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A call to end the epidemic of adolescent E-cigarette use*

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1. Introduction

E-cigarette nicotine delivery systems (ENDS), also known as electronic cigarettes (e-cigarettes) were introduced to the global market around 2007 (Pauly et al., 2007). The popularity of these products has soared rapidly, generating \$900 million in revenue in 2014. Market analysts predict that the e-cigarette industry could be worth \$10 billion by 2018 (Herzog, 2015).

With the growing popularity of e-cigarettes, the overall impact of e-cigarettes on public health has been heavily debated among health professionals and policy makers. The main controversy is how to balance the risks and benefits of the potential use of these products. Proponents of the products state that e-cigarettes can be an effective harm reduction or cessation option for cigarette smokers given that they have lower levels of toxicants commonly present in cigarettes, and that therefore they should not be regulated and should be freely available to reduce the scourge of smoking combustible products. These claims are disputed by opponents who state that there is limited evidence of the safety of these products or their efficacy for harm reduction or cessation of combustible tobacco products, and that these devices may enable smokers to bypass smoke-free laws and maintain their addiction, and importantly, perpetuate nicotine addiction by introducing nicotine to non-users, especially adolescents. There is also concern that the wide availability of these devices could renormalize combustible tobacco use behaviors.

This article provides a brief overview of e-cigarette devices and e-liquids, as well as the existing literature on general safety concerns of e-cigarette use, the potential use of e-cigarettes as aides for combustible tobacco harm reduction or cessation, and then largely focuses on e-cigarette use among adolescents. We will discuss epidemiological evidence documenting adolescent e-cigarette use rates, associations between e-cigarettes and other tobacco/substance use, existing evidence on the use of e-cigarettes for adolescent smoking cessation, and reasons for e-cigarette popularity among adolescents. We will also discuss

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regulatory and prevention efforts that are urgently needed to curb the e-cigarette epidemic among youth.

2. E-cigarette devices and e-liquids

E-cigarettes are battery-powered devices that vaporize liquid solutions (i.e., e-liquid, e-juice), which contain propylene glycol and vegetable glycerin, and other ingredients including flavorings and nicotine, to create an aerosol (referred to as vapor) that users inhale or “vape”. The e-cigarette device commonly consists of an aerosol generator, a flow sensor, a battery, and a storage compartment which contains an e-liquid in either a cartridge or an open tank system (Brown and Cheng, 2014).

There are numerous varieties of e-cigarette devices. In 2014, more than 460 e-cigarette brands were identified (Zhu et al., 2014). The devices range from “closed systems” like cigalikes, which resemble cigarettes, to advanced generation e-cigarettes (e.g., rechargeable, pen-like devices, tanks, cartridges, mods/mech-mods) that are larger devices and do not resemble cigarettes (FDA, 2017). Other known e-cigarette devices are vaporizers, hookah pens, and e-pipes (FDA, 2017). The advanced generation e-cigarettes are “open systems” with many interchangeable parts that allow users to modify their devices, such as modifying voltage (hence temperature) to control puff volume. All these devices and parts are available for sale in brick and mortar stores (e.g., convenience stores, tobacco shops, vape shops) and online stores.

E-liquids primarily contain different ratios of propylene glycol and vegetable glycerin as carriers; the users can modify the proportion of these two constituents to achieve better throat hit or thicker vapor clouds. E-liquids also contain varying concentrations of nicotine, water, and flavorings. Some e-liquids also contain other solvents like ethyl alcohol, sometimes in high enough levels to negatively impact psychomotor performance (Valentine et al., 2016). E-liquids are currently available in over 7000 flavors (Zhu et al., 2014) and each flavor is made up of a mixture of chemicals, which are primarily aldehydes and vanillins, as well as maltol, ethyl maltol, benzyl and ethyl alcohol, ethyl butyrate and ethyl acetate, and other confectionary flavor chemicals (Tierney et al., 2015).

