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E-cigarettes: An Up to Date Review and Discussion of the Controversy

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Abstract
Electronic cigarettes (e-cigarettes) present a novel method for nicotine delivery that is reportedly advantageous when compared to traditional cigarette usage. Manufacturers and consumers claim reduced chemical exposure, decreased symptom profiles, and efficacy in smoking reduction and cessation greater than conventional nicotine replacement therapies (NRT). However, these products present new challenges and concerns to legislators, clinicians, and public health advocates.

Questions of authority in state and federal legislation, establishing product quality control, assessing long-term studies on e-cigarettes and quantifying usefulness in harm reduction represent only a portion of the many unanswered topics being discussed. The purpose of this article is to assess the literature on e-cigarettes and establish perceptions and attitudes on this controversial subject.

Introduction
Electronic cigarettes (e-cigarettes) are a recent addition to the marketplace of tobacco products, fitting into the broader category of electronic nicotine delivery systems (ENDS). First patented in the 1960s, manufacture of the modern e-cigarette did not begin until 2004 when Chinese company Ruyan® produced a prototype electronic device capable of emulating the subjective experience of smoking while delivering nicotine in the absence of burning tobacco. They began circulating internationally as early as 2007-2008, gaining the reputation as a safer alternative to conventional cigarettes while offering a socially acceptable way to mimic smoking in smoke-free environments.

These products are designed to resemble their conventional tobacco counterparts but deliver nicotine through vaporizing a humectant carrier, the most common of which is propylene glycol, and can be mixed with flavorants. Devices consist of a disposable nicotine-containing cartridge, a heating element, a flow trigger, battery, and LED light. Nicotine along with the propylene glycol humectant and any flavorants are drawn from the cartridge towards the heating element as the user applies suction to the mouthpiece. This activates the flow trigger and exposes the contents of the cartridge to the heating element, vaporizing the nicotine solution into a mist that is inhaled. The LED light serves as an indicator for when the flow trigger is open and mimics the burning end of a tobacco cigarette.

ENDS sales in the United States started as early as 2007, mostly with internet sales. As popularity of these devices grew, they started appearing in shops and mall kiosks, drawing attention of state and federal regulators who established complicated and non-uniform regulations on e-cigarettes. While there are claims reporting markedly less chemical exposure compared to tobacco cigarettes and suggesting usefulness in smoking cessation strategies, there remain many issues to be addressed: questions of legal authority, the absence of consistent quality control, long-term studies of safety, and usefulness in nicotine harm reduction.

While attitudes towards ENDS devices remain mixed, they are a quickly evolving source of interest. A search of NCBI’s PubMed database using the search terms “e-cigarette” and “electronic cigarette” yielded 102 and 495 search results, respectively. The literature on the subject remains equivocal in many respects and subjective data is only beginning to be published. What is certain about electronic cigarettes is that they pose a significant area for continued research.

E-Cigarette Culture and User Expectations
Electronic cigarettes are marketed strongly in television, and movies. These products are presented as harmless devices that aid in smoking cessation and find their way onto shows such as ‘The Doctors’ and ‘The Late Show with David Letterman.’ Advertisers market...
just as heavily to the celebrities as they do to the common consumer, going so far as to make e-cigarettes gifts at the Grammy Awards. However, unique amongst other tobacco products is the presence of e-cigarettes on the internet. By 2010, Google internet searches for ENDS increased dramatically. Fifty to seventy five percent of these searches in the United States were directed towards sites specifically dedicated to selling these products and of the top Google search results for e-cigarettes, eight of the first ten were online distributors.

An entire culture has sprung up surrounding the use of e-cigarettes, with users self-identifying as “vapors” and enthusiastically embracing activities related to the use of ENDS and in some cases acting as what one study referred to as unpaid evangelicals. Internationally, the United States has one of the most informed populations regarding e-cigarettes and those most likely to have heard of e-cigarettes are white males who are heavy smokers and are young, educated, have higher income, and have at least one close friend who smokes tobacco. Use has been reported to mirror similar variables however other research suggests that despite hearing of such products less often than their well-educated male counterparts, female current smokers with less than a high school education and of lower socioeconomic status are more likely to have tried an e-cigarette.

Those who try such products usually are in their teens or twenties but continued use correlates with higher educational status. Non-daily smokers are, according to one study, twice as likely to try e-cigarettes than daily smokers and if perceived to be less harmful than tobacco cigarettes are over four times more likely to try ENDS. Non-daily smokers make use of e-cigarettes more than daily smokers and both use them more than those who recently ceased tobacco use. Awareness of e-cigarettes is on the rise, with a doubling of awareness and a quadrupling of ever use from 2009 to 2010 but use of ENDS products occurs less often in the Southwest United States compared to other states.

