

Electronic Nicotine Delivery Systems or E-cigarettes: American College of Preventive Medicine's Practice Statement



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Introduction: E-cigarettes or electronic nicotine delivery systems (ENDS) have rapidly gained popularity in the U.S. Controversy exists about the safety and efficacy of ENDS. The American College of Preventive Medicine's Prevention Practice Committee undertook a consensus-based evidence review process to develop a practice statement for the American College of Preventive Medicine.

Methods: A rapid review of the literature was performed through June 2017 to identify efficacy, patient-oriented harms, and the impact on population health.

Results: On an individual level, limited evidence suggests that ENDS may be effective at reducing cigarette use among adult smokers intending to quit. There is insufficient evidence addressing potential long-term harms of ENDS, and limited evidence is available about short-term harms of ENDS and the impact of secondhand exposure. Although ENDS appear safer than combustible cigarettes, they are not without risk. Among youth there is no known benefit and significant concern for harm. On a population level, there may be significant harms associated with ENDS, particularly among youth nonsmokers. The long-term balance of potential benefits versus harms from the individual and population perspectives are unclear.

Conclusions: The American College of Preventive Medicine developed practice recommendations that include encouraging screening for ENDS use, strategies to prevent the initiation of ENDS use in nonsmokers, particularly in youth, adoption of a harm reduction model for smokers intending to quit in those who refuse or fail to quit with evidence-based smoking-cessation methods, recommendations on policy and regulatory strategies to decrease public use of ENDS and regulation of their components, and future research needs.

Am J Prev Med 2019;56(1):167–178. © 2019 American Journal of Preventive Medicine. Published by Elsevier Inc. All rights reserved.

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0749-3797/\$36.00

<https://doi.org/10.1016/j.amepre.2018.09.010>

INTRODUCTION

E-cigarettes, or electronic nicotine delivery systems (ENDS), were introduced in the U.S. in 2007. Lack of early regulation of ENDS likely contributed to widespread availability and uptake.¹ Despite the rapid growth in use of ENDS, limited safety and efficacy studies guide public policy and clinical recommendations. E-cigarettes are perceived as safer than traditional combustible cigarettes, and as an effective method of smoking cessation,² despite scientific uncertainty.

Among adults, the National Health Interview Survey 2016 data showed that 15.4% of adults aged 18 years and older had ever used an e-cigarette, up from 12.6% in 2014.³ Current use was lower among adults, at 3.2%. Younger adults (ages 18–24 years) were the most likely to have ever used an e-cigarette (23.5%), with increasing age associated with less likelihood of ever using an e-cigarette.⁴ Population studies of adult use showed current smokers had the highest rates of e-cigarette use, followed by former smokers, with little use among never smokers.^{5–7}

Among youth, tobacco product use overall has declined in the last 2 years, but ENDS have surpassed combustible cigarettes as the most used youth tobacco product in the U.S.⁸ Between 2011 and 2015, use of ENDS had tripled among middle and high school students, but decreased somewhat in 2016–2017, with use of e-cigarettes among middle schoolers at 0.6% in 2011 and 3.3% in 2017, and among high school students at 0.6% in 2011 to 3.3% in 2017.⁸

Youth uptake is of concern because of increased vulnerability to nicotine addiction and the potential long-term nicotine impacts on the developing brain.⁹ There is also emerging evidence that youth use of ENDS is associated with increased future use of combustible cigarettes.¹⁰

Numerous types of ENDS are available that use different means of aerosolizing a variety of refill liquids. The primary ingredients include nicotine, flavorings, propylene glycol, and glycerol.¹¹ There is poor correlation between labeling and nicotine content.^{11,12} A myriad of flavors exist, including tobacco, mint, cocoa, and strawberry shortcake, among others. One of the major appeals of the ENDS is the flavoring, with both adults and youth preferring sweet flavors.¹³ Additional compounds may include a variety of chemical constituents, including tetrahydrocannabinol (the psychoactive ingredient in marijuana)^{14,15}; carcinogens; and others with potential toxic effects.^{11,12}

Arguments favoring e-cigarettes include possible efficacy as a tobacco cessation tool, or as a less dangerous alternative to combustible, toxin-laden, conventional cigarettes. Arguments against e-cigarettes include lack of evidence supporting efficacy; lack of evidence on harms;

appeal to youth (potentially facilitating conventional tobacco use initiation); and the risk of creating new vaping norms or acceptability, which may lead to increased tobacco smoking.

The American College of Preventive Medicine (ACPM), therefore, examined the balance of benefits and harms of e-cigarettes, at the population and individual levels, to develop this practice statement.