3. E-cigarette safety and health effects

Crucial to the debate on the role of e-cigarettes in public health is an understanding of the health effects of these devices and liquids. Because e-cigarettes are relatively new to the market the long-term health effects of e-cigarette use still remains to be determined. To date, the most frequently reported adverse events associated with e-cigarette use have been minor, such as nausea, throat and mouth irritation, headache, and dry cough (U.S. Department of Health and Human Service, 2014). Although e-cigarettes are free of combustion, and therefore, free of toxicants contained in burned tobacco through inhalation, they have different chemicals that could pose harm to health like propylene glycol and glycerin (FDA, 2014; Pisinger and Døssing, 2014). While there is limited information on long term inhalational exposure to propylene glycol in humans, short term exposure to propylene glycol mist at levels that are commonly used in aviation emergency training scenarios has

been shown to cause ocular and upper airway irritation (Wieslander et al., 2001). Glycerin when exposed to elevated temperatures is known to result in acetaldehyde and acrolein, which are known sensory and pulmonary irritants and also known carcinogens. Therefore, it is no surprise that aerosol produced from heating e-liquids contains carbonyls like formaldehyde, acetaldehyde, and acrolein (Goniewicz et al., 2014b; Kosmider et al., 2014). E-cigarettes deliver these ultra-fine particles deep into the lungs, which can have adverse pulmonary and cardiovascular effects (Grana et al., 2014; Lerner et al., 2015) and lower immune responses (Sussan et al., 2015). While the levels of carbonyls in e-cigarettes are lower than those found in combustible cigarettes (Goniewicz et al., 2014b), carbonyl levels are affected by e-liquid solvent characteristics and the temperatures they are exposed to. In particular, while these compounds are highest in aerosol generated by e-liquids with greater propylene glycol content and exposure to higher temperatures (Kosmider et al., 2014), it appears that formation of such carbonyls are observed even at low wattages/temperatures (Geiss et al., 2016).

The safety of flavorants in e-cigarettes also remains to be established. Most flavorants consist of chemicals that are generally recognized as safe for the purpose of ingestion; however, many of these flavor chemicals when vaporized, especially at high temperatures, result in toxic levels of inhalational irritants like benzaldehyde (Kosmider et al., 2014) and trigger oxidative and inflammatory responses in lung cells and tissues (Behar et al., 2014; Lerner et al., 2015). Scientific studies also raised concerns about the toxicity levels of certain e-cigarette flavors that contain chemicals like diacetyl (in buttery flavors known to associated with “popcorn lung”) and cytotoxic levels in cinnamaldehyde (in flavors like “atomic cinnacide”) (Allen et al., 2016; Behar et al., 2014), which has led to guidance from the Medicines and Healthcare Regulatory Agency of the United Kingdom to disallow ingredients, including diacetyl, from e-liquids (Medicines & Healthcare Products Regulatory Agency, 2016).

Finally, it is important to note e-liquids also contain nicotine, which raises concern of development and/or maintenance of nicotine dependence. Further concerning is that exposure of e-liquids to high temperatures can result in increased blood levels of nicotine (Talih et al., 2015a), which raises concerns about nicotine toxicity. In sum, thus far, there is limited evidence on the safety of e-cigarettes (Pisinger and Døssing, 2014). There is a need for more rigorous studies that are methodologically sound to support the safety of these products and establish the short-and long-term harm of e-cigarettes on public health.

4. The potential for e-cigarettes as harm reduction/cessation aids

As stated earlier, proponents of e-cigarettes believe that the availability of e-cigarettes will help reduce use of combustible cigarettes. Combustible tobacco use poses a substantial health burden and cost to the individual, and to society as a whole. Quitting smoking can lead to reduced risk of serious illnesses, such as lung cancer, chronic lung diseases and cardiovascular diseases (World Health Organization, 2011). Despite the known serious health consequences of tobacco use, nicotine dependence is a chronic relapsing disorder and quitting is difficult even with the availability of evidence-based cessation programs (Fiore et al., 2008). Quitting without the aid of an intervention is more difficult; adult smokers who

attempt to quit on their own relapse within the first month of abstinence and only about 3–5% achieve prolonged abstinence (Hughes et al., 2004). Many experts believe that e-cigarettes can serve as a highly appealing harm reduction or quitting approach for combustible tobacco users (Etter, 2010; Polosa et al., 2011).

Studies have started to examine the potential for e-cigarettes for smoking cessation for adults. An observational pilot study with 40 regular smoking adults in Italy examined if the use of e-cigarettes led to smoking reduction and abstinence. This study showed that the use of e-cigarettes for four weeks resulted in 50% reduction in the number of cigarettes used per day and 22.5% of participants achieved smoking abstinence at 24 weeks (Polosa et al., 2011). This sample was then provided with e-cigarettes for 6 months, and a 24-month follow up (N = 23) observed that 12.5% were abstinent from cigarettes (Polosa et al., 2014). While this evidence is encouraging, the results from existing randomized controlled trials (RCTs) of e-cigarettes are not as supportive.

