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Author

Chaffee, Benjamin W

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Electronic Cigarettes: Trends, Health Effects and Advising Patients Amid Uncertainty

Benjamin W. Chaffee, DDS MPH PhD

University of California San Francisco

Abstract

Dental professionals can be effective tobacco prevention and cessation partners. Electronic cigarettes (e-cigarettes), which deliver aerosolized nicotine but fewer toxicants than found in cigarette smoke, present new and contentious questions for clinicians, patients, and researchers. Evidence suggests e-cigarettes are not harmless but are less dangerous than cigarettes. Smoking cessation effectiveness is unproven and oral and systemic health effects remain under study. Dental professionals must stay informed to provide patients truthful information as new data emerge.

Introduction

The dental professional is well positioned to address tobacco use in clinical practice. Through frequent recall appointments, team-based care, and trusting patient partnerships, evidence-based tobacco cessation and prevention interventions delivered by dentists and other members of the dental care team are both effective¹ and associated with enhanced patient satisfaction.² However, dental professionals as a whole lag behind their medical peers in terms delivering advice to quit,³ often citing perceived patient resistance, lack of remuneration, and not knowing where to refer as barriers to engaging in tobacco cessation in practice.⁴ Professional training has been shown to improve dentists' attitudes and behaviors related to tobacco cessation.⁵ The American Dental Association (ADA), World Dental Federation, U.S. Public Health Service, and World Health Organization Framework Convention for Tobacco Control all strongly encourage that dentists actively engage in tobacco use prevention and cessation.^{6, 7} Given that patient counseling as brief as 10 minutes increases the probability of a successful quit attempt,⁶ the dental practitioner can address patient tobacco use even with minimal time investments.

Use of tobacco products, including cigarettes, cigars, and smokeless tobacco, wreaks havoc on the oral cavity, with potential consequences ranging from tooth staining and heavy plaque to periodontal disease, tooth loss, implant and surgical failures, and oral cancer.⁸ Approximately 15% of U.S. adults were current cigarette smokers in 2015, down from nearly 21% in 2005.⁹ Despite this meaningful progress, tobacco use remains the leading cause of preventable mortality nationally, causing 480,000 deaths annually.¹⁰ Eliminating tobacco use improves clinical outcomes and saves patient lives.

While cigarette smoking accounts for the vast majority of tobacco-related illness worldwide, dentists and other clinicians face a changing tobacco landscape. New and emerging tobacco products, policy and regulatory changes, and shifting use patterns all challenge the practitioner to look beyond cigarettes when discussing tobacco use with patients.¹¹

At the forefront of this new tobacco landscape are electronic cigarettes (e-cigarettes). These devices quickly rose in popularity in the early part of this decade,¹² with many users viewing them as a less harmful nicotine delivery alternative to combustible cigarettes. E-cigarettes have been met with no shortage of controversy and uncertainty. Reputable public health and medical organizations have taken contrasting stances.^{13, 14} Proponents tout e-cigarettes as a disruptive technology with the potential to save the lives of cigarette smokers who switch.¹³ More skeptical viewpoints note the unknown long-term health effects, limited data on effectiveness as a smoking cessation tool, and the potential to lure youth.¹⁴

Dental clinicians are certain to encounter patients using or considering use of e-cigarettes and will be expected to respond to patient concerns related to e-cigarette health effects, effectiveness for smoking cessation, and implications for dental treatment. However, patient surveys suggest that very few dentists discuss either the potential benefits or harms of e-cigarettes with their patients.¹⁵ This narrative review covers the current evidence related to e-cigarette health effects, systemically and orally, and use as smoking cessation aids. Practical suggestions for the dental clinician are provided, emphasizing the need to remain informed at this time of evolving e-cigarette science and policy.

