Electronic nicotine delivery systems (ENDS), which include electronic cigarettes, or e-cigarettes, are growing in popularity, but their safety and efficacy as a smoking cessation aid are not well understood. Some argue that they have the potential to reduce tobacco-related morbidity and mortality and could be a useful tool for reducing tobacco-related harm. Others express concern that the health effects of ENDS use are unknown, that they may appeal to young people, and that they may encourage dual use of ENDS and traditional tobacco products. Although ENDS are a new and unregulated product, the U.S. Food and Drug Administration has proposed regulations that would deem ENDS to be subject to the Family Smoking Prevention and Tobacco Control Act, which regulates cigarettes and other tobacco products. In this position paper, the American College of Physicians offers policy recommendations on ENDS regulation and oversight, taxation, flavorings, promotion and marketing, indoor and public use, and research. This paper is not intended to offer clinical guidance or serve as an exhaustive literature review of existing ENDS-related evidence but to help direct the College, policymakers, and regulators on how to address these products.

In its 2010 paper, “Tobacco Control and Prevention,” the American College of Physicians (ACP) called for regulation and oversight of ENDS, noting that the products may expose users and bystanders to toxic constituents (7). The College developed this position paper to provide updated policy and regulatory guidance to policymakers to address the growing ENDS market. This paper does not intend to provide specific clinical guidance regarding ENDS, but instead offers recommendations on product regulation, flavorings, taxation, marketing and promotion, indoor air laws, and additional research. While the long-term public health consequences of ENDS are unknown, the College believes that efforts should be made to oversee these novel products to protect the health of ENDS users and nonusers and strongly prohibit youth access. Further, robust research is needed to better understand the potential benefits and harms associated with ENDS. This Executive Summary provides a synopsis of the full position paper, which is available in the Appendix (available at www.annals.org).

**Methods**

This policy paper was drafted by the ACP’s Health and Public Policy Committee, which is charged with developing and assisting with implementation of ACP pol-
Electronic Nicotine Delivery Systems

An appropriate federal agency, such as the Agency for Healthcare Research and Quality, National Institutes of Health, or Centers for Disease Control and Prevention, should commission an evidence review to evaluate the current research and data related to benefits and harms of ENDS that can be utilized as a basis for a clinical guideline.

From the American College of Physicians, Washington, DC.

Disclaimer: The authors of this article are responsible for its contents, including any clinical or treatment recommendations.

Acknowledgment: The authors thank Jorge Fuentes, MD, for his contributions to this article.

Financial Support: Financial support for the development of this guideline comes exclusively from the ACP operating budget.

Disclosures: Disclosures can be viewed at www.acponline.org. Author contributions are available at www.annals.org.

References


Types of ENDS

ENDS are available in various forms, brands, and flavors (14). A disposable e-cigarette model, such as OneJoy (NJOY, Scottsdale, Arizona), resembles a cigarette and is intended to be thrown away after the aerosol has depleted. Rechargeable e-cigarettes, such as certain Blu e-Cigs models (Lorillard), contain a battery and may have a component that regulates inhalation duration. Pen-style rechargeable ENDS such as Storm (Vapor King) contain prefilled or refillable nicotine cartridges. Tank-style devices are substantially larger than cigarette-style ENDS and have a higher battery and nicotine liquid capacity. Quality of ENDS and their components varies, and the FDA has raised concern about “substandard or nonexistent” quality control standards (15). The ENDS liquids are often flavored; in early 2014 there were 7764 different flavors of e-cigarette products (16). Flavors include chocolate, bubble gum, and Belgian waffle.

Are ENDS Safe?

ENDS products often contain nicotine, a highly addictive drug. Nicotine may promote tumor growth, compromise cancer treatment, and negatively affect the neurologic development of adolescents (10, 17). ENDS use may also harm the lungs. ENDS aerosol contains particulate matter in size and distribution similar to that of combustible cigarettes, with higher levels found in ENDS with higher nicotine content. The human toxicity of inhaled particulate matter is not yet known (18). ENDS use may affect lung function: One study found that after inhaling ENDS aerosol for 5 minutes, participants (healthy smokers) showed an increase in airway resistance (19). The study acknowledged that further research is needed to determine the long-term effects of inhalation of ENDS aerosol on lung function.