An RCT conducted in Italy randomized 300 smokers to receive either 7.2 mg of e-cigarettes with nicotine for 12 weeks, 7.2 mg the first 6 weeks and 5.4 mg the last 6 weeks, or no nicotine containing e-cigarettes for 12 weeks (Caponnetto et al., 2013). This study observed no differences in quit rates between the groups, and reported overall quit rates of 10.7% at the end of 12 weeks and 8.7% at the end of 52 weeks. Another RCT that examined differences between 12 weeks of treatment with e-cigarettes with and without nicotine and nicotine patches in adult smokers seeking treatment (N = 657) observed quit rates of 7.3% with e-cigarettes with nicotine, 5.8% with nicotine patches, and 4.1% with e-cigarettes with no nicotine at 6-month follow up (Bullen et al., 2013).

A 2014 Cochrane review (McRobbie et al., 2014) examined 13 studies (observational and RCTs), two of which were the RCTs discussed above, and concluded that while there was some evidence that e-cigarettes help smokers quit or reduce smoking, the lack of high-quality RCTs reduces the certainty of these effects. In addition, a meta-analysis of clinical trials, cohort studies, and cross-sectional studies came to the conclusion that e-cigarette use in the real world is not associated with quitting smoking (Kalkhoran and Glantz, 2016). Therefore, there is limited evidence of the efficacy of e-cigarettes in promoting reduction or cessation of combustible tobacco use.

5. Adolescent e-cigarette use: why are we concerned?

Nicotine addiction is a pediatric disease (Kessler et al., 1997) and nicotine exposure to the developing adolescent brain has been shown to have long-term cognitive and behavioral impairments (Abreu-Villaça et al., 2003; Dwyer et al., 2009; England et al., 2015). Tobacco and nicotine addiction is established during adolescence with close to 90% of adult daily smokers starting before the age of 18 (U.S. Department of Health and Human Services, 2012). Although cigarette smoking has declined in recent years, e-cigarette use among adolescents has grown at phenomenal rates; uptake among adolescents has been shown in many local (Barrington-Trimis et al., 2015; Krishnan-Sarin et al., 2015; Leventhal et al., 2015; Wills et al., 2014) and national datasets in the U.S.A. (Johnston et al., 2016; Singh et al., 2016a). According to the U.S. Centers for Disease Control and Prevention, past-30-day

use of e-cigarettes among high school students has increased 11-fold between 2011 and 2015 1.5% to 16% (Singh et al., 2016a). Similar increases in youth e-cigarette use, specifically among younger adolescents, were also observed in the Monitoring the Future survey in 2015 (Johnston et al., 2016) but more recent evidence suggests that rates may be stabilizing and even going down in the U.S.A. (Johnston et al., 2017). High e-cigarette use rates among adolescents are also seen globally, including South Korea (Lee et al., 2014), the Russian Federation (Kong et al., 2016), Poland (Goniewicz et al., 2014a; Goniewicz and Zielinska-Danch, 2012), and New Zealand (White et al., 2015).

E-cigarette use now exceeds cigarette smoking among U.S. adolescents (Johnston et al., 2017; Singh et al., 2016a). Of concern, e-cigarettes are often the first tobacco product used by younger adolescents (Anand et al., 2015; Krishnan-Sarin et al., 2015), and a substantial proportion of adolescents who are not using cigarettes or other combustible tobacco products are using e-cigarettes (Barrington-Trimis et al., 2015). For instance, among adolescents in 2014, greater than 40% of adolescents who had used an e-cigarette in the past 30 days reported having never tried a combustible tobacco product (Barrington-Trimis et al., 2015).

