EXECUTIVE SUMMARY

Objective. This report updates and expands information presented in CSAPH Report 6-A-10. This is an important issue for physicians and other health care professionals who are being asked to counsel patients and communities about the safety and efficacy of e-cigarettes in the midst of conflicting or inconsistent research findings, a changing regulatory landscape, and the expanding influence of major tobacco companies. The CSAPH deems that another report is needed to educate and inform the House of Delegates on this evolving topic.

Methods. English-language articles were selected from searches of the PubMed and Google Scholar databases from 2010 to July 31, 2014 using the search terms “electronic cigarettes,” “e-cigarette,” and “electronic nicotine delivery systems” in the article title and/or abstract. Internet sites managed by federal agencies and applicable health professional organizations and tobacco control advocacy organizations also were reviewed for relevant information. Additional articles were culled from the manual search of reference lists contained in pertinent articles and other publications. Recognizing the dynamic nature of research being published on this topic, the Council deemed it appropriate to summarize the findings and conclusions of a comprehensive background paper prepared for the World Health Organization Tobacco Free Initiative and to evaluate literature published subsequent to the publication of the background paper.

Results. The popularity of e-cigarettes has grown steadily since their introduction into the U.S. marketplace in 2007. Since that time, awareness and use of e-cigarettes has increased considerably among adolescents and adults. Rapid penetration of e-cigarettes in the marketplace is occurring with no federal oversight despite many unanswered questions about their safety, efficacy, and total impact on public health. No requirements exist for e-cigarette manufacturers to adhere to established consumer safety practices that list ingredients and produce consistent products with uniform concentrations and defined maximum doses of nicotine. The lack of regulatory oversight has resulted in inconsistent labeling, insufficient or nonexistent child protective packaging, and product design and flavoring that may encourage young people to explore and experiment with these products. The U.S. Food and Drug Administration has the legal authority to regulate e-cigarettes as a tobacco product; a proposed rule has been issued for public comment that would extend the agency’s authority to regulate e-cigarettes and other tobacco products.

Conclusion. The safety and efficacy of e-cigarettes in aiding smoking cessation have not been demonstrated scientifically and those concerned are advised strongly not to use e-cigarettes until these products are found to be safe and effective. The value of e-cigarettes as a substitute for conventional cigarettes has been questioned because of high levels of dual use with conventional cigarettes. Evidence-based policies and regulations are needed that protect all ages and populations in the context of how the e-cigarette industry is marketing and promoting these products. To minimize the potential negative impacts on prevention and cessation, and the undermining of existing tobacco control measures, e-cigarette use should be prohibited where tobacco cigarette use is prohibited and the products should be subject to the same sales and marketing restrictions as tobacco cigarettes. Considering the expanding awareness and use of e-cigarettes among adolescents and adults, it is likely physicians will need to consider how best to counsel patients about these products.
REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 2-I-14

Subject: Electronic Cigarettes, Vaping, and Health: 2014 Update

Presented by: Stuart Gitlow, MD, Chair

Referred to: Reference Committee K (Hugh Taylor, MD, Chair)

INTRODUCTION

CSAPH Report 6-A-10, “Use of Electronic Cigarettes in Smoking Cessation Programs,” reviewed the manufacture and characteristics of electronic cigarettes (e-cigarettes), applicable regulations, potential health impacts of these products, and the potential role of e-cigarettes in smoking cessation. E-cigarettes were a relatively new product when the Council developed this report. Since that time, the marketplace has experienced rapid penetration of these products despite ongoing concern about their potential impact on public health. This is an important issue for physicians and other health care professionals who are being asked to counsel patients and communities about the safety and efficacy of e-cigarettes in the midst of conflicting or inconsistent research findings, a changing regulatory landscape, and the expanding influence of major tobacco companies. The CSAPH deems that another report is needed to educate and inform the House of Delegates (HOD) on this evolving topic. In addition to this report, the HOD will continue to be apprised of issues and developments related to e-cigarettes via the “Annual Tobacco Report,” which is submitted to the HOD each June.

METHODS

This report updates and expands information presented in CSAPH Report 6-A-10. English-language articles were selected from searches of the PubMed and Google Scholar databases from 2010 to July 31, 2014 using the search terms “electronic cigarettes,” “e-cigarette,” and “electronic nicotine delivery systems” in the article title and/or abstract. Internet sites managed by federal agencies and applicable health professional organizations and tobacco control advocacy organizations also were reviewed for relevant information. Additional articles were culled from reference lists contained in pertinent articles and other publications.