Electronic cigarettes

E-cigarettes are capable of delivering nicotine without tobacco combustion.^{16, 17} These battery-powered devices create an inhalable aerosol, commonly called “vapor,” by heating a liquid mixture (e-liquid), which typically contains propylene glycol or glycerin, along with nicotine, flavorants, and other additives.¹⁶ E-cigarettes are known under many other names, including electronic nicotine delivery systems (ENDS), vapor pens, e-hookah, and vape pipes, and vary considerably in design. Use is often called “vaping.” The devices have been heavily marketed, frequently as a less harmful alternative to conventional cigarettes.^{17–19} E-cigarette aerosol has been found to contain ultrafine particles and known toxins, such as acetaldehyde, acrolein, toluene, and formaldehyde, albeit at much lower levels than found in cigarette smoke.²⁰

E-cigarette awareness and use expanded rapidly in the first half of this decade.^{12, 21, 22} By 2013–2014, 3.3% of U.S. adults had reported using e-cigarettes everyday or some days.²³ Use is higher among current cigarette smokers and also among young adults, LGBT individuals, and those of low socio-economic status.²⁴ One national study estimated that in 2014 nearly 15% of U.S. adults had ever used e-cigarettes, with greater use among young adults (23%), those earning <\$15,000 annually (23%), and those reporting self-perceived “poor” health status (27%), but with no statistically significant association with gender or race/ethnicity.²⁵ Since 2014, e-cigarettes have been the most common form of tobacco product used by U.S. middle and high school students, eclipsing conventional cigarettes.²²

E-cigarettes are highly heterogeneous and evolving in design (Figure). While often cited as invented by Chinese pharmacist Hon Lik in 2003, related devices had been under development by major cigarette companies years earlier.²⁶ Currently marketed e-cigarettes include “first generation” devices that resemble cigarettes in appearance (“cigalike”) and can be recharged or discarded after use.¹⁶ Slim, cigarette-shaped first generation e-cigarettes generally produce aerosol at a fixed puff duration or frequency, while larger “second generation” devices often include refillable e-liquid cartridges, more powerful batteries, and allow the user to adjust the length and frequency of puffs and activate the heating coil at the press of a button.¹⁶ Tank-type, including modifiable, “third generation” devices typically feature high capacity batteries, refillable cartridges, and greater ability for user control and customization, such as adjustable voltage or power, which influences the nicotine (and potential toxin) content of the aerosol produced.²⁷ Different e-liquid nicotine levels (including nicotine free) and flavorants²⁸ also contribute to the variability across e-cigarette products.

The Food and Drug Administration (FDA) officially announced its authority and intention to regulate e-cigarettes in 2016.²⁹ However, in 2017, the FDA announced that it would delay e-cigarette regulation until 2022.³⁰ In the absence of federal regulation, some municipalities have instituted local measures: for example, to extend clean indoor air laws to e-cigarettes or include e-cigarettes under restrictions on the sale of flavored tobacco products.³¹ Meanwhile, multinational cigarette manufacturers, who have developed and/or acquired e-cigarette brands,³² and independent e-cigarette companies alike are highly invested in an industry expected to reach \$47 billion globally by 2025.³³

Harm reduction and controversies

Using an e-cigarette is almost certainly less dangerous than smoking a cigarette. What remains contentious is: 1) *how* much less harmful an e-cigarette may be to the user; and 2) the net impact of widespread e-cigarette availability on society as a whole. Both sides of the e-cigarette debate have been fueled with impassioned language.³⁴ The arrival of e-cigarettes has been hailed as “one of the greatest public health wins of all time”³⁵ and, alternatively, “an emerging public health epidemic.”³⁶

The premise of harm reduction is that for individuals unwilling or unable to avoid a highly dangerous behavior, at least in the short-term, substitution with less dangerous behavior will ultimately improve health. For example, while motorcycle enthusiasts are unlikely to give up riding, imposing helmet laws will reduce injuries.³⁷ Injection drug abuse is a complex social problem, but clean needle and syringe programs might prevent the spread of blood-borne pathogens.³⁸ E-cigarettes could serve a harm-reducing role for the cigarette smoker otherwise unwilling or unable to quit - a view the tobacco industry has firmly embraced.³⁹ The cigarette industry has an ignominious history with harm reduction, promoting “low tar” and filtered cigarettes, which offered no discernable health benefit,⁴⁰ sometimes in misleading and manipulative relationships with government researchers and potential regulators.⁴¹

