



Review

The rise of e-cigarettes, pod mod devices, and JUUL among youth: Factors influencing use, health implications, and downstream effects

Matthew C. Fadus*, Tracy T. Smith, Lindsay M. Squeglia

Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, 67 President Street, Charleston, SC, 29425, USA

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ABSTRACT

Background: Electronic cigarettes (e-cigarettes) were first introduced in the U.S. market in 2006, with the more recent evolution of "pod-mod" e-cigarettes such as JUUL introduced in 2015. Although marketed as a smoking cessation tool, e-cigarettes are rarely used for this purpose in youth. This review aims to synthesize the literature regarding e-cigarette use among youth, and provides a resource for clinicians, educators, and families that helps answer commonly asked questions about e-cigarettes.

Methods: PubMed, Scopus, and PsycINFO search was performed using search terms "Electronic Nicotine Delivery Systems," "e cigarettes," "e-cigarettes," "electronic cigarettes," "vaping," "JUUL," "e-cigs," and "vape pens." Search results were filtered to only include those related to adolescents and young adults.

Results: E-cigarette use among youth is common, with rates of use increasing from 1.5% in 2011 to 20.8% in 2018. Pod mod devices such as JUUL have gained favor among youth for their sleek design, user-friendly function, desirable flavors, and ability to be used discreetly in places where smoking is forbidden. Adolescents are often uninformed about the constituents of e-cigarettes, and little is known about the long-term effects of e-cigarettes. Studies have suggested a "gateway" effect for combustible cigarettes and cannabis use.

Conclusions: E-cigarette use is becoming increasingly common among youth, leading to a myriad of questions and concerns from providers, educators, and family members. More research is needed to determine the ultimate public health impact of e-cigarette use. The authors provide a summary table of frequently asked questions in order to help clarify these common concerns.

1. Introduction

Electronic cigarettes (e-cigarettes) first entered the U.S. market in 2006, acclaimed as a smoking cessation tool and a safer alternative to smoking (Cahn and Siegel, 2011; Hon, 2013). E-cigarettes have evolved from early generation cigarette lookalikes (cigalikes), to modifiable tank-style e-cigarettes, to the latest, more inconspicuous device type known as pod mods or "pods." Among pod mods, the most well known is JUUL, which was first introduced in 2015. JUUL is currently the most popular retail e-cigarette brand in the USA, accounting for 76% of the retail e-cigarette market at the end of 2018 (Craver, 2019; Huang et al., 2019). JUUL has become so popular among youth that the term "JUULing" has become synonymous with "vaping" among teens and young adults (Teitell, 2017). JUUL devices are small, rechargeable, battery-powered e-cigarettes which aerosolize liquid solutions containing glycerol, propylene glycol, natural oils, extracts and flavor, nicotine, and benzoic acid (JUUL, 2019). Modern e-cigarettes and pod mod devices like JUUL have become a more socially acceptable

alternative to combustible cigarettes among adolescents and young adults, and have become popular among this age group as a result of (1) sleek designs, (2) user-friendly functions, (3) less aversive smoking experiences, (4) desirable flavors, and (5) the ability to be used discreetly in places where smoking is forbidden (Allem et al., 2018; Barrington-Trimis and Leventhal, 2018; Kavuluru et al., 2019; Kinouani et al., 2017; McKeganey et al., 2018; Pepper et al., 2016; Ramamurthi et al., 2018; Yingst et al., 2018).

JUUL has been described as the "iPhone of e-cigarettes" (Radding, 2015) due to its modern and user-friendly design that requires only sliding a flavor pod (nicotine cartridge) into the device before use, a significant improvement over previous models of e-cigarettes (Barrington-Trimis and Leventhal, 2018). JUUL utilizes protonated nicotine, which the company claims provides a more satisfying experience to the user by reducing aversive experiences of taste, smell, and throat irritation (Barrington-Trimis and Leventhal, 2018; Bowen and Xing, 2015). The appealing flavorings available (e.g., mango, fruit medley, menthol) in JUUL (JUUL, 2019) can mask unwanted tastes and

* Corresponding author.

E-mail address: fadus@musc.edu (M.C. Fadus).

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smells, and are often cited as a reason for experimentation among young JUUL users (Ayers et al., 2017; Chen, 2018 Kavuluru et al., 2019; Kong et al., 2015). The size of JUUL and its resemblance to a USB flash drive allow it to be easily concealed from authority figures and discreetly used in places where smoking is forbidden, also known as “stealth vaping” (Allem et al., 2018; Kavuluru et al., 2019; Ramamurthi et al., 2018; Yingst et al., 2018). Given the novel user experience, appealing flavors, and product design of JUUL and other pod mod devices, they may be more appealing to youth than prior e-cigarette products. In one recent report, 80% of 15–24 year olds who reported that they had ever tried JUUL were also past 30-day users (Willett et al., 2019), suggesting that youth who try JUUL are highly likely to continue using it.

