Asthma + Respiratory FOUNDATION NZ

2018 ACC expert consensus decision pathway on tobacco cessation treatment.

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6.9. Other tobacco products

6.9.1. Smokeless tobacco

Approximately 3.4% of U.S. adults use smokeless tobacco products.[1] Products used in the United States are primarily oral snuff (moist ground tobacco placed between the lips and gums) or chewing tobacco (shredded flavored tobacco). Smokeless tobacco products that are sucked and dissolve in the mouth are also sold in a variety of forms.

Smokeless products contain nicotine and sodium bicarbonate, which increases pH to increase nicotine absorption across the oral mucosa. They also contain carcinogenic nitrosamines, low levels of other combustion products generated during curing, and other potential toxins.[2]

The major health risks of smokeless tobacco use are diseases of the oral cavity, including periodontal disease and tooth decay, and a slightly higher risk of oral cancer.[3] Smokeless tobacco use has also been associated with an increased risk of pancreatic and esophageal cancer in some studies.[4]

Whether long-term smokeless tobacco use can cause or aggravate CVD is less certain because evidence is conflicting.[5-7] A meta-analysis of 11 studies found an increased risk of fatal MI (relative risk: 1.13; 95% confidence interval: 1.06 to 1.21) and fatal stroke (relative risk: 1.40; 95% confidence interval: 1.28 to 1.54) among smokeless tobacco users compared with nonusers.[8] The studies included in that meta-analysis from the United States and Sweden showed an increased risk of death from myocardial infarction and stroke.[8]

A review by the American Heart Association concluded that although smokeless tobacco use may convey a much lower risk of CVD than does cigarette smoking, it does pose some risk, particularly in patients with CVD.[9] Given the overall evidence, the committee recommends against the use of smokeless tobacco, particularly in patients with CVD. Providers should screen for smokeless tobacco use, advise smokeless users to stop, and offer treatment.

Evidence for treatment of smokeless tobacco dependence is less well-established than treatment for cigarette smoking because fewer studies have been conducted. The strongest evidence to date favors varenicline and behavioral support to promote quitting.[10] Nicotine lozenges also appeared to enhance quitting. Studies testing use of a nicotine patch and/or bupropion for cessation of smokeless tobacco use have not found these treatments to be effective.[10]

6.9.2. Alternative tobacco products: e-cigarettes

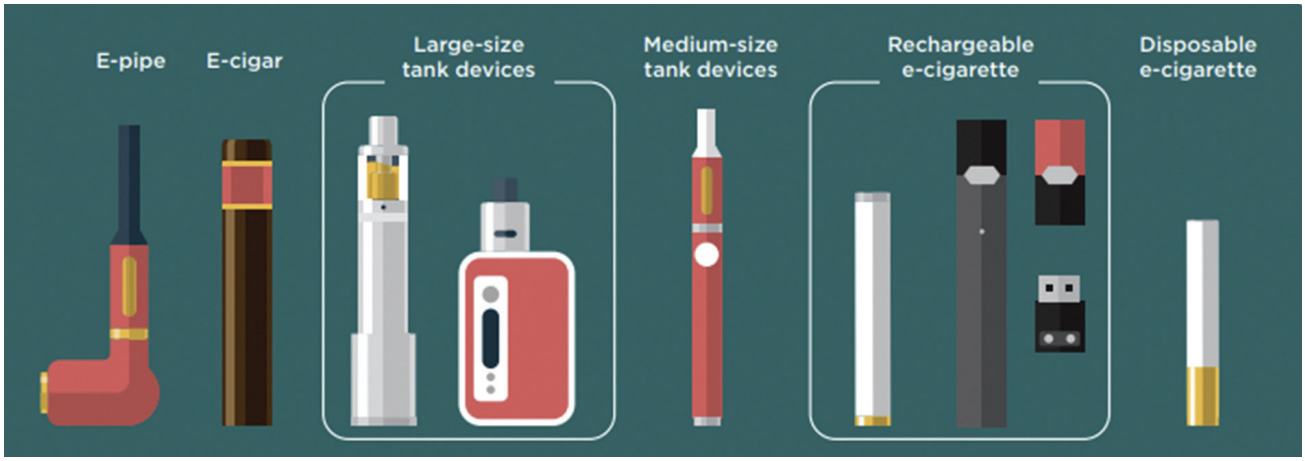
E-cigarettes, also known as electronic nicotine delivery systems, differ from cigarettes and other combustible tobacco products in that they do not produce smoke by burning tobacco. Instead, they heat a solution (e-liquid) that usually contains nicotine, propylene glycol or vegetable glycerin, and flavorings to generate an aerosol that the user inhales.[11]