The literature search revealed an extensive list of peer-reviewed publications on e-cigarettes published since 2010. Recognizing the dynamic nature of research being published on this topic, the Council deemed it appropriate to summarize the findings and conclusions of a recent authoritative review and to evaluate any recent pertinent literature. In December 2013, the Center for Tobacco Control Research and Education at the University of California, San Francisco, released an extensive background paper on e-cigarettes for the World Health Organization (WHO) Tobacco Free Initiative. The WHO Background Paper reviewed the literature on e-cigarettes that was available as of September 2013, and includes an update of tobacco industry involvement in the e-cigarette market, research recommendations, global regulations pertaining to e-cigarettes, and...
potential options for regulation. A highly condensed version of the WHO Background Paper, which includes five additional studies, was published in May 2014. Relevant articles that were not included in the WHO Background Paper are cited, as appropriate, in this report; readers should refer to the WHO Background Paper for more detailed information and for primary source citations.

In July and August of 2014, the Forum of International Respiratory Societies, the American Heart Association, and the WHO released reports and policy recommendations that accord with findings and recommendations in the WHO Background Paper.

BACKGROUND

Cigarette smoking remains the leading preventable cause of sickness and mortality in the United States, responsible for more than 400,000 deaths each year. The most dire health consequences associated with smoking (e.g., cancer and heart disease) are linked to inhalation of tar and other chemicals produced by tobacco combustion and the heat of inhaled smoke; the pleasurable, reinforcing, and addictive properties of smoking are produced primarily by the nicotine contained in tobacco. The prevalence of current cigarette smoking among adults has declined from 42% in 1965 to 18% in 2012. However, more than 42 million Americans still smoke. Tobacco has been linked to the premature deaths of more than 20 million people since the first U.S. Surgeon General’s report on this topic was published in 1964.

E-cigarettes and other electronic nicotine delivery systems (ENDS) are designed to simulate the act of tobacco smoking by producing a flavored aerosol that looks and feels like tobacco smoke but without the toxic chemicals produced by burning tobacco leaves. While e-cigarettes do not contain tobacco, most contain nicotine, which can be harmful and is associated with toxicity and addiction. In most e-cigarettes, puffing activates a heating device to vaporize nicotine and other ingredients, which simulate the visual, sensory, and behavioral aspects of smoking without the combustion of tobacco. The resulting aerosol or vapor is then inhaled (called “vaping”). Because they deliver nicotine without burning tobacco, e-cigarettes are marketed as a safer, less toxic alternative to conventional cigarettes. Theoretically, the extent to which these products are less harmful to health than conventional cigarettes and help some smokers quit could help reduce the overall death and disease burden from tobacco product use in the United States.

Many health professionals are concerned that e-cigarettes may have an adverse impact on users’ health, encourage smoking initiation, perpetuate the use of nicotine and tobacco products among smokers who might otherwise quit, and counter the effectiveness of smoke-free policies. There is concern about potential health effects of acute and chronic inhalation of the vaporized base components of these products. Whereas some experts welcome e-cigarettes as a potential pathway to the reduction or cessation of tobacco use, opponents characterize them as dangerous products that could undermine efforts to denormalize smoking. Opponents of e-cigarettes argue that these products can serve as initiators for new tobacco users before they migrate to cigarettes or other tobacco products, or for existing users to become dual users (i.e., users of e-cigarettes and conventional tobacco cigarettes). The increasing popularity of e-cigarettes has raised concern that these products might undercut significant gains associated with tobacco cessation efforts and limits on public use and advertising. Experts have also raised concerns that the marketing of products such as e-cigarettes can increase nicotine addiction among young people or serve as a gateway to try other tobacco products, including conventional cigarettes, which are known to cause disease.

* For this report, these products are collectively referred to as “e-cigarettes” for the purpose of brevity and simplicity.
and lead to premature death. The temporal and causal relationships between e-cigarette use and smoking among youth have not been determined.

The U.S. Food and Drug Administration (FDA) has the legal authority to regulate e-cigarettes as a tobacco product; a proposed rule, which is discussed in this report, would extend the agency’s tobacco authority to cover additional tobacco products. In the meantime, e-cigarettes have grown to become a multibillion dollar industry with no federal oversight. Rapid e-cigarette product penetration in the marketplace is occurring despite many unanswered questions about their safety, efficacy for harm reduction and for facilitation of cessation of use of tobacco products, and their total impact on public health.

PRODUCT CHARACTERISTICS

Wide variability exists in e-cigarette product engineering, including varying concentrations of nicotine in the solution (also called “e-liquid”) used to generate the aerosol, varying volumes of solution in the product, different carrier compounds (most commonly propylene glycol with or without glycerol [glycerin]), a wide range of additives and flavors, and battery voltage. Battery voltage differences and device circuitry can result in variability in the ability of these products to heat and convert the e-liquid to an aerosol and, consequently, may affect actual delivery of nicotine and other chemicals to users emitted in the exhaled aerosol or “vapor” (which looks like smoke). Some e-cigarettes have refillable cartridges, which may provide a means for users (or others, including children) to expose themselves to potentially toxic levels of nicotine when refilling the cartridges. These cartridges also could be filled with substances other than nicotine, thus possibly serving as an alternate delivery route for other drugs.