This review examines the rise of use in e-cigarettes and pod mod devices such as JUUL, and discusses factors which are implicated in their initiation and sustainment of use. The perception of these products among adolescents and young adults will also be examined, as well as current research available regarding the potential benefits of e-cigarettes and pod mod devices as a harm reduction model for those who use combustible cigarettes. Alternatively, this review will also examine the risk of e-cigarette use as a “gateway” to combustible cigarette use and cannabis use. This review is meant to serve as an updated, meaningful summary of adolescent e-cigarette and pod mod use from a clinical perspective, with Table 1 as a general reference to commonly asked questions that many researchers, providers, educators, and families often have regarding e-cigarettes.

2. Methods

Pubmed, Scopus, and PsycINFO search was performed using search terms "Electronic Nicotine Delivery Systems," "e cigarettes," "e-cigarettes," "vaping," "electronic cigarettes," "JUUL," "e-cigs," and "vape pens." Search results were filtered to only include those related to adolescents and young adults. Review of peer-reviewed articles included original research articles and review articles pertinent to adolescent e-cigarette, vaping, and pod mod use.

3. Epidemiology and rising prevalence of use

Although there recently has been a significant decline in youth combustible cigarette use, the overall use of nicotine products among youth has increased as a result of e-cigarettes and pod mod devices such as JUUL (Miech et al., 2018; Mirbolouk et al., 2018). In the United States, past 30-day vaping among high school students has risen from 1.5% in 2011 to 11.7% in 2017 to 20.8% in 2018 (Cullen et al., 2018), whereas 30-day prevalence rates of combustible cigarette use among high school seniors decreased over the same time period (18.7% in 2011, 9.7% in 2017, 7.6% in 2018) (Miech et al., 2018). In 2018, Monitoring the Future data found a ten percentage point increase in high school seniors who reported vaping in 2017, the largest one-year increase in any substance use over the 44 years that Monitoring the Future has been tracking adolescent substance use (Miech et al., 2018). E-cigarette use is also increasing among middle school students, as prevalence of past 30-day use increased from 0.6% in 2011 to 4.9% in 2018 (Cullen et al., 2018).

Outside of the United States, e-cigarette use among youth varies; for example, a 2017 study found 3.6% of university students in France were users of e-cigarettes (Kinouani et al., 2017), whereas a 2015 study in Switzerland of 8th grade and high school students found a rate of 24% (Surís et al., 2015). Prevalence of ever using e-cigarette use varies widely across European countries (Filippidis et al., 2017; Goniewicz et al., 2014a; Kinnunen et al., 2015), as well as other countries such as South Korea (Cho et al., 2018) and Taiwan (Chen, 2018). Prevalence varies for many reasons including regulation, access, and perceived norms (Cho et al., 2018). For example, in Switzerland, e-cigarettes were sold without nicotine until as recently as 2018, indicating why previous

studies of Swiss youth may have found higher high rates of e-cigarette use compared to other countries (Surís et al., 2015; Swissinfo.ch, 2018).

4. Health concerns related to E-cigarettes and JUUL

Combustible cigarette smoking is the leading cause of preventable death (Courtney, 2015), and e-cigarettes are largely viewed as a safer alternative to combustible cigarettes (Cahn and Siegel, 2011). Unlike traditional cigarettes, e-cigarettes are free from the process of combustion, which releases pulmonary carcinogens including polycyclic aromatic hydrocarbons, *N*-nitrosamines, and other cytotoxic compounds that are inhaled by the user (Courtney, 2015; Hecht, 1999). An emerging product also free of combustion, IQOS (FDA approved as of April 2019), heats tobacco rather than burns it; IQOS is similar to an e-cigarette in that it confers the benefit of limiting the harm from combustible tobacco (IQOS; PMI, 2019).

Studies have found that the vapor in e-cigarettes has a significantly reduced level (between 9–450 times reduced) of toxic substances compared to combustible cigarettes (Goniewicz et al. 2014b), although there is still concern regarding carcinogens that are present in e-cigarette vapors (Rubinstein et al., 2018). Given that e-cigarette vapor is generally safer, there is an opportunity for potential harm reduction models among smokers unwilling to quit or looking to transition away from combustible cigarettes.

However, there is a growing body of evidence suggesting that e-cigarettes are not without health risks. Propylene glycol and vegetable glycerin, the primary constituents of e-liquid, form toxic aldehydes when heated and little is known about the long-term effects of their inhalation as well as the inhalation of flavoring chemicals (Chun et al., 2017; Sleiman et al., 2016). Although e-cigarette manufacturers may advertise that constituents such as propylene glycol or vegetable glycerin are “FDA approved” or “generally recognized as safe,” this designation only applies to consumption, not aerosolization and inhalation (Chun et al., 2017). The long-term effects of these constituents when inhaled is unknown.

