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The Harmful Consequences of Vaping

A Public Health Threat

Brenda Douglass, DNP, APRN, FNP-C, CD E, CTTS ❍
Susan Solecki, DrPH, APRN, FNP-BC, PPCNP-BC ❍ Theresa Fay-Hillier, DrPH, MSN, PMHCNS-BC

Abstract

The vaping of nicotine products has overwhelmingly gained national attention as the new public health crisis. The use of electronic nicotine delivery systems and products such as electronic cigarettes, JUUL, pods, or vaporizers is now a worldwide multibillion dollar industry. Despite the notable gains decreasing harmful smoking behaviors of traditional cigarettes among youth, these public health initiatives have been significantly nullified by the indiscriminate exposure of these highly addictive products by nicotine manufacturers to the adolescent population. Although touted as a safer alternative to traditional tobacco smoking and an effective cessation method to quit traditional cigarette smoking, there are no definitive data, to date, substantiating that this is true. Currently, adolescents are the predominant population using electronic nicotine delivery systems and at the greatest risk to the negative effects of nicotine exposure (U.S. Department of Health & Human Services, 2016). The purpose of this article is to identify the health impact and potential dangers related to the vaping epidemic that conflict with teens' risk beliefs that vaping is harmless. To protect American youth, a comprehensive approach for harm reduction to this deadly problem is imperative, including product warnings and regulation, public media campaigns, economic and social strategies, and policy initiatives.

Keywords: e-cigarette, electronic cigarette, electronic nicotine delivery systems (ENDS), harm reduction, JUUL, tetrahydrocannabinol (THC), vaping

Global use of tobacco is undergoing a rampant change since the development and proliferation of electronic nicotine delivery systems (ENDS). Vaping refers to the inhalation of substances (nicotine, flavorings, cannabis, or other popular substances) where oil, liquid, or plant material is heated from these high-tech battery-powered electronic devices to a temperature resulting in the release of an aerosolized water vapor and its active ingredients (Unger & Unger, 2018). Individuals use ENDS, which are noncombustible tobacco products including electronic cigarettes (e-cigarettes), refillable atomizers, and other novel devices, as an alternative or in addition to traditional cigarettes (Farsalinos et al., 2014). ENDS are known by many different names such as e-cigs, e-hookahs, vapes, vape pens, tank systems, or mods (Food and Drug Administration [FDA], 2020a). There are more than 250 ENDS brands available in the U.S. market that come in many different shapes and sizes, with some resembling regular cigarettes, pens, or larger devices (FDA, 2020a; Kaur et al., 2018). E-cigarette solutions, often known as e-juice or e-liquid, are commonly advertised to contain nicotine, flavoring chemicals, and solvent carriers (propylene glycol and vegetable glycerin), but toxicants, ultrafine particles, and carcinogens have also been found in e-cigarette solutions and emissions, many of which are known to cause adverse health effects (Walley et al., 2019).

JUUL AND NICOTINE SALTS

One of the most popular vape products used by adolescents is JUUL, a brand of e-cigarette that is shaped like a USB flash drive and contains twice the amount of nicotine concentrate as other e-cigarette brands (Boudi et al., 2019). JUUL e-cigarettes can be concealed in the palm of the hand and are hard to detect because they give off very little vapor or smell (American Cancer Society, 2020). Educators report widespread use of JUUL by teenagers who covertly use the product during school, even in the classroom (American Cancer Society, 2020). The nicotine level in a single JUULpod is equivalent to that of one pack of cigarettes (Boudi et al., 2019; Centers for Disease Control and Prevention [CDC], 2020b). Nicotine concentration can vary, both in the reported concentration and in the actual concentration of ENDS solutions (Walley et al., 2019). Besides higher nicotine concentrations, nicotine salts are among escalating concerns for additional reasons. When compared with free-base nicotine in traditional cigarettes, which have a higher pH level, nicotine salt formulations in e-cigarettes have a lower pH level allowing for less throat irritation when e-liquid aerosol is

Brenda Douglass, DNP, APRN, FNP-C, CDE, CTTS, Susan Solecki, DrPH, APRN, FNP-BC, PPCNP-BC, and Theresa Fay-Hillier, DrPH, MSN, PMHCNS-BC, Drexel University College of Nursing and Health Professions, Philadelphia, PA.