ENDS aerosol contains toxic chemicals, such as formaldehyde and acetaldehyde, at rates 9 to 450 times lower than that of combustible cigarettes but higher than that of a nicotine inhaler (14, 20). In a comprehensive review of ENDS health effects studies, Grana and colleagues concluded that “although data are limited, it is clear that e-cigarette emissions are not merely ‘harmless water vapor,’ as is frequently claimed and can be a source of indoor air pollution” (14).

Propylene glycol and glycerin are found in ENDS liquid. Propylene glycol can irritate the eye and respiratory system (14, 21). Heavy metals, such as tin, lead, and nickel, have also been discovered in a brand of ENDS nicotine liquids and aerosols. These metals can
negatively affect the nervous and respiratory systems (22).

ENDS Use Among Youth

Use of e-cigarettes among young people is growing. The number of high school students who never used tobacco but had tried ENDS tripled between 2011 and 2013 (23, 24). Previous data from the Centers for Disease and Prevention estimated that e-cigarette use had more than doubled among U.S. middle and high school students from 2011 to 2012 (25). Some argue that this percentage is higher when noncigarette ENDS, such as electronic hookahs or “vape pipes,” are included in the count (26). The National Institute on Drug Abuse’s 2014 Monitoring the Future survey found that 8.7% of 8th graders, 16.2% of 10th graders, and 17.1% of 12th graders reported using ENDS in the past month and that use surpassed combustible cigarette smoking among teens (27).

Although this is debated in the literature (28), evidence suggests that adolescents who start using ENDS also use or intend to use combustible tobacco products (29, 30). The 2011-2013 National Youth Tobacco Survey found that 44% of nonsmoking youths who had tried ENDS stated they intended to start smoking combustible cigarettes within the next year (31). Of those who had not tried ENDS, only 21.5% said they would try combustible tobacco in the coming year. The survey also found that among young people who smoked combustible cigarettes, 20% reported that they also had tried ENDS (23). A press release on the aforementioned 2014 Monitoring the Future survey noted that it was unclear whether teens who exclusively used ENDS went on to use traditional cigarettes (32).

Potential for Smoking Cessation?

Some argue that ENDS have potential as smoking cessation aids and that the devices deliver nicotine to the user without many of the harmful constituents found in combustible tobacco smoke (33). Further, say proponents, ENDS mimic the tactile and sensory experience of smoking. Some evidence suggests that ENDS help combustible tobacco smokers reduce or abstain from use. A study by Polosa and colleagues found a 50% reduction in cigarette smoking among 32.5% of participants (27 of 66) who participated in the 24-week study, leading the authors to conclude that “the use of e-Cigarette substantially decreased cigarette consumption without causing significant side effects in smokers not intending to quit” (34). Bullen and colleagues (35) compared smoking abstinence rates at 6 months for those who used ENDS, nicotine patches, and placebo ENDS (nicotine-free). Verified abstinence rates at 6 months were 7.3% for nicotine ENDS users, 5.8% for nicotine patch users, and 4.1% for placebo ENDS users (35). Another study found that smokers rated electronic cigarettes higher than nicotine inhalers on measures of satisfaction, reward, acceptability, and perceived cessation benefits (36). However, others conclude that the potential of ENDS to help smokers quit is not clear. The World Health Organization’s 2014 report on ENDS found “insufficient evidence” to support ENDS as a smoking cessation aid and reiterated its recommendation that existing approved cessation aids be used (37). A policy statement from the American Heart Association notes that “[c]urrent evidence suggests at best a modest effect on cessation, likely equal to or slightly better than nicotine patches without behavioral support” and maintains that further research and regulation is urgently needed (16, 38).

Although many combustible tobacco smokers cite the desire to reduce or quit smoking as motivation for using ENDS, many also report using the devices to skirt smoke-free zone laws (39). Dual use of ENDS and combustible cigarettes is substantial among adults and youth (29); the 2011 and 2012 National Youth Tobacco Survey found that 76% of young people in grades 6 to 12 who currently used electronic cigarettes were also current conventional cigarette smokers (25).