As a result of the nicotine salt formulation, pod mod vapors are able to deliver high concentrations of nicotine in a formulation that is less aversive than it would be if it were delivered in a free-base formulation (Bowen and Xing, 2015). Although patent research is not peer-reviewed, Pax labs (makers of JUUL) found peak concentrations of nicotine in the blood and total amount of nicotine delivered to be comparable to a traditional cigarette (Bowen and Xing, 2015). Additionally, nicotine exposure among youth who use pod mod e-cigarettes is higher than among those who exclusively smoke combustible cigarettes (Goniewicz et al., 2018).

The most frequently reported short term adverse events associated with the use of e-cigarettes are mild and include throat and mouth irritation, headache, dry cough, and nausea; however, these side effects are often self-limited and resolve over time (Courtney, 2015). E-cigarette use has cardiovascular effects as well, elevating heart rate and diastolic blood pressure, but less so than combustible cigarettes (Yan and Ruiz, 2015). E-cigarettes are also associated with development of respiratory symptoms in adolescents (Cho and Palik, 2016; Wang et al., 2016), and reduced pulmonary immune function (Hwang et al., 2016).

In addition to health effects of inhalation, the appeal of the flavoring pods to very young children may lead them to ingest the liquid, and reports of accidental e-cigarette ingestions in young children are common, with the majority of cases in those under the age of five (Gummin et al., 2018; Seo et al., 2016). This is concerning given that a standard e-cigarette liquid container can contain several times the lethal dose of nicotine in children (Normandin and Benotti, 2015).

The most serious concern regarding adolescent e-cigarette use is the potential for long-term effects on brain development and behavior (Yuan et al., 2015; Squeglia and Gray, 2016). Nicotinic acetylcholine receptors regulate critical aspects of brain development, and low doses of nicotine exposure can adversely affect brain development, leading to

Table 1
 Frequently Asked Questions from Families and Clinicians.