METHODS

The ACPM Prevention Practice Committee (PPC) advances scientific knowledge in preventive medicine among medical professionals, employers, healthcare consumers, and national advisory and policy-making bodies by developing practice statements for the ACPM. The PPC developed a working group on ENDS to draft an ACPM practice statement for review and approval by the ACPM Board of Regents followed by publication and dissemination to members of the College, and the public health community at large.

The ACPM e-cigarette working group defined the scope of the topic to include the following key questions (KQs): Primary: (1) How effective are ENDS at helping people quit cigarette smoking? and (2) What are the comparative risks of ENDS, compared to smoking cigarettes or non-exposure to smoking or vaping? Additional questions: (3) What are the associated harms of secondhand aerosol? (4) How do the characteristics, marketing, perception, and availability of the product affect the incidence of ENDS use in population subgroups? (5) Are policy measures effective at reducing the number of new vapers or exposure to secondhand aerosol?

The population included tobacco smokers and nonsmokers of all ages. Interventions included any vaporized nicotine delivery system with or without other substances. Comparators included placebo ENDS (non-nicotine devices); cigarette smoking; not smoking (never smoking or quitting); and Food and Drug Administration–approved pharmacotherapy. Outcomes of interest included short- and long-term quit rates, incidence of new users of ENDS or other tobacco (especially among adolescents), use of other substances of abuse, and tobacco-related morbidity and mortality.

The ACPM PPC e-cigarette working group decided to conduct a rapid review of the literature. Rapid reviews synthesize the knowledge in a given field more quickly than a systematic review by shortening or eliminating steps required in a full systematic review.¹⁶ A medical librarian conducted a PubMed, English language, literature search for each of the five KQs above, using keywords and Medical Subject Headings terms appropriate for each for a 10-year period from May 2007 to June 2017. The search yielded systematic reviews, meta-analyses, clinical trials, observational studies, and policy statements. All titles and abstracts were independently reviewed by two members of the working group to determine which ones should be selected for full-text review and again independently reviewed for inclusion in the development of the ACPM practice statements for KQs 1 and 2. For KQs 3–5, a single member of the working group reviewed abstracts for full-text review and inclusion. Discrepancies were resolved by

consensus within the working group. Studies that did not meet the population, interventions, and outcomes of interest listed above and trials that were published before the most recent systematic review were excluded.

Systematic reviews and meta-analyses were prioritized based on their relevance to the particular KQ, their year of publication, and their quality based on the AMSTAR (A Measurement Tool to Assess Systematic Reviews) risk of bias assessment.¹⁷ Clinical trials and observational studies were also considered by the working group based on their date of publication (i.e., included only if more recent than the systematic reviews/meta-analyses) but the risk of bias of each study was not formally assessed. Authors did not formally assess strength of evidence by KQ with prescribed criteria (e.g., Grading of Recommendations, Assessment, Development and Evaluations [GRADE]). Table 1 below summarizes the number of articles reviewed at the title/abstract and full-text levels by KQ.

A survey of position statements on ENDS from governmental agencies and professional and health organizations also was performed to help define the policy landscape. The ACPM PPC developed consensus recommendations based on the available evidence of the net benefits and harms to the individual (based on observational studies and clinical trials) and to populations (based on cross-sectional and ecologic studies) in the context of recommendations from others.

RESULTS

Key Question 1: How Effective Are ENDS at Helping People Quit Cigarette Smoking?

Two authors reviewed the KQ1 literature search, selected 30 studies for full-text review, and excluded 53 studies. The most common reasons for exclusion were lack of inclusion of ENDS as the intervention (seven studies); lack of focus on tobacco cessation (17 studies); being published prior to a more recent systematic review (12 studies); or not a study (17 articles). Studies of benefit are in adult populations and do not apply to youth.

The literature search identified several acceptable quality systematic reviews relevant to this KQ: two published in 2017, four published in 2016, and one published in 2015 (Table 2). The systematic reviews varied in the

number of studies included, interventions, comparisons, length of outcomes, and length of follow-up; however, there was significant overlap in the studies. The GRADE quality of the evidence synthesized in the reviews included not reported, very low, and low. The pertinent reviews that addressed KQ1 subquestions are discussed below.

a. Compared with other pharmacologic and non-pharmacologic (placebo) treatments. Glasser et al.⁷ published a 2017 systematic review of 687 articles covering nine topics related to the use of ENDS. The use of ENDS with versus without nicotine for smoking cessation was evaluated based on five RCTs; 28 longitudinal observational studies (13 with and 15 without a comparison group); 22 cross-sectional surveys; two clinical laboratory studies; and one case series. Although observational studies showed either no change or a negative correlation (i.e., less quitting among those using ENDS), the authors concluded qualitatively based on four of five RCTs that ENDS were effective in helping some adults quit or reduce cigarette consumption.