Public Health England, a United Kingdom advisory agency to government and health authorities, published a report stating the e-cigarettes are “95% less harmful” than smoking.¹³ That 95% estimate was loudly criticized as based on “flimsy” evidence⁴² - criticism the report authors claim detracts from the main message that e-cigarettes are less harmful than smoking.⁴³ In 2017, Public Health England backed television messages encouraging cigarette smokers to consider e-cigarettes.⁴⁴ In contrast, since 2015, the California Department of Public Health has run statewide television messages warning of e-cigarette dangers.⁴⁵ Some countries, including Brazil, Norway, and Singapore, have effectively banned e-cigarettes.

For e-cigarettes to yield meaningful public health gains, their use must be substantially less harmful than cigarette smoking. Additionally, e-cigarettes must serve as an effective substitute for cigarettes among smokers, aiding long-term quitting rather than enabling ongoing dual use of e-cigarettes and conventional cigarettes in combination. Finally, e-cigarette availability should not encourage tobacco and nicotine uptake among nonsmokers, including among youth or former smokers. These ideas are examined below.

E-cigarettes and systemic health

Due to the absence of tobacco combustion, e-cigarettes do not produce many of the toxins present in cigarette smoke, such as carbon monoxide, although some tobacco-derived chemicals, including volatile organic compounds and nitrosamines²⁰ and heavy metals and silicate particles from the device heating elements,^{20, 46} may be present in e-cigarette aerosol at low but potentially biologically relevant levels. Lower toxin exposure is the main reason e-cigarettes are presumed to cause less harm than conventional cigarettes, and in fact, among cigarette smokers switching to e-cigarettes for two weeks, biomarkers of exposure to key carcinogens and toxins were substantially reduced.⁴⁷ It is highly plausible that e-cigarette use will prove less carcinogenic than cigarette smoking. However, cancer only accounts for a portion of cigarette related-deaths: the majority of those killed by smoking die from non-malignant pulmonary or cardiovascular diseases.¹⁰

Collected data from in vitro and animal models, as well as human clinical studies, suggest that pulmonary toxicity could be a serious concern.⁴⁸ The FDA designates glycerol and propylene glycol as “generally recognized as safe” to consume orally but has not evaluated the chemicals for inhalation, which could cause respiratory irritation.⁴⁹ Diacetyl, acetyl propionyl, and other aldehydes are associated with toxic effects when inhaled and are found as flavoring agents in many e-liquids.^{28, 50} Human exposure studies suggest that acute e-cigarette use may trigger oxidative stress and increased airflow resistance.^{51, 52} E-cigarette use may alter the secretion of immune system proteins in human airways.⁵³ Epidemiologically, e-cigarette use is positively associated with asthma among adolescents,⁴⁹ but the causal nature of this relationship is uncertain. Together, the evidence points toward meaningful respiratory effects, but further research is necessary to address variability in e-cigarette design and e-liquid contents, as well as the implications of long-term use.⁴⁸

Chemicals delivered during e-cigarette use, notably nicotine, oxidants, and particulates, could enhance cardiovascular risk.⁵⁴ Studies have associated e-cigarettes with increased

heart rate,⁵⁵ endothelial cell toxicity,⁵⁶ and impaired flow-mediated dilatation,⁵⁷ all of which may contribute to damaging cardiovascular events. Short-term cardiovascular changes have not been found in all studies, and in some studies, cardiovascular changes were less pronounced with exposure to e-cigarette aerosol versus cigarette smoke.⁵⁴ While the evidence continues to accumulate, it appears likely that e-cigarettes contribute to cardiovascular risk, particularly among individuals with underlying cardiovascular disease, although the cardiovascular risks posed by e-cigarettes are likely to be less severe than those of cigarette smoking.⁵⁴

