



E-Cigarettes: Different But Not Safe

The pressing need to assess the health risks of
e-cigarettes in the face of rising teen use

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Rapidly rising teen use underscores the need for effective risk communication to adolescents

It's only halfway through first period of 9th grade biology class, and Tess is already itching to leave. She raises her hand to go to the bathroom and checks her pocket to make sure the small, flash drive-shaped device is there. Once inside the bathroom stall, she takes a puff, exhales, and watches the vapor fill the small space around her. Blowing out the thick cloud was something she had liked from the very beginning. She started vaping because the older girls in her group of friends were doing it. They'd told her she could get the liquid without nicotine, and that it was only water vapor. She'd gotten an old device from one of the girls and started swiping liquid from her older brother. The label said the nicotine level was low, certainly not enough to be addictive. Tess tried to stick with liquids that were labeled with no, or low levels of nicotine, but now she could barely make it through a full class without feeling like she needed to take another hit.

Introduction

The 1965 patent for an electronic cigarette (e-cigarette) lauded its potential to help smokers quit tobacco. Over the past several years, the popularity and use of e-cigarettes has exploded. However, the demographics of e-cigarette users have shifted from adult conventional cigarette users trying to quit smoking to rapidly increasing numbers of first users amongst high school and even middle school students. The sharp rise in e-cigarette use amongst this vulnerable

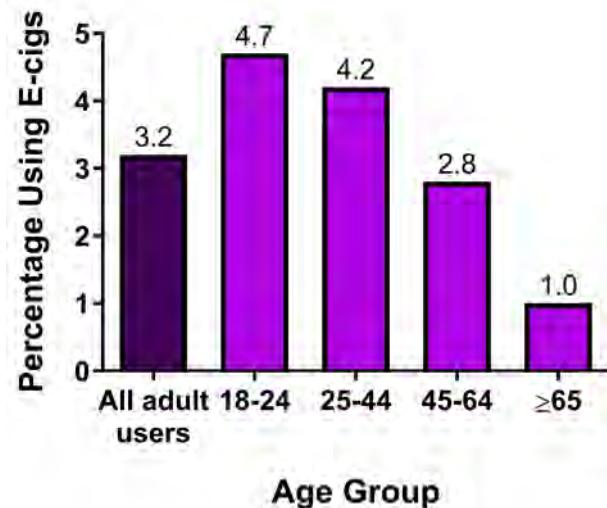


Figure 1: Amongst adults in the U.S. who use tobacco products, e-cig usage is more prevalent in younger adults than older adults. Data modified from National Health Interview Survey, 2016.

population, combined with growing concerns of health risks associated with vaping (defined as inhaling and exhaling vapor produced by an e-cigarette), underscore the pressing need for strategies to effectively communicate the risk of e-cigarettes to adolescents, parents, teachers and healthcare providers.

What is an e-cigarette?

E-cigarettes, or e-cigs, which are also known as electronic nicotine delivery systems (ENDS), are battery-powered devices intended to deliver nicotine by heating a liquid solution to form an aerosol, which is then inhaled in a fashion that mimics smoking. In contrast, conventional