Another 2017 systematic review compared ENDS or placebo ENDS (non-nicotine devices) with no smoking-cessation aids or alternative smoking-cessation aids.¹⁸ The use of ENDS for smoking cessation for 6–12 months was evaluated based on three randomized trials including 1,007 participants and nine cohorts including 13,115 participants. Results provided by only two RCTs suggest a possible increase in tobacco smoking cessation with ENDS in comparison with non-nicotine devices (RR=2.03, 95% CI=0.94, 4.38). Results from cohort studies suggested a possible reduction in quit rates with use of ENDS compared with no use of ENDS (OR=0.74, 95% CI=0.55, 1.00). The authors concluded that there is very limited evidence regarding the effectiveness of ENDS or non-nicotine devices on tobacco smoking cessation.

Malas and colleagues¹⁹ published a 2016 systematic review of primary cessation outcomes (smoking abstinence or reduction) or secondary outcomes (abstinence-related withdrawal symptoms and craving reductions)

Table 1. Literature Search by Key Question and Full-Text Review by Study Design

| Key question | Title and abstract review | Full-text review | | | |
|--------------|---------------------------|---|-----------------|--------------------------|--------|
| | | Systematic reviews/ meta-analyses ^a | Clinical trials | Observational studies | Policy |
| 1 | 707 | 18 | 8 | 0 | 4 |
| 2 | 693 | 17 | 4 | 2 | 1 |
| 3 | 82 | 2 | 17 | 1 | 4 |
| 4 | 611 | 5 | 9 | 2 | 3 |
| 5 | 302 | 2 | 0 | 2 | 0 |

^aSystematic reviews included all that met A Measurement Tool to Assess Systematic Reviews (AMSTAR) risk of bias quality criteria.

Table 2. Literature Search Results for Key Question 1

| Author, year | Study designs included | Population intervention comparison | Length of follow-up | Outcome | Measure of effect |
|-----------------------------------|--|---|---------------------|---|--|
| Glasser, 2017 ⁷ | 5 RCT 13 cohort 15 longitudinal without comparison 22 cross-sectional | Current smokers ENDS with vs without nicotine | 6+ months | Smoking cessation Cigarette consumption | 4 of 5 RCTs found a positive association In cohort studies, no or negative association |
| El Dib, 2017 ¹⁸ | 3 RCT 9 prospective cohort | Current smokers ENDS and/or electronic non-nicotine delivery systems (non-nicotine devices) with versus NRT or without smoking-cessation aid | 6–12 months | Tobacco smoking cessation | RR=2.03, 95% CI=0.94, 4.38; $p=0.07$; $I^2=0\%$, RD=64/1000 with ENDS vs non-nicotine devices OR=0.74, 95% CI=0.55, 1.00; $p=0.051$; $I^2=56\%$ with ENDS vs no ENDS |
| Malas, 2016 ¹⁹ | 62 studies | Current smokers ENDS with versus without nicotine NRT No aid | Any | Smoking cessation Reduction Withdrawal Urge to smoke | Majority of studies found a positive association, but the evidence is inconclusive because of low quality |
| Khoudigian, 2016 ²⁰ | 4 RCT 1 before–after | Adult smokers ENDS with versus without nicotine | 1 day to 9 months | Smoking cessation Desire to smoke Withdrawal | RR=2.02, 95% CI=0.97, 4.22 |
| Kalkhoran, 2016 ²³ | 2 CT 15 cohort 3 cross-sectional | Current smokers ENDS with versus without nicotine | 7 days to 6 months | Smoking cessation | OR=0.72, 95% CI=0.57, 0.91, against use of ENDS |
| Hartman-Boyce, 2016 ²¹ | 3 RCTs (2 included in meta-analysis) 21 cohort | Current smokers ENDS with versus without nicotine NRT | 6 months | Smoking abstinence | RR=2.29, 95% CI=1.05, 4.96 |
| Rahman, 2015 ²² | 2 RCT 2 cohort 2 cross-sectional | Current smokers ENDS with versus without nicotine NRT No aid | 6–24 months | Smoking cessation | Pooled effect size=0.20, 95% CI=0.11, 0.28 |

ENDS, electronic nicotine delivery systems; NRT, nicotine replacement therapy; RD, risk difference

with ENDS versus non-nicotine devices; nicotine replacement therapy (NRT); or no aids, based on 62 articles including 25 with moderate or strong data quality. Meta-analyses were not reported. The authors concluded that although the majority of studies found a positive association between e-cigarette use and smoking cessation compared with NRT and no cessation aid, the evidence was inconclusive because of the low quality of the published research.