E-cigarettes and oral health

Studies of the potential oral health effects of e-cigarette use are limited. However, there are plausible mechanisms through which e-cigarettes could harm oral tissues. Up to half of U.S. periodontal disease cases can be attributed to tobacco use,⁵⁸ and damage to the periodontium from smoking at least partly results from nicotine exposure. At doses equivalent to heavy smoking, nicotine inhibits osteoblast proliferation,⁵⁹ impedes neutrophil phagocytosis,⁶⁰ and stimulates inflammatory cytokine production from human gingival fibroblasts.⁶¹ E-cigarettes can deliver nicotine at levels comparable to conventional cigarettes⁶² in addition to other potentially toxic aerosol components.

Aerosol temperature could affect oral tissues. However, the temperature at which e-cigarette aerosols are produced depends on device characteristics and user modifications, for example, varying from 130°C to 350°C in devices known as “direct drip atomizers.”⁶³ Nicotine stomatitis features hyperkeratinization and inflammation of the minor salivary glands of the hard palate and can be attributed to exposure to high-temperature smoke, particularly from pipes. Anecdotal accounts have reported palatal stomatitis in e-cigarette users,⁶⁴ but formal case reports or epidemiologic studies have not confirmed this finding.

A number of in vitro studies have examined the response of oral-derived cells and tissues to e-liquids. Exposure of human gingival fibroblasts to e-cigarette liquids, both with and without nicotine, resulted in morphological changes, with nicotine-containing e-liquids found to be particularly cytotoxic.⁶⁵ In another study, human periodontal ligament fibroblasts and human gingival tissue models exposed to e-cigarette aerosols exhibited increased markers of oxidative stress and inflammation, suggesting a pathogenic pathway.⁶⁶

The cell culture studies give reason for caution but do not necessarily translate to clinically meaningful effects. Two studies of periodontal parameters in e-cigarette users have been published. Suppression of the inflammatory response and reduced bleeding on probing is a well-documented clinical consequence of tobacco smoking.⁶⁷ A cross-sectional study of 94 patients in Saudi Arabia compared periodontal status between cigarette smokers, daily exclusive e-cigarette users, and tobacco never-users.⁶⁸ The e-cigarette group exhibited a lower percentage of sites with bleeding on probing than never-smokers, similar to the percentage seen for cigarette smokers.⁶⁸ In England, 18 cigarette smokers, none with a pocket depth >4mm, were provided e-cigarettes to substitute for smoking over 2 weeks.⁶⁹ The mean percentage of site with bleeding on probing increased on follow-up, although mean plaque scores remained similar.⁶⁹ These initial clinical studies should be interpreted

cautiously in light of small sample sizes, convenience sampling, brief observation periods, and the heterogeneity of e-cigarette devices, e-liquids, and patterns of use in the general population. Larger, more rigorous studies are likely forthcoming.

In addition to any oral health implications of e-cigarettes under intended use conditions, there are multiple documented cases of oral and facial trauma caused by explosions and fires from e-cigarette device malfunctions.⁷⁰⁻⁷² The dental practitioner may encounter burns, alveolar fractures, and tooth evulsions, stemming from e-cigarette explosions near the mouth.⁷¹ This potential for facial injury is a harm unique to e-cigarettes relative to conventional tobacco products and one example in which, despite the promise of lower levels of known toxins, the proliferation of e-cigarettes may be accompanied by new and unexpected risks.

E-cigarettes and smoking cessation

Dental professionals may encounter patients who achieve smoking cessation with e-cigarettes. Both implicit and explicit smoking cessation claims, including testimonials from e-cigarette users, are commonly featured in commercially sponsored e-cigarette social media channels and other marketing.⁷³ E-cigarette heavy-users often report being motivated by a desire to quit smoking, with many also reporting cessation success.⁷⁴ While smoking cessation is possible with e-cigarettes, 75% to 82% of U.S. adults who use electronic cigarettes use in combination with at least one other form of combustible tobacco,^{25, 75} and only 20% of e-cigarette users are recent quitters of combustible cigarettes.²⁵