Recommendations

1. The American College of Physicians recommends that the Food and Drug Administration extend its regulatory authority granted through the Family Smoking Prevention and Tobacco Control Act to cover electronic nicotine delivery systems (ENDS).

In its 2010 position paper, “Tobacco Control and Prevention,” the American College of Physicians (ACP) recommended that “the FDA should be authorized to regulate electronic cigarettes until convincing evidence develops that they are not addictive of harmful” (7). The College based this position on evidence that ENDS contained harmful toxins, such as ethylene glycol; that device quality control was limited; and that youth access and marketing were unrestricted in many jurisdictions.

In April 2014, the FDA released a proposed rule that would deem ENDS as subject to regulatory oversight as outlined in the Tobacco Control Act. Under the proposed regulation, which also extends to such products as cigars, pipe tobacco, waterpipe/hookah tobacco, and dissolvable products, ENDS manufacturers would be required to register with the FDA, disclose product ingredients, and refrain from making unsubstantiated risk-reduction claims. Retailers would not be allowed to distribute free samples or sell ENDS in vending machines accessible to youths. Product packaging would display health warnings regarding the addictiveness of nicotine. The rule would also establish age verification requirements for deemed products.

Regulation of ENDS remains an important goal. Access and use has exploded in the last few years in the United States and abroad. The devices are now a $2
billion a year industry in the United States, and global sales were expected to reach $5 billion in 2014 (40). Major tobacco companies have taken notice, with R.J. Reynolds, Lorillard, and Altria Group all offering electronic cigarettes products.

Quality control remains a major concern. Nicotine yields vary widely, potentially exposing users to higher-than-expected levels of the chemical. A study of 16 ENDS models found that efficacy and consistency of nicotine vaporization were not uniform (41, 42). Product labels are often inaccurate: One study found that ENDS marketed as being free of nicotine actually did contain the addictive drug (43). The FDA’s proposed regulation would provide the necessary oversight to ensure that ENDS manufacturers adhere to quality control guidelines and disclose accurate product information, including nicotine content.

It is also apparent that young people are able to access ENDS. Use of electronic cigarettes among high school students rose from 4.7% to 10% from 2011 to 2012, and only 33 states have established age restrictions to prevent young people from purchasing the devices (30, 44). The FDA’s proposed rule would prohibit ENDS sales to persons aged 18 years and younger and allow states to establish higher age restrictions.

Unregulated ENDS packaging and product design also pose a danger to young children. Poison control centers across the nation have reported an increase in the number of children poisoned by nicotine derived from ENDS, with more than half of these exposures affecting children younger than 6 years (45). The ACP has joined with other medical societies to call for future rulemaking that would mandate childproof ENDS packaging (46).

The proposed rule does not apply many regulatory provisions established in the Tobacco Control Act to deemed products, such as ENDS. These include prohibitions on the sponsorship of sporting and entertainment events; self-service retail displays; and tobacco product-branded merchandise, such as clothing that displays a tobacco company logo. The FDA should extend these requirements to deemed tobacco products to ensure consistent application of the law.

The College supports the following specific regulatory provisions:

A. Requiring health warnings on all packaging, sales displays, and promotional and marketing materials. Warnings should be updated as scientific evidence related to the health effects of ENDS emerges.

B. Establishing product safety and manufacturing standards, including childproof designs for all ENDS-related devices and nicotine liquid cartridges.

C. Prohibiting ENDS-related promotion and sponsorship of entertainment and sporting events, self-service retail displays, distribution of free samples, sales of ENDS products in vending machines accessible to youth, and tobacco product-branded merchandise.

D. Prohibiting sales to persons younger than age 18 years and requiring age verification.

E. Applying requirements on misbranding and adulteration, ingredient disclosure, manufacturer registration and inspection, premarket review, and the prohibition of unsubstantiated health claims to ENDS products.

2. The American College of Physicians recommends that characterizing flavors should be banned from all tobacco products, including ENDS.

