

Electronic cigarettes are the most common form of nicotine delivery used by youth and young adults, and in 2018, the US Surgeon General declared this to be an epidemic. The developing adolescent brain is vulnerable to nicotine exposure, which can lead to long-lasting cognitive and mood disorders. Screening rates for vaping are low and lack of knowledge by adolescents, clinicians, parents, and caregivers is high. This article reviews the components of vaping, prevalence, adverse reactions, regulation, treatment, and prevention strategies related to vaping in youth and young adults.

**Keywords:** electronic cigarettes, e-cigarettes, e-liquid, vaping, youth, screening

#### Learning objectives

- Describe the epidemiology of e-cigarette use in youth and young adults.
- List the potential detrimental health effects of e-cigarette use.

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DOI:10.1097/01.JAA.0000654384.02068.99

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lectronic cigarettes, or e-cigarettes, are noncombustible tobacco products that have become the most common form of nicotine consumption among US youth and young adults, surpassing combustible cigarettes. These extremely popular vaping devices produce a near-odorless vapor, are easily obtained and concealed, and users may believe that they are a healthier alternative to cigarettes (Figure 1).2 Flavorings added to e-liquids used in vaping are attractive to young people, and devices can be used to deliver tetrahydrocannabinol (THC). Lack of knowledge about electronic cigarettes among youth, adults, and healthcare workers is pervasive, and many people do not realize that the most common devices deliver higher nicotine levels than traditional cigarettes and that early exposure to nicotine increases the likelihood of lifelong nicotine addiction.<sup>3</sup> Smoking during adolescence also affects brain development, which has lasting effects on cognitive function and increases the risk for developing mood disorders later in life.4

Despite rules to restrict marketing and sales of cigarettes to minors, US cigarette manufacturers appear to target young people in their advertising.<sup>5,6</sup> Use of vaping products has increased at unprecedented rates among youth and is underreported in clinical settings.<sup>7</sup> In 2018, 21% of US high school seniors reported using an e-cigarette in the past 30 days; that same year, the US Surgeon General declared vaping an epidemic among youth.<sup>7,8</sup>

## Key points

- More than 27% of high school students and 10% of middle school students have used e-cigarettes in the past 30 days.
- The developing adolescent brain is vulnerable to nicotine, which can cause long-term adverse neurochemical changes.
- No clinical practice guidelines exist for treating youth and young adults addicted to e-cigarettes.

#### **E-CIGARETTE BACKGROUND**

China introduced the world to e-cigarettes in 2003 and most are manufactured there. The first e-cigarette entered the US market in 2007 and the vaping industry's estimated retail sales were \$5.5 billion in 2018.

E-cigarettes use a battery to heat a coil that vaporizes a liquid, commonly referred to as e-liquid (Figure 2). The smoker inhales this vapor, which often is odorless or may produce a mild transient odor.

The most common devices in use today are vape pens, mods, and pods. These devices have USB rechargeable batteries and prefilled or refillable reservoirs that hold e-liquid.

The *vape pen* closely resembles a pen and is compatible with most prefilled e-liquid cartridges.

A *vape mod* is a modifiable device with various sizes of tanks and a battery of varying strength and quality. Because the heating of the liquid is done indirectly via a coil, the user can adjust the power, which affects the amount of nicotine delivered per inhalation. Stronger batteries can deliver a much higher dose of nicotine per inhalation.

The device used most commonly by youth and young adults is a *vape pod*, the most popular being the JUUL, which owns a 75% market share of e-cigarettes.<sup>5</sup> This device is sleek and shaped like a USB flash drive, and can be used in a concealed manner.

