

Counseling Patients on the Use of Electronic Cigarettes

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CME Activity

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Learning Objectives: On completion of this article, you should be able to (1) list the components of an electronic-cigarette (e-cigarette), (2) recall the available evidence regarding the efficacy of e-cigarettes for smoking cessation, and (3) describe the characteristics of e-cigarette users.

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Abstract

Electronic cigarettes (e-cigarettes) have substantially increased in popularity. Clear evidence about the safety of e-cigarettes is lacking, and laboratory experiments and case reports suggest these products may be associated with potential adverse health consequences. The effectiveness of e-cigarettes for smoking cessation is modest and appears to be comparable to the nicotine patch combined with minimal behavioral support. Although a role for e-cigarettes in the treatment of tobacco dependence may emerge in the future, the potential risk of e-cigarettes outweighs their known benefit as a recommended tobacco treatment strategy by clinicians. Patients should be counseled on the known efficacy and potential risks of e-cigarettes.

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From the Robert D. and Patricia E. Kern Center for the

Affiliations continued at the end of this article.

Modern electronic cigarettes (e-cigarettes) were invented in the early 2000s by a Chinese pharmacist seeking a non-combusted form of nicotine inhalation after his father died of tobacco-attributable lung cancer.¹ The basic e-cigarette design is a lithium battery attached to a heating element (atomizer) that vaporizes a humectant (propylene glycol, vegetable glycerin, and/or polyethylene glycol 400) that contains liquid nicotine (Figure 1).

Vaporization allows for inhalation of vapor, referred to as vaping, and produces an aerosol similar in appearance but substantially different in substance to conventional cigarette smoke.

Varieties of e-cigarette brands exist that can be grouped into 3 main categories: cigalikes, resembling cigarettes; eGos, larger than cigalikes with tanks that can be filled and refilled with e-fluid or e-juice (ie, nicotine combined with a humectant and flavoring);

and mods, constructed from basic components or by modifying commercially available products.² E-cigarettes are sold as single-use disposable devices or as reusable devices. E-cigarettes purchased as reusable devices can be attached to prefilled combined atomizers and cartridges called cartomizers. E-juice can also be dripped directly onto the heating element with the use of a drip tip. As of January 2014, more than 7500 unique flavors of e-juice were available.² New-generation e-cigarettes deliver more nicotine to the user because of larger atomizers, batteries, and electronic circuitry for setting atomizer power, but the amount of nicotine delivery is still substantially less than a conventional cigarette.³

E-cigarettes are attractive because they address the psychopharmacologic (ie, nicotine), social, and behavioral aspects of smoking. Use of the device can simulate the experience of smoking a cigarette with the vapor that simulates tobacco smoke, handling of the device that simulates the hand-to-mouth experience, and flavorings that simulate cigarette taste. Similar to a conventional cigarette, e-cigarette vapor particles are small enough to make their way to the alveoli where nicotine is absorbed,⁴ leading to relief of nicotine withdrawal symptoms⁵ and potentially providing behavioral reinforcement for continued use. A variety of reasons are reported for using e-cigarettes, with the most common being to quit or reduce smoking, to use a product perceived to be healthier than conventional cigarettes, to circumvent smoking restrictions, and to reduce costs associated with tobacco dependence.⁶

Significant uncertainty exists about e-cigarette safety and efficacy, rendering patient discussions about these devices challenging. The goal of this article is to provide the clinician with information that can be incorporated into counseling patients about the use of e-cigarettes.

REGULATORY STATUS

Regulation of e-cigarettes varies around the globe, ranging from no regulation to complete bans. The US Food and Drug Administration (FDA) does not regulate e-cigarettes as drug delivery devices. Rather, e-cigarettes and other products made or derived from tobacco are regulated as tobacco products under the Family Smoking Prevention and Tobacco Control Act

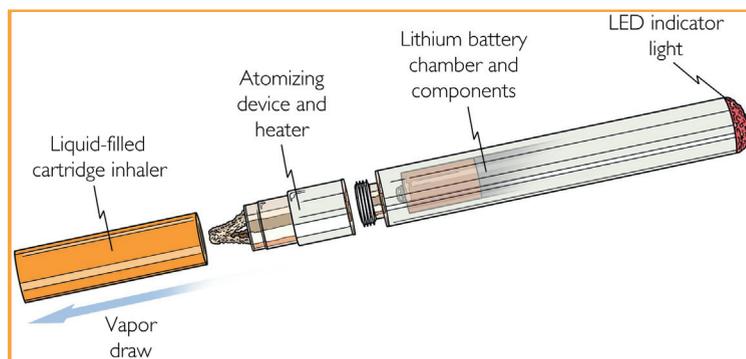


FIGURE 1. Simple anatomy of the electronic cigarette. Used with permission of Mayo Foundation for Medical Education and Research. All rights reserved.

