moving away from traditional cigarettes and toward e-cigarettes. Educate patients on known and suspected harms associated with e-cigarette use, and emphasize that much is unknown about the implications of long-term use. Use the e-cigarette terminology recognized by younger patients. Be aware of risk factors that may indicate a patient is more likely to use e-cigarettes, and educate parents on behaviors that may suggest that their adolescent is using e-cigarettes. All of these strategies can help to better protect adolescents from adverse reactions to vaping. JAAPA

Earn Category I CME Credit by reading both CME articles in this issue, reviewing the post-test, then taking the online test at http://cme.aapa.org. Successful completion is defined as a cumulative score of at least 70% correct. This material has been reviewed and is approved for 1 hour of clinical Category I (Preapproved) CME credit by the AAPA. The term of approval is for 1 year from the publication date of September 2022.

REFERENCES

- US Department of Health and Human Services. E-Cigarette Use Among Youth and Young Adults. A Report of the Surgeon General. Atlanta, GA. 2016. https://e-cigarettes.surgeongeneral. gov/documents/2016_SGR_Full_Report_non-508.pdf. Accessed July 8, 2022.
- Walley SC, Wilson KM, Winickoff JP, Groner J. A public health crisis: electronic cigarettes, vape, and JUUL. *Pediatrics*. 2019; 143(6):e20182741.
- 3. Vincent D, Potts J, Durbin J, et al. Adolescent use of electronic nicotine delivery systems. *Nurse Pract.* 2018;43(3):17-21.
- 4. Huang J, Duan Z, Kwok J, et al. Vaping versus JUULing: how the extraordinary growth and marketing of JUUL transformed the US retail e-cigarette market. *Tob Control.* 2019;28(2):146-151.
- Cullen KA, Ambrose BK, Gentzke AS, et al. Notes from the field: use of electronic cigarettes and any tobacco product among middle and high school students—United States, 2011-2018. MMWR Morb Mortal Wkly Rep. 2018;67(45):1276-1277.
- Cullen KA, Gentzke AS, Sawdey MD, et al. e-Cigarette use among youth in the United States, 2019. JAMA. 2019;322(21):2095-2103.
- Centers for Disease Control and Prevention. About electronic cigarettes (e-cigarettes). www.cdc.gov/tobacco/basic_information/ e-cigarettes/about-e-cigarettes.html. Accessed June 27, 2022.
- Villarroel MA, Cha AE, Vahratian A. Electronic cigarette use among US adults, 2018. NCHS Data Brief, no. 365. Hyattsville, MD: National Center for Health Statistics; 2020.

- Office of the Surgeon General. Surgeon General's advisory on e-cigarette use among youth. 2018. https://e-cigarettes.surgeon general.gov/documents/surgeon-generals-advisory-on-e-cigaretteuse-among-youth-2018.pdf. Accessed June 21, 2019.
- Wills TA, Knight R, Williams RJ, et al. Risk factors for exclusive e-cigarette use and dual e-cigarette use and tobacco use in adolescents. *Pediatrics*, 2015;135(1):e43-e51.
- Kornfield R, Huang J, Vera L, Emery SL. Rapidly increasing promotional expenditures for e-cigarettes. *Tob Control*. 2015; 24(2):110-111.
- Luo C, Zheng X, Zeng DD, Leischow S. Portrayal of electronic cigarettes on YouTube. BMC Public Health. 2014;14:1028.
- Huang J, Kornfield R, Szczypka G, Emery SL. A cross-sectional examination of marketing of electronic cigarettes on Twitter. *Tob Control.* 2014;23(suppl 3):iii26-iii30.
- 14. Jenssen BP, Walley SC. Section on Tobacco Control. E-cigarettes and similar devices. *Pediatrics*. 2019;143(2):e20183652.
- Pew Research Center. Teens, Social Media & Technology 2018. www.pewresearch.org/internet/2018/05/31/teens-social-mediatechnology-2018. Accessed July, 8, 2022.
- 16. Pew Research Center. Social media fact sheet. www.pewresearch. org/internet/fact-sheet/social-media. Accessed June 27, 2022.
- 17. Arane K, Goldman RD. Electronic cigarettes and adolescents. *Can Fam Physician*. 2016;62(11):897-898.
- Carpenter CM, Wayne GF, Pauly JL, et al. New cigarette brands with flavors that appeal to youth: tobacco marketing strategies. *Health Aff (Millwood)*. 2005;24(6):1601-1610.
- Pepper JK, Ribisl KM, Brewer NT. Adolescents' interest in trying flavoured e-cigarettes. *Tob Control*. 2016;25(suppl 2):ii62-ii66.
- Pepper JK, Farrelly MC, Watson KA. Adolescents' understanding and use of nicotine in e-cigarettes. *Addict Behav.* 2018;82:109-113.
- 21. Westling E, Rusby JC, Crowley R, Light JM. Electronic cigarette use by youth: prevalence, correlates, and use trajectories from middle to high school. *J Adolesc Health*. 2017;60(6):660-666.
- Goldenson NI, Leventhal AM, Stone MD, et al. Associations of electronic cigarette nicotine concentration with subsequent cigarette smoking and vaping levels in adolescents. *JAMA Pediatr*. 2017;171(12):1192-1199.
- 23. JUUL. www.juul.com/shop. Accessed June 27, 2022.
- 24. Solarino B, Rosenbaum F, Riesselmann B, et al. Death due to ingestion of nicotine-containing solution: case report and review of the literature. *Forensic Sci Int.* 2010;195(1-3):e19-e22.
- 25. Palazzolo DL. Electronic cigarettes and vaping: a new challenge in clinical medicine and public health. A literature review. *Front Public Health*. 2013;1:56.
- National Poison Data System, American Association of Poison Control Centers. E-cigarettes and liquid nicotine. https://aapcc. org/track/ecigarettes-liquid-nicotine. Accessed June 27, 2022.
- Moheimani RS, Bhetraratana M, Yin F, et al. Increased cardiac sympathetic activity and oxidative stress in habitual electronic cigarette users: implications for cardiovascular risk. *JAMA Cardiol.* 2017;2(3):278-284.
- McConnell R, Barrington-Trimis JL, Wang K, et al. Electronic cigarette use and respiratory symptoms in adolescents. *Am J Respir Crit Care Med.* 2017;195(8):1043-1049.
- Barrington-Trimis JL, Samet JM, McConnell R. Flavorings in electronic cigarettes: an unrecognized respiratory health hazard? JAMA. 2014;312(23):2493-2494.
- Hajek P, Etter J-F, Benowitz N, et al. Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefit. *Addiction*. 2014;109(11):1801-1810.
- Kosmider L, Sobczak A, Fik M, et al. Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine Tob Res.* 2014;16(10):1319-1326.
- 32. Centers for Disease Control and Prevention. Outbreak of lung injury associated with the use of e-cigarette, or vaping, products.