Another 2016 systematic review by Khoudigian et al.²⁰ compared ENDS with non-nicotine devices. Of 569 articles identified, five were eligible for inclusion in meta-analyses. Use of ENDS was associated with a statistically nonsignificant higher smoking cessation rate compared with non-nicotine devices (RR=2.02, 95% CI=0.97, 4.22).²⁰ Meta-analyses showed no difference in withdrawal symptoms or non-serious side effects between the two groups. Length of follow-up ranged from 1 day to 9 months.

A 2016 Cochrane review by Hartmann–Boyce²¹ concluded that abstinence at 6 months or greater, verified by exhaled carbon monoxide, was more likely in ENDS users compared with non-nicotine device users (RR=2.29, 95% CI=1.05, 4.96, based on two RCTs). No significant difference in 6-month abstinence rates were observed in the one study that compared ENDS with nicotine patches (RR=1.26, 95% CI=0.68, 2.34).

Rahman and colleagues²² published a 2015 systematic review of the association between ENDS, with and without nicotine, with and without NRT on smoking cessation or reduction. Six studies were included, with two RCTs. The authors quantitatively concluded that ENDS with nicotine compared with ENDS without nicotine were effective for cessation (pooled RR=2.29, 95% CI=1.05, 4.57). Compared with controls, ENDS were positively associated with smoking cessation (pooled effect size=0.20, 95% CI=0.11, 0.28) and qualitatively associated with smoking reduction.

b. Compared with no intervention, in all smokers versus smokers motivated to quit. Kalkhoran²³ published a 2016 systematic review and meta-analysis on the effectiveness of ENDS on smoking cessation in adult cigarette smokers irrespective of their motivation for using ENDS. A total of 38 studies were included in the review and 20 in the meta-analysis. E-cigarette use was negatively associated with quitting cigarettes (OR=0.72, 95% CI=0.57, 0.91), meaning those using e-cigarettes were less likely to quit. The association was not significantly different when restricted to smokers interested in cigarette cessation.

Key Question 2: What Are the Comparative Risks of ENDS Compared with Smoking Cigarettes or Non-exposure to Smoking or Vaping?

Thirty-three studies were selected for full-text review. The most common reasons for exclusion were lack of

focus on patient-oriented harms and being published before a more recent systematic review.

Many of the studies looking specifically at harms focus on individual biomarkers or immediate physiologic impacts in a controlled laboratory environment,⁷ rather than on patient-oriented outcomes. A systematic review by Pisinger et al.²⁴ included 76 studies, with 34 examining the content/effect of fluid or vapor of e-cigarettes, 20 reporting adverse events, 21 human experimental studies, and one animal experimental study. The most common adverse events reported were lightheadedness, throat irritation, dizziness, and cough. Given concerns about methodologic problems with the studies, the authors concluded inadequate information was available to draw firm conclusions; however, ENDS are certainly not harmless. They also raise concerns about mislabeling of ingredients and inclusion of some toxic ingredients (e.g., cinnamon flavor).

A Cochrane systematic review including 24 studies (three RCTs and 21 cohort studies) found no reported serious adverse events.²¹ Similar rates of minor adverse events (such as mouth and throat irritation) were reported between e-cigarette users and placebo. The authors note that the long-term safety is unknown.

A systematic review including five controlled clinical trials that evaluated adverse effects found no difference between ENDS and controls (NRT or placebo) on irritability, restlessness, poor concentration, depression, hunger, or average number of non-serious adverse events.²⁰ However, only two of the studies adequately reported on adverse effects and only one on serious adverse events. Although serious adverse events were higher in the ENDS group (19.7%) compared with the non-nicotine device group (13.9%) and patches (11.8%), the authors reported that “no serious adverse events in any groups were related to product use.”²⁵ Similarly, a more recent systematic review that included 12 studies (three RCTs and nine cohort studies)¹⁸ found that in all studies except one,²⁶ there was no reported difference in serious side effects when comparing groups using ENDS versus placebo ENDS.

No studies were found examining the potential harms of ENDS in pregnant women.^{26,27}

A systematic review of case reports included 26 case reports of 27 individuals with three categories of harm: systemic health effects (13); nicotine poisonings (12); and mechanical injury (two).²⁸ Additionally, between 2012 and 2015, there have been 92 incidents of overheating, fire, and explosion events that injured 47 people (including some life-threatening and permanently disabling injuries) and caused property damage in 67 cases.²⁹

Key Question 3: What Are the Associated Harms of Environmental (“Secondhand”) E-cigarette Vapor?