<p>“I have heard that e-cigarettes like JUUL are really popular at my child’s school, but I don’t know if my child has tried them. Should I talk to him/her about this? What should I say?”</p>	<p>Some families will be hesitant to discuss talking about e-cigarettes like JUUL out of concern that they may inadvertently encourage their child to start using the product, which is very unlikely to be true. You should talk with your child about why his or her peers may use e-cigarettes, the known and unknown health risks of e-cigarettes, and their association with an increased risk of cannabis and combustible cigarette smoking. Tell your child that cigarettes are still the most harmful tobacco product available, but that e-cigarettes are not safe. E-cigarettes like JUUL contain nicotine and can lead to addiction, meaning that it will be hard to stop using these products once they start.</p>
<p>“How much nicotine does a JUUL pod usually contain?”</p>	<p>Although combustible cigarettes and JUUL pods vary in nicotine content, JUUL reports that each JUUL pod contains a similar amount of nicotine as a pack of cigarettes (JUULpod Basics 2019).</p>
<p>“My son is in high school, how many other kids his age are using e-cigarettes? Are more kids using e-cigarettes than regular cigarettes?”</p>	<p>E-cigarettes are now more popular than cigarettes. In 2018, a nationwide study found that 21% percent of US high school seniors reported vaping in the past month, while 8% of high school seniors reported combustible cigarette use in the past month (Miech et al., 2018).</p>
<p>“Are devices like JUUL technically a tobacco product?”</p>	<p>Yes. The nicotine in e-cigarettes is derived from tobacco, and the FDA finalized a rule in 2016 which deemed e-cigarettes to be tobacco products under their control (United States Food and Drug Administration, 2016).</p>
<p>“Why are so many kids using e-cigarettes like JUUL?”</p>	<p>For many reasons; specifically for JUUL, it has a sleek, iPhone-like design, user-friendly functions, desirable flavors, and can be used discreetly in places where smoking is forbidden (such as schools). The social pressures and peer influence of use with e-cigarettes are significant.</p>
<p>“I have a friend at work who uses their e-cigarette to help reduce their cigarette use, but this doesn’t seem to be what my son or daughter is using it for, right?”</p>	<p>Less than 8% of adolescents who use e-cigarettes do so for combustible cigarette cessation (Tsai et al., 2018), in contrast to 85% of adults who do (Patel et al., 2016). Adolescents may use pod mod devices like JUUL as a result of evolving social norms, peer influences, appealing flavors, and decreased perceptions of risk, but less commonly for cigarette cessation.</p>
<p>“My daughter has been using her JUUL daily for the last six months. Is this a gateway drug to cigarettes and other substances?”</p>	<p>We don’t know if e-cigarette and pod mod devices like JUUL directly lead to cigarette or other substance use, but we do know that youth who use e-cigarettes are three times more likely to try cigarettes (Soneji et al., 2017), and four times more likely to try cannabis (Audrain-McGovern et al., 2018).</p>
<p>“My son said that other kids at school were using JUUL to smoke marijuana, is this true?”</p>	<p>Pod mod devices like JUUL provide a new method of inhaling cannabinoids or other psychoactive drugs (Giroud et al., 2015). In 2018, almost one in ten high school seniors vaped cannabis (Miech et al., 2018). Preparing cannabis in a JUUL or pod mod device can allow youth to smoke discreetly without the characteristic smell of cannabis that would otherwise lead them to be detected (Giroud et al., 2015; Hayes, 2018). However, vaping marijuana does appear to be a safer alternative to smoking it (Earleywine and Barnwell, 2007; Giroud et al., 2015).</p>
<p>“Do most high school students and young adults know what exactly is in the JUUL they are using?”</p>	<p>Most adolescents and young adults do not. In a recent survey, 63% did not know that nicotine is present in JUUL products (Willet et al., 2019), 19% believed that smoke from e-cigarettes was only water (Gorukanti et al., 2017), and 23% believed that e-cigarettes were not a tobacco product (Gorukanti et al., 2017).</p>
<p>“Are e-cigarettes like JUUL safer than combustible cigarettes?”</p>	<p>Yes, unlike traditional cigarettes, e-cigarettes are not combusted, which makes them substantially less harmful than traditional cigarettes (Courtney, 2015; Hecht, 1999). Studies have found that the vapor in e-cigarettes has a significantly reduced level (between 9–450 times) of toxic substances compared to combustible cigarettes (Goniewicz et al., 2014a).</p>
<p>“What are some of the health concerns related to using e-cigarettes like JUUL? What about the nicotine?”</p>	<p>Little is known about long-term effects (including those on brain development) as these are such new products (Chun et al., 2017; Sleiman et al., 2016). Nicotine receptors in the brain regulate critical aspects of brain development, and low doses of nicotine exposure can adversely affect brain development, leading to cognitive issues and development of more problematic levels of use (Dwyer et al., 2009; England et al., 2015; Goriounova and Mansvelder, 2012; Yuan et al., 2015). The most frequently reported short term adverse events associated with the use of e-cigarettes include throat and mouth irritation, headache, dry cough, and nausea, however these side effects are often self-limited and resolve over time (Courtney, 2015).</p>
<p>“Since JUUL is an electronic cigarette, does that mean that they have less nicotine than regular cigarettes?”</p>	<p>As a result of the nicotine salt formulation, JUUL can deliver high concentrations of nicotine by increasing the amount and rate of nicotine uptake (Bowen and Xing, 2015). Studies have found that nicotine exposure among youth who use e-cigarettes is just as high or higher than those who smoke combustible cigarettes (Goniewicz et al., 2018). Although nicotine exposure may be higher in JUUL, they are regarded as safer than traditional cigarettes since they are free from combustion.</p>
<p>“My daughter uses JUUL and regular cigarettes. She says that she is using JUUL to stop cigarette smoking. What should I do?”</p>	<p>Using both e-cigarettes and cigarettes is common, as 75% of adolescent e-cigarette users reported concurrent use of other forms of tobacco (Anand et al., 2015). However in youth, using both e-cigarettes and cigarettes is not often a temporary state, indicating that e-cigarettes may not be facilitating smoking cessation in the way that they are advertised among this age group (Barrington-Trimis et al., 2018). Youth who use e-cigarettes and cigarettes are more likely to continue using traditional cigarettes than to transition away from their use (Barrington-Trimis et al., 2018), and are more likely to develop a dependence on nicotine (Lee et al., 2013). There is limited data for treatments of tobacco use disorder (particularly e-cigarettes) among youth, but it is something that should be discussed with your child’s healthcare provider.</p>
<p>“My son uses JUUL because he says it is the only thing that can help with his stress and anxiety. It seems to help. What should I do?”</p>	<p>Although nicotine use may have favorable short-term effects in stress reduction and alleviating anxiety, exposure to nicotine during adolescence is associated with an increased risk of mood and attention symptoms (National Academies of Sciences, Engineering, and Medicine 2018). Outpatient follow-up with a mental health provider should be encouraged to help explore healthier and more appropriate ways to manage stress.</p>

cognitive issues and development of more problematic levels of use (Dwyer et al., 2009; England et al., 2015; Goriounova and Mansvelde, 2012; Yuan et al., 2015). Vulnerability to nicotine in earlier stages of adolescence may help explain why the age of a first cigarette is clinically indicative of the severity of nicotine use later in life, as well as predictive of future cessation success (Cengelli et al., 2012; Kendler et al., 2014). Youth who initiate and quickly progress in tobacco smoking are at a higher risk of becoming chronic smokers later in adulthood (Courtney, 2015), and symptoms of tobacco dependence are evident among adolescents who used a single tobacco product on as few as one to two days during the previous month (Apelberg et al., 2014). Exposure to nicotine during adolescence is also associated with an increased risk of mood and attention symptoms (National Academies of Sciences, Engineering, and Medicine, 2018).