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Correspondence related to content to: Brenda Douglass, DNP, APRN, FNP-C, CDE, CTTS, Drexel University, College of Nursing and Health Professions, 1601 Cherry Street, Philadelphia, PA 19102.

E-mail: bld46@drexel.edu

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inhaled, a more rapid delivery, and a higher potency of nicotine delivery (National Academies of Sciences, Engineering, and Medicine et al., 2018).

JUUL is one of a few brands of e-cigarettes that contains nicotine salts, which allows for markedly higher levels of available nicotine to be readily inhaled by masking the harshness of nicotine with less irritation than the free-base nicotine used in traditional tobacco products (CDC, 2020b). JUUL has an e-cigarette solution containing benzoic acid at a much higher advertised nicotine concentration of 59 mg/ml compared with a conventional cigarette with a typical nicotine absorption of 1 mg/ml (Walley et al., 2019). Evidence has purported that the use of nicotine salt in JUUL use has provided superior emotional and physical satisfaction compared with traditional cigarette use attributed to nicotine salt formulations (Bach, 2020). The CDC's Principal Deputy Director informed the House Oversight and Reform Committee's panel on consumer products that health care providers (HCPs) believe the salts allow nicotine to "cross the blood brain barrier and lead to potentially more effect on the developing brain in adolescents" (Medical Brief, 2016). Those adverse effects include difficulty with memory, learning, and attention, as well as potentially priming the body to become addicted to nicotine and other harmful substances (Medical Brief, 2016).

The evidence of JUUL's recent spike in popularity is shown by sales data that revealed that, in August 2018, JUUL sales were 72.1% of the market share of e-cigarette market in the United States, compared with 13.6% in the first quarter of 2017 (Walley et al., 2019). Despite that JUUL manufacturers claim they do not sell to youth under 21 years old, marketing campaigns and appealing flavors have undoubtedly targeted toward a youthful demographic (Walley et al., 2019). In December 2018, JUUL sold over one third of the stake to the tobacco company Altria, formerly known as Philip Morris, for $13 billion, increasing additional concerns about the company's strategy to amplify the use of their products by teenagers (Kim et al., 2019; Walley et al., 2019). Because of the controversy over JUUL's marketing practices and the growing incidences of vaping-related illnesses, the $38-billion company has become the face of the youth vaping crisis currently experiencing congressional investigations, critical scrutiny from the FDA, lawsuits from school districts across the country, and a potential nationwide ban in the United States (Kim et al., 2019).

THE DEADLY ALLURE OF FLAVORINGS

Most brands of ENDS solutions are available in a variety of youth-appealing flavors ranging from fruits, desserts, candy, and soda to traditional tobacco (Walley et al., 2019). Menthol has been used as an additive in approximately 25% of cigarettes manufactured in the United States alone, with adolescents, especially from ethnic minority subgroups, more likely to progress from experimentation of menthol cigarettes to regular smoking (Ferris & Connolly, 2004; Giovino et al., 2004; Kaur et al., 2018; Kreslake et al., 2008; Robinson et al., 2006). Currently, 68% of high school children have reported smoking e-cigarettes with flavorings and are often named as a primary reason for e-cigarette use (Cullen et al., 2018). There are 8,000 different flavorings in the U.S. market alone, with the manufacturers marketing these e-liquids with alluring names that appeal to youth, such as cotton candy, milk and honey, apple pie, melon mania/watermelon, cheese cake, cherry, chocolate, coconut, licorice, cappuccino, crème brule, oatmeal cookie, cinnamon roll, and tutti frutti (Allen et al., 2016; Chen & Zeng, 2017; Kaur et al., 2018; Kim et al., 2016). Although flavoring agents are well documented to be safe for ingestion through the digestive tract, recent reports of lung toxicity caused by inhaled flavoring agents in tobacco and nontobacco products have emerged (Kaur et al., 2018). The composition of flavors differs as these are not FDA regulated and may pose a potential hazard in ENDS users when they are aerosolized into ultrafine particles reaching deep into smaller airways of the lungs (Kaur et al., 2018). Several studies have shown that, when e-liquid ingredients are heated with ENDS, carbonyl compounds such as formaldehyde, acetaldehyde, acrolein, and glyoxal have been found in the emitting aerosols and considered potentially hazardous to the health of ENDS users (National Academies of Sciences, Engineering, and Medicine et al., 2018).

