

E-CIGARETTES – ARE THEY SAFE?

A UPDATE FOR PRIMARY CARE PHYSICIANS



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Learning objectives:

- List the adverse reactions of e-cigarette usage
- Explain the limitations of research on e-cigarette usage as a tobacco reduction strategy
- Describe the uncertainty of amounts of nicotine in ENDS

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Electronic cigarettes (E-cigarettes/E-cigs) are tobacco products that deliver nicotine via a battery-operated device, with a heating element that turns a flavored liquid into a vapor, which the user inhales¹. They were first developed by a Chinese pharmacist in 2003 and introduced into Europe and the United States in the mid-2000s². E-cigarettes entered the market as consumer products without much government regulation. Since 2010, sales have risen exponentially with more than 400 brand names and over 7,000 flavorings, especially due to widespread advertising campaigns by tobacco companies in television, print, and the media³. Yet there is still much uncertainty about the long-term health effects of e-cigarettes and whether they are ultimately safe to use⁴.

inhaling their vapors may expose people to toxic substances like tin, lead, cadmium and nickel^{5,2}. Most e-cigarette users are also traditional cigarette

The safety and efficacy of using e-cigs as tobacco cessation products is still unknown.⁷

The AAFP encourages all members to screen for e-cigarette use in all age groups, to discuss the potential harms of e-cigarette use, and to recommend evidence-based smoking cessation interventions with e-cigarette users.³⁷

smokers⁶, and surveys show that a majority of smokers see e-cigs as a tool to help them quit or reduce their smoking³, yet the safety and efficacy of using e-cigs as tobacco cessation products is still unknown⁷. Moreover, the manufacture and distribution of e-cigarettes is not well regulated and the exact amounts and components or health consequences are uncertain⁸. There is also growing public health concern on the effect e-cigarettes may have on smoking prevalence or the potential to be used as gateways to other tobacco or illicit drugs, particularly among the youth⁴. The Surgeon General recently issued a report discussing the potential health effects of nicotine and e-cigarettes on America’s youth and the increase in consumption in recent years, calling to action health care providers, teachers, and society to educate about the dangers of nicotine and to discourage tobacco use in any form⁴. Family physicians often encounter patients who use or ask about e-cigarettes, and it is important to keep up

Often perceived to be more innocuous than traditional cigarettes because they do not have combustion products of tar, ash, or carbon monoxide, e-cigarettes still contain nicotine and

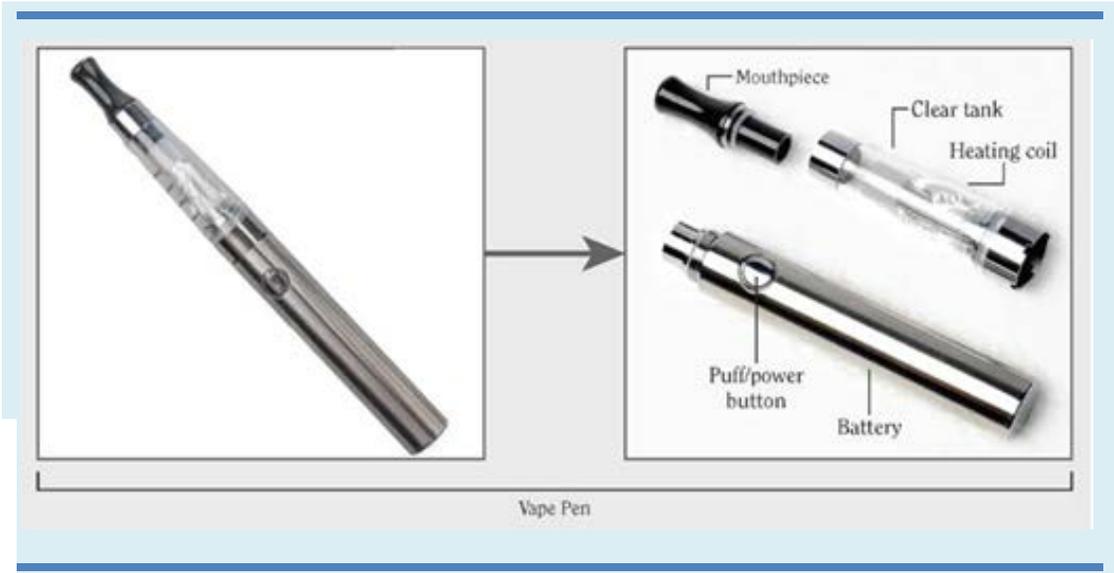


Figure 1: from USDHHS 2016

with the latest information. Below is a brief overview to help make informed counseling decisions.