## **E-LIQUID**

Also referred to as vape juice or e-juice, e-liquid has four components: water, flavorings, a propellant (typically propylene glycol or vegetable glycerin), and almost always



FIGURE 1. An e-cigarette

nicotine. In many cases, the nicotine concentration is much greater than in combustible cigarettes. JUUL creates its e-liquids through a patented process that uses benzoic acid to transform the nicotine into nicotine salt. This causes a higher nicotine concentration that does not have the same harsh effect on the throat and lungs as combustible cigarettes.<sup>5</sup>

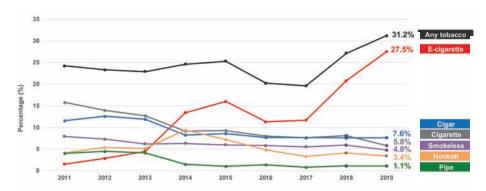
The e-liquid forms a vapor when heated. Vapor contents vary based on the type of propellant used but all produce carbonyls such as formaldehyde, acetaldehyde, acrolein, and acetone, all of which have established toxic or carcinogenic properties. The levels present in vapor vary based on the device's battery voltage and type of solvent. Devices that use high-voltage batteries have levels of formaldehyde similar to that found in combustible tobacco smoke. Metals, likely derived from the heating coil, also are present in vapor and include lead, chromium, nickel, and manganese, all of which are toxic when inhaled. Levels vary significantly based on brand, voltage, and frequency of coil change.<sup>5</sup>

### **EPIDEMIOLOGY AND PATTERNS OF USE**

E-cigarette use among youth has become a public health concern. Although males have always had a higher rate of combustible smoking than females, this gap is decreasing. Data are mixed, with about 50% of studies showing no

FIGURE 2. Parts of an e-cigarette





**FIGURE 3.** Tobacco use among high school students (Centers for Disease Control and Prevention. National Youth Tobacco Survey, 2011-2019)

gender gap and others showing a slight trend toward male predominance.<sup>9</sup> In US high schools, Hispanics (43%) and whites (38%) are the most common races to report ever using e-cigarettes.<sup>1</sup> The US Surgeon General reported e-cigarette use among high school students grew 900% from 2011 to 2015.<sup>1</sup> In 2019, 27.5% of US high school students reported using an e-cigarette in the last 30 days, compared with 1.4% of adults (Figure 3).<sup>10,11</sup> From 2017 to 2018, e-cigarette use among US high school students rose 78%, the highest year-over-year increase for any substance in the past 44 years.<sup>10</sup>

The most commonly cited reasons that youth and young adults report using e-cigarettes include curiosity, flavorings/ taste, social acceptance, lack of odor, quick use, easy concealment, and the perception that they are more healthful than cigarettes. E-cigarettes also are appealing because they can be used in places where combustible cigarettes are restricted. Youth reported vaping "everywhere" at school, particularly in bathrooms, staircases, and cafeterias.<sup>12</sup>

Young people are most commonly introduced to vaping by friends, and device-sharing is very common. <sup>13,14</sup> E-cigarettes frequently are used as conversation starters and something for youth to hold in their hands at parties. Youth also may vape when they feel anxious, such as before and after tests or to calm social anxiety. <sup>15</sup> Most do not perceive the risks of vaping to outweigh the benefits, and adolescents tend to hold the belief that they can simply "stop in a few years." <sup>15</sup>

### **PATHOPHYSIOLOGY**

The brain undergoes structural and neurochemical maturation during adolescence. One of the last areas of the brain to mature is the prefrontal cortex, which does not fully develop until age 25 years. This part of the brain controls judgment, emotional and self-regulation, planning, reasoning, and social skills. Exposure to nicotine during adolescence changes the natural course of brain development, particularly in the prefrontal cortex, and can lead to reduced impulse control, deficits in attention and cognition, and long-term mood disorders. These changes are not seen in adults who start smoking after the brain is fully developed.