Tobacco use usually begins in adolescence, and tobacco companies have targeted this vulnerable and impressionable age group by offering flavored products that appeal to young palates (47). This is not a new strategy; internal tobacco company memoranda going back to the early 1970s have revealed that flavored tobacco has long been discussed as a means to introduce young people to smoking. A 1972 Brown and Williamson company document discussing a potential “youth cigarette” states that “Apples connote goodness and freshness and we see many possibilities for our youth-oriented cigarette with this flavor” (48). Fruit flavorings used in tobacco are often the same as artificial fruit flavorings used in candy. For example, the chemical flavorings used in “cherry” Jolly Rancher, Zotz, and Life Savers candies were also prevalent in cherry-flavored tobacco products, leading study authors to conclude that “[t]he same, familiar, chemical-specific flavor sensory cues that are associated with fruit flavors in popular candy and drink products are being exploited in the engineered designs of flavored tobacco products. What we are seeing is truly candy-flavored tobacco” (49). It is also evident that young people who initiate smoking flavored products often develop a long-term addiction. A 2013 study published in the American Journal of Preventive Medicine found that “young adults were more likely to use flavored tobacco products” and concluded that “those most likely to use flavored products are also the most at risk of developing established tobacco-use patterns that persist through their lifetime” (50). Another study found that young adult waterpipe/hookah tobacco users erroneously believed that fruit flavorings filtered out unsafe toxins from the tobacco, making them safer to use than unflavored products.

The Tobacco Control Act bans characterizing flavors (with the exception of tobacco and menthol) from cigarettes, but leaves it to federal regulators to extend the ban to other tobacco products. ENDS products are available in thousands of enticing flavors (51), including chocolate, cotton candy, and Georgia peach, and are just as popular with young people as their combustible counterparts. A survey of young adult ENDS users (age 18 to 24 years) found that they “exclusively” used flavors...
vored electronic cigarettes compared with just 65% of older survey respondents (52, 53). Because flavored electronic cigarettes appeal to young people and may encourage them to initiate tobacco product use, federal regulators should ban all flavorings in all tobacco products.

3. The American College of Physicians reiterates its support for taxing tobacco products, including ENDS devices and nicotine liquids, to discourage use among children and adolescents. Local governments should be permitted to establish higher tax rates for ENDS and related products than state levels.

The evidence shows that young tobacco users are especially price sensitive. Governments have often increased tobacco taxes as a means to discourage use. According to the World Health Organization, “on average, a 10% price increase on a pack of cigarettes would be expected to reduce demand for cigarettes by about 4% in high-income countries,” with even greater reductions in low- and middle-income countries (54). The ACP supports policies to increase taxes on tobacco products, especially to fund tobacco use control and prevention efforts (7). The College believes that ENDS and nicotine liquids should be subject to taxation policies that discourage use among young people.

ENDS-related taxation policy is complex. As of August 2014, only a handful of states had enacted policies that subject ENDS to tobacco taxes (55). Minnesota specifically applies electronic cigarettes to the state’s tobacco tax and defines the devices and nicotine liquids as tobacco products (1). Vermont and Missouri apply an excise tax to all “tobacco-derived products” or similar language, rather than explicitly naming ENDS. The American Heart Association supports “taxing e-cigarettes at a rate high enough to discourage youth use, while retaining or increasing the differentials with combustible products by increasing taxes on combustibles” and recommends directing at least some of the revenue to tobacco cessation and prevention programs (38). Whatever the path taken by policymakers, such laws should be written to ensure that existing tobacco prevention and control laws (such as those committed to reducing youth uptake, restricting indoor use, and establish taxes on combustible and other tobacco products) remain intact.

4. The American College of Physicians supports legislative or regulatory efforts to restrict promotion, advertising, and marketing for ENDS products in the same manner as for combustible cigarettes, including a prohibition on television advertising. Youth tobacco prevention efforts, such as antismoking media campaigns and school-based interventions, should include information about the potential risks for ENDS use.