HARMFUL EFFECTS OF E-CIGARETTE AEROSOL

The aerosol emanated by e-cigarettes is breathed into and out of the lungs by the user, with some of the generated aerosol being directly released into the surrounding environment and depositing on surface areas (Jenssen & Walley, 2019). Individuals in the vicinity of the vaper are exposed to this secondhand and thirdhand aerosol in a similar mode to that of secondhand and thirdhand cigarette smoke (Jenssen & Walley, 2019). Known harmful toxicants and carcinogens, including polycyclic aromatic hydrocarbons, nicotine, volatile organic compounds, metal (aluminum, nickel, lead, tin), and silicate particles, have been detected in e-cigarette emissions (Jenssen & Walley, 2019). Of particular concern is that both fine and ultrafine particulate matter found in indoor air after vaping sessions contain particles that can be inhaled deeply into the lungs and enter the systemic circulation, leading to inflammation and potential cardiovascular disease (Walley et al., 2019). There is limited data on the human health effects of e-cigarette emissions; however, there is increasing evidence of the pulmonary effects of e-cigarette use, particularly for adolescents with asthma. Investigators report that adolescents who used e-cigarettes have an increase in asthma exacerbations and that secondhand aerosol exposure increased the odds of an asthma attack by 27% (Bayly et al., 2019).

VAPING CANNABIS

The vaping phenomena has created a new culture on the use of marijuana containing tetrahydrocannabinol (THC), cannabidiol, and other addictive substances (Boyer et al., 2020). Because vaping avoids the characteristic smell of burning marijuana, inhalation of THC by vaping can be highly discreet allowing its more overt and less stigmatized use, minimizing the social

contexts surrounding THC use (Boyer et al., 2020). The amount of THC that some users vape can be exorbitant, nearing 50-mg THC inhaled in a single session, with a total consumption of up to 700 mg per day, in comparison with a typical "joint" of marijuana that remits approximately 12 mg of inhaled THC (Boyer et al., 2020). Unlike smoking tobacco or marijuana cigarettes, the more rapid and higher concentrations of vaping nicotine and THC can result in acute toxicity exhibited by hallucinations, psychotic reactions, and hyperemesis syndrome (Boyer et al., 2020). Some vapers increase the concentration of THC delivery by "dripping," a method where THC solutions are applied directly to a heating coil to produce a thicker and more flavorable vapor to be inhaled (Boyer et al., 2020; Krishnan-Sarin et al., 2017). Many patients experiencing vape-related complications reported using THC-containing products in the past, leading the FDA to believe that THC played a role in the vape-related illness outbreak (Boudi et al., 2019).