Epidemiologic studies have been inconsistent regarding whether e-cigarette use among adult smokers is associated with long-term smoking abstinence. Some large population-based surveys have reported that e-cigarette use among combustible cigarette smokers is positively associated with quit attempts and actual quitting.^{76, 77} In contrast, other longitudinal studies have reported no association with cessation⁷⁸ or the inverse association: more quitting among participants who did not use e-cigarettes.⁷⁹ A meta-analysis including 18 observational studies and 2 trials concluded that e-cigarette use was associated with less cessation.⁸⁰ For some adult cigarette smokers, e-cigarettes are viewed a way to evade smoke-free policies, and current e-cigarette marketing is seen as reframing smoking as normative and socially acceptable.⁸¹

A small number of randomized trials have assessed the effectiveness of nicotine-containing e-cigarettes as a smoking cessation aid. In New Zealand, participants who received e-cigarettes via mail achieved a similar level of smoking abstinence at 6-months (7%) as those who received vouchers redeemable for nicotine patches (6%).⁸² In Italy, participants given nicotine-containing e-cigarettes were more likely to quit smoking at 12-months (11% to 17%, depending on nicotine concentration supplied) than those given non-nicotine e-cigarettes (4%), although differences were not statistically significant.⁸³ A systematic review of these studies graded the evidence as “low” that nicotine-containing e-cigarettes improve smoking cessation but noted that more trials are underway.⁸⁴

Among other factors, whether e-cigarette users are successful in quitting smoking may depend on the type of e-cigarette device and frequency of use.^{74, 77, 85} “Tank” devices that deliver more nicotine and daily use may be more effective than “cigalike” devices or non-daily use in achieving quitting.^{74, 77, 85}

E-cigarettes and youth smoking initiation

Multiple longitudinal studies, summarized in a recent meta-analysis,⁸⁶ have shown consistently that adolescents who use e-cigarettes are at elevated risk of progression to combustible cigarette smoking. The association with future smoking persists after adjustment for known smoking risk factors and is independent of use of other tobacco products, such as cigars and smokeless tobacco.⁸⁷ Several mechanisms may explain the relationship. For example, youth who experiment with e-cigarettes may thereafter perceive cigarettes as less dangerous than they did previously.⁸⁸ Additionally, youth initially attracted to e-cigarettes, potentially due to greater social acceptability, variety in flavors and styles, or lower perceived health risks, may later find conventional smoking more attractive for satisfying nicotine dependence or sensory stimulation.⁸⁹

In contrast, it is possible that the association between e-cigarettes and smoking is not a causal pathway but rather a reflection of youth with a high affinity for risk-taking trying both e-cigarettes and other forms of tobacco. Some youth may choose to use e-cigarettes in place of smoking. Cigarette smoking among U.S. middle and high school students declined during the same period that e-cigarette use rapidly expanded.⁹⁰ However, existing tobacco control measures have contributed to a nearly two-decade decline in U.S. youth smoking, without clear evidence that e-cigarettes accelerated that decline.⁹¹

For the dental provider, e-cigarette use by adolescent patients should be considered a strong risk indicator of future smoking and other tobacco use, regardless of the mechanism underlying the association. The U.S. Surgeon General concludes that e-cigarette aerosol is itself not harmless and that use of any nicotine-containing product poses dangers to youth.⁹² Thus, asking and advising young patients about e-cigarettes are necessary elements to providing tobacco prevention guidance and counseling.

Patient communication

Dentists have a professional obligation to act in the interest of their patients’ overall health. Consistent with this responsibility, engaging in tobacco use prevention and cessation is an essential component of every patient visit. This entails relapse prevention for former users, discouraging initiation among never users, and motivating current tobacco users to make a cessation attempt. For the dental patient interested in trying e-cigarettes as a method of quitting combustible tobacco, above all, the clinician should encourage and reinforce that desire to quit.