Marketing of ENDS has increased dramatically in the past few years. New manufacturers and long-established tobacco companies, such as the tobacco giant Lorillard, have devoted millions of dollars to promoting the nicotine delivery products. In 2013, the largest e-cigarette companies spent $60 million on marketing, and ENDS company NJoy has said that it plans to spend $30 million on United States–based marketing in 2014 (56, 57). Young people are getting the message: Youth exposure to ENDS television advertisements increased 256% from 2011 to 2013, and young adult exposure increased 321% during the same period (58). According to a survey, 73% of teens aged 12 to 17 years were exposed to television and print advertisements for the popular Blu ENDS products, owned by Lorillard (59). ENDS ads promote the products as being “newer, healthier, cheaper and easier to use in smoke-free situations, all reasons that e-cigarette users claim motivate their use” (60). In addition, ENDS companies infer through affiliate marketing and advertising that their products are useful as a cessation devices (61).

ENDS products can circumvent marketing and advertising restrictions that apply to other tobacco products, such as combustible cigarettes and smokeless tobacco. ENDS products can be advertised in print and on television, and companies may sponsor entertainment and sporting events that attract young people. The FDA’s proposed rule on deemed tobacco products largely avoids restricting advertising and marketing for ENDS products, although the regulation would require ENDS packaging to display a warning label regarding the addictiveness of nicotine.

Cigarette commercials have been banned from television since the passage of the Public Health Cigarette Smoking Act in the early 1970s. A ban on smokeless tobacco ads followed in the mid-1980s. Legal interventions, such as the Tobacco Master Settlement Agreement, have prohibited most outdoor advertising for tobacco products, and the Tobacco Control Act of 2010 placed additional restrictions on tobacco advertising and marketing. Before the release of the FDA’s proposed rule, Advertising Age magazine predicted that the agency would ban ENDS television advertising (62).

The ACP strongly supports prohibitions on tobacco advertising and marketing, especially when directed toward young people. A major concern among public health advocates is that the popularity of ENDS may reverse the progress made to stigmatize smoking and reduce its appeal among young people (26). Promotion, marketing, and advertising of ENDS have used imagery, messaging, and celebrity endorsements that appeal to young people; for example, an advertisement for Blu electronic cigarettes invites viewers to “take our freedom back,” and the company sponsors music festivals and auto racing teams (63). The College is concerned that tobacco product advertising results in increased awareness of ENDS products, creates a mis-

Annals of Internal Medicine • Vol. 162 No. 8 • 21 April 2015
www.annals.org
conception that ENDS are safe, and may give people an unsubstantiated view that ENDS are a clinically accepted means of smoking cessation. Most concerning, ENDS advertising, promotion, and marketing may encourage young people to start using such products, potentially leading to a lifetime of nicotine addiction or use of other tobacco products, such as combustible cigarettes.

Some evidence suggests that many young people believe that ENDS do not pose a substantial risk to health; the 2014 Monitoring the Future survey found that only 15% of eighth graders said that regular ENDS use could pose great harm to one’s health (32). To combat ENDS marketing, youth-oriented education campaigns to prevent and control tobacco use should stress the potential dangers of ENDS and strongly maintain that they are not a safe alternative to other tobacco products. Similar messaging should be ingrained in education campaigns targeted at adults.

5. The American College of Physicians recommends that federal, state, and local regulators should take action to extend indoor and public place clean air laws that prohibit smoking in public places, places of employment, commercial aircraft, and other areas to ENDS products.

Some studies suggest that ENDS vapor exposure may be harmful. ENDS aerosol exposes bystanders to nicotine and other toxins at levels substantially lower than those in combustible tobacco smoke but higher than those in air; however, the long-term effects of such exposure is not yet known (12, 14). An evidence review published in the journal Circulation recommends that clinicians advise patients not to use ENDS indoors or around children because of the potential threat of secondhand exposure (14). ENDS product marketing often promotes the ability of users to “smoke anywhere,” including public places, where use of traditional combustible tobacco products is not allowed (64). Permitting indoor ENDS use where smoking is banned may facilitate the “normalization” of smoking; complicate indoor air law enforcement; and establish the misconception that indoor tobacco use is lawful, safe, and socially acceptable.