Inhaled nicotine crosses the blood-brain barrier within 10 to 20 seconds of inhalation.4 Once in the brain, it mimics acetylcholine and binds to the nicotinic acetylcholine receptors (nAChR), causing desensitization, upregulation, and reduced synaptic transmission, which interferes with cholinergic signaling in the prefrontal cortex. This leads to an increase in dopamine as well as a prolonged effect. Dopamine signals a pleasurable experience and is critical for the reinforcing effects of nicotine. Nicotine also

leads to persistent changes in gene expression and likely produces changes in prefrontal cortex neurons such as increased dendritic length and spine density.<sup>16</sup>

#### PHYSICAL EXAMINATION FINDINGS

No published articles identify or suggest abnormal clinical examination findings in people who use e-cigarettes. Some reports cite complaints of nosebleeds and excessive thirst due to dry mucosa. In contrast to combustible cigarettes, patients who use e-cigarettes have no nicotine odor and no nicotine staining on their fingers or teeth. This highlights the importance of screening.

# **SCREENING FOR THE USE OF E-CIGARETTES**

Among adults who become daily smokers, 88% start by age 18 years and 99% start by age 26 years.<sup>17</sup> Therefore, focusing prevention efforts on youth and young adults is crucial.18 Ask about e-cigarette use in tobacco screening questions that are part of every health examination. Current screening rates are exceptionally low and the reasons are multifactorial. Although the electronic health record (EHR) has been successful at increasing traditional smoking screening rates, it lacks specific embedded words to prompt questions about e-cigarette use.<sup>19</sup> Research has shown that by adding specific e-cigarette terms into the EHR such as vape, e-cig, or electronic cigarette, documented vaping rates rose exponentially.<sup>19</sup> Clinician lack of knowledge of e-cigarettes also contributes to the low screening rate. Many youth and young adults do not consider vaping to be smoking and some do not consider the JUUL device to be an electronic cigarette. 15 When screening for smoking, ask patients if they use tobacco products such as cigarettes, e-cigarettes, or JUUL.

#### **ADVERSE HEALTH EFFECTS**

To date, relatively little research has been conducted on the human health effects of e-cigarettes. Adverse reactions can arise from nicotine exposure and vapor contents including propellant byproducts and metals. **Nicotine effects** Acute effects of nicotine are due to sympathetic stimulation and include increases in BP, pulse, and myocardial contractility. These symptoms vary based on the nicotine concentration of the e-liquid. The main long-term health effect of nicotine use, particularly in the developing adolescent brain, is addiction resulting in the aforementioned brain and neurochemical changes. The synaptic changes can make young smokers more vulnerable to lifelong mood disorders. The use of e-cigarettes also is associated with greater risk for use of combustible cigarettes among youth and young adults. <sup>1</sup>

Respiratory effects Although e-cigarettes may be less harmful to the lungs than inhaling smoke from combustible cigarettes, they still have many effects on the respiratory tract. Acrolein and acetone irritate mucous membranes in the nose and throat, one of the most common reported adverse reactions to e-cigarettes. Metals found in vapor (lead, chromium, nickel, and manganese) are known to be toxic when inhaled; however, the human effects from the levels of metals inhaled from vaping are unknown and research is ongoing. Formaldehyde is a known human carcinogen and has been implicated in nasopharyngeal cancer.

Other frequently reported symptoms of e-cigarette use include cough, phlegm production, and wheezing, which raises the concern about harm to users with asthma and other chronic lung diseases. E-cigarette vapor has been shown to be toxic to alveolar macrophages and causes impaired bacterial clearance due to phagocytosis inhibition.<sup>20</sup> Because of the link between bronchiolitis obliterans and the microwave popcorn additive diacetyl (also found in many e-liquids), vaping may cause bronchiolitis obliterans, also known as "popcorn lung," although no cases have been attributed to vaping.<sup>21</sup>

In August 2019, the CDC began investigating an outbreak of severe pulmonary disease associated with the use of e-cigarettes. Now known as e-cigarette, or vaping, product use-associated lung injury (EVALI), this condition has resulted in 2,291 hospitalizations and 48 deaths as of December 2019.<sup>22</sup> This outbreak is mostly associated with THC-containing e-liquid, and the additive vitamin E acetate is a chemical of concern.<sup>22</sup> A CDC update provides guidance to healthcare providers to diagnose and manage EVALI.<sup>23</sup> Evaluate the patient's history for e-cigarette use and use of other substances such as THC or cannabis oil. Screen for respiratory issues, obtain vital signs including pulse oximetry, as well as chest imaging and appropriate laboratory testing. Patients with suspected EVALI, Spo, below 95%, respiratory distress, and comorbidities should be admitted to the hospital. Outpatient management may be considered for clinically stable patients.<sup>23</sup>