5. Influences of E-cigarette use among adolescents and young adults

5.1. Cognitive influences: attitudes, knowledge, and misperceptions

Overall, youth are very open to using non-cigarette tobacco products such as e-cigarettes (Mays et al., 2015), and studies have indicated that perceptions of e-cigarettes as less risky, more popular, and more socially acceptable than combustible cigarettes have contributed to their increased use among youth (Ambrose et al., 2014; Anand et al., 2015; Berg et al., 2015; Chaffee et al., 2015; Choi and Forster, 2014; Copeland et al., 2017; Gorukanti et al., 2017; Kong et al., 2015; Mays et al., 2015; Pokhrel et al., 2014; Reditis et al., 2016; Saddleson et al., 2015, 2016; Sutfin et al., 2013; Trumbo and Harper, 2013). Youth not only endorse views that e-cigarettes are safer alternatives to cigarettes, but report higher acceptance levels for public and indoor e-cigarette use (Carroll Chapman and Wu, 2014; Gorukanti et al., 2017; Latimer et al., 2014; Trumbo and Harper, 2013). Additionally, adolescents also believe that fruit-flavored e-cigarettes are less harmful to health than tobacco flavored e-cigarettes (Pepper et al., 2016).

In addition to perceptions of social norms, expectancies influence attitudes and decisions related to e-cigarette use. Expectancies refer to the outcomes that are expected from engaging in certain behaviors. One cross-sectional study found that positive expectancies of e-cigarette use were associated with increased likelihood of current use (Pokhrel et al., 2014). Positive expectancies among youth included social enhancement (gaining respect of friends, increasing chances of being liked, improving social status and popularity), affect regulation (feeling calm, reducing stress or boredom), and sensory experiences (enjoying taste and smell). Negative expectancy factors such as health concerns, addiction, and an aversive sensory experience were reported as deterrents toward initiating e-cigarette use (Pokhrel et al., 2014). Among current e-cigarette users, nearly half believed that e-cigarettes were not bad for their health, but the same belief was held among only 7.5% of those who had never used them before (Barrington-Trimis et al., 2015), suggesting that perceived health risks may be a determinant of whether youth experiment with e-cigarettes.

Youth commonly hold misperceptions about e-cigarettes, particularly regarding overall safety profile, nicotine content, and efficacy for smoking cessation, which may lead to an increased likelihood of use (Gorukanti et al., 2017; Pepper et al., 2016, 2018). Among high schoolers and young adults, 60% believed e-cigarettes to be safe or to have minimal health hazards (Anand et al., 2015), 19% believed that smoke from e-cigarettes was only water (Gorukanti et al., 2017), 63% did not know that nicotine is present in JUUL products (Willett et al., 2019), and 23% believed that e-cigarettes were not a tobacco product (Gorukanti et al., 2017). Although 40% of adolescents believe that e-cigarettes are used for smoking cessation (Gorukanti et al., 2017), the majority of them do not use them for that purpose, as the most common reasons for use include enjoyment and novelty (Ayers et al., 2017; Bold et al., 2016; Choi and Forster, 2014; Gorukanti et al., 2017; Kinouani

et al., 2017; Patrick et al., 2016; Saddleson et al., 2016; Suris et al., 2015; Sutfin et al., 2013). In fact, less than 8% of adolescents who use e-cigarettes do so for combustible cigarette cessation (Tsai et al., 2018), in contrast to the 85% adults who do (Patel et al., 2016).

5.2. Social and peer influences

Among youth and young adults, the social environment for e-cigarettes is much more favorable than for combustible cigarettes (Barrington-Trimis et al., 2015). Much like how combustible cigarettes gained popularity among youth (Maxwell, 2002), peer influences are among the most common reasons for e-cigarette experimentation among high school and college students. Perceptions of e-cigarettes as “cool” are often cited as a reason for experimentation (Bold et al., 2016; Kong et al., 2015), and the social transmission and modeling effects of e-cigarettes are significant, as e-cigarette use is strongly associated with having family members (3-fold increase) and friends (7-fold increase) who use e-cigarettes (Khouri et al., 2016). Studies examining Twitter posts have found that e-cigarettes are portrayed in light of a positive social image (Ayers et al., 2017), and that youth who believed that their friends would have a “friendly” or “very friendly” response to e-cigarette use were significantly more likely to use e-cigarettes than peers who believed that their friends would have an “unfriendly” or “very unfriendly” response (Barrington-Trimis et al., 2015). Adolescents may harbor misperceptions of peer substance use rates, and their perceptions are often biased in the direction of their own use or non-use, known as the *false consensus effect* (Henry et al., 2011). As a result, adolescents may overestimate the number of their peers who use various tobacco products (Noland et al., 2016), and these perceptions of perceived norms can influence behaviors and decision-making (Rajiv and Kevin, 2005).