Device Components:

E-cigarettes are electronic nicotine delivery systems (ENDS), which may also be referred to by other names such as: e-cigs, cigalikes, e-hookahs, mods, vapes, vape pens, or tank systems¹⁰. Typically, they have three main components: a cartridge that contains a solution (an e-liquid with nicotine, propylene glycol or glycerol and flavorings), an atomizer (or vaporization chamber with a heating element), and a battery¹¹ (see figure 1). There are multiple generations of products. First-generation e-cigs often mimic conventional cigarettes in their shape and design with a tan body and white mouthpiece. Newer second-generation models are shaped more like pens (“vape pens” or “eGos”) with larger cartridges, refillable tanks and replaceable batteries. Third/fourth-generation devices are more diverse and modifiable (“mods”), allowing the user to customize the atomizers and batteries, producing widespread variability in the amount of nicotine and levels of chemicals present in the aerosolized vapor¹².

The amount of nicotine exposure in e-cigarettes also varies depending on the concentration of e-liquid, user experience, puffing intensity & frequency, device components and characteristics, as well as vaping technique^{18,19}

Prevalence:

By 2012, consumption of e-cigarettes doubled, and by 2014, about 4% of adults in the United States reported using e-cigarettes every day or some days¹³. Many consumers are also dual users. A recent Journal of Family Practice article cited 52% of conventional cigarette smokers also use e-cigarettes¹⁴. A majority (79%) perceived them as a tool for smoking cessation, yet they did not perceive a greater likelihood of quit success¹⁴. This potentially exposes them to the dangers and toxicity of compounds in both tobacco and e-cigarettes. Rates of e-cig use also appear to be increasing among current and former conventional tobacco smokers. This is particularly prevalent in adolescents and young adults, where 16% of high

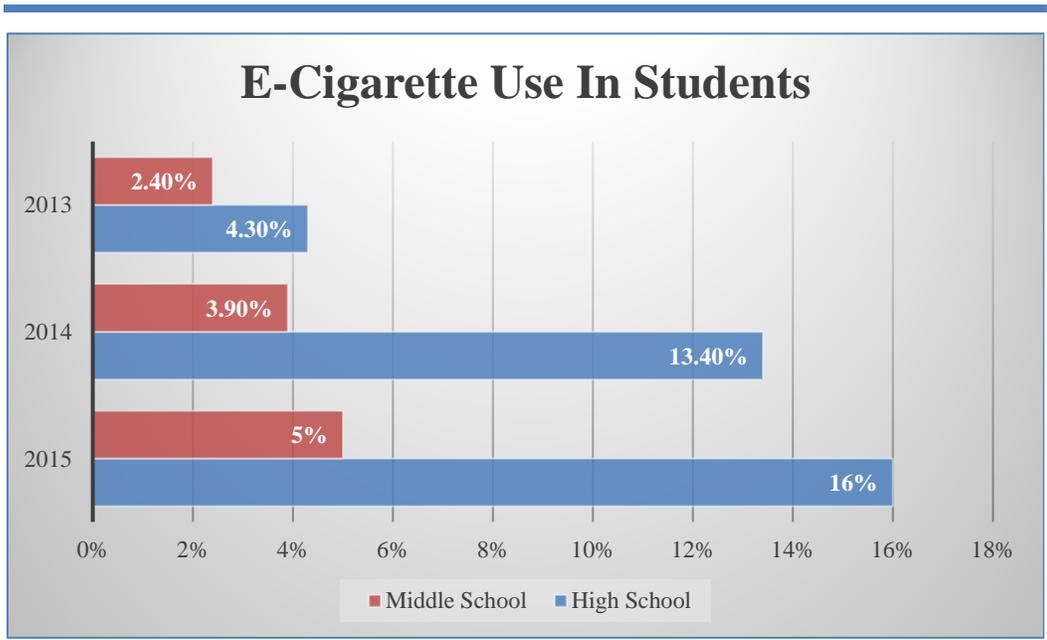


Figure 2: CDC/CDC National Youth Tobacco Survey USDHHS 2016

According to a 2015 survey, e-cigs were the most commonly used tobacco product among high school and middle school students – 620,000 middle school students and 2.4 million high school students reported using e-cigs in the past 30 days)¹⁵.

school students and young adults 18-24 years of age (compared to 13% in 2014) and 5% of middle school students (compared to 3% in 2014) reported using e-cigs in the past 30-days in 2015⁴. (see figure 2) All in all, e-cigarette use has grown 900% among high school students from 2011 to 2015 based off this data⁴.