A question that is often raised is whether adolescents are using e-cigarettes with nicotine. The evidence on this issue, while limited, suggests that nicotine use in e-cigarettes varies; while 37.4% of e-cigarette using adolescents report using e-cigarettes with nicotine, and 28.5% report using nicotine free e-liquids, 34.1% report not knowing whether their e-liquids contain nicotine, which raises concerns that many adolescents may not really know that they are using in e-cigarettes (Morean et al., 2016b). Among adolescents who use nicotine, use of higher nicotine concentration is associated with cigarette smoking, being male, and purchasing e-cigarettes from tobacco shops. Preliminary evidence seems to suggest that adolescents who initiate tobacco products with e-cigarettes without nicotine are switching to nicotine-containing e-cigarettes (Krishnan-Sarin et al., 2015). These findings, in combination with evidence that e-cigarettes are being used by adolescents who are naïve to combustible tobacco use, raises concerns about whether e-cigarettes could lead adolescents who would not have otherwise used tobacco products to nicotine dependence and future use of combustible tobacco products.

Indeed, emerging longitudinal evidence suggests that e-cigarette use does lead to initiation of combustible tobacco use (Leventhal et al., 2015; Wills et al., 2017). Adolescents who use e-cigarettes more frequently also seem to progress to heavier cigarette smoking (Leventhal et al., 2016). Moreover, among adolescents who have never smoked a cigarette, those who had ever used e-cigarettes are more likely to state that they intend to smoke cigarettes in the future than those who never tried e-cigarettes (Park et al., 2016). There is also compelling evidence that e-cigarette use among adolescents is associated with the use of multiple other tobacco products (Anand et al., 2015; Camenga et al., 2014; Gilreath et al., 2016; Huang et al., 2016b; Morean et al., 2016a; Simon et al., in press), and other substances like marijuana and alcohol (Morean et al., 2016a; Unger et al., 2016). Longitudinal evidence also suggests that initiation with e-cigarettes leads to greater initiation of use of multiple combustible tobacco products (Huh and Leventhal, 2016). The association between e-cigarette use and combustible smoking onset appears to be greater among adolescents who are at low risk for smoking initiation (Wills et al., 2017) or those who have never smoked a cigarette

(Leventhal et al., 2016), again raising concerns that adolescents who are naïve may be introduced to nicotine and combustible cigarettes through the use of e-cigarettes.

6. Potential for e-cigarettes as harm reduction/cessation among adolescents

Could e-cigarettes be beneficial to adolescents who are already using tobacco products by aiding in tobacco cessation? After all, existing reviews highlight that current strategies are not especially effective in helping adolescents quit smoking (Simon et al., 2015; Sussman and Sun, 2009). In addition, adolescents have more difficulties in quitting smoking than adults do (Bancej et al., 2007).

While to the best of our knowledge there are no observational studies or RCTs that have examined the efficacy of e-cigarettes for quitting in adolescent smokers, prospective studies among adolescents have shown that e-cigarette use among ever smokers did not change the frequency of smoking one year later (Wills et al., 2017). One recent study did observe that some adolescent smokers may be using e-cigarettes to quit smoking (Camenga et al., 2016). In this study, 41.8% of adolescents who had used 100 or more cigarettes in their lifetime indicated using e-cigarettes to quit smoking; however, 84.8% of these individuals still reported smoking cigarettes in the past 30 days, suggesting that their use of e-cigarettes for quitting was not successful. Thus, the limited available literature does not seem to support the use of e-cigarettes for quitting smoking among adolescents.

7. Why are e-cigarettes so popular among adolescents?

A better understanding of the e-cigarette popularity among adolescents can inform regulatory strategies and prevention efforts to prevent adolescents e-cigarette use. In the following sections, we discuss attributes that contribute to the e-cigarette popularity among adolescents. These attributes include availability of appealing flavors, marketing strategies, low harm perceptions, and alternative use behaviors.

7.1. Adolescents find e-cigarette flavors highly appealing

Flavored tobacco products are known to be extremely appealing to adolescents who are more likely than adults to use tobacco flavors (King et al., 2014; Klein et al., 2008). Flavors may promote combustible tobacco use among adolescents by reducing harshness of tobacco/nicotine and increasing appeal (Carpenter et al., 2005). Although all flavors, with the exception of menthol, are banned from cigarettes, e-cigarettes are available in a wide variety of flavors. In 2014, more than 7000 e-cigarette flavors were identified and this number is still growing (Zhu et al., 2014). In addition to existing flavors, users can also mix various flavors to create their own unique combinations which also increases appeal. Flavors are also marketed with exotic names that often do not resemble any flavors to pique interest (e.g., unicorn milk, vampire blood).