Specific to e-cigarettes, clinicians should send the clear message that no form of tobacco or nicotine is safe. The healthiest long-term goal is to live completely nicotine and tobacco free. However, patients should also understand that combustible cigarettes are more dangerous than e-cigarettes. Limited evidence suggests that e-cigarettes might help some

smokers to quit, but at this time, the consistent, high-quality studies needed to reach a scientific consensus are lacking. E-cigarettes are not harmless, and their long-term health risks are unknown.

The ADA does not recommend the use of e-cigarettes as a method to quit smoking or as a harm reduction alternative to other forms of tobacco. The ADA does not support marketing some tobacco products as less harmful than others and does support policies to regulate, limit sales, and tax both traditional and non-traditional tobacco products.⁹³ The American Medical Association⁹⁴ and American Heart Association⁹⁵ have similarly taken cautious positions on e-cigarettes, prioritizing prevention of youth use and not recommending e-cigarettes for smoking cessation. In contrast, the Royal College of Physicians in the United Kingdom has largely embraced e-cigarettes as a safer alternative to smoked tobacco.⁹⁶ The dental professional is left to navigate these divergent positions via careful evaluation of the available evidence.

For tobacco-using patients motivated to make a quit attempt, the dental practitioner has multiple evidence-based tobacco cessation approaches on which to rely. Brief counseling, even lasting no more than a few minutes, can increase the probability that a patient remains tobacco-free long-term.⁶ The “5-A’s” approach: ASK (about all tobacco use), ADVISE (not to use), ASSESS (readiness to quit), ASSIST (in the quit attempt), and ARRANGE (for follow-up care), is both effective and easily implemented.⁶ Pharmacotherapy, which includes both nicotine replacement therapy and the non-nicotine medications bupropion and varenicline, alone or in combination, substantially improves cessation outcomes.⁹⁷ Dental professionals are encouraged to refer patients for additional tobacco cessation support, such as local tobacco cessation programs and telephone quitlines, which have been proven effective and can be accessed at no cost to patients.⁹⁸ In California, patients can call 1–800-NO-BUTTS or call 1–800-QUIT-NOW nationwide. Tobacco cessation is an ideal opportunity for interprofessional collaboration with physicians, pharmacists, and other healthcare providers: receiving assistance from multiple clinician types is more effective than from one clinician type alone.⁶

Quitting tobacco can be extremely difficult. Nicotine is a highly addictive drug that alters brain functioning.⁹⁹ Additionally, many tobacco users come to associate particular social or environmental cues with the urge to use tobacco again.⁹⁹ Thus, it may take the average cigarette smoker many quit attempts before achieving lasting tobacco cessation.¹⁰⁰ Although the probability that any given quit attempt will succeed is low, dental professionals can increase the chances of success with supportive counseling and proven pharmacological aids, particularly when used in combination.

E-cigarettes are unlikely to make quitting tobacco easy. However, for some patients unwilling to consider other approaches, e-cigarettes could offer a palatable option. For such patients, the clinician must stress the ultimate goal of becoming completely tobacco and nicotine free rather than continuing dual-use of both e-cigarettes and combustible tobacco. The currently available evidence suggests that e-cigarettes are less dangerous than combustible tobacco, both for systemic and oral health. However, e-cigarettes are not harm

free and are not proven cessation aids. The tobacco industry did not make major investments in the e-cigarette industry expecting that e-cigarettes would put them out of business.