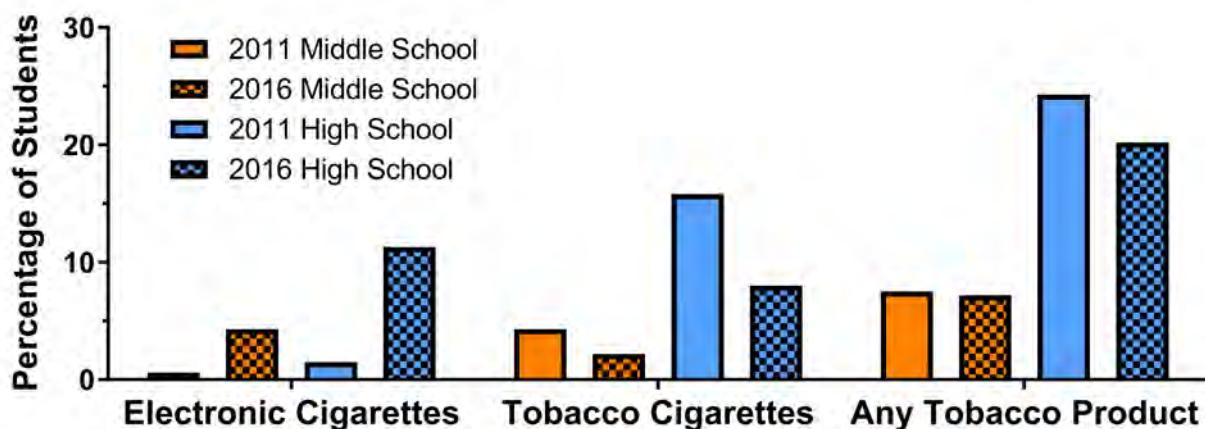


Figure 2: Tobacco product use by middle and high school students. Adolescent users of e-cigarettes compared to other tobacco products have increased in both middle school and high school populations. In contrast, conventional cigarette usage has decreased in both populations. Data modified from Centers for Disease Control and Prevention Mortality and Morbidity Weekly Reports, 2011 and 2016

cigarettes contain tobacco leaves that undergo chemical combustion to produce smoke that delivers nicotine. The e-cig was originally conceived as a hand-held device that aerosolized nicotine to prevent exposure to carcinogens produced by burning tobacco. The devices have evolved from the first-generation designs produced and tested in the consumer market in 2004, which were similar to conventional cigarettes in appearance, to the currently marketed compact devices that are more discrete, as exemplified by recent models that look similar to thumb drives. Additionally, the market is offering an increasing variety of e-liquids, or e-juices, the nicotine-containing solution inside of an e-cig, which is often supplemented with diverse chemical flavorings and additional chemical solvents.

The rapidly changing demographics of e-cig users

While e-cigs were originally intended to replace or reduce conventional cigarette use by adult smokers, demographic data from the U.S. indicate that the predominant users amongst adult consumers of tobacco products are young adults from age 18-24 (Figure 1). As these users continue to use e-cigs, the

percentage of users in the older age groups is expected to increase. Of concern is the rapid increase of e-cig use amongst high school, and even middle school, students (Figure 2). Conventional cigarettes have all but disappeared in high schools around the U.S., but they are being replaced in the pockets of teenagers by e-cigs. Indeed, e-cigs have become the most popular tobacco product among high school students. A recent survey from a Colorado high school estimated that 42% of students vaped, and 38% of those students felt they were addicted to nicotine.

Most adolescent e-cig users are first time tobacco product users. This demographic is attracted to these products in part because of the slick marketing, which includes the modern appearance of the devices – Juul brand e-cigs, which are currently the most popular e-cig on the market, are sleek, inconspicuous, and go largely unrecognized amongst teachers and parents – and the wide range of added flavorings, such as cherry, vanilla, and buttered popcorn, which are packaged to resemble popular food products (Figure 3). However, a major factor driving increased use amongst teenagers is their widespread belief that e-cigs are safe.