Manufactured e-liquids contain variable concentrations of nicotine. Analysis of simulated e-cigarette use found that individual puffs contained from 0 micrograms (μg) to 35 μg of nicotine. Assuming a high nicotine delivery of 30 μg/puff, an individual would need to take about 30 puffs to deliver the 1 mg (milligram) of absorbed nicotine typically delivered by smoking a conventional cigarette. The amount of nicotine delivered to the user is likely to be dependent on the temperature achieved by the heat source in the e-cigarette and how the product is used. The variability in nicotine delivery from these products is evident from an FDA analysis, which involved the simulated use of three different cartridges for the same e-cigarette product (labeled as menthol high strength; 18 mg nicotine). Testing yielded nicotine delivery concentrations of 26.8, 34.9, and 43.2 ug/100 mL puff from the respective cartridges.

An analysis of 20 models of 10 popular brands of e-cigarette refill liquids found that the nicotine content measured in the refill bottles corresponded closely to the labels on the bottles, with concentrations ranging from 6.0 mg/mL to 29.0 mg/mL. Some brands had levels of impurities above acceptable limits for pharmaceutical products. To ensure that e-liquids meet the quality standards required of nicotine replacement medications, the study authors suggest that e-liquid manufacturing processes should be controlled and that standard testing and quality control procedures be implemented. For some brands of e-liquids, the manufacturing process or control systems are probably below required standards for nicotine-based medications.

SALES AND MARKETING

The popularity of e-cigarettes has grown steadily since their introduction into the U.S. market in 2007. The estimated market for these products approached $2 billion in 2013, and is estimated to rise to $10 billion by 2017. It is further estimated that e-cigarette sales will surpass sales of conventional cigarettes by 2023. As of January 2014, there were more than 400 different e-cigarette brands being sold on the Internet.
Most e-cigarettes are marketed and sold independently; however this changed in 2012 when Lorillard, the manufacturer of Newport cigarettes, acquired the blue-cigarette brand. The two other major U.S. tobacco companies followed suit, with Reynolds American (maker of Camel) launching its VUSE brand and the Altria Group (maker of Marlboro) debuting its MarkTen e-cigarette in select test markets in 2013; national launches were announced for some time in the second half of 2014. With the entry of these established tobacco companies into the marketplace, e-cigarette advertising is becoming more aggressive. Brands now use celebrity endorsements, event sponsorships, and advertisements on cable television, print, and web media to promote their products. “Vaping bars” are being located in many communities to promote the use of e-cigarettes and the glamorization of such use.

In addition to traditional media outlets, e-cigarettes have established a strong advertising presence on the Internet, and e-cigarette companies heavily advertise their products through electronic communication. Another innovation employed effectively by e-cigarette marketers and retailers is the use of social media and viral video sharing. Given the substantial research demonstrating the effect of viewing smoking in the movies on smoking initiation, the addictive nature of nicotine, and the lack of regulatory assurance of their quality or safety, tobacco control experts cite the important need to keep e-cigarettes from being sensationalized through the use of celebrity promotion or product placement in movies or other entertainment media.

In September, 2013, federal legislators launched an investigation into the practices of nine commonly sold e-cigarette brands. E-cigarette manufacturers have significantly increased marketing spending, more than doubling expenditures between 2012 and 2013. In total, six e-cigarette companies spent $59.3 million in 2013 to market e-cigarettes. E-cigarette companies are marketing their products using some of the same claims, tactics, and media channels -- including television and radio -- that were effective at marketing conventional cigarettes to attract young people and deter smokers from quitting before use of these channels to market cigarettes was banned. Among the most popular claims are that e-cigarettes are healthier, cheaper, and cleaner than cigarettes, can be smoked anywhere, can be used to circumvent smoke-free policies, and do not produce secondhand smoke. Cessation-related claims (ranging from overt statements that one can use the product to quit smoking to indirect claims such as “you’ll never want to smoke tobacco cigarettes again”) were found on many of the sites. Claims about effects on bystanders frequently included statements that e-cigarettes emit “only water vapor” that is harmless to others. All nine companies surveyed were using marketing practices that appeared to appeal to youth. Seven e-cigarette companies were airing television and radio advertisements during events and programs, including those with youth viewership. Six e-cigarette companies were marketing e-cigarettes in flavors that could appeal to children and teens. For example, e-cigarette manufacturers are marketing flavors like Cherry Crush, Chocolate Treat, Peachy Keen, and Grape Mint.