E-CIGARETTE, OR VAPING, PRODUCT USE-ASSOCIATED LUNG INJURY

E-cigarette or vaping product use-associated lung injury (EVALI) was first distinguished by the CDC in August of 2019 after the incidence of multistate outbreaks of serious lung illness associated with using e-cigarette and vaping products (CDC, 2020a). EVALI is mostly a diagnosis of exclusion as its clinical presentation is similar to many other respiratory diseases (American Lung Association, 2020). Signs and symptoms include shortness of breath, fever and chills, dry cough, chest pain, vomiting, diarrhea, headache, dizziness, rapid heart rate, and body aches (American Lung Association, 2020). As there is no single diagnostic test for EVALI, HCPs depend on their evaluation of a history of e-cigarette use and other vaping devices and imaging studies such as chest x-rays or computed tomography scans to identify lung opacities that indicate tissue damage (American Lung Association, 2020). The treatment of EVALI is based on clinical judgment and the severity of the illness (American Lung Association, 2020). Medication regimens can encompass antibiotics, antivirals, and corticosteroids to combat infection and inflammation in the lungs (American Lung Association, 2020). Individuals with severe symptoms are hospitalized often requiring ventilator assistance to breathe, and even patients who have less severe symptoms may need supplemental oxygen (CDC, 2020a). Because EVALI is a new medical phenomenon, the course of illness has been found to be unpredictable (American Lung Association, 2020). Even after patients have been medically stabilized to breathe on their own and discharged to home, there have been incidences of some patients relapsing, and even dying, soon after release from the hospital (American Lung Association, 2020). Medical experts recommend that all patients, regardless of severity, be referred to follow-up with a pulmonologist within 48 hours after being discharged from the hospital (American Lung Association, 2020).

Progress has been made in identifying the cause of EVALI. Although not the only cause of EVALI, health officials from the CDC and the FDA have linked Vitamin E acetate as the primary cause of the EVALI outbreak (CDC, 2020a). Vitamin E acetate is an oily chemical added to thicken or dilute vaping liquids in some THC-containing e-cigarettes (CDC, 2020a). Vitamin E is also available as a dietary supplement and contained in many foods, including vegetable oils, cereals, meat, fruits, and vegetables, as well as a component in many cosmetic products, like skin creams (CDC, 2020a). When Vitamin E acetate is ingested in food, as a vitamin, or applied to the skin, it usually does not cause any harm (CDC, 2020b). However, research now indicates that, when Vitamin E acetate is inhaled, it can interfere with normal lung functioning (CDC, 2020a). A CDC report analyzed bronchoalveolar lavage (BAL) fluid from a large sample of patients with EVALI from 16 states in comparison with BAL fluid from healthy people (American Lung Association, 2020). Along with similar results from the FDA and state laboratories, they found Vitamin E acetate in BAL fluid from 48 of 51 patients with EVALI and none in any of the BAL fluids of healthy people (American Lung Association, 2020).

Evidence is still insufficient in some of the reported EVALI cases to eliminate other chemicals of concern in either THC or non-THC products (CDC, 2020a). For example, some EVALI cases presented with symptomatology aligning with bronchiolitis, a lung infection normally caused by bacteria or virus (Boudi et al., 2019). Many patients who had vape-related illnesses, though, experienced damage to the alveoli inconsistent with an infectious etiology (Boudi et al., 2019). Instead, these cases aligned more with an acute toxic lung injury called "popcorn lung," an occupational illness found to be prevalent in factory workers of microwave popcorn plants nearly 20 years ago (Boudi et al., 2019). "Popcorn lung" is formally known as bronchiolitis obliterans, a condition that results in the scarring of the tiny air sacs in the lungs, resulting in the thickening and narrowing of the airways (American Lung Association, 2018). Although it is known that diacetyl causes popcorn lung, this chemical has been added to complement flavorings such as vanilla, maple, and coconut in many e-cigarette liquids or "e-juices" (American Lung Association, 2018). So although diacetyl was hastily removed from popcorn products because it could cause this devastating disease among factory workers, e-cigarette users are now directly inhaling this harmful chemical into their lungs (American Lung Association, 2018). The American Lung Association (2018) has commissioned the FDA to require that diacetyl and other hazardous chemicals be banned from e-cigarette cartridges.

