

## E-cigarettes Evidence Brief: March 2018

### What are E-cigarettes?

Originally introduced in China in 2003, electronic nicotine delivery devices (e-cigarettes) entered the U.S. and European markets in 2006 and have grown into a multibillion dollar industry with over 466 brands and 7,764 flavors (Lieberman, 2017). E-cigarettes deliver nicotine rapidly to the brain without burning tobacco. The e-cigarette heats a liquid solution of nicotine via a battery-powered device producing nicotine-containing vapor for inhalation (Lieberman, 2017).

### Prevalence/Trends

Among adults in the United States, awareness of e-cigarettes increased from 41% in 2010 to 80% in 2013. In this same time frame, prevalence of ever use increased from 10% to 37% among smokers; from 3% to 10% among former smokers. Among never smokers, prevalence of use remained unchanged at 1% between 2010 and 2014 (King, 2014).

According to the Centers for Disease Control and Prevention (CDC) 2015 survey, 13.5% of middle school and 37.7% of high school students had ever used e-cigarettes while past 30-day use was at 5.3% for middle school students and 16% for high school students. Both ever and past 30-day rates among middle and high school students have more than tripled since 2011 (USDHHS, 2016).

Another CDC survey found that in 2013-2014, e-cigarette use among young adults surpassed that of adults for both ever and current use. In young adults, ever use was at 35.8% compared to 16.4% in adults. Current use was 13.6% in young adults and 5.7% in adults (USDHHS, 2016).

### Tobacco Cessation

There is insufficient evidence to support e-cigarettes as effective aids for smoking cessation compared to standard FDA approved therapies.

The U.S. Preventive Services Task Force (USPSTF) did not find sufficient evidence to recommend electronic nicotine delivery systems (ENDS) for tobacco cessation in adults, including pregnant women. Instead, they recommended that clinicians direct patients who smoke tobacco to other cessation interventions with established effectiveness and safety (USPSTF, 2015).

A 2016 meta-analysis of 2 randomized controlled trials, 15 cohort studies and 3 cross-sectional studies found that smokers using e-cigarettes (irrespective of intent to quit smoking) were not more likely to quit smoking than those who did not use e-cigarettes (Kalkhoran, 2016). A more recent 2017 meta-analysis of 3 randomized controlled trials and 9 cohort studies confirmed these findings. It did find evidence from cohort studies of a possible reduction in quit rates with the use of nicotine e-cigarettes compared with alternatives (nicotine replacement therapy, cigarette use, behavioral interventions, no nicotine e-cigarette use) (El Dib, 2017).

The evidence (randomized controlled trials, cohort and cross-sectional studies) on which these systematic reviews and meta-analyses are based on have methodological issues and only few randomized controlled trials

are available. Overall quality of evidence is either low or very low. No trials (only observational studies) compared the direct effects of e-cigarette use on smoking cessation to standard therapies such as nicotine replacement therapy. The trials that are available studied the efficacy of nicotine e-cigarettes vs. placebo e-cigarettes. These trials showed mixed results, and because of the low quality evidence, no clear inferences can be drawn (Hartmann-Boyce, 2016; Khoudigian, 2016, El Dib, 2017).

## Safety

Because e-cigarettes contain lower levels of toxins than conventional cigarettes, they are considered by some as a safer alternative. A 2017 health risk assessment found that compared with e-cigarettes, conventional cigarettes had more contaminants with exposure levels higher than the international guideline levels (Chen, 2017).

A systematic review of 687 articles found that conventional cigarette smokers who report switching to e-cigarettes have been shown to have positive outcomes such as reduced blood pressure, improved lung function, and improved lung disease symptoms (Glasser, 2017). A 2016 systematic review of 3 randomized controlled trials and 21 cohort studies found no serious adverse events from e-cigarette with irritation of the mouth and throat reported as the most common side effects (Hartmann-Boyce, 2016). Additional side effects may include nausea, headache, and dry cough (Gualano, 2014, Glasser, 2017; Hajek 2014).