Cardiovascular effects Recent data found that adult e-cigarette users had a 71% higher risk of stroke, 59% higher risk of myocardial infarction, and 40% higher risk of heart disease compared with nonusers.<sup>24</sup> Although this study was limited, it is the largest study ever to have examined a possible association between e-cigarettes and stroke.

Other substance use Substantial evidence points to e-cigarette use among youth and young adults increasing their risk of ever using combustible cigarettes. This raises concerns that e-cigarettes are acting as a gateway to using more dangerous nicotine products. Many young people do not use e-cigarettes daily; however, the Doran study pointed out that even nondaily smokers who use e-cigarettes are at greater risk for chronic tobacco use compared with those who never vape. <sup>25</sup>

E-cigarette use by adolescents also is associated with the use of other substances. In 2016, one-third of e-cigarette users reported using these devices to deliver marijuana. When people vape rather than smoke marijuana, they tend to consume higher amounts of THC.<sup>26</sup>

Other adverse reactions Other dangers of e-cigarettes and e-liquids include defective e-cigarette batteries, which have caused fires and explosions, some of which have resulted in serious injuries. This prompted the US Federal Aviation Administration to prohibit e-cigarettes in checked baggage.<sup>27</sup> Children have been poisoned by swallowing, breathing, or absorbing e-liquid through their skin or eyes. Most of the children affected (84%) were under age 3 years and ingestion was the most common complaint (93%).<sup>28</sup> High nicotine exposure caused the vast majority of symptoms and although most were not severe, some included seizure, coma, or cardiac arrest.<sup>28</sup> In 2019, poison control managed nearly 5,200 exposures related to vaping.<sup>29</sup>

## **ANTICIPATORY GUIDANCE**

Anticipatory guidance for e-cigarette use is an important part of the youth and young adult primary care visit and should begin before patients are in middle school. Provide clear, personally relevant, and age-appropriate messages. Many young patients do not realize that nicotine is a common ingredient in e-cigarettes, so explain to them that one JUUL typically contains the amount of nicotine in a pack of cigarettes.<sup>30</sup> Stress that nicotine in any amount is addictive and unsafe for youth. Reinforce that it causes damage to the young developing brain, that nicotine addiction happens very quickly, and that youth who vape are more likely to smoke traditional cigarettes. Inform them that tobacco companies are marketing to them with misinformation. When counseling youth, providing factual information in a way they can understand and relate to is more effective than using an authoritative tone. Attempting to reverse the appeal of vaping is important but undoubtedly an uphill battle. Avoid telling youth that e-cigarettes have not been around long enough to know their long-term health effects—this message does not seem to deter use.<sup>15</sup>

Educate parents about the increasing use of e-cigarettes in schools. Many parents also hold misconceptions about youth use of e-cigarettes. Many feel that they are safe alternatives to smoking and are unaware of the nicotine content.<sup>31</sup> Tell parents that e-cigarettes may be safer for adults, but this does not mean that they are safe for the developing brains of

youth. Counsel parents to start and maintain a dialogue with their child as early as kindergarten. Parents should not smoke or vape around their children and should prepare their children for peer pressure and practice appropriate responses.

Provide parents and youth with printed materials that highlight the dangers of vaping and list resources for quitting. Because terminology and popular flavors can vary geographically, learn local trends and counsel accordingly. The American Academy of Pediatrics (AAP) has developed a JUUL fact sheet for pediatricians and families that is available at www.aap.org/en-us/Documents/AAP-JUUL-Factsheet.pdf.