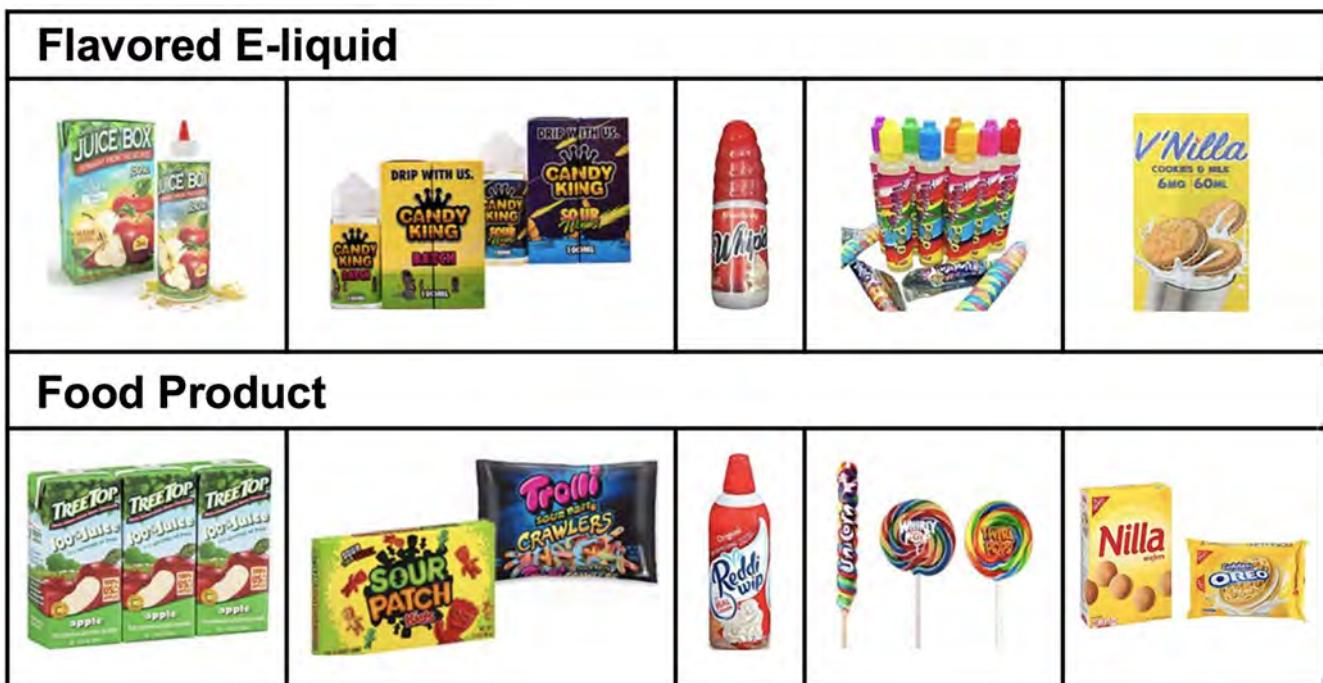


Figure 3: Packaging of flavored e-liquids resembles that of commercially available food products. Examples of vaping products flagged by the U.S. Food and Drug Administration for using packaging that resembles that of juice boxes and candy. These products, which appeal to younger e-cig users, do not contain childproof safety locks to prevent accidental ingestion. Images adapted from FDA Newsroom.

Myths about e-cig safety

Studies of young adults who use e-cigs indicate a predominant reason they started using e-cigs was their perception that e-cigs are safe, especially compared to other tobacco products. They believe that e-cigs not only pose fewer health risks to the user, but also that secondhand emissions are less toxic to non-users.

Unfortunately, neither of these perceptions is supported by empirical evidence (Figure 4). One factor contributing to these misconceptions is the wide-spread belief that e-cigs do not contain tobacco; however, e-juices often contain ingredients from tobacco plants, including the addictive compound nicotine.

Another myth is that all the ingredients in e-juice are safe, e.g., "it is just water vapor". However, e-liquids are comprised mostly of glycerol and propylene glycol. While generally regarded as safe for ingestion as foods, heating these chemicals promotes their breakdown into more toxic compounds such as formaldehyde and acrolein (Figure 5). Moreover, propylene

glycol is a known lung irritant that causes airway dehydration. E-liquid flavorings are a major draw for adolescent users, but some flavorings may be hazardous to human health. The buttered popcorn flavor molecule, diacetyl, can cause an irreversible pulmonary disease, bronchiolitis obliterans, which is characterized by airway obstruction. Cinnamaldehyde, the spicy flavoring molecule used in cinnamon flavored e-liquids, is toxic to cultured lung epithelial cells. Although there is not yet sufficient evidence to identify flavorings as carcinogens, many modify proteins and DNA in experimental models.

The physical components of the e-cig device, such as the heating coils and battery, pose additional hazards. If constructed or used improperly, heating coils can leach metal ions into the aerosol that are known to be toxic to humans. Battery design and safety is another concern. Faulty e-cig batteries can overheat and explode during use, transport, and charging, which has resulted in severe burns to the user and fires in the surrounding area.



FACT: E-cig aerosols are heated propylene glycol and glycerin.

FACT: Many e-cig aerosols contain detectable levels of metals, acrolein, and formaldehyde, and have similar PM_{2.5} levels as conventional cigarettes.