of 2009 (Tobacco Control Act)⁷ and are not considered drugs or devices unless they are marketed for therapeutic purposes. This regulatory approach to e-cigarettes emerged from a 2010 US Court of Appeals ruling. In April 2014, the FDA, using tools provided through the Tobacco Control Act to regulate tobacco products but not specifically e-cigarettes, proposed to subject e-cigarettes to regulatory oversight. The FDA proposed to prohibit the sale of e-cigarettes to individuals younger than 18 years, require the display of health warnings on packaging, ban dispensing in vending machines, prohibit the provision of free samples, require registration of products and ingredients by manufacturers, and require scientific evidence before making harm reduction claims.⁸ At the writing of this article, no decision has been made as to any potential changes in FDA regulation of e-cigarettes. The Tobacco Control Act does not preempt state or local policies, and more than half of the states in the United States have taken the initiative to regulate e-cigarettes in the absence of federal regulation.⁹

PREVALENCE OF USE

Nearly 6% of all US adults and 21% of US adult smokers have tried e-cigarettes.¹⁰ Among US middle and high school students, 50.3% are aware of e-cigarettes,¹¹ and the percentage reporting use of e-cigarettes increased from 4.7% in 2011 to 10.0% in 2012 (Figure 2).¹² Data from the United States, United Kingdom, Canada, and Australia suggest that almost half of current and former smokers are aware of e-cigarettes, and awareness is predictably higher in countries where these products are legal (73% in the United States vs 20% in Australia).¹³

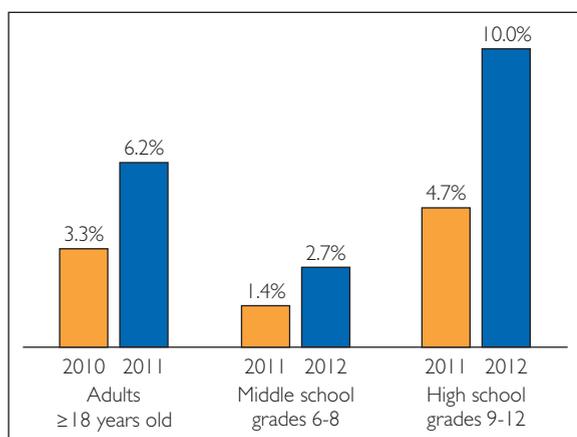


FIGURE 2. Changes in electronic cigarette use over time. For adults, data are from the HealthStyles Survey 2013.¹⁰ For middle school and high school students, data are from the National Youth Tobacco Survey 2013.¹²

Current e-cigarette use is higher among both nondaily smokers and heavier smokers (≥ 20 cigarettes per day) than among daily smokers and smokers of fewer cigarettes.¹³ More than three-quarters of current and former smokers consider e-cigarettes less harmful than conventional cigarettes.¹³

Among US middle and high school students reporting having ever used e-cigarettes, 20.3% reported never smoking conventional cigarettes.¹² The use of e-cigarettes among nonsmoking youth is associated with increased intentions to smoke cigarettes.¹⁴ Adolescent e-cigarette users are more likely to be male, white, and older¹⁵ and to have more education.¹⁶ Experimentation with e-cigarettes may be associated with adolescent sensation seeking,¹⁷ and adolescent e-cigarette use is unlikely to be related to tobacco reduction or cessation behavior.

SAFETY

Considerable variability exists among different e-cigarette products,¹⁸ adding to the complexity of trying to counsel patients regarding their safety. Currently available data on the safety of e-cigarettes are limited and inconsistent.

Self-reported adverse events have been identified during randomized clinical trials and longitudinal studies. The longest duration of systematic follow-up of patients using e-cigarettes has been 24 months.¹⁹ Clinical trial data have found no significant differences in adverse events between e-cigarette use and

nicotine patches.²⁰ Consistent with this, other clinical trials have reported either clinically minor adverse events with the use of e-cigarettes (eg, mouth irritation, cough, and nausea)²¹ or lower rates of adverse events than conventional cigarettes.²²