## TREATMENT OPTIONS

No clinical practice guidelines exist for treating youth and young adults addicted to e-cigarettes. Traditional methods that are successful in helping adults stop smoking are largely ineffective in youth.<sup>32</sup> Few alternative treatment options exist other than pharmacologic interventions and behavioral therapy.

**Medications** Pharmacotherapy including nicotine replacement therapy, bupropion, and varenicline is recommended by the AAP for certain adolescents who are moderately to severely addicted to tobacco and who want treatment.<sup>33</sup> The AAP's 2015 clinical practice policy refers to tobacco dependence and does not specifically address e-cigarettes.<sup>32</sup> Also, the drugs used for smoking cessation in this age group have not been FDA-approved for quitting e-cigarettes or vaping and are not approved for youth under age 18 years. Nicotine replacement therapy typically is well tolerated by adolescents but has limited efficacy given their high rates of nonadherence and frequent relapse after stopping treatment.<sup>34</sup> Nicotine replacement therapy doses also may be inadequate because many e-cigarette users receive a higher total daily nicotine dosage compared with those who use combustible cigarettes. Although some forms of nicotine replacement therapy are available overthe-counter for patients age 18 years and older, minors need a prescription from a licensed healthcare provider.

Bupropion SR formulation has proven to be beneficial in adults for smoking cessation and relief of nicotine withdrawal symptoms. However, this drug is not particularly effective in adolescents because of low adherence, and is not FDA-approved for use in children.<sup>35</sup> Bupropion carries a black box warning of increased risk of suicidal thoughts in youth and young adults, and is contraindicated in patients with seizure disorders. The role of bupropion in e-cigarette use has not been assessed.<sup>35,36</sup>

Varenicline also is an effective agent for adult smoking cessation but is not recommended for youth age 16 years and younger, as it has not proven effective for this age group.<sup>37</sup> A recent study using varenicline for smoking cessation in teens did not significantly reduce sustained quit rates and a trial in the United Kingdom to assess varenicline for adult e-cigarette cessation is underway.<sup>38,39</sup>

**Behavioral** All youth and young adults who use e-cigarettes should be offered behavioral therapies, although

finding an acceptable program for youth and young adults can be challenging. Traditional smoking cessation programs have not been tested for efficacy in patients who want to quit vaping. Most adolescents who vape do not consider themselves smokers and may not want to participate in programs designed for smokers.

The Truth Initiative has developed a free vaping cessation program for teens and young adults called "This is Quitting." This low-key, anonymous text-based platform lets users engage and set a quit date, or not. Users simply text QUIT to 202-804-9884. The program began in January 2019 and enrolled more than 30,000 young people in its first 12 weeks. Most set a quit date and at 14 days, nearly 61% of respondents indicated they had reduced or stopped using e-cigarettes. <sup>40</sup> This indicates that a low-barrier text

# More than 80% of youth reported their first use of an e-cigarette was a flavored product.

message intervention to promote e-cigarette cessation is desired by and acceptable to young people.

Coping from cravings from nicotine withdrawal is one of the greatest challenges of quitting e-cigarettes. Exercising, creating an environment to avoid temptations, using a distraction, and finding stress solutions have been suggested to address cravings from vaping.

Although the data and guidelines for helping youth and young adults quit e-cigarettes are lacking, there is consensus that clinicians should not recommend e-cigarettes to youth and young adults as a method of quitting combustible cigarettes.<sup>32</sup>

**Follow-up** Approach nicotine addiction as a chronic disease. Individualize therapy and provide frequent follow-up to combat the high rate of nonadherence to therapy in this age group.<sup>32</sup>

#### MARKETING AND ADVERTISING

Youth exposure to advertising correlates with increased use of e-cigarettes, according to the 2014 National Youth Tobacco Survey. In 2016, an estimated 80% of US middle and high school students were exposed to e-cigarette advertisements, which was up significantly from 2015. The most exposure was in retail stores and social media.