E-cigarette flavors are very popular among adolescents; 85.3% of adolescent e-cigarette users start with flavored e-cigarettes (Ambrose et al., 2015), and adolescent users report flavors as a top reason for e-cigarette initiation (Kong et al., 2015). Recent evidence also

suggests that flavored e-cigarette use may put adolescents at risk for combustible cigarette smoking (Dai and Hao, 2016). Never smoking adolescent e-cigarette users who use flavored e-cigarettes are more likely to be susceptible to cigarettes relative to those who do not use e-cigarettes. Among adolescent e-cigarette users who also smoke cigarettes, using flavored e-cigarettes is associated with lower intentions to quit cigarettes and lower harm perceptions toward tobacco products than those who do not use e-cigarettes (Dai and Hao, 2016).

Currently, e-cigarette flavors are marketed heavily without any restrictions. Not surprisingly, e-cigarette advertisements that emphasize appealing flavors appeal to adolescents. An experimental study showed that adolescents who had never tried e-cigarettes but who were exposed to flavored e-cigarette advertisements had greater intention to use and buy e-cigarettes than their counterparts who were exposed to advertisements of e-cigarettes without flavors (Vasiljevic et al., 2016).

Thus, flavors may be one the primary reasons for initiation of e-cigarette use among adolescents. In fact, as suggested by Harrell et al. (2017) restricting the range of flavors in e-cigarettes may significantly benefit adolescents and young adult e-cigarette prevention efforts.

7.2. E-cigarettes are aggressively marketed in venues that are accessible to adolescents

E-cigarettes are marketed in traditional media, such as the television and print advertisements (Kim et al., 2014), with themes that emphasize health benefits (e.g., e-cigarettes are healthier, cheaper, and cleaner than cigarettes; e-cigarettes can be used to bypass smoke-free policies; e-cigarettes do not produce secondhand smoke; Grana and Ling, 2014). Interestingly, newer e-cigarette brands are less likely to compare their products to combustible cigarettes and make claims of smoking cessation but are more likely to emphasize other features, such as appealing flavors (Zhu et al., 2014). E-cigarette marketing also includes evocative themes that appeal to adolescents, such as statements of independence, identity, and a lifestyle choice through the use of celebrities and other appealing components (Andrade et al., 2013).

E-cigarette marketing is highly effective in reaching adolescents. In the U.S.A., adolescents exposure to e-cigarette TV advertisement increased by 256% from 2011 to 2013 (Duke et al., 2014). Recent national data indicate that 69% of U.S. adolescents (18.3 million) are exposed to e-cigarette advertisements (Singh et al., 2016b). Television is the most common source of e-cigarette advertisement exposure. Most adolescents reported learning about e-cigarettes from television (Anand et al., 2015). Television advertisement is problematic because the mere presence of e-cigarette marketing on television may perpetuate low harm given that combustible cigarettes are not advertised on television.

While marketing using traditional media is an effective way to reach adolescents, e-cigarette companies are also using the Internet to market and sell their products (Chu et al., 2016; Freeman, 2012; Grana and Ling, 2014; Mackey et al., 2015; Richardson et al., 2014). The Internet is an ideal place to market e-cigarettes, especially to adolescents because of its rapid and wide-spreading reach, low cost, and lack of regulation (Elkin et al., 2010). Approximately, 40% of U.S. adolescents (10.5 million) report seeing an e-cigarette

advertisement online (Singh et al., 2016b). Analyses of e-cigarette-related content on social media show that promotional content is widespread (Chu et al., 2016; Huang et al., 2016a; Huang et al., 2014; Kim et al., 2015). For instance, over 90% of tweets on Twitter (text-based social media) related to e-cigarettes have promotional content (Huang et al., 2014). Additionally, 70% of e-cigarette vendors use social media to market and promote e-cigarette use (Mackey et al., 2015). Most importantly, while most e-cigarette websites contain some barriers to prevent youth access, these barriers are relatively simple (i.e., including questions like “Are you over 18 years of age?”) and can be easily bypassed by adolescents (Mackey et al., 2015). Given that social media use is particularly high among adolescents (Lenhart, 2015), regulation of e-cigarette marketing on the Internet is urgent.