5.3. Environmental influences: advertising and social media

By the end of 2018, JUUL accounted for 76% of the retail e-cigarette market (Craver, 2019), however its share of the overall market is still unclear, as vape shops and online sales account for significant portion of e-cigarette sales but are not included in retail statistics. The rapid growth of e-cigarettes and pod mod devices such as JUUL appears to be related to the millions of youth who were exposed to their advertising and social media campaigns, as these led to a significant impact on the increase in appeal, experimentation, and initiation of e-cigarettes (Center for Disease Control and Prevention, 2019; Huang et al., 2019).

Much of the information that adolescents receive regarding pod mod devices and e-cigarettes does not appear to be evidence-based, but instead is delivered through claims of peers and social media. Social media has been scrutinized as a prominent source of exposure to e-cigarettes and pod mod devices among vulnerable adolescents who are at risk for tobacco use (Hébert et al., 2017), and has been found to influence perceptions of reduced harm among tobacco products (Petrescu et al., 2017). Among youth, social media and peer-based information are so influential because they not only are highly accessible, but they also convey the use of e-cigarettes as more socially acceptable and do not often encourage e-cigarette use solely for smoking cessation (Anand et al., 2015; Luo et al., 2014). For example, one study found that less than 1% of posts on twitter were related to smoking cessation (Allem et al., 2018).

Specifically, JUUL’s marketing campaigns have come under criticism for directly targeting advertisements toward youth (Harty, 2015; Kavuluru et al., 2019; Stanbrook, 2016; Trumbo and Kim, 2015). Examination of the official Instagram account of JUUL, *JUULvapor* (prior to its deactivation November 2018, see below), found that over 90% of posts were related to lifestyle appeal, displaying pictures and videos meant to evoke feelings of relaxation, freedom, and sex appeal in the context of the JUUL product and flavor images (Huang et al., 2019). Online, users of JUUL will often post images related to blowing large

clouds of aerosol, in addition to discussing preferred devices and flavors (Chu et al., 2016). The digital influence and social transmission of JUUL is common, as JUUL-related posts on social media discuss bonding and sharing experiences of JUUL with others, or notifying a friend about purchasing a JUUL (Allem et al., 2018). In response to regulations from the FDA in November 2018 (Office of the Commissioner, Center for Tobacco Products, 2018), JUUL deactivated their U.S.-based social media accounts on Facebook and Instagram, and their YouTube account is now only used for posting testimonials of former adult smokers who switched to the JUUL system (Burns, 2018).

6. E-cigarettes may lead to combustible cigarette use among youth

The ultimate impact of e-cigarettes on public health will depend on their influence on the overall prevalence of cigarette smoking (National Academies of Sciences, Engineering, and Medicine, 2018). In contrast to adult e-cigarette users who are almost exclusively current and former cigarette smokers, many youth and young adult users had never used a tobacco product before initiating e-cigarette use (Barnett et al., 2015; Barrington-Trimis et al., 2015; Barrington-Trimis et al., 2016; Camenga et al., 2014; Hamilton et al., 2015; Ireland et al., 2015; Lee et al., 2013; Moore et al., 2016; Surís et al., 2015). Almost 90% of adult smokers started before the age of 18 (Substance Abuse and Mental Health Services Administration, 2011), and those who do not initiate smoking during adolescence are unlikely to ever do so (Sussman, 2003). Meta-analyses and other studies have suggested that e-cigarette use predicts combustible cigarette use (Aleyan et al., 2018; Barrington-Trimis et al., 2016, 2018; Bold et al., 2017, 2018; Chaffee et al., 2018; East et al., 2018; Hammond et al., 2017; Leventhal et al., 2016; Leventhal et al., 2015; Loukas et al., 2018; Primack et al., 2018; Spindle et al., 2017; Wills et al., 2017; Wise, 2016), with an estimated threefold increase in the risk of subsequent cigarette initiation with e-cigarette use (Soneji et al., 2017).

The “gateway” hypothesis of e-cigarettes suggests that many youth who use tobacco products such as combustible cigarettes would have been unlikely to use tobacco products in the first place if e-cigarettes were not made available (Barrington-Trimis et al., 2016; Dutra and Glantz, 2017). Additionally, other non-cigarette forms of tobacco use are becoming particularly common, and the increasing use of multiple types of tobacco products such as hookah, smokeless tobacco, and snus heightens the concern about e-cigarettes as a gateway to further tobacco use (Lee et al., 2014).