www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html. Accessed June 27, 2022.

- Layden JE, Ghinai I, Pray I, et al. Pulmonary illness related to e-cigarette use in Illinois and Wisconsin—final report. N Engl J Med. 2020;382(10):903-916.
- Blount BC, Karwowski MP, Shields PG, et al. Vitamin E acetate in bronchoalveolar-lavage fluid associated with EVALI. N Engl J Med. 2020;382(8):697-705.
- 35. Aberegg SK, Cirulis MM, Maddock SD, et al. Clinical, bronchoscopic, and imaging findings of e-cigarette, or vaping, product use-associated lung injury among patients treated at an academic medical center. *JAMA Netw Open.* 2020;3(11):e2019176.
- 36. Eaton DL, Kwan LY, Stratton K, eds. National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Review of the Health Effects of Electronic Nicotine Delivery Systems. Public health consequences of e-cigarettes. Washington, DC: National Academies Press; 2018. www.ncbi.nlm.nih.gov/books/NBK507171. Accessed June 27, 2022.
- Goriounova NA, Mansvelder HD. Short- and long-term consequences of nicotine exposure during adolescence for prefrontal cortex neuronal network function. *Cold Spring Harb Perspect Med.* 2012;2(12):a012120.
- Primack BA, Soneji S, Stoolmiller M, et al. Progression to traditional cigarette smoking after electronic cigarette use among US adolescents and young adults. *JAMA Pediatr.* 2015;169(11):1018-1023.
- 39. Oh KH, Lee CM, Oh B, et al. The relationship between electronic cigarette use with or without cigarette smoking and alcohol use among adolescents: finding from the 11th Korea youth risk behavior web-based survey. *Korean J Fam Med.* 2019;40(4):241-247.
- 40. Audrain-McGovern J, Stone MD, Barrington-Trimis J, et al. Adolescent e-cigarette, hookah, and conventional cigarette use and subsequent marijuana use. *Pediatrics*. 2018;142(3): e20173616.
- Trivers KF, Phillips E, Gentzke AS, et al. Prevalence of cannabis use in electronic cigarettes among US youth. JAMA Pediatr. 2018;172(11):1097-1099.
- 42. Spindle TR, Cone EJ, Schlienz NJ, et al. Acute effects of smoked and vaporized cannabis in healthy adults who infrequently use cannabis: a crossover trial. *JAMA Netw Open.* 2018;1(7): e184841.
- 43. US Food and Drug Administration. Some e-cigarette users are having seizures, most reports involving youth and young adults. www.fda.gov/TobaccoProducts/NewsEvents/ucm635133.htm. Accessed June 27, 2022.
- 44. Wharton JD, Kozek LK, Carson RP. Increased seizure frequency temporally related to vaping: where there's vapor, there's seizures? *Pediatr Neurol.* 2020;104:66-67.
- 45. Quezada T, Sianati B, Valeriano J. Vaping and seizure risk: a case report. *Neurology*. 2020;94(15 suppl):1814.
- Tatum PS, Oster JM. Seizures and vaping—a report of two cases. Mil Med. [e-pub July 17, 2021]
- 47. US Food and Drug Administration. Deeming tobacco products to be subject to the federal Food, Drug, and Cosmetic Act as amended by the Family Smoking Prevention and Tobacco Control Act; restrictions on the sale and distribution of tobacco products and required warning statements for tobacco products. www.federalregister.gov/documents/2016/05/10/2016-10685/ deeming-tobacco-products-to-be-subject-to-the-federal-fooddrug-and-cosmetic-act-as-amended-by-the. Accessed June 27, 2022.
- 48. US Federal Drug Administration. FDA denies authorization to market JUUL products. www.fda.gov/news-events/pressannouncements/fda-denies-authorization-market-juul-products. Accessed July 7, 2022.
- 49. Centers for Disease Control and Prevention. State Tobacco Activities Tracking and Evaluation (STATE) system. www.cdc. gov/statesystem/factsheets/ecigarette/ECigTax.html. Accessed July 7, 2022.

30 www.JAAPA.com