7.3. Adolescents think e-cigarettes are safe

Marketing of e-cigarettes with claims of low health risks may also influence general harm perceptions of the product (Grana and Ling, 2014). Harm perceptions of tobacco products are associated with adolescents’ initiation and continued use of tobacco products (Chaffee et al., 2015; Halpern-Felsher et al., 2004; Song et al., 2009). Indeed, adolescents perceive lower harm from using e-cigarettes than smoking combustible cigarettes (Barrington-Trimis et al., 2015; Hammal and Finegan, 2016). Low harm perceptions of e-cigarettes are also associated with increased e-cigarette use among adolescents (Ambrose et al., 2014; Roditis et al., 2016). Moreover, adolescents perceive e-cigarettes to have the lowest harm relative to all other tobacco products (Roditis et al., 2016). Adolescents also hold many misperceptions about e-cigarettes, such as believing e-cigarette vapor is water and that e-cigarettes are not a tobacco product (Gorukanti et al., 2017). Thus, the general perception that e-cigarettes are safe may also promote use among adolescents.

7.4. Adolescents engage in alternative e-cigarette use behaviors

Adolescents may be attracted to e-cigarettes because of the countless available options to customize the device and its constituents. A majority of adolescents use advanced generation e-cigarette devices, which are open systems that allow users to easily modify temperatures, puffing behaviors, and concentrations and composition of e-liquids (Barrington-Trimis et al., in press). The ease with which this device can be manipulated has led to emergence of a variety of other use behaviors especially among adolescents.

Adolescents use e-cigarettes for “dripping” (inhaling vapors from dripping e-liquid directly onto an atomizer’s coil to vaporize e-liquid at high temperature) to intensify nicotine and flavor and to create bigger volume of exhaled vapor (Krishnan-Sarin et al., 2017). While there is limited research on the prevalence rates of this behavior, recent data from Connecticut indicate that 26% of adolescent e-cigarette users are “dripping.” The high rates of “dripping” among adolescents is alarming because e-liquids are exposed to high temperatures during this behavior which can yield greater levels of nicotine and toxicants than previously reported from regular vaping with e-cigarettes (Talih et al., 2016).

In addition, adolescents also find the appeal of doing “smoke tricks” appealing (Kong et al., 2015). “Smoke tricks” refer to using or manipulating the e-cigarettes to produce large and dense amounts of vapors or make various shapes with the exhaled vapor. To create these

smoke tricks, users customize the ratio of the e-liquid constituents (e.g., increase propylene glycol content which is responsible for the visible exhaled vapor), use higher temperatures, and alter their puffing behaviors. This is also concerning because greater propylene glycol concentrations are associated with higher levels of carbonyl compounds (as discussed above; Kosmider et al., 2014).

Adolescents are also using e-cigarettes to administer marijuana (Morean et al., 2015). Adolescents use e-cigarettes to vape hash oil, and wax infused with THC; 26.5% of adolescents who use both e-cigarettes and marijuana and 18% of adolescents who only use e-cigarettes reported using e-cigarettes to vaporize THC (Morean et al., 2015). While it is still unknown as to whether adolescents are using nicotine and marijuana together in e-cigarettes, it is known that co-use of these two substances poses additive health risks from toxicant exposure (Meier and Hatsukami, 2016).

In sum, adolescents are engaging in a number of alternative e-cigarette use behaviors that have unknown health risks. Future research needs to focus on developing a better understanding of these alternative use behaviors and include them in determinations of e-cigarette use risk.

8. E-cigarette regulations to protect adolescents

The Family Smoking Prevention and Tobacco Control Act of 2009 gave the US Food and Drug Administration (FDA) authority to regulate tobacco products. However, this act was limited to cigarettes, roll-your-own (loose tobacco), and smokeless tobacco. The exclusion of e-cigarettes allowed e-cigarettes to be marketed and sold without any federal regulatory oversight. However, in August, 2016, the FDA extended their authority over various other tobacco products, which included e-cigarettes, cigars, pipe tobacco, nicotine gel, hookah, and dissolvable tobacco (FDA, 2017).

The new e-cigarette regulations that immediately went into effect as of August, 2016 included a minimum age of purchase (18 years old), mandatory age verification with photo IDs of individuals under 27 years old, prohibition of free samples of e-cigarettes, and prohibition of e-cigarettes in vending machines unless they are in an adult-only location. The new regulations also require that products not on the market as of February 15, 2007 obtain FDA approval, all tobacco products to have health warning labels, and any manufacturers of the e-cigarette products and e-liquids must register with the FDA and provide a detailed list of ingredients and manufacturing processes; the manufacturers have two years to comply with these latter requirements. Overall, these regulations will make significant inroads into reducing adolescents access and use of e-cigarettes. However, more needs to be done to reduce e-cigarette use among adolescents.