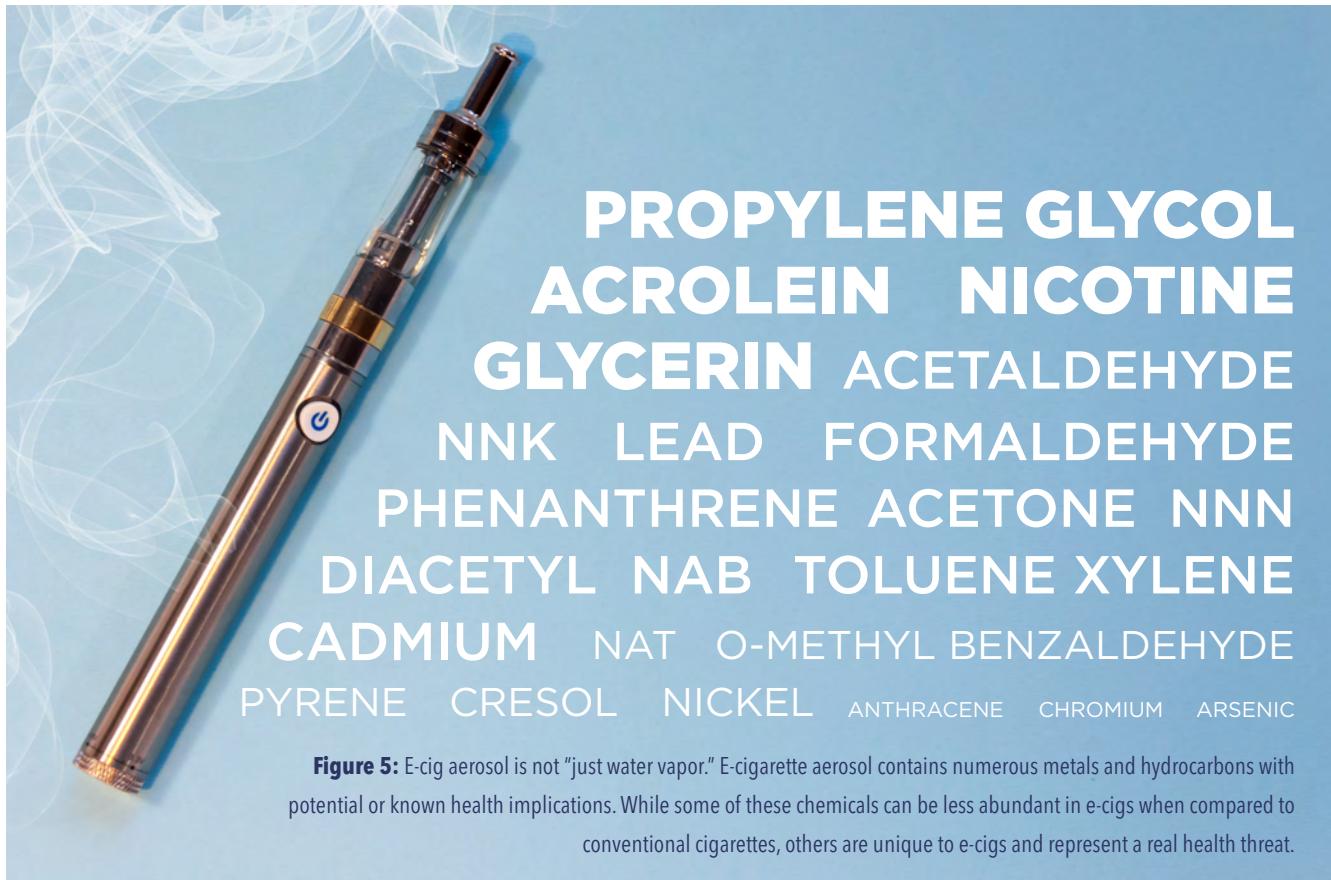
FACT: Exhaled e-cig aerosols contain fractions of the original vapor as well as metabolites that can be inhaled by others and stick to surfaces. This includes nicotine and its carcinogenic derivatives.

Figure 4: E-cig myths and facts. Many statements made in the defense of e-cigarette usage do not withstand scientific scrutiny. While e-cigarettes may be a better alternative than conventional cigarettes, they should not be viewed as a safe option for non-smokers.