The FDA has received reports of both minor adverse events associated with the use of e-cigarettes, including headache, chest pain, nausea, and cough, and major adverse events, such as hospitalizations for pneumonia, congestive heart failure, seizure, rapid heart rate, and burns related to routine use.²³ Case reports of lung disease attributable to the use of e-cigarettes have also been published.^{24,25} Importantly, direct causality has not been established for any of these symptoms and cases, and some may be related to preexisting medical conditions. Data collected through online e-cigarette forums suggest that adverse effects occur most often in the mouth, throat, and respiratory, neurologic, sensory, and digestive systems, with some symptom improvement occurring in the respiratory system.²⁶

Results of laboratory experiments also provide evidence that e-cigarette use may be associated with adverse health consequences. In a study evaluating the immediate effects of e-cigarettes on pulmonary function among 30 healthy smokers, 5 minutes of e-cigarette use was associated with significant increases in lung airflow resistance.²⁷ Another study assessed the cytotoxicity of e-cigarettes on embryonic and adult cells and discovered evidence of decreased cellular survival due to the flavoring agents,²⁸ suggesting that the flavoring agents, not the nicotine, are the potentially harmful ingredients in e-juice. Cinnamaldehyde has been specifically identified as a highly cytotoxic substance in cinnamon-flavored refill fluids.²⁹ The FDA has detected levels of carcinogens and toxins, such as diethylene glycol, a harmful ingredient found in antifreeze, in laboratory analyses of 18 flavors and various cartridge types of e-cigarettes.³⁰ Diacetyl and acetyl propionyl, approved for food use but associated with respiratory disease when inhaled, have been found in sweet-flavored e-juice.³¹

E-cigarettes can also have adverse health effects on nonusers. E-cigarettes may be a potential source of thirdhand exposure to nicotine,³² and e-cigarettes with tank systems producing more vapor may increase this exposure. Importantly,

the number of calls to poison centers involving unintentional exposure to e-cigarettes and e-juice, including ingestion, inhalation, or skin absorption by young children, has increased markedly as e-cigarette use has proliferated.³³ The lethal dose of nicotine to a previously unexposed person is approximately 0.5 to 1 g,³⁴ and bottles of nicotine solution that contain this amount of nicotine can be purchased over the Internet for home mixing.

Cases of individuals being injured by exploding lithium batteries have also been reported in the news. Some lithium batteries are poorly designed, contain low-quality materials, or have manufacturing flaws and defects. Improper use and handling of these batteries can contribute to thermal runaway, where the internal battery temperature increases and causes fires or explosions.³⁵ Some of these explosions have resulted in house and car fires and severe skin burns.

The perception that e-cigarettes are safer than conventional cigarettes may increase their use during pregnancy.³⁶ The cytotoxic effects associated with e-cigarette refill fluids on stem cells could translate into embryonic loss or developmental defects.²⁸ More needs to be understood about the risks associated with embryonic exposure to the chemical constituents in e-cigarettes.

EFFICACY FOR SMOKING CESSATION

Direct claims about cessation efficacy are prohibited by law, but it has been easy for e-cigarette manufacturers to make indirect claims about cessation through product user testimonials. Case reports³⁷ and a small prospective study³⁸ have suggested potential efficacy for e-cigarettes as an aid to smoking cessation.

Only 2 large randomized clinical trials evaluating the efficacy of e-cigarettes for smoking cessation and reduction have been published. In a 12-month randomized clinical trial of 300 cigarette smokers not intending to quit tobacco, participants were randomized to 1 of 3 e-cigarette groups: (1) a 12-week supply of 7.2-mg e-cigarette nicotine cartridges, (2) a 6-week supply of 7.2-mg e-cigarette nicotine cartridges and then a 6-week supply of 5.4-mg e-cigarette nicotine cartridges, and (3) a 12-week supply of cartridges that contained no nicotine.²² Decreases in cigarettes smoked per day and exhaled carbon monoxide levels were observed across all 3 groups. At the end of the treatment period, the

percentage reduction in cigarettes per day was 26%, 20%, and 21% for the 3 groups, respectively. Tobacco abstinence rates at 12 weeks were 11%, 17%, and 4%, respectively ($P=.04$). However, no significant differences were observed between the groups at 6 and 12 months. Another clinical trial randomized 657 smokers wanting to quit to 16-mg nicotine e-cigarettes, 21-mg nicotine patches, or placebo e-cigarettes.²⁰ Low-intensity behavioral support was provided via voluntary telephone counseling. Smoking abstinence was confirmed by measuring exhaled carbon monoxide levels. At 6 months, biochemically confirmed smoking abstinence was 7.3% with nicotine e-cigarettes, 5.8% with nicotine patches, and 4.1% with placebo e-cigarettes. No significant differences were observed in the study groups. Notably, the quit rates in this study were comparable to quit rates observed in studies of over-the-counter nicotine replacement therapy when minimal or no behavioral support is provided.