JUUL and other e-cigarettes can deliver higher concentrations of nicotine than some combustible cigarettes, and evidence suggests that higher nicotine concentrations may heighten the risk of transitioning from e-cigarette use to combustible cigarette use (Daynard, 2018; Leventhal et al., 2016). There is also concern that an increase in e-cigarette use may renormalize a smoking culture among young people, subverting decades of anti-smoking efforts (Barrington-Trimis et al., 2015; Bell and Keane, 2014; Franck et al., 2016; Kandel and Kandel, 2015; Stanwick, 2015). The public use of e-cigarettes may contribute to this renormalization, as 60% of United States e-cigarette users reported using e-cigarettes in public areas where combustible cigarette smoking was disallowed (Shi et al., 2017; Stanwick, 2015).

Despite strong evidence which points toward e-cigarettes as a gateway to combustible cigarette use, time-trend analyses have indicated a decline in past 30-day smoking prevalence among US youth and young adults, which decreased more rapidly as vaping started to increase in popularity (Levy et al., 2018). Although combustible cigarette use among youth has been decreasing over the last twenty years (Miech et al., 2018), these findings support the *diversion hypothesis*, which suggests that at a population level, e-cigarette use partially replaces and/or substitutes completely for combustible cigarette smoking, mitigating some of the concerns of widespread e-cigarette use (Levy et al., 2018). Proponents of the diversion hypothesis have suggested that the concern surrounding a gateway hypothesis may be premature,

because many of these studies include smoking a single cigarette as the primary outcome, and e-cigarette users may be only temporarily experimenting with cigarettes and unlikely to progress to more frequent smoking. Researchers supportive of this hypothesis have suggested that e-cigarettes have not been available and popular for a long enough time period to determine whether if they lead to long-term cigarette use (Audrain-McGovern et al., 2004; Colder et al., 2001; Levy et al., 2018; Riggs et al., 2007).

7. E-cigarettes and Cannabis use

The relationship between combustible cigarette use and the initiation, maintenance, and escalation of cannabis use is well-established (Agrawal et al., 2013; Peters et al., 2012), and research suggests that e-cigarettes may confer a similar risk (Azagba, 2018; Dai et al., 2018).

E-cigarette use at 14 years of age was associated with almost a four-fold increase in the odds of initiating and consistently using cannabis two years later (Audrain-McGovern et al., 2018). Nicotine exposure in adolescence may prime the brain’s reward system to increase the pleasure that is experienced from using cannabis, setting up potential for a more rapid progression of use (Agrawal et al., 2013; Huang et al., 2013; Levine et al., 2011; Yuan et al., 2015). As a result of e-cigarette smoking, physiologic changes occur within the respiratory tract that can facilitate a transition to future cannabis use, as smoking can result in reduced sensitivity to the irritation caused by inhalation of smoke (Audrain-McGovern et al., 2018).

The emergence of e-cigarettes may provide adolescents an additional method of inhaling cannabinoids or other psychoactive drugs (Eggers et al., 2017; Kenne et al., 2017), and there are a significant number of websites which provide instructions on how to prepare cannabis-derived liquids for use in e-cigarettes such as JUUL (Giroud et al., 2015). As of 2018, 7.5% of US high school seniors report vaping cannabis, an increase from 4.9% in 2017 (Miech et al., 2018). Preparing cannabis in an e-cigarette such as JUUL can allow youth to smoke discreetly without the characteristic smell of cannabis that would otherwise lead them to be detected (Giroud et al., 2015; Hayes, 2018). Although there are concerns related to e-cigarettes and cannabis use, puffing on cannabis vapors generated at lower temperatures through an e-cigarette may be less risky than inhaling smoke formed in a combustible cannabis joint (Earleywine and Barnwell, 2007; Giroud et al., 2015).

8. E-cigarettes, pod mod devices, and smoking cessation

More than half of youth who smoke combustible cigarettes are interested in quitting, and many adults who endorse e-cigarette use utilize the devices to quit smoking (Babb et al., 2017). Despite the urge to quit smoking, U.S. smokers report significant difficulty abstaining from nicotine use; within a given year, 34% of smokers will attempt to quit, but only 1% will remain tobacco free for at least one year (Stratton et al., 2001). In addition to the physiological addiction that occurs as a result of nicotine exposure, the behavioral cues of smoking are one of the strongest habit-forming properties of traditional combustible cigarettes (Caponnetto et al., 2011; Frances, 2011). The regular hand-to-mouth action and the production of smoke are behavioral cues that make e-cigarettes a viable option to treat both the physiological effects of nicotine while replicating some of the behavioral cues as well.