Regulation of e-cigarettes

During the early years of marketing to the public, e-cigs were unregulated, and even minors could purchase and use e-cigs. The 2009 Family Smoking Prevention and Tobacco Control Act (TCA) extended the authority of the U.S. Food and Drug Administration (FDA) to regulate all tobacco products in the U.S., including e-cigs and e-liquids. Under the TCA, the legal age limit for purchasing e-cigs was raised to 18, and a number of labeling and manufacturing guidelines and restrictions were instituted. However, implementation of these new regulations has been slow, with 3 to 5 years before compliance becomes mandatory, and tobacco companies have exploited loopholes in the TCA. Currently, there are no safety guidelines or regulations for the physical components of e-cig components.

The nicotine content of e-liquid is a key focus of FDA regulation. Unlike conventional cigarettes, which require selective breeding or chemical manipulation to alter nicotine levels, manufacturers of e-liquids can directly control the amount of nicotine in the product. Unfortunately, accurate labeling of e-liquid contents has not been mandated. Several studies have shown disparities between nicotine concentrations listed on the label and those in the e-liquid, with nicotine detected in e-liquids advertised as "nicotine free." In an effort to address nicotine addiction in the U.S., the FDA has issued an advanced notice of proposed rulemaking that focuses on reducing nicotine levels in conventional cigarettes to non-addictive levels. This legislation could serve as precedent for future regulation of nicotine levels in other tobacco products, such as e-cigs; it would also introduce standards for



testing and accurately reporting nicotine content on product labels.

Marketing of e-cigs: another concern

Debate has erupted over the marketing of e-cig products. Many of the promotions used by companies are appealing to young consumers. While it is impossible to prove that e-cig advertisers deliberately target teens, e-cig ads often feature themes of friendship, sex, and humor, and 32% percent of video ads employ youth actors. Additionally, an overwhelming number of video ads for e-cigs use production techniques known to be effective in capturing the attention of a younger audience, such as rapid editing, sound effects, and animation.

Social media also plays a key role in teen awareness of e-cigs. Not only are webpages a frequent location for e-cig ads, but certain sites have bots programmed to post phrases related

to vaping. Networking sites enable e-cig users to gather for conventions specifically dedicated to vaping, which have been shown to significantly increase nicotine residues on facility surfaces that persist for several days.

What are the health risks of electronic cigarettes?

While the health effects of tobacco smoke have been extensively studied and are widely known, the available information regarding the effects of e-cigs on human health, especially long-term effects, are relatively limited, in large part because the wide-spread use of e-cigs is relatively recent. The vaporization reaction of e-cigs is inherently different from the combustion reaction of tobacco cigarettes, yet studies have shown that e-cig vapor contains many of the same chemical constituents as the smoke from tobacco cigarettes, but at different concentrations. Thus, it is difficult to predict

PROS	CONS
<ul style="list-style-type: none"> Fewer hazardous chemicals than conventional cigarettes Flavorings, additives, and nicotine content are customizable and optional May be beneficial as a cessation product for current tobacco users Reduced environmental harm from tobacco combustion and cigarette butts Reduced health risks for current users of tobacco cigarettes who switch to e-cigs 	<ul style="list-style-type: none"> Contains hazardous chemicals not found in conventional cigarettes Similar PM_{2.5} profile to tobacco cigarettes Some flavorings are unsafe for inhalation Label reported nicotine levels are inaccurate Nicotine uptake is more efficient than conventional cigarettes, increasing risk of addiction High usage in first-time users introduces new predominantly adolescent demographic to potential nicotine addiction Environmental harm from disposable plastic cartridges and heating coils E-cig liquids pose poisoning risk due to lack of safety features E-cig mods can pose injury hazard due to battery heat, including explosion

Figure 6: Pros and cons of e-cigarette use.

whether the long-term health effects of e-cigs will be different or the same as tobacco smoke. However, the epidemiological studies and experimental investigations of aerosol exposure to laboratory animals or isolated cells published to date in the peer-reviewed literature suggest that e-cigs negatively impact human health. Health outcomes of concern include:

Poisoning. Nicotine is one of the most common chemicals in e-cigs. E-liquid solutions can contain up to 720 mg of nicotine, an amount that is twelve times higher than the oral lethal dose for children. The packaging of e-liquid solutions and e-cig cartridge refills mimic commercially available food products, which appeal to young children (Figure 3), and e-liquid containers do

not have child-prevention locks. Additionally, the FDA has released reports of children choking on e-cig cartridges.