However, there is also concern that they are not a harm-free alternative (Chen, 2017; Glasser, 2017; Fernandez, 2015; Hajek 2014, Hess 2016).

There is conflicting literature regarding particular substances in e-cigarettes and the potential for toxicity and harm (Chen, 2017; Burstyn, 2014). Further complicating this issue of toxins is the variability of the delivery systems. Most e-cigarettes share a similar basic design, with common components including an aerosol generator, a flow sensor, a battery, and a liquid solution storage area (Brown, 2014). Yet, there is significant variability in configuration and functionality which therefore leads to varied nicotine delivery and variable exposure to other substances (Brown, 2014; Cheng, 2014).

The effect of e-cigarettes on bystanders is not fully understood. While the exposure to toxins is much less than with conventional cigarettes, the risk is unclear. A systematic review by Hess et. al (2016) found that passive exposure to e-cigarette vapor had the potential to lead to adverse health events because of elevated levels of chemicals such as nicotine, particulate matter, glycerine, propylene glycol, formaldehyde, acetaldehyde, polycyclic aromatic hydrocarbons, and metals (Hess, 2016). Abidin (2017) found that current studies were inconsistent in methodology and findings on indoor air quality related to e-cigarettes. (Abidin, 2017)

In youth, a 2018 study on 103 adolescents with an average age of 16.4 years old found significantly higher levels of toxic chemicals, including carcinogens, in those who used both e-cigarettes and traditional cigarettes compared to e-cigarette use alone as well as significantly higher levels in those youths who used e-cigarettes alone compared to those who never used e-cigarettes or traditional cigarettes. The harmful toxins were found in both nicotine and non-nicotine e-cigarettes. (Rubinstein, 2018)

Other safety issues of e-cigarettes include accidental poisoning, explosions, and vaping of other substances (Glasser 2017, Brown 2014). Between 2012 and 2015, e-cigarettes accounted for 14.2% of the nicotine single-exposure calls among children five years old and under (Glasser, 2017). There were 92 reports of overheating,

fire, or explosion events from 2012 to 2015 in the United States, with about 50% of those resulting in injuries (Glasser, 2017). There is also concern that the e-cigarette apparatus may be used to vaporize other chemical substances (Brown, 2014).

Many of the flavorings are in the same class of flavorings that have been shown to cause bronchiolitis obliterans (Kreiss, 2008). Caution should be exercised when using flavoring products.

### **Youth: Potential Gateway to Addiction**

According to the 2016 U.S. Surgeon General Report on e-cigarettes, nicotine exposure during adolescence can cause addiction and harm brain development (USDHHS, 2016).

Low to moderate evidence from systematic reviews and meta-analyses of observational studies suggests that young adults who use e-cigarettes may be at higher risk for future cigarette smoking.

A 2016 meta-analysis of six studies (91,051 participants, including 1452 with ever e-cigarettes use) found that never-smoking adolescents and young adults who used e-cigarettes had higher likelihood of increased intent to smoke cigarettes in the future (Zhong, 2016). A 2017 systematic review and meta-analysis of 9 studies of 17,389 adolescents and young adults found that never cigarette smokers who used e-cigarettes in the past 30 days had higher likelihood for subsequent cigarette smoking initiation (Soneji, 2017).

### **Discussing E-Cigarettes with Patients - Key Takeaways**

Adapted from Ebbert, 2015: Counseling Patients on the Use of Electronic Cigarettes (Mayo Clinic Proceedings)

1. They are not demonstrably superior to FDA-approved medications for smoking cessation.
2. They may not be effective for smoking cessation and dual use (i.e., using e-cigarettes and continuing to smoke) will prolong exposure to tobacco.
3. They are not FDA-approved for the treatment of tobacco dependence.
4. The long-term health risk of exposure to e-cigarette constituent chemicals is unknown.
5. No regulatory oversight, such as requirements for good manufacturing practices, is currently in place for e-cigarette devices.
6. For adolescents, use of e-cigarettes may increase likelihood of use of conventional cigarettes.
7. The safety of flavorings have not been documented and there is some evidence that it could be hazardous.

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