E-cigarette devices vary considerably in design (Figure 5). First-generation products are disposable devices that mimic the appearance and experience of smoking a combustible cigarette. Second-generation devices are larger and have rechargeable batteries and/or replaceable cartridges of e-liquid. Third-generation e-cigarette designs allow the user to customize the devices by manipulating features such as batteries, temperature, and dose of nicotine.[12]

The design features of an e-cigarette can have a large impact on cost, safety, and nicotine delivery. Users' exposure to nicotine and other chemicals in the aerosol depends on the type of device, the components of the e-liquid, and on how the devices are used. Experienced users can achieve levels of nicotine intake similar to that obtained from smoking combustible tobacco cigarettes.[12]

Recently, a novel vaping device emerged that differs from previous e-cigarettes in its technology, product design, and marketing. Exemplified by JUUL, the device is designed to resemble a computer flash drive and encapsulates nicotine, flavorings, and other contents in small replaceable cartridges called "pod-mods" (Figure 5).[13,14] The device's battery, rechargeable via a USB port, heats the liquid to produce vapor. The product differs from prior e-cigarettes in the

FIGURE 5: **Electronic nicotine delivery systems, including electronic cigarettes**



Source: U.S. Department of Health and Human Services, 2016

chemical formulation of nicotine used in the product. Pod-mod devices use nicotine salts, which produces more protonated nicotine at a lower pH than the free-base form of nicotine used in other e-cigarettes, which has a higher pH and activates nicotine sensory receptors. Therefore, the nicotine in the newer devices is less irritating when inhaled. Additionally, these devices can deliver a higher concentration of nicotine to the user.[14] A higher dose of nicotine might benefit adult smokers who are seeking to quit cigarettes but might also promote nicotine dependence among nonsmoking adolescents and young adults.[15] The product's sleek design, sweet flavors, marketing strategy and social-media presence appear to have made it more attractive to youths than earlier e-cigarette products. During 2017, JUUL's sales accelerated and it captured the largest share of the e-cigarette retail market.[13] Although national data on youth use of the products are not yet available, multiple anecdotal reports of youth uptake of JUUL devices appeared in the media during 2018.[14]

E-cigarettes have the potential for large public health benefit if they help smokers to quit smoking combustible cigarettes, especially smokers who have not been willing or able to quit using current treatments. This potential benefit must be balanced against e-cigarettes' own long-term health risks, which are largely unknown at this time, and against the potential for e-cigarettes to attract youth and young adults who might not otherwise smoke to take up their use and perhaps increase the uptake of cigarettes.

In August 2016, the FDA gained regulatory authority over e-cigarettes, allowing it to enforce laws preventing the sale of e-cigarettes to persons under the age of 18 years, ban provision of free product samples, and regulate the labeling and content of e-cigarettes. A 2018 systematic evidence review by the National Academies of Sciences, Engineering, and Medicine (NASEM) concluded that while scientific evidence is insufficient to allow reliable conclusions to be made about the long-term health effects of e-cigarettes (including CV outcomes or measures of subclinical atherosclerosis), such risks could be less than those associated with smoking, because toxicants and carcinogens present in cigarette smoke are absent or present at much lower concentrations in e-cigarette aerosols.[12]