Addiction. Upon inhalation, nicotine binds to nicotinic receptors in the human brain. There it promotes the release of dopamine and GABA, neurotransmitters interpreted by the brain as a reward, which promotes addictive behaviors. Activation of nicotinic receptors also releases opioids, which reduce pain sensation. Moreover, flavoring agents, such as menthol, bind to nicotinic receptors, which increases the addictive properties of nicotine.

Cardiovascular risks. Metals, chemical oxidants, particulates, and nicotine – all of which can be

found in e-cigs - are known causes of tobacco-induced cardiovascular effects. E-cig usage can acutely increase heart rate, and possibly diastolic blood pressure. Several studies have shown increased oxidative stress and inflammation in cultured cardiac tissue exposed to e-cig aerosol. Although there is currently no evidence that e-cig use is associated with long-term cardiovascular outcomes, given the recent introduction of e-cigs to the public, it may take years for adverse clinical outcomes to surface.

Oral health. Periodontal disease, a known outcome of long-term tobacco use, is characterized by inflammation, gum recession, ligament loss, bone reabsorption, and loss of teeth. Exposure to e-cig aerosol can cause inflammation, cell death and decreased cell viability in oral tissues. There are limited data from clinical studies indicating that switching to e-cigs from smoking tobacco may improve oral health; however, there is also evidence that vaping can adversely affect oral health in those who do not smoke tobacco.

Obesity. Although some reports indicate that vaping may help users to lose weight, others have linked e-cig use to obesity and related metabolic abnormalities. There is a clear relationship between e-cigs and hypertension, low HDL cholesterol, high triglyceride levels, and high fasting glucose, all of which are diagnostic criteria for metabolic syndromes, including diabetes. Vaping also worsens preexisting fatty liver disease. These effects occur even with nicotine-free e-cigs, but the lack of standardization of e-juices makes it challenging to determine which mixtures of chemicals are responsible for these effects.

Cancer. Although e-cigs have yet to be definitively linked to cancer, the combustion of tobacco products is the single greatest cause of cancer among adults. Many regions of DNA associated with tumor activity are active at similar levels in cells exposed to e-cig vapor vs.

conventional cigarette smoke. Cellular processes for repairing damaged DNA regions are impaired after exposure to e-cig aerosol, increasing the probability of mutations that generate or promote cancerous growths. In fact, there is emerging evidence that DNA damage is greater from e-cig aerosol than from conventional cigarette smoke.

Use during pregnancy. The use of nicotine-containing products during pregnancy is known to adversely impact fetal growth and development. While there are limited data specific to e-cigs, particularly in humans, maternal vaping, even in the absence of tobacco, has been associated with impaired learning and memory, increased impulsiveness, decreased anxiety, and hyperactivity in children. In lab animals, maternal exposure to e-cig vapor during pregnancy interferes with muscle and cartilage formation, resulting in craniofacial defects, and increases expression of neuropeptides that regulate food intake, thereby increasing obesity risk.

Conclusion

In summary, while data are just starting to emerge, numerous health risks associated with conventional cigarette use are being identified as possible adverse health outcomes of vaping. While some studies suggest that e-cigs mitigate problems associated with smoking tobacco in conventional cigarette users, these risk are not reduced to zero. It also seems likely there will be other risks that are unique to e-cigs, particularly in those who have not previously smoked conventional cigarettes (Figure 6). A major concern surrounding the cultural phenomenon of vaping amongst adolescents is the unique biological and psychological vulnerability of this population. It will be important to teach teens to be skeptical of information claiming that e-cigs are safe. Additionally, we need to stimulate serious discussions about the advertising, packaging,

child proofing, and safety of these devices to ensure that minors and young children are not only protected from accidental ingestion and involuntary exposure to e-cig aerosol and liquid but also not targeted as consumers. Once the risks are understood and the misconceptions laid to rest, the future of e-cigs may look different...and possibly safer.

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This eBook was written by the trainees and training faculty of the NIEHS T32 training program, "Advanced Training in Environmental Health Sciences", University of California, Davis (UC Davis), grant # T32 ES007059, <http://niehs.etox.ucdavis.edu/>

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