Seven studies were selected for full-text review based on relevance. Four of these were excluded because they were published prior to a more recent systematic review, not specifically relevant to the question, or did not include patient-oriented outcomes.

A recent systematic review included 16 heterogeneous studies and concluded that environmental e-cigarette aerosol may pose a health hazard to bystanders, although this risk is likely to be less than the harm posed by conventional cigarettes.³⁰ The authors raised concerns that studies funded by those with potential conflicts came to different conclusions (i.e., that secondhand vaping was non-harmful) versus the conclusions of studies whose authors were without conflicts (i.e., there is potential harm).

Another systematic review evaluated the composition of aerosols emitted by human vaping. The review identified eight studies, all published in 2013 or 2014, most of which took place in highly controlled enclosed settings.³¹ The authors concluded that a variety of potentially toxic compounds are increased in e-cigarette emissions, such as organic volatile compounds, nicotine, and metals (although at lower levels than with combustible cigarettes).

One RCT found that passive inhalation of either ENDS or combustible cigarettes increased smokers’ urge to smoke a combustible cigarette.³²

Key Question 4: How Do the Characteristics, Marketing, Perception, and Availability of the Product Affect the Incidence of ENDS Use in Population Subgroups?

Twenty-eight citations were included for full-text review. Other citations were excluded for not including interventions of interest or not having outcomes data.

Factors impacting the usage of ENDS products vary among different population subgroups. One example is the effect of advertising. ENDS advertisements have increased substantially over recent years, often with false claims.⁷ One study found that advertising exposure increased e-cigarette use among black smokers, but not among whites. Whites reported more ad exposure from stores and on the Internet, whereas blacks reported more ad exposure from radio and television.³³ Three studies found that advertisements increased youth uptake of e-cigarettes,^{34–36} although one study found mixed results.³⁷

Other common reasons cited for use of ENDS among youth and young adults are curiosity, flavorings, and low perceived harm compared with traditional cigarettes.^{7,38} These factors may also have variable impact among different age and ethnic groups. In a 2015 study of retailers in the United Kingdom, some retailers perceived that

flavored products had greater appeal to younger customers aged 18–21 years. Retailers also reported a much higher profit margin from e-cigarette sales than conventional cigarette sales.³⁹ This may affect the way in which ENDS are marketed.⁷

Another recent systematic review also found that youth and adolescents believe e-cigarette flavoring is less harmful than traditional cigarettes,⁴⁰ a factor leading to initiation or experimentation.⁴⁰ This lack of perceived harm may also be influenced by ease of obtaining ENDS products, and the way in which retailers choose to display health warning messages on their products. ENDS are generally less expensive than cigarettes.² Youth may access ENDS through online retailers because of a lack of appropriate age verification methods,^{41,42} and a 2015 survey of e-cigarette Internet vendors found that of 57 Internet vendors, 68.4% displayed one or more health warnings on their website often in smaller font, or in their terms and conditions.⁴² Lack of strong health warnings may increase the probability of ENDS use among youth.²

Age, education, and race all impact use of ENDS. Among middle and high school students, being male and Hispanic was associated with higher rates of ENDS use; being black was associated with lower rates. These differences persist among adults. Those attaining less than a high school degree were much more likely to smoke ENDS compared with those with college degrees.³⁸

Some studies suggest a relationship between ENDS use and later combustible cigarette use.^{38,43} Although uncommon, e-cigarette use can also occur in those who have never tried a conventional cigarette—in one survey of college students, 12% of ever e-cigarette users had never smoked a conventional cigarette.⁴³ An RCT of combustible cigarette smokers found reductions in intention to smoke and withdrawal-related cravings among participants who were told their ENDS contained nicotine (whether or not nicotine was present). Gender differences were found, in that women demonstrated shorter latency between usages when believing the ENDS contained nicotine.⁴⁴

There are multiple types of ENDS devices. Nicotine delivery varies by device depending on characteristics, such as battery size, device type, propylene glycol–vegetable glycerin ratio, and nicotine liquid concentration, and user differences.² Geiss and colleagues¹¹ determined that the most popular style of e-cigarette is the “second generation” refillable device, which resembles a regular tobacco cigarette. “Tobacco-like” flavoring has been found by some studies to be the most commonly sold on the market,¹¹ which may reflect greater ENDS use among adults than youth.