The NASEM report also reviewed existing evidence about the effects of e-cigarette exposure on intermediate disease outcomes. It found "substantial" evidence that short-term exposure to e-cigarette aerosols can cause acute endothelial cell dysfunction, DNA damage, and signs of oxidative stress, as well as temporarily increase heart rate. However, the report noted that the long-term consequence of these changes or the effects of chronic e-cigarette exposure on CV or other biomarkers of chronic disease remain unknown.[16]

A subsequent crosssectional study using nationally-representative self-report data found a positive association between daily e-cigarette use and a history of MI.[17] However, the study's cross-sectional design precluded a conclusion about any causal relationship between these two events. The study had no assessments of temporality in exposure, and it is unclear if e-cigarettes were used prior to or after the MI events. More robust studies will be needed to confirm the association between MI and e-cigarette use.

The NASEM noted other safety concerns with e-cigarette devices, such as defective batteries causing explosion and injuries as well as risks of accidental or intentional exposure due to ingestion of or contact with the e-liquids.[12] The NASEM report also noted that certain flavorings sometimes found in e-liquids (i.e., diacetyl, cinnamaldehyde) may pose a health hazard and should be avoided.[12]

The NASEM report concluded that completely switching

TABLE 9:

Recommended actions regarding secondhand smoke (SHS) exposure

- *Routinely ask all patients (especially nonsmokers) about their exposure to SHS.*
- *Inform patients that SHS exposure increases the risk of cardiovascular events in nonsmokers.*
- *Advise all patients (especially nonsmokers) to adopt a smoke-free policy for their home and car and avoid other sites of SHS exposure.*
- *Actively support smoke-free policies for worksites, including healthcare*

from combustible tobacco products to e-cigarettes should reduce short-term adverse health effects of continued smoking, indicating e-cigarettes' potential for harm reduction.[12] However, the report found far less evidence that dual use of both cigarettes and e-cigarettes reduces exposures to toxicants or health risks. Currently 60% of adult e-cigarette users also continue to smoke cigarettes.[18] The concern is especially relevant to CVD risk, because smoking even one cigarette daily increases CVD risk in epidemiological studies.

The NASEM report found only limited evidence that e-cigarettes are effective as cessation aids when compared with no treatment or current FDA-approved cessation therapies, but it found moderate evidence that e-cigarettes may be more likely to lead to smoking cessation when used more frequently as compared to infrequent or intermittent use.[12] However, the report found substantial evidence that e-cigarette use by adolescent never-smokers increases their likelihood of subsequently trying a cigarette and moderate evidence that this increases the frequency and intensity of subsequent smoking.[12]

There is widespread agreement that regulatory oversight of e-cigarettes is needed to reduce the risk of youth use of e-cigarettes and transition to combustible cigarettes.

Despite gaps in the evidence base about the effectiveness of e-cigarettes for smoking cessation, many smokers are asking physicians in clinical practice for guidance about e-cigarettes.[19]

Writing committee members were unanimous on 3 points (Table 9). First, the clinician's role is to encourage and support a smoker's efforts to stop using cigarettes and other combustible tobacco products. Second, given the uncertainties of the long-term effects of e-cigarettes on health, a clinician should advise cigarette smokers seeking to quit to use evidence-based, FDA-approved, safe, and effective smoking cessation pharmacotherapies as first-line treatments in preference to e-cigarettes. Third, clinicians should be prepared to discuss the risks and benefits with patients who ask about or are already using an e-cigarette.

If a smoker decides to use e-cigarettes, the committee felt that the clinician should play a supportive role, helping the patient to use the product in a way that minimizes risk to themselves and others and indicating that the eventual goal is complete abstinence from all products, including e-cigarettes. Table 10 provides some guidance for clinicians' discussions with patients about e-cigarette use.

Committee members had a range of opinions about the use of e-cigarettes as a cessation aid, reflecting differing interpretations of the limited evidence about e-cigarettes' effectiveness for smoking cessation and possible health effects. Approximately one-half of the committee felt e-cigarettes are associated with less short-term harm than combustible cigarettes and may be of benefit for smokers who have been unable to quit smoking after multiple attempts using FDA-approved medications and behavioral support or for smokers who are unwilling to quit but seek to reduce tobacco-related health harms.