KNOWLEDGE GAPS

Continued efforts are needed to track the adoption and use of e-cigarettes in the population so we can understand how e-cigarettes positively and negatively affect tobacco use patterns. Consistent data on the safety and efficacy of e-cigarettes for increasing long-term (≥ 6 months) smoking abstinence are also needed. The potential efficacy of e-cigarettes for the treatment of tobacco dependence will predominantly depend on the route, speed, and amount of nicotine delivery. Early human laboratory studies observed that e-cigarettes delivered very little nicotine, although they suppressed symptoms associated with tobacco abstinence and were associated with increased subjective acceptability ratings.³⁹ Subsequent studies found better nicotine delivery and suggest that nicotine delivery increases with longer durations of e-cigarette use by experienced users.⁴⁰ New generation e-cigarette devices appear to deliver nicotine more efficiently.³

Little is known about the concentration of nicotine required to approximate the nicotine delivery of conventional cigarettes. Investigators have proposed that the concentration of e-juice in an e-cigarette cartridge needs to be 50 mg/mL to approach nicotine delivery from smoking.³ However, decisions are being made about the upper limits of fluid concentrations based on relatively few data. For

example, a new regulation in the European Union has set an upper limit of 20 mg/mL of nicotine in liquids. This regulation potentially places an arbitrary ceiling on nicotine delivery from e-cigarettes. Uncertainty remains as to the potential effect of increased nicotine delivery with e-cigarettes on the likelihood of dual use (ie, using e-cigarettes and conventional tobacco).

CLINICAL CONSIDERATIONS

Policy makers and tobacco control advocates embrace a concept known as the continuum of risk.⁴¹ On one end of this continuum are conventional cigarettes; on the other end is medicinal nicotine replacement therapy. Somewhere on this continuum is the e-cigarette, but we do not know exactly where it is. If clear and convincing evidence can be produced that e-cigarettes are safe for long-term use and can increase smoking abstinence among patients who want to quit use of conventional cigarettes, the overall net health benefit across the population could be positive. However, if e-cigarettes either increase or have a neutral effect on the prevalence of smoking by undermining cessation, harm across the population could be increased.

For the practicing clinician, the American Heart Association suggests that clinicians should not recommend e-cigarettes as primary cessation aids, and if a patient is using e-cigarettes, he/she should be advised to consider a quit date for using them and not plan to use them indefinitely.⁴² The American Heart Association also suggests that if initial treatment fails in a patient or a patient has refused conventional treatments and wishes to use e-cigarettes to aid quitting that it "is reasonable to support the attempt."^{42,p1427}

Dual use of e-cigarettes and conventional tobacco remains a significant concern. Many smokers who use e-cigarettes will likely reduce their smoking rate without actually achieving tobacco abstinence, undermining tobacco abstinence, and prolonging exposure to tobacco. Smoking reduction is arguably not a relevant clinical outcome because a significant increase in tobacco-related risk occurs at low levels of exposure. As clinicians, we should remind our patients who smoke that a reduction in the number of cigarettes smoked should only be a waypoint on the journey to complete tobacco abstinence. This clinical conviction emanates

from the nonlinear relationship between exposure to cigarette smoke and cardiovascular risk. Although the excess risk of ischemic heart disease from actively smoking 20 cigarettes per day is 80%, the excess risk in smokers of 5 cigarettes per day is approximately 50%.⁴³ Even secondhand smoke is associated with a significant increase in cardiovascular risk. No safe level of tobacco smoking exists. Higher smoking abstinence rates can be achieved than those observed in the e-cigarette randomized trials by providing first-line pharmacotherapies combined with more intensive behavioral support.

CONCLUSION

Clinicians are ethically obligated to promote smoking cessation using evidence-based treatment strategies. Smokers will ask about e-cigarettes, and we must be prepared to offer appropriate counseling. With the evidence available to date, clinicians must be circumspect in recommending e-cigarettes for use by cigarette smokers interested in quitting smoking for the following reasons:

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 (ie, 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. Short-term safety data suggest they may cause airway reactivity.
5. The long-term health risk of exposure to e-cigarette constituent chemicals is unknown.
6. No regulatory oversight, such as requirements for good manufacturing practices, is currently in place for e-cigarette devices or e-juice.

More clinical safety data and increased product reliability and regulation are needed before e-cigarettes can assume a place in the standard clinical approaches to the treatment of tobacco dependence.

Abbreviations and Acronyms: FDA = Food and Drug Administration

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