Key Question 5: Are Policy Measures Effective at Reducing the Number of New Vapers or Exposure to Secondhand Aerosol?

No studies were found in the literature search that directly addressed this question.

Policy Landscape

In August 2016, the Food and Drug Administration's regulatory authority over tobacco products was extended to ENDS.⁴⁵ The new rule restricts youth access to these newly regulated products. Youth access to ENDS is further restricted to varying degrees by state law in all states.⁴⁶ Preliminary evidence suggests that policy restrictions have had an impact on previously reported increases in youth uptake of e-cigarettes.⁴⁷ Table 3 details national governmental and international organizations' policy stance on ENDS.

In the U.S., the development of clean air regulations that apply to ENDS has been stepwise and with significant variation across the country. Most of the regulations have been developed first at the municipal level then at the state level.⁵⁴ A number of states have instituted additional regulations on ENDS, such as increasing the minimum age requirement to purchase ENDS (to 19 or 21 years) and applying smoke-free policies equally to ENDS.⁴⁶ Most states do not tax e-cigarettes,^{46,55} which may lead to a competitive advantage over taxed conventional tobacco products.

DISCUSSION

The evidence behind the safety and efficacy of ENDS has not caught up with the rapid increase in widespread use of these products. Limited evidence supports the short-term efficacy of exclusive use of nicotine-containing ENDS in adults desiring to quit, with several RCTs demonstrating positive results compared with observational studies that often do not show benefit. These studies compared ENDS with no treatment, non-nicotine ENDS, or, in rare cases, NRT. There is insufficient evidence comparing the efficacy of ENDS to established evidence-based treatments.

Clinical studies evaluating short-term patient-oriented harms of ENDS in adults compared with combustible cigarettes appear to be mostly minor (e.g., mouth and throat irritation, cough, lightheadedness, and nausea) but worse than non-vaping, and long-term harm data are unavailable. In youth, and adult nonsmokers, the greatest harm is in the possibility of inducing dependence with long-term use of ENDS (with unknown long-term effects) or combustible cigarettes (with well-described serious morbidity and mortality implications). Serious adverse events related to ENDS are rare but do

occur and are mostly related to overheating, fires, and explosions. In terms of environmental (secondhand) exposure, very short-term experimental studies suggest that environmental toxic exposures are substantially less than with conventional cigarettes, but not negligible, and that exposure to certain components (e.g., nicotine) may equal conventional cigarettes. Of concern, one RCT³² identified in this review found that passive exposure to ENDS increases the desire to smoke conventional cigarettes among smokers.

At the individual level, the benefit/harm balance may weigh in favor of ENDS compared to no treatment for tobacco cessation, in a very specific population of adult smokers who are trying to quit, based on limited evidence and a harm reduction approach if they are able to reduce use of combustible cigarettes through use of ENDS. There are other effective, evidence-based methods for smoking cessation; therefore, ENDS would only be appropriate in those unwilling to try or who have failed evidence-based smoking-cessation therapies and are interested in trying ENDS.

In youth, there are no known individual benefits of ENDS use and significant potential for harm (including another forum for use of psychoactive substances, such as tetrahydrocannabinol, and developing dependence on nicotine). Youth use of ENDS should be actively discouraged, similar to combustible tobacco products.

At the population level, there is a public health concern that ENDS use may have a negative potential impact on youth smoking and impact the cultural norms around cigarette use, increasing the acceptability and appeal of cigarette smoking. Given that there are significant potential harms at the population level and at the individual level, a clear benefit of ENDS has not yet been proven and long-term harms are completely unknown, restrictive policy strategies are indicated, and at the individual clinical level, caution is advised in adults.

Limitations

This evidence review has a number of limitations. First, a rapid review methodology was employed rather than a systematic review. This methodology allows for a more rapid process but is a less rigorous methodology. Risk of bias was assessed for systematic reviews but was not for individual clinical and observational studies. Strength of evidence for KQ conclusions was not assessed by predefined criteria. The second major limitation relates to the very rapid development of evidence in this field, which means that new studies have been published since the last search date. Given the evolving evidence, new reviews of the literature and potential revisions to the practice statement will be necessary. The third major