Fortunately, there has been a decline of EVALI cases across the United States since its notable peak incidence in September of 2019 (CDC, 2020a). Multiple factors that may have contributed toward the decline of the EVALI outbreak is the rapid public health response that increased awareness of the risk associated with THC-containing e-cigarettes or vaping products, the removal of Vitamin E acetate from some products, and law enforcement interventions related to illicit products (CDC, 2020a). Although EVALI cases are decreasing, new cases continue to be reported to the CDC, FDA, and other health agencies with ongoing testing of samples connected to patients with EVALI (CDC, 2020a). A current number of hospitalized

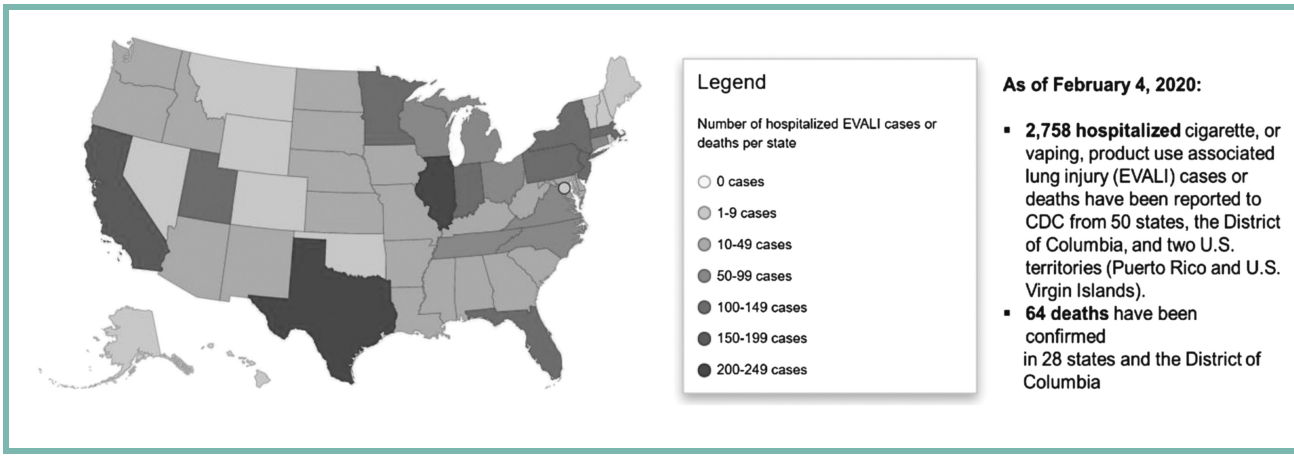

Figure 1. Number of hospitalized e-cigarette or vaping product use-associated lung injury cases or deaths reported to the Centers for Disease Control and Prevention as of February 4, 2020. Photo source: https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html#map-cases.

EVALI cases or deaths reported to the CDC are presented in Figure 1.

Increasing public awareness of this harmful condition supports the implementation of comprehensive, population-based interventions for this preventable disease (Boudi et al., 2019). The CDC continues to partner with the FDA, state health departments, public health agencies, and clinicians by providing consultation and technical assistance on communication, public health alerts, community outreach, and surveillance (CDC, 2020a).

OTHER INJURIES AND RISKS RELATED TO THE USE OF ENDS

There has been other injuries and risks reported related to the use of ENDS with investigators still learning about the unknown health effects of these varied products (U.S. Department of Health & Human Services [USDHHS], 2020). Defective e-cigarette batteries have been reported to explode resulting in serious burns and causing fires (USDHHS, 2020). Approximately 50% of calls to poison control centers in the United States are related to e-cigarette exposure to kids 5 years old or younger (USDHHS, 2020). Children have been inadvertently poisoned by swallowing, breathing, or absorbing nicotine-containing e-cigarette liquid through their eyes or skin (USDHHS, 2020). Nicotine base absorbs easily through the skin, thereby the basis for their use in nicotine transdermal systems known as nicotine patches (National Academies of Sciences, Engineering, and Medicine et al., 2018). Therefore, contact of users or nonusers, especially in children and infants, with nicotine-containing e-liquids, even in small amounts, can lead to potentially harmful systemic nicotine exposure (National Academies of Sciences, Engineering, and Medicine et al., 2018). Fortunately, accidental ingestions and exposures have decreased in part to education, as well as the Child Nicotine Poisoning Prevention Act of 2015, which requires that nicotine-containing ENDS solutions be sold in child-resistant packaging (Walley et al., 2019).