Adverse Health Effects:

Currently, there is no observational data examining the long-term health effects of e-cigarettes, although a *JAMA* study found that e-cig use for at least one year was associated with increased oxidative stress and cardiac autonomic balance, factors correlated with increased cardiovascular risk¹⁶. Although it is not known whether the particles cause toxicity, the vapor from e-cigarettes contains particulate matter, with some reports suggesting concentrations similar to conventional cigarettes². A *Chest* study found changes in airway respiratory function but to a much smaller extent than conventional cigarettes¹⁷. The amount of nicotine exposure in e-cigarettes also varies depending on the concentration of e-liquid, user experience, puffing intensity & frequency, device components and characteristics, as well as vaping technique^{18,19}. Nicotine exposure during adolescence has been shown to cause addiction and can hurt the developing brain⁴. It is also harmful for the fetus in pregnancy, as nicotine crosses the placenta and has known adverse effects on postnatal development, resulting in health consequences such as Sudden Infant Death Syndrome, deficits in auditory processing and even obesity⁴.



The health effects of aerosolized constituents of e-liquids (solvents, flavorings, and toxicants) are not completely understood yet, although preliminary data does show linkage to bronchial irritation, causing chronic cough and phlegm, due to changes in airway respiratory function²⁰. A relationship between cytotoxicity and certain flavorings, especially sweet and cinnamon, has also been shown²¹, and cherry-flavored e-liquids have been linked to higher levels of benzaldehyde, a respiratory irritant²². Other compounds like nicotine, carbonyl compounds and volatile organic compounds are present and known to have health consequences⁴. At high temperatures, excess levels of formaldehyde, aldehyde and acrolein (known carcinogens) are present through heating of e-liquid solvents (propylene glycol and glycerin) and heavy metals (lead and cadmium) have been found in some e-cigarette aerosols⁴. Ingestion or skin exposure to e-liquids can cause toxicity in various quantities, as well. Most e-cig poisonings are caused by unintentional exposure to nicotine from e-liquid refills via ingestion, skin absorption, inhalation or dropping into eyes⁴. Consequences of e-liquid nicotine intoxication at low doses include nausea, vomiting, dizziness, headaches, and diarrhea; however high doses may cause tachycardia, seizures, abdominal pain, confusion and even death²³.

Role in Smoking Cessation:

Although tobacco companies make claims for use of e-cigs as smoking cessation aids, there is not. Few randomized controlled trials have evaluated e-cigarettes as smoking cessation tools, but one RCT that did, found quit rates did not differ significantly from other smoking cessation tools²⁵. Multiple observational studies found e-cigs are not associated with higher rates of quitting or reduced smoking²⁶. Some studies propose e-cigarettes may decrease nicotine cravings and withdrawal enough data to support their efficacy and safety²⁴. symptoms, insinuating the potential use as a harm reduction tool²⁷. Countries like Great Britain are recommending their use as nicotine-replacement aids, but more data is needed before an official recommendation is made by the FDA⁴.

Public Health Concerns:

The potential impact of e-cigarettes on public health is uncertain and widely controversial. There is concern that e-cigarettes' appeal to youth may potentially cause "renormalization" (reverse gains made in social norms about smoking acceptability), discouraging successful future quit attempts and encouraging smoking relapse and initiation rates²⁸. However, there is no real evidence that renormalization is occurring at present. There is also concern that unregulated e-cigarette use may erode gains in smoking cessation and smoke-free laws¹.

Accidental poisoning in children associated with e-cigarettes is another growing public health concern, as there have been increasing calls to poison control centers²⁹. A 5ml vial of e-liquid may contain a nicotine concentration of 20mg/ml (100mg/vial) and a lethal dose of nicotine in a child is about 10mg³⁰. A 2014 CDC report cited 51% of calls to poison control centers about e-cigarettes predominately involved children less than 5 years of age and were typically from unintentional exposure to e-liquids⁴.

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There is also concern over unknown health risks of secondhand exposure to vapor, although limited evidence suggesting harm exists. Passive exposure to e-cig vapor produces increases in cotinine (a metabolite of nicotine found in the saliva) but is like that of conventional cigarettes. Secondhand exposure to vapor is expected to be less toxic than combustible cigarette smoke according to a *BMC Public Health Journal* study³¹, but the amount and concentration of vapor released widely depends on user technique, temperature, device and other factors. With limited regulation and no standardization of e-cig products, it is hard to assess potential long-term health impacts.

Evidence indicates that nicotine may prime the adolescent brain for illicit drug use⁴. This is most concerning, as public health experts worry e-



cigarettes might appeal to youth, causing nicotine addiction and related harmful consequences. This is especially troubling because of the tobacco industry's successful marketing tactics and appealing flavors (like bubble gum, chocolate, and cotton candy). Adolescents are particularly vulnerable to the damaging consequences of nicotine exposure, specifically the increases in drug-seeking behavior³² and attention/cognition deficits and mood disorders³³. A 2014 *New England Journal of Medicine* study proved that nicotine has a molecular basis as a gateway drug³². This could have profound public health consequences with the increasing widespread use of e-cigarettes (which are pure nicotine delivery devices) by increasing the prevalence of tobacco and drug use in a whole new generation⁴.