Table 3. Policy Statements and Recommendations by Others

| Organization | Target population | Policy statement/recommendations |
|---|--------------------------------------|---|
| HHS, Office of the Surgeon General (HHS, 2016) ³⁸ December 2016 | Youth and young adults | Include ENDS in smoke-free indoor air policies. Restrict youth access to ENDS in retail settings. Formulate tobacco-related licensing requirements for a business to manufacture, distribute, or sell tobacco products. Establish specific packaging requirements. |
| U.S. Preventive Services Task Force (USPSTF, 2016) ⁴⁸ November 2015 | All adults, including pregnant women | Current evidence insufficient to recommend ENDS for tobacco cessation in adults. USPSTF recommends clinicians to direct patients to other cessation interventions with established effectiveness and safety. |
| U.S. Food and Drug Administration (U.S. FDA, 2016) ⁴⁵ August 2016 | U.S. population | Since August 2016, the FDA's regulatory authority to regulate manufacturing, distribution, and marketing of tobacco products was extended to electronic cigarettes or ENDS. The new rule restricts youth access to newly regulated tobacco products (no products sold to those younger than 18, requiring age verification by photo ID, and no tobacco products in vending machines). |
| National Governors Association (National Governors Association, 2016) ⁴⁹ August 2016 | U.S. population | No current conclusive scientific evidence that ENDS are effective for long-term cessation from conventional cigarettes. Insufficient evidence exists to support claims that ENDS do not constitute a health risk, especially as a result of long-term use. As of March 2016, a total of 21 states have included ENDS in smoke-free air laws and regulations, and three states (Louisiana, Minnesota, and North Carolina) and the District of Columbia have imposed taxes on ENDS. |
| Public Health England and other United Kingdom public health organizations (Public Health England, 2016) ⁵⁰ July 2016 | United Kingdom population | ENDS are significantly less harmful than smoking. Because of the public health opportunity, smokers may be encouraged to try vaping to stop smoking tobacco completely. ENDS use is the most popular quitting tool in the country, but using local stop smoking services is the most effective way to quit. |
| WHO ⁵¹ August 2016 | All countries | Prohibit health claims. Prohibit use of ENDS indoors. Regulate advertising, promotion, and sponsorship. Include health warnings. Prohibit sales to minors. Prohibit health claims. |
| Government of Australia; Quit line Victoria ^{52,53} | Youth and adults | Nicotine e-liquid is Schedule 7 (dangerous poison) and against the law. E-cigarettes are not approved by the Therapeutic Goods Administration as a quit smoking aid. A precautionary approach to future regulation is contemplated as with other combustible products. |

Table 4. ACPM Practice Statement on Electronic Nicotine Delivery Systems (ENDS) or E-cigarettes

| Dimension | Recommendation | SORT grade |
|--------------------------------------|--|-------------------------------------|
| Screening | | |
| | Clinicians should screen youth for exposure to ENDS as part of tobacco screening and provide education and brief counseling to prevent initiation of e-cigarette and tobacco use. (This recommendation is adapted from the USPSTF 2013 recommendation on interventions to prevent tobacco initiation in children and youth, which is currently being updated.) | C |
| | Clinicians should discuss potential harms of e-cigarettes. Youth identified as active ENDS users should be advised to quit. Clinicians should screen all adults for ENDS use as part of tobacco screening. Those who smoke or vape should be advised to quit (or cut down) tobacco and ENDS use and be given evidence-based options for control of nicotine addiction, including counseling and pharmacologic strategies. | C |
| | Clinicians should screen pregnant women for the use of ENDS as part of tobacco screening. Those who smoke or vape should be advised to quit all nicotine products and provided with evidence-based tobacco cessation interventions including behavioral interventions and financial incentives. | C |
| Prevention | | |
| | Clinicians and public health officials should support efforts to prevent experimentation and initiation of ENDS particularly in youth, because the long-term health effects are unknown and ENDS has the potential to serve as a gateway to cigarette smoking. | C (NASEM conclusions 16-1, 2, 3) |
| | Clinicians should advise patients to keep ENDS away from children and pets due to the potential for hazards, including poisoning and battery explosions. | C |
| Tobacco cessation and harm reduction | | |
| | Clinicians should advise patients that ENDS are not considered evidence-based smoking-cessation therapy. If patients have refused or failed these treatments and are more willing to try ENDS as a harm reduction or nicotine-cessation approach, than a first-line evidence-based strategy, clinicians should use a shared decision-making approach and address the following issues: Nicotine-containing ENDS have limited short-term evidence to support their use as a clinical tool to help smokers quit; there is a lack of evidence around long-term efficacy or harms, and the ingredients are currently unregulated; and rare but serious harms, including burns, explosions, and childhood poisonings, may occur. Clinicians should monitor for the effectiveness of ENDS in their patients and for any adverse effects. | B (NASEM conclusions 17-1, 2, 3, 4) |
| | Clinicians should counsel patients about the inconsistent nicotine content of liquids, the possibility that flavorings may sometimes include toxic components, unreliable labeling, and the significant variations in drug delivery associated with ENDS devices that limit the expected efficacy of ENDS as a smoking-cessation measure and possibly could result in harm. | C |
| | Clinicians should advise pregnant women who smoke cigarettes to use evidence-based treatments (e.g., behavioral counseling and financial incentives) rather than recommending ENDS. | C |
| Policy/regulatory | | |
| | Given the potential population effects of widespread availability and appeal of ENDS, particularly to youth, ENDS should be regulated. | C |
| | Policies should be adopted to prohibit access as well as exposure to marketing for ENDS to anyone under the age of 21 years. | C |
| | Regulations should require standardization of ENDS products, including labeling and nicotine content and delivery, and flavorings should only be included if known to be non-toxic. | C |
| | All environmental restrictions on combustible cigarette smoking, such as smoke-free workplaces, should equally apply to ENDS. | C |
| | ENDS are a potential environmental occupational hazard, and regulatory authorities should limit or eliminate their presence in high-risk environments (e.g., airplanes). | C |