Dental professionals are trained to have truthful and nuanced conversations with patients. Providers must utilize these communication skills when conveying the complexity and current uncertainty regarding the health implications of e-cigarettes. In this rapidly changing landscape, the dental provider has a responsibility remain informed as new evidence and new products emerge, with the potential for e-cigarettes regulation and practice guidelines in the future.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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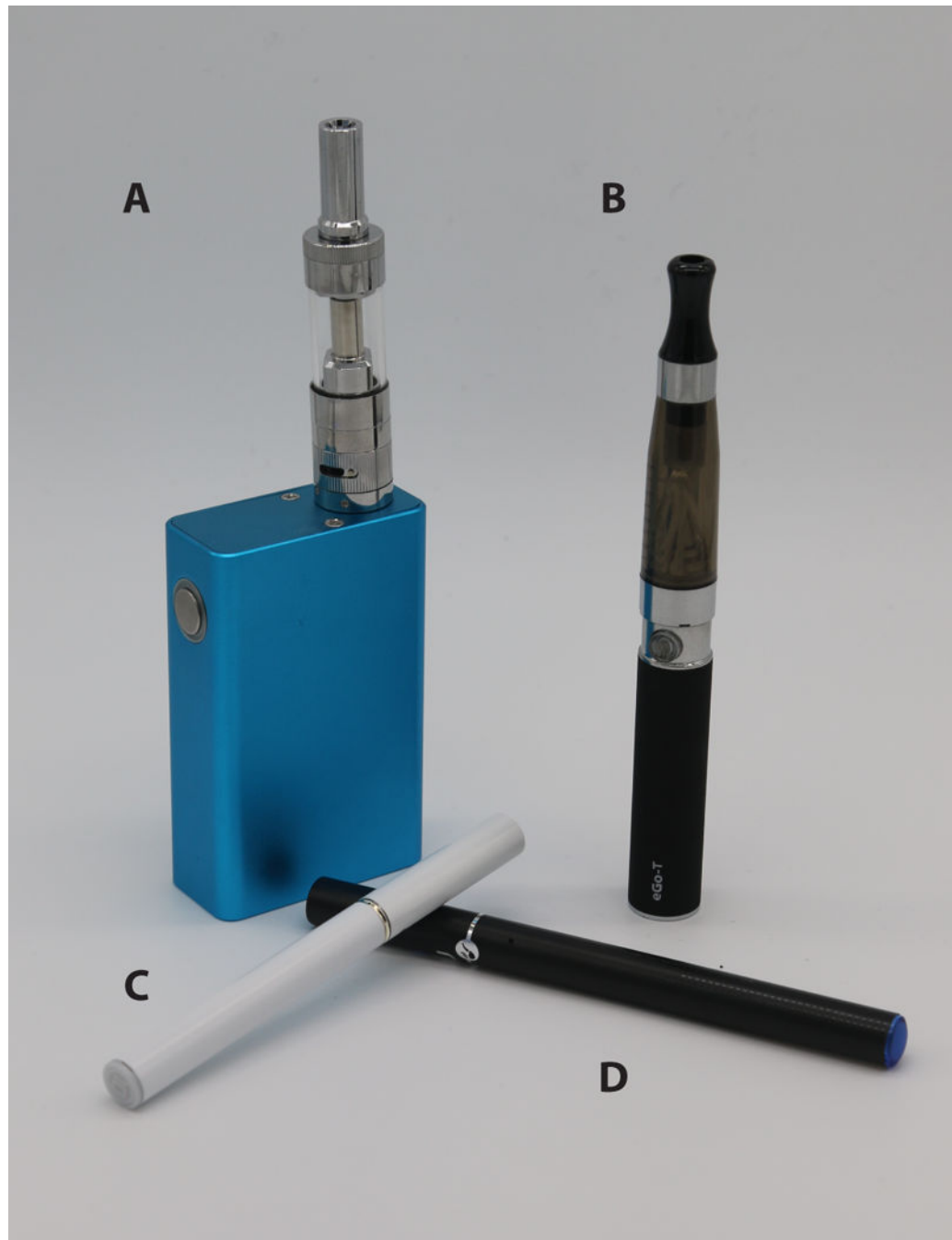


Figure. Example electronic cigarette devices

Legend: Common types of electronic cigarettes (e-cigarettes) currently available in the United States. A) Modifiable tank-type devices are typically larger than earlier designs and often allow user to adjust battery voltage or device power, along with other modifications. B) Pen-type or tank “second generation” devices are rechargeable, refillable, and button-activated. C) Rechargeable “cigalike” devices resemble a cigarette in appearance. D)

Disposable “cigalike” devices are not intended to be refilled or recharged and are discarded after use.

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