Regulation:

Acknowledging additional data is needed, the World Health Organization (WHO)³⁴ issued a report suggesting regulations were needed to stop promotion of e-cigarettes to nonsmokers and young people, to minimize exposure to users and nonusers, and to restrict advertising and indoor use³⁴. However, some countries like Great Britain disagree and believe the risks of e-cigarettes might be overstated, so they have adopted a balanced regulatory approach to ensure product safety while

encouraging e-cigarettes as a smoking cessation device³⁵. As of 2014, countries like Canada, Singapore, Brazil, and Uruguay have banned e-cigarettes altogether². In the United States, the 2009 Family Smoking Prevention and Tobacco Control Act allowed the US Food and Drug Administration (FDA) authority over regulation of cigarettes and smokeless tobacco, although this did not include e-cigarettes. In May 2016, the FDA issued a “deeming rule” to extend its authority to include e-cigs and their components. This was a huge milestone, for it granted the FDA oversight conducting premarket review of all e-cig products and mandated ingredient and health risk disclosure of all tobacco products⁴. This is currently being challenged by lobbyists and tobacco companies.

Practice Implications:

With no clear data on health consequences of e-cigarettes or their efficacy in smoking cessation, no evidence-based recommendations can be made. Some research shows that e-cigarettes do not increase long-term tobacco abstinence among smokers², so now, many organizations do not recommend using them as smoking cessation aids, especially since many people continue as dual users and end up exposed to the dangers and toxicities of both. Although e-cigarettes are probably less harmful than conventional tobacco cigarettes overall, their safety to users and second-hand exposure is still unknown. Several medical societies, such as the American Heart Association, have provided policy statements with guidance addressing e-cig use in clinical practice¹. The AHA maintains that “e-cigarette use should be part of tobacco screening questions incorporated into clinical visits” and that there is not enough evidence to recommend e-cigarettes as primary cessation aids, however “clinicians should be educated about e-cigarettes...and prepared to counsel their patients regarding comprehensive tobacco cessation strategies”¹ (see Figure 3). The FDA has neither approved e-cigarettes for smoking cessation nor endorsed their safety. As of now, clinicians should offer FDA-approved nicotine-replacement and smoking cessation aids and pharmacotherapy.

Summary of Current Recommendation for Clinical Guidance

E-cigarettes use should be included in tobacco screening questions that are part of every health examination.

Clinicians should be educated about e-cigarettes and should be prepared to counsel their patients regarding comprehensive tobacco cessation strategies.

Patients should be separated into 3 treatment categories based on their tobacco/e-cigarette use status:

1. Tobacco product users who are willing to quit should receive intervention to help them quit.
2. Tobacco product users unwilling to quit at the time should receive interventions to increase their motivation to quit.
3. Those who recently quit using tobacco products should be provided relapse prevention treatment

There is not yet enough evidence for clinicians to counsel their patients who are using tobacco products to use e-cigarettes as a primary cessation aid.

If a patient has failed initial treatment, has been intolerant to or refused to use conventional smoking cessation medication, and wishes to use e-cigarettes to aid quitting, it is reasonable to support the attempt.

However, patients should be informed that although e-cigarette aerosol is likely to be much less toxic than cigarette smoking, the products are unregulated, may contain low levels of toxic chemicals, and have not been proven to be effective as cessation devices.

In the absence of long-term safety studies of e-cigarette use, it may be appropriate to advise the patient to consider setting a quit date for their e-cigarette use and not to plan to use it indefinitely (unless needed to prevent relapse to cigarettes)

It is also important to stress that patients should quit smoking cigarettes entirely as soon as possible, because continued cigarette smoking, even at reduced levels, continues to impose tobacco-induced health risks.

For patients with existing CVD or stroke, or at risk for CVD event, intensive cessation counseling and pharmacotherapy should be offered as soon as possible.

Figure 3: Bhatnagar, A. et al. "Electronic Cigarettes: A Policy Statement from The American Heart Association". *Circulation* 130.16 (2014):1418-1436³⁶

The USPSTF recommends prescribing behavioral techniques and/or pharmacologic devices for smoking cessation.

Conclusion:

In order to prevent and reduce the use of tobacco and any potential negative health consequences of e-cigarettes, we must work together as a society. Broad educational programming, research initiatives, legislative & regulatory actions, and other public health strategies need to be adopted on local, state and national levels to prevent all forms of tobacco use, particularly among children and adolescents. In the meantime, physicians can, and should, educate their patients and the public about risks associated with tobacco in all forms. They should screen patients for e-cigarette use and educate them about its potential harm. Above all, physicians should recommend all patients use evidence-based smoking cessation interventions for both tobacco and e-cigarette users.

With no clear data on health consequences of e-cigarettes or their efficacy in smoking cessation, no evidence-based recommendations can be made. However, physicians should discuss, screen for e-cigarette use and recommend proper interventions.

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