For its launch in 2015, JUUL spent more than \$1 million to market its product on social media, including Twitter, Instagram, and YouTube, with images associating JUUL with being cool, having fun, relaxing, and sex appeal. <sup>44</sup> JUUL ads feature models in their 20s with trendy wardrobes engaged in poses and movements more consistent with teenagers. The JUUL e-cigarette brand now dominates the vaping market and claims it only markets to adults. <sup>6</sup> However, in a recent study, nearly half of users following

the @JUULvapor Twitter account were younger than the legal age (18 years) to buy e-cigarettes.<sup>6</sup> The US Federal Trade Commission recently announced that it is investigating whether JUUL's advertising practices target youth.

E-liquid flavors also attract youth and young adults to tobacco products. More than 80% of youth and young adults reported their first use of an e-cigarette was a flavored product, and cite flavors as a major reason for vaping. 45 Nearly 8,000 liquid flavors are available, including Fruity Pebbles, gummy bear, and mango. 46

## **REGULATION**

In the United States, the FDA gained primary regulatory authority over tobacco products in 2009 through the Family Smoking Prevention and Tobacco Control Act (TCA).<sup>47</sup> This act was amended in 2014 to include the regulation of e-cigarettes, and in August 2016 it established a federal minimum age (18 years) to purchase the products.<sup>47</sup> The FDA bans e-cigarette vending machine sales, except in facilities where only those over age 18 years are allowed. The FDA also requires a warning statement on packages and advertisements for e-cigarettes, including most e-liquids, stating that the product contains nicotine, an addictive chemical. The TCA requires manufacturers to submit to the FDA a premarket application that includes ingredients and health documents for all vaping products; however, this requirement had been deferred until August 8, 2022. In response to this delay, the AAP and its partners filed a lawsuit in 2018 against the FDA, Department of Health and Human Services (HHS), and the individual heads of the FDA and HHS.<sup>47</sup>

In May 2019, a federal judge ruled in favor of the AAP, stating that the FDA cannot delay their premarket approval until 2022 as previously planned. The judge ordered that applications for vaping products such as devices and e-liquids that were on the market as of August 8, 2016, must be submitted to the FDA no later than May 12, 2020, but in most cases these products can remain on the market pending FDA review and approval. Products not on the market as of August 8, 2019, are required to receive premarketing authorization from FDA before the product may enter the market or they will be subject to enforcement. Of particular significance is that the FDA will require all vaping products to demonstrate a net benefit to public health to receive marketing authorization. The products must demonstrate the increased likelihood that current tobacco users will stop using certain products or reduce the likelihood that nonusers will start using the products. 48

No federal regulations address e-liquid flavors or indoor vaping restrictions, or ban e-cigarette companies from event sponsorships, and no federal excise tax is charged on e-cigarettes.

States and local governments, territories, and tribes also have the ability to regulate the sales, marketing, advertising, and use of all tobacco products (including e-cigarettes) by persons of any age. Seventeen states have raised the minimum age to buy e-cigarettes and e-liquids to age 21 years.<sup>49</sup> Others have laws that regulate indoor use. Many states have simply added e-cigarettes to existing smoking restrictions.

International regulations vary significantly. As of June 2019, 42 countries had banned the sale of e-cigarettes, 56 countries regulated the sale, and 30 regulate the content, such as nicotine concentration. <sup>50</sup> Public Health England released a campaign to promote the use of vaping as a quit aid for cigarette smoking and minimizes the safety concerns. <sup>51</sup> Public Health England acknowledges the rise in teen vaping but points to the lack of studies that show vaping increases tobacco use among young people in the United Kingdom. <sup>51</sup>

## **CONCLUSION**

Electronic cigarettes are extremely popular devices that deliver nicotine and THC in an easily concealed manner. Youth and young adults are using the devices at unprecedented rates. Despite an epidemic being declared by the US Surgeon General, there is still a profound lack of knowledge of the dangers and public health effect of e-cigarettes. Clinicians should include e-cigarettes when screening for adolescent smoking; adding vaping-specific terms into the EHR can help. Start anticipatory guidance before middle school and provide quitting resources when appropriate. JAAPA

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