Adolescents between the ages of 11 and 19 have reported awareness of e-cigarettes and among those individuals eighteen percent have expressed a willingness to try them. Use among middle and high school students has approximately doubled from 2011 to 2012 with about 1.78 million students in 2012 having ever tried an e-cigarette. Furthermore, while older users of e-cigarettes are more likely to use these products as a means for tobacco cessation, college users do not appear to be motivated by a desire to quit. A South Korean study reports that...
among adolescents, in addition to the propensity for males to try e-cigarettes reported elsewhere.\textsuperscript{34} Other precipitating factors include peer influence, dissatisfaction in school life, and a previous history of cigarette use.\textsuperscript{35} This growing trend of e-cigarette experimentation among minors presents concerns of e-cigarettes serving as gateways to nicotine addiction.\textsuperscript{3,38}

Users of e-cigarettes cite numerous reasons for their continued use and most report overall satisfaction with their devices.\textsuperscript{42} Chief among these is the belief that e-cigarettes present a reduced risk of harm when compared to tobacco cigarettes.\textsuperscript{3,7,34,36,42} E-cigarettes are perceived to decrease tobacco cigarette use \textsuperscript{3,8,36} and ultimately maintain tobacco cessation and abstinence in a large number of cases.\textsuperscript{3,7,8,42} The biobehavioral feedback mechanisms simulated by vaping, the term for smoking an e-cigarette, are also cited as reasons for e-cigarette use, noting that these devices are able to address the oral fixation seen in current and former smokers, successfully mimicking the sensation of smoke against the throat (a term called “throat-hit”), copying the gestures and actions seen in conventional cigarette use, and alleviating symptoms of craving and withdrawal.\textsuperscript{3,8,33,42} Numerous health benefits are attributed to a transition from tobacco to e-cigarettes including respiratory improvement, decreased cough, reduced weight gain after tobacco cessation, and increased exercise tolerance.\textsuperscript{3,8} Smokers also highlight reductions in loss of smell and taste, the avoidance of tobacco odor on clothing, and absence of smoker’s breath.\textsuperscript{3,33} Less significant reasons are absence of any open flames during product use, cheaper overall price, avoiding bothering other people with cigarette smoke, dealing with smoke free situations, and serving as a complete alternative to smoking.\textsuperscript{3,7,42} Not all reasons cited for the use of ENDS products are a reduction in negative effects of tobacco products. Many users reported positive aspects of ENDS usage including social benefits through a sense of belonging to an online vaping community, hobby elements as users purchase and customize their e-cigarettes, and establishing a sense of personal identity in calling themselves vapers.\textsuperscript{15,33} Many e-cigarette users enjoy modifying (or “modding”) their products to include larger batteries for fewer charges between uses or to sustain larger amounts of vapor for larger throat hits.\textsuperscript{3}

While users are quick to point out that these devices can help achieve a successful nicotine taper, they are firm in drawing the distinction between smoking cessation and nicotine cessation. Eliminating the harmful effects of cigarettes while still maintaining the ‘good’ effects of nicotine is seen by users as a desirable outcome.\textsuperscript{33} Although similar to the goals of conventional nicotine replacement therapies (NRT) and in many instances used similarly by former smokers to avoid relapses or to bolster smoking cessation,\textsuperscript{42} users of ENDS report a stronger preference to the e-cigarette with fewer reported side effects.\textsuperscript{7,8,33,42}

**Positive Data Findings on E-Cigarettes**

Although there is relatively little data to objectively lend credibility to assertions of harm reduction, the data available does show promise. Whereas up to 80% of individuals who use conventional NRT for smoking cessation return to smoking by one year,\textsuperscript{9} e-cigarettes may help reduce the number of cigarettes smoked, maintain abstinence at six months after initial purchase, and reduce dependence on nicotine.\textsuperscript{22} While some studies report only modest improvements, likening their use to nicotine patches\textsuperscript{23} smokeless tobacco including e-cigarettes is reported to be 90-99% less deadly than tobacco cigarettes\textsuperscript{24} and effective at delivering nicotine into the blood, decreasing withdrawal symptoms associated with smoking cessation.\textsuperscript{24} E-cigarettes may decrease tobacco cigarette consumption in those who have no intention to quit smoking while maintaining a reduced side effect profile compared to tobacco cigarettes.\textsuperscript{1,3,25-31} Interestingly, the abstinence induced by these products seems to be irrespective of nicotine concentration\textsuperscript{25} once again strengthening the possible explanation that this is due to the biobehavioral feedback mechanisms mimicked in e-cigarettes compared to other forms of NRT.\textsuperscript{3,31}

Furthermore, e-cigarettes have been effective in treating patients who are refractory to all other forms of tobacco cessation.\textsuperscript{43} Public health has also seen improvements with e-cigarettes. In Sweden the introduction of smokeless tobacco products including e-cigarettes has greatly decreased smoking related fatalities.\textsuperscript{13} American studies also report the public health benefits of e-cigarettes as a harm reduction strategy compared to traditional tobacco cigarette usage.\textsuperscript{3,4,31,44} These series of studies admit it may be premature to make sweeping conclusions, but they feel that there are no serious health concerns when compared to traditional cigarette use due to drastic reductions in harmful toxicants by an order of anywhere from 9-450%.\textsuperscript{44} Analyses of e-cigarette vapor yielded reductions in nicotine, carbon monoxide, tobacco specific nitrosamines (TSN) including N’-nitrosornornicotine (NNN), N’nitrosoanatabine (NAT), N’tobalabasine (NAB), and 4-(methylthiobalobino)-1-(3-pyrindyl)-1-butane (NNK), carbonyl compounds including formaldehyde, acetaldehyde, acrolein, and o-methylbenzaldehyde, volatile organic compounds such as toluene and pim-xylene, the metals cadmium, nickel, and lead, and polyaromatics.
hydrocarbons.\textsuperscript{44,45} When compared to the emissions found in tobacco cigarettes, authors of these articles claim these levels pose no apparent risk to human health.\textsuperscript{45}