Several studies have demonstrated a potential for e-cigarettes to be used for smoking cessation in adults and young adults (Hartmann-Boyce et al., 2018; Kalkhoran and Glantz, 2016; Kinouani et al., 2017; Kulik et al., 2018), however there is little evidence for their efficacy among youth (Conner et al., 2018; Doran et al., 2017; Farsalinos et al., 2016; Gmel et al., 2016; Park et al., 2016; Wang et al., 2017; Wills et al., 2017). A 2016 systematic review found that the evidence for e-cigarettes as smoking cessation agents for all ages remains inconclusive due to low quality published research, and evidence is currently

assessed as *very low* or *low* (Malas et al., 2016). Specifically, the analysis revealed little to no evidence regarding cessation efficacy among adolescents and young adults.

Dual-use of combustible cigarettes and e-cigarettes could indicate that adolescents are using e-cigarettes to help reduce combustible cigarette smoking or to transition away from combustible cigarettes altogether. Dual-product use is common, as 75% of adolescent e-cigarette users reported concurrent use of other forms of tobacco (Anand et al., 2015). However dual-use is often not a temporary state, indicating that e-cigarettes may not be facilitating smoking cessation in the way that they are advertised. One study found that 51% of adolescent dual-users were still using both products at a six-month to two-year follow-up, and an additional 16% were smoking combustible cigarettes only (Barrington-Trimis et al., 2018). Dual-product users were more likely to continue using cigarettes rather than transitioning toward exclusive e-cigarette use or smoking cessation altogether (Barrington-Trimis et al., 2018). Dual-product users were also more likely to smoke cigarettes daily and more heavily than students who smoked only combustible cigarettes (Goniewicz et al., 2016). These findings indicate evidence to the contrary of adult studies that suggest e-cigarettes may promote smoking cessation (Glantz and Bareham, 2018; Kalkorhan and Glantz, 2016; Kulik et al., 2018).

9. E-cigarette regulation in the United States

Although e-cigarettes were not initially included in the Family Smoking Prevention and Tobacco Control of 2009, the FDA finalized a rule in 2016 that extended its regulatory authority to all tobacco products, including e-cigarettes (United States Food and Drug Administration, 2016). As a result, the new law required health warnings on e-cigarettes, and e-cigarettes were held to public health standards set by the law. Additionally, mounting pressure from the FDA and other public-health related agencies led JUUL to suspend the retail sale of most of its flavored e-cigarettes in an attempt to reduce the accessibility to youth (Kaplan and Hoffman, 2018).

New FDA rules as of November 2018 are requiring stronger age verification for online sales

of e-cigarettes, as well as the removal of e-cigarette products that are marketed to children or are appealing to youth, such as those with names of products favored by youth such as bubble gum or cotton candy (Office of the Commissioner, Center for Tobacco Products, 2018). In response, JUUL has developed an action plan to reduce the accessibility of nicotine products to youth by limiting retail sales, using sophisticated age verification measures for online purchases, increasing secret shopper programs to ensure retail store adherence, and deactivating their own U.S.-based social media accounts (Burns, 2018).

10. Conclusion

Youth are using e-cigarettes and pod mod devices such as JUUL now more than ever. Given the increasing prevalence of use among impressionable and vulnerable adolescent populations, there is concern that electronic cigarettes may be exposing a significant number of youth to nicotine who would have not otherwise be using tobacco. Although the use of e-cigarettes is generally considered safer in comparison to combustible cigarettes, concerns remain. The developing adolescent brain is susceptible to the harmful effects of nicotine, and earlier use of nicotine predicts concerning patterns of future nicotine use. Among youth, e-cigarettes have little to no evidence as a smoking cessation tool, and very few report using it for such purposes. Recent FDA regulations have aimed to reduce access to these appealing nicotine products among youth as a result of the potential harms that they are thought to introduce, and further research is warranted to definitively determine if e-cigarettes such as JUUL predict combustible cigarette use. If research continues to suggest that e-cigarette use predicts combustible cigarette use among other substances, e-cigarettes pose a

significant public health concern and the potential to renormalize a social environment of smoking among young people.

In regards to e-cigarette use, providers, educators, and families have questions that often go unanswered, particularly those related to the potential gateway effects of vaping to combustible cigarettes and cannabis use. Table 1 provides a list of questions commonly asked of clinicians about e-cigarettes and pod mod devices such as JUUL. Based on the information in this review, brief answers to these common questions are included in the hopes of informing clinicians, educators, researchers, and families.

Contributors

Matthew C. Fadus formulated and wrote the manuscript. Tracy T. Smith provided significant guidance and helped edit and write the manuscript. Lindsay M. Squeglia provided significant guidance and helped edit and write the manuscript. All authors agree to the final submitted version of the manuscript.

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Conflict of interest

No conflict declared

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