As public health officials scramble to respond to the emergence of multiple health problems, including deaths, among users of ENDS, the FDA has also received reports over the last decade identifying more than 100 seizures and other neurological problems linked to e-cigarettes and vaping devices (Samson, 2019). Underscoring the importance of these suspected complications are reports of seizures occurring in first-time ENDS users, as well as with experienced ENDS users, and some having seizures occurring after only a few puffs or up to 1 day of use (Samson, 2019). Of greatest concern in the FDA's list of neurological cases is the relatively young age of the subjects, the lack of any prior seizure history, and their exposure to much higher levels of nicotine than with products like cigarettes or chewing tobacco (Samson, 2019).

NICOTINE DEPENDENCE AND HARM

The nicotine in an e-cigarette is quickly absorbed in the bloodstream. Once nicotine enters the bloodstream, the adrenal glands are stimulated and release the hormone epinephrine also known as adrenaline. Epinephrine stimulates the central nervous system, which results in an increased heart rate, blood pressure, and breathing. Nicotine also activates the brain's reward circuits and also increases levels of a neuro-messenger chemical in the brain called dopamine, which reinforces rewarding behaviors. Pleasure caused by nicotine's interaction with the reward circuit motivates some people to use nicotine repeatedly, despite risks to their health and well-being (Hammond et al., 2014, 2019; Jensen & Nutt, 2015). Once the reward circuit in an adolescent is activated by an addictive substance, there is an increased risk for continued engagement in the use of the addictive substance. In addition, because the white matter and hippocampus are still maturing during adolescence, there is an increased risk for adolescents exposed to addictive substances to experience the destructive effects of the drugs on their working memory, motor coordination, and prefrontal cortex. A large new study reports a strong association between vaping nicotine and major depression and suicidal behavior (Boudi et al., 2019;

Obisesan et al., 2019). Other long-term effects can increase the risk for the development of mood disorders and attention-deficit disorders and the permanent reduction of impulse control (Hammond et al., 2014, 2019; Jensen & Nutt, 2015).

As conjectured by ENDS manufacturers, there are no sufficient data to date that support the use of ENDS and other nicotine replacement therapies resulting in the cessation or reduction of tobacco smoking (Unger & Unger, 2018). On the contrary, current research supports a causal role of youth nicotine exposure on the brain as a "gateway drug" that ultimately encourages subsequent drug use, potentially increasing the risk of addiction to smoking cigarettes and other illicit drugs in the adolescent population (Ren & Lotfipour, 2019).

DISCUSSION

The escalation in adolescent use of nicotine products demands the need to raise awareness of the detrimental effects of developmental nicotine exposure (Ren & Lotfipour, 2019). Because of the accelerated economic and societal costs, along with deaths associated with ENDS use, it is imperative to obtain a more complete understanding of nicotine's harmful effects during adolescence (Ren & Lotfipour, 2019). HCPs should practice with heightened regard when interacting with adolescents with a history of ENDS use, taking an individualized approach to treatment, providing resources for patients and their families, and continuing to inform about the risks of vaping (Ren & Lotfipour, 2019). This increased education and advocacy may result in improved care coordination, greater adherence to treatment plans, and optimal clinical outcomes (Ren & Lotfipour, 2019). As an example, research showed that, in the first 2-years of the FDA's first tobacco prevention campaign, "The Real Cost," the public health education prevented over a half a million youth, aged 11–19 years, from initiating smoking with its central message of "smokeless does not mean harmless" (FDA, 2020b). To control the vaping public health crisis, regulatory and public health agencies need to establish and enforce a legislation that promotes age restrictions on the purchase of nicotine products (Ren & Lotfipour, 2019).

CONCLUSION

Until further research is more comprehensive with analyzing the multiple health effects of ENDS on youth and young adults, the guiding principle should be that ENDS is harmful for the short- and long-term health of youth, until proven otherwise (Walley et al., 2019). A collaborate strategy of building partnerships among HCPs, politicians, community advocates, youth leaders, tobacco-control groups, and departments of public health is imperative to strengthen the needed response to disseminate information, improve outcomes, and enforce regulations to combat the harmful effects of the vaping public health crisis.

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