(continued on next page)

Table 4. ACPM Practice Statement on Electronic Nicotine Delivery Systems (ENDS) or E-cigarettes (continued)

| Dimension | Recommendation | SORT grade |
|---------------|---|--|
| Research gaps | Screening and documentation of ENDS use should be incorporated into electronic health records and built into metrics related to tobacco use. | C |
| | NIH, CDC, and other funding agencies should sponsor research in youth and adults into the long-term (i.e., >10 years) effects of ENDS on nicotine cessation; harms of use and risk of conventional cigarette smoking initiation; and the comparative effectiveness of ENDS compared to behavioral and pharmacologic strategies. Targeted studies of the use of ENDS in special populations, such as pregnant women and individuals with mental disorders, are needed. | B (NASEM recommendations 15-1, 15-2, 20-1) |
| | Health services research is needed on the effectiveness of policies and regulations designed to curtail use of ENDS and their impact on overall tobacco use. | C |
| | Further surveillance and research is needed on the toxic and hazardous effects of ENDS, particularly in children. | C (NASEM conclusions 15-1) |
| | Research is needed on the effects of ENDS on adolescent brain development. | C |
| | Further research should evaluate the impact of secondhand exposure to aerosol. | C (NASEM conclusions 6-1) |

SORT grades include A (good-quality, patient-oriented evidence); B (inconsistent or limited-quality patient-oriented evidence); and C (consensus, disease-oriented evidence, usual practice, expert opinion, or case series for studies of diagnosis, treatment, prevention, or screening).⁵⁶
 CDC, Centers for Disease Control and Prevention; NASEM, National Academies of Science, Engineering, and Medicine; SORT, Strength-of-Recommendation Taxonomy from American Academy of Family Physicians.

limitation is that the current evidence does not adequately address the long-term (i.e., more than 10 years) effects of ENDS on nicotine cessation, harms of use and risk of conventional cigarette smoking initiation, nor the comparative effectiveness of ENDS compared with evidence-based behavioral and pharmacologic strategies, yet ACPM makes recommendations to inform current practice knowing that further evidence could result in changes to its practice statement.

Through an evidence-informed consensus process, the ACPM has developed 18 prevention practice statements related to ENDS (Table 4).

Recently the National Academies of Science, Engineering, and Medicine (NASEM), Committee on the Review of the Health Effects of ENDS published a consensus study report entitled the Public Health Consequences of E-cigarettes.⁵⁷ Where there is overlap in the conclusions between the NASEM report and the ACPM, specifically in the areas of prevention, tobacco cessation, and harm reduction, this is noted in Table 4.

CONCLUSION

The evidence on the benefits versus harms of e-cigarettes is still emerging. There are significant population health concerns, and it is unclear if the potential benefit to the individual adult smoker interested in quitting outweighs the potential harms of attractiveness to youth, including a gateway to cigarette smoking and changing norms around vaping and smoking.

ACKNOWLEDGMENTS

The authors would like to heartily acknowledge Anita Balan, MPH, MCHES, for her assistance in preparation of the manuscript. Also, the authors appreciate the input of Christopher Novak, MD, MPH, Dave Cundiff, MD, MPH, and Lidia Nelkovski, MD, in the development of the practice statement.

The findings and conclusions of the manuscript are those of the authors and do not necessarily reflect the views of the U.S. Defense Agency, the Agency for Healthcare Research and Quality, HHS, the U.S. Department of Defense or the Federal Government.

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No financial disclosures were reported by the authors of this paper.

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