As of July 2014, a handful of state and local governments had taken action to extend indoor smoking bans to ENDS. North Dakota prohibits ENDS use in all smoke-free venues, including nonhospitability workplaces, bars and restaurants, and gambling facilities. Other states regulate ENDS indoor use in specific areas, such as school district property, correctional facilities, or state agency buildings (65). Many large cities, including Seattle, Washington; Boston, Massachusetts; Los Angeles, California; and New York City, New York, have also implemented regulations to ban ENDS use indoors. Many municipalities have extended the ban on indoor ENDS use to other public places, such as city parks (66). Further, the National Association of County and City Health Officials recommends that local health departments, legislators, and regulators “use broadly-defined language to include e-cigarettes in new smoke-free legislation for indoor and outdoor environments” (67). The College recommends that indoor air laws be clarified to include ENDS. Relevant entities should initiate public information campaigns to educate people about indoor clean air laws and their application to ENDS.

6. The American College of Physicians recommends that the federal government should authorize and appropriate funding to rigorously research the health effects of ENDS use, chemical content, and toxicity; effects of ENDS vapor exposure; dual-use rates; and effects of ENDS-derived nicotine on human health. An appropriate federal agency such as the Agency for Healthcare Research and Quality, National Institutes of Health, or the Centers for Disease Control and Prevention, should commission an evidence review to evaluate the current research and data related to benefits and harms of ENDS that can be utilized as a basis for a clinical guideline.

Published research on the efficacy and health effects of ENDS has proliferated in recent years, yet consensus on their clinical merit and safety has not been met. Although supporters tout electronic cigarettes for their potential as a smoking cessation aid or safer alternative to combustible tobacco smoking, at this time empirical data on their efficacy to help smokers quit are limited and inconclusive (68, 69).

The FDA has distributed $270 million dollars to 48 projects to study ENDS (70). In addition to studying the chemical content of ENDS cartridges and the effect of vapor on the respiratory system, grant recipients are also studying underage consumers’ response to different ENDS retail display configurations, evidence of consumer nicotine container tampering to vary dosage, and the toxicity of vapor from higher-voltage refillable tank devices, among other considerations. The FDA began studying ENDS in 2012, and some projects will conclude in 2018.

Physicians and other health care professionals may be misinformed about ENDS safety and efficacy. A survey of North Carolina physicians found that 67% believed ENDS products to be a helpful smoking cessation tool and 35% recommended them to patients. Thirteen percent thought that the FDA had approved electronic cigarettes for smoking cessation (71). At this time, the U.S. Preventive Services Task Force has not issued recommendations on use of ENDS as smoking cessation aids. The devices (as well as other products not approved by the FDA for such use) were excluded from the Task Force’s “Behavioral Counseling and Pharmacotherapy Interventions for Tobacco Cessation in Adults, Including Pregnant Women” final research plan.
despite calls from the American Cancer Society and others for their inclusion in the evidence review (72, 73).

A survey of existing evidence conducted by Breland and colleagues (12) underscores the need for more knowledge:

The most important roles that science can play in the current ECIG debate are to identify and then fill the substantial knowledge gaps that exist today. The review of the literature presented here highlights clearly that very little is known about the acute and longer-term effects of ECIG use for individuals and the public health, especially given the dramatic variability in ECIG devices, liquids, and user behavior.

Rigorous, extensive testing is needed to determine whether ENDS are indeed useful smoking cessation aids, particularly when compared with FDA-approved nicotine replacement therapy and medications. Further study is also needed to determine the long-term physiologic, psychological, and environmental effects of regular ENDS use; use among adolescents and younger users and the effect on development; dual-use habits; effect of normalization of smoking; and other considerations.

Conclusion

Despite the widespread popularity and availability of ENDS, little is known about the direct and second-hand long-term effects of their use or their potential as a smoking cessation aid. The College supports strong regulations to ensure product safety and transparency, policies that prevent use among young people, in- creased research to better determine their health effects, strong limits on marketing and promotion to discourage interest among young people, and application of indoor air laws to protect the health of bystanders.

Web-Only References