For example, a significant exclusion from the FDA regulation are flavors in e-liquids and other combustible tobacco products (e.g., cigars/cigarillos). Given the overwhelming evidence showing that e-cigarette flavors are highly appealing to adolescents, are a top reason for adolescents e-cigarette initiation, and may pose harms that are yet unknown, the FDA must restrict the marketing and sale of e-liquid flavors.

Federal authorities also need to put into place appropriate monitoring measures to ensure compliance with the regulations that are directed at protecting adolescents from accessing e-cigarettes. For example, prior to federal regulations, evidence obtained in Connecticut in 2015 (when Connecticut had a rule that prohibited the sale of e-cigarettes to minors) showed that underage adolescents (i.e., younger than 18 years old) were easily able to purchase e-cigarettes in both physical (i.e., brick and mortar stores) and online stores (Kong et al., 2017). Other studies have also found that underage purchasing of e-cigarettes online is particularly easy because of poor monitoring and restriction systems (Williams et al., 2015). Approximately 61% of online e-cigarette vendors have age verification processes that are easy to cheat (a click on a pop-up agreeing to the fact they are over 18 years of age allows access to the site) and almost 35% of online e-cigarette vendors do not even have age verification systems (Mackey et al., 2015). Regulating e-cigarette marketing on the Internet is a new challenge that tobacco control stakeholders must address.

Although popular source of e-cigarette acquisition among adolescents are physical and online stores, adolescents also obtain e-cigarettes from their peers and parents (Kong et al., 2017). Adolescents cite peer use as a reason for e-cigarette initiation (Kong et al., 2015) and report learning about e-cigarettes from the peers (Anand et al., 2015). Thus, when considering effective prevention campaigns/resources for youth, the powerful effect of peers must be addressed. These prevention campaigns also need to highlight misperceptions about harms and benefits of e-cigarettes and need to be directed not just at youth but also their parents. Education campaigns to relay convincing and salient prevention messages about e-cigarettes and regulating marketing content are urgently needed.

Finally, adolescents are using more advanced generation e-cigarettes and engaging in “dripping” that aerosolize e-liquids in high temperatures to intensify nicotine, flavors, and visible vapor (often to do “smoke tricks”), which could expose adolescents to numerous health risks. Regulating the products to disallow the modified use of e-cigarettes for these risky behaviors is also imperatively needed to protect youth.

9. Conclusions and recommendations to end the adolescent e-cigarette epidemic

The free and unregulated availability of e-cigarettes has led to increases in use of these devices by youth. Youth e-cigarette use should not be dismissed as a phase of experimentation that occurs in adolescence. Rather, the youth e-cigarette use epidemic should be taken seriously as any form of nicotine exposure among youth is harmful (Abreu-Villaça et al., 2003; Dwyer et al., 2009; England et al., 2015) and emerging evidence suggests a substantial portion of youth e-cigarette users are naïve to other combustible tobacco products and e-cigarettes are the first tobacco product they have used (Anand et al., 2015; Barrington-Trimis et al., 2015; Krishnan-Sarin et al., 2015; Johnston et al., 2016). E-cigarette use could initiate nicotine dependence in a new generation of youth which could progress to use of combustible tobacco products. Recent evidence suggests that rates of e-cigarette use may be going down among youth (Johnston et al., 2017) which is encouraging news. However, youth use rates are still high and we need more evidence on the health

effects of e-cigarettes among youth (U.S. Department of Health and Human Services, 2016). These critical concerns should not be dismissed because of the potential for e-cigarettes to help with quitting smoking. Public health officials need to balance the potential for e-cigarettes as a harm reduction/quitting device for combustible product users against the potential for nicotine addiction among youth.

Investigations into the emergence of alternative e-cigarette use behaviors and the short and long-term safety of these and regular e-cigarette use are critical. Additionally, as highlighted in the recent Surgeon General's report, local and federal policies that address e-cigarette use among adolescents, including advertising restrictions, health warning labels on the products, and prevention efforts that target youth e-cigarette use via the use of effective mass media campaigns (directed at youth and parents) are urgently needed (U.S. Department of Health and Human Services, 2016). Preventing the initiation of nicotine dependence in youth should be a top priority and a major goal of tobacco control efforts.

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