TABLE 10

Guidance for clinicians' discussions of e-cigarettes with patients

Recommendations:

- *Emphasize to smokers the importance of the goal of complete cessation of all combustible tobacco products. Even a single cigarette per day increases cardiovascular risk.*
- *Recommend that smokers use evidence-based, FDA-approved smoking cessation aids, which are known to be safe and effective.*
- *Clinicians should be prepared to discuss the evidence about e-cigarettes' risks and benefits with patients who ask about them.*

Points to cover in a discussion with a patient who asks about e-cigarettes:

- *E-cigarettes are devices that heat a nicotine-containing liquid, producing an aerosol that differs from the smoke produced by burning tobacco.*
- *E-cigarettes contain chemicals in addition to nicotine, including propylene glycol, glycerin, and flavoring chemicals that may pose a risk.*
- *Because they do not burn tobacco, e-cigarettes expose the user to fewer and lower levels of toxic compounds than smoking a cigarette does.*
- *Therefore, if used as a complete substitute for combustible tobacco products, e-cigarettes are expected to be less harmful than smoking combustible tobacco products in the short-term, but their long-term safety is uncertain.*
- *Because e-cigarettes are new products, scientific information about their health effects and effectiveness to help smokers quit is limited and rapidly evolving. They are not currently approved by the FDA as safe and effective cessation aids.*
- *E-cigarettes vary considerably in their design, in the contents of the e-liquids, and in nicotine and toxicant delivery to the user.*

If smoker chooses to use e-cigarettes, provide evidence-based advice:

- *Switch completely to e-cigarettes. Avoid dual use of both combustible tobacco products and e-cigarettes.*
- *The eventual goal is cessation of e-cigarettes as well as combustible cigarettes, because of uncertainty about e-cigarettes' long-term health risks. After stopping combustible tobacco, plan to taper off e-cigarettes.*
- *Heed safety instructions. Choose products with child-proof packaging to minimize the risk of nicotine poisoning of children. Follow instructions for device maintenance, battery recharging, and storage to minimize the risk of explosion.*
- *Avoid using e-cigarettes around children.*

FDA – U.S. Food and Drug Administration

In these situations, e-cigarette use is likely to minimize risk if smokers switched completely to e-cigarettes, avoided dual use, and used e-cigarettes temporarily as an aid to cessation of both cigarettes and e-cigarettes.

Other committee members felt that the limited evidence of benefit of e-cigarettes for cessation of combustible tobacco products and the insufficient evidence regarding long-term health effects outweighed any potential benefits of e-cigarettes at this time.

Like smokers using conventional cessation therapies, those using e-cigarettes should be followed regularly by the clinician or smoking cessation professional. Although there are no data yet to show that behavioral support enhances the potential effectiveness of e-cigarettes for cessation, it is reasonable to encourage e-cigarette users to use the standard resources for behavioral support.

6.9.3. Alternative tobacco products: HNB tobacco

"Heat-not-burn" devices are also alternative tobacco products that, like e-cigarettes, do not burn tobacco.[20] Unlike e-cigarettes, which heat a nicotine-containing liquid, HNB products heat tobacco itself. A pen-like device heats a tobacco stick to a temperature lower than that required for combustion but high enough to release an aerosol that users inhale. Several tobacco companies are developing these products. They claim that the products mimic the experience of conventional combustible cigarettes, providing the taste of tobacco without smoke, ash, or odor, and thereby reducing the health risks of smoking cigarettes.[20]

Studies funded by the manufacturers have reported that HNB products produce lower levels of harmful chemicals compared with conventional cigarettes.[21] Studies from independent researchers replicating this work are just beginning to be published and raise some question about whether HNB products may actually burn tobacco and whether some harmful chemicals are generated.[22-24]

Consequently, little is known about the health effects of HNB products. Novel HNB products are not currently approved for sale in the United States, but one tobacco company has applied to the FDA for approval to market its product as a modified-risk tobacco product.[12]

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