**Negative Data Findings on E-Cigarettes**

While there may be benefits to e-cigarette usage, there are still drawbacks and consequences. Currently e-cigarettes lack regulation of manufacture, enforcement of sanitary conditions, guidelines in handling pharmaceutical-grade ingredients, and incomplete or absent listing of constituents.\textsuperscript{3} The most egregious of these offenses is the lack of quality control, with brands having wildly different concentrations of nicotine.\textsuperscript{46,47} Products listed as having no nicotine reveal significant concentrations upon analysis.\textsuperscript{3,6,48} There are even products claiming to possess E-Cialis (tadalafil) and rimonabant for erectile dysfunction and dieting, respectively, without ever assessing the validity or safety of such claims.\textsuperscript{48} Among the chemicals known to be present in e-cigarettes, propylene glycol presents possible carcinogenic concerns\textsuperscript{6} and initial exposure causes sore throat, dry cough, and dizziness.\textsuperscript{3,48} Other humectants such as glycine and diethylene glycol, not advertised as present in e-cigarettes, are also found and present health concerns in poorly quality controlled settings.\textsuperscript{6} However the FDA reports that in the measurements it has made on a limited number of products it has not found lethal concentrations of these substances.\textsuperscript{3} Other miscellaneous irritants including butyl acetate, diethyl carbonate, benzoic acid, quinolone, diocyl phthalate, and 2,6-dimethyl phenol were also found as unlisted ingredients but have unclear significance.\textsuperscript{6} “Passive vaping,” a form of second-hand smoke for e-cigarettes, has also been confirmed however it too is in early stages of study.\textsuperscript{50}

Additional product concerns include fluid leaks from cartridges, difficulties assembling apparatuses without spilling nicotine fluid, poor labeling, poor or absent instruction on how to properly dispose of spent cartridges, failed safety features, baseless claims, and errors in filling orders.\textsuperscript{5,10} Furthermore, whereas traditional cigarettes have only 1-2 mg of nicotine each, nicotine cartridges carry far greater concentrations. With lethal doses of nicotine anywhere from 30-60 mg, there is concern that children or even adults may accidentally expose themselves to its effects.
themselves to fatal overdoses if not properly handling their devices.6,17,31

Of concern is the use of e-cigarettes among children and populations heretofore abstinent from nicotine products. Companies have been known to distribute free samples3 and there are concerns that these will encourage novices to become addicted to what they perceive as a safer smoking product.4 Children are targeted for addiction with the addition of flavorants including strawberry and chocolate to mask the otherwise bitter taste of the product.5,38,40

Legislation

Currently e-cigarettes are in a state of legal ambiguity. The FDA met resistance from the DC Circuit Court in the 2011 case Sottera Inc. v. FDA, in which the court ruled that e-cigarette regulation at the federal level is outlined according to the 2009 Family Smoking Prevention and Tobacco Control Act and not the Federal Food, Drug, and Cosmetic Act (FDCA). While the FDA attempted to regulate and control the sale of e-cigarettes, claiming they were in fact misbranded drug device combinations and thus deserving of regulation as medical devices, Sottera Inc. successfully appealed that the FDA can only regulate tobacco products marketed as therapeutic. In so doing, the court prohibited the FDA’s ability to effectively regulate these devices, drastically hindering any efforts to ensure quality control or safety.11,12,16,19

It took three years to overcome this setback, but, in April 2014, the FDA proposed a rule to extend their authority to include regulation of additional tobacco products including e-cigarettes. Importantly, the new rule would allow the FDA to prohibit free samples, limit the sale of the products to adults, and limit any health claims to those supported by scientific evidence.52

States have been able to take local action to regulate the sale and use of e-cigarettes to a degree, mirroring laws in place for traditional tobacco products. California, Utah, and New Jersey do not allow the sale of ENDS to minors and Oregon does not sell ENDS at all. New Jersey and New York ban the sale and public use of the devices.11 The United States Air Force bans the devices on their premises.54

Conclusion

Presently there is a scarcity of trials with long term follow up of e-cigarette use 2 and an absence of nonclinical, animal, clinical, and public health studies to draw sufficient conclusions to make definitive statements.52

Until these studies are performed, clinicians should advise patients that there is not enough evidence to definitely say that these products are safe or effective to use for smoking cessation.2

References


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CME Post-Test

1. Awareness of e-cigarettes in the US quadrupled from 2009-2010
   True False

2. Forty to fifty-five percent of Google searches for e-cigarettes are for sites selling the devices
   True False

3. Use among middle school and high school students ever trying e-cigarettes doubled from 2011-2012
   True False

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