A recent article, based on results from the Centers for Disease Control and Prevention (CDC) National Youth Tobacco Survey, showed that flavored smoking products are used by 42% of middle-school and high-school students who smoke. The study authors conclude that advertising for flavored tobacco products is a tactic to target youth. Because flavors can mask the natural harshness and taste of tobacco, flavored tobacco products are easier for young people to use and flavoring increases their appeal.
AWARENESS AND USE OF E-CIGARETTES BY ADULTS

E-cigarettes are increasing rapidly in popularity: prevalence of ever use among adult smokers in the United States appears to have increased from approximately 2.5% in 2010 to more than 7% in 2012. In 2010, approximately 40% of adults reported awareness of e-cigarettes, rising to nearly 70% in 2011. Population-based studies of adults show the highest rate of e-cigarette use among current smokers (dual use), followed by former smokers, with little use among nonsmokers; e-cigarette use rose in each of these categories over the past few years. Awareness is more prevalent among men, but trying e-cigarettes is more prevalent among women. The most common reasons given by adults for trying e-cigarettes are for use in places where smoking is restricted, to reduce smoking, because they believe e-cigarettes are less harmful than combustible cigarettes, and for help with quitting smoking.

AWARENESS AND USE OF E-CIGARETTES BY YOUTH

Data on e-cigarettes for adolescents are limited but, like adults, show rapid increases in awareness and use. Awareness among teens and young adults appears to be higher than awareness among adults. According to a recent survey published by the Legacy Foundation, awareness of e-cigarettes among young people is nearly ubiquitous, ranging from 89% for those between 13 and 17 years of age to 94% for young adults between 18 to 21 years of age. Awareness was even higher in both age groups for individuals who had either ever or currently used traditional cigarettes. Analyses by race/ethnicity found that e-cigarette awareness was similar across racial/ethnic groups.

The first national estimates of e-cigarette use among U.S. youth from the CDC National Youth Tobacco Survey indicate rapid growth of e-cigarette use among middle school and high school students in the United States from 2011 to 2012. Among middle school youth (grades 6 through 8), prevalence of “ever trying” an e-cigarette doubled from 1.4% in 2011 to 2.7% in 2012. Similarly, current use (past 30-day use) rose from 0.6% to 1.1%. Among high school youth, ever use doubled from 4.7% in 2011 to 10.0% in 2012, with current use rising from 1.5% in 2011 to 2.8% in 2012. Notably, dual use with cigarette smoking accounts for most of the past 30-day e-cigarette use among middle school youth (61.1%) and high school youth (80.5%). Initiation of nicotine exposure with e-cigarettes is apparent in that 20% of middle school youth who had tried an e-cigarette and 7.2% of high school youth who had tried an e-cigarette had not yet tried a conventional tobacco cigarette. These results indicate rapid market penetration of e-cigarettes among youth. Moreover, although youth who had tried to quit were more likely to use e-cigarettes, most adolescent e-cigarette users are dual users with conventional smoking, suggesting that use of e-cigarettes is not leading to abstinence from smoking among adolescents.

Analysis of data from the 2011, 2012, and 2013 National Youth Tobacco surveys of middle and high school students in the United States found that the number of students who say they have tried e-cigarettes but not traditional cigarettes increased by about 60% from 2012 to 2013. The study found that non-smoking youth who used e-cigarettes were nearly twice as likely to say they plan to start smoking tobacco cigarettes compared to those who never used e-cigarettes (about 43.9% versus 21.5%, respectively). Survey results indicate that more than 263,000 middle and high school students who had never smoked before used e-cigarettes in 2013, up threefold from 79,000 in 2011. The study also showed that 21.9% of youth who had never smoked conventional cigarettes intended to try them in the next year.
PRODUCT SAFETY

Electronic cigarettes vaporize and deliver to the lungs a chemical mixture typically composed of nicotine, propylene glycol (a known irritant when inhaled), and other chemicals often of unknown dose and identity. While e-cigarettes are often promoted as safer alternatives to traditional cigarettes, little is actually known about the short- and long-term health effects of using these devices. Though the FDA states that propylene glycol and glycerin food additives are “generally regarded as safe,” the long-term effects of inhaling rather than ingesting these substances are unknown, especially in the heated vaporized form delivered by an operational e-cigarette.

Acute Toxicity

Between 2008 and early 2012, 47 adverse event reports were filed with the FDA Center for Tobacco Products regarding e-cigarettes; these include reports of eye irritation, nausea, headaches, sore throat, vomiting, and coughing. Eight reports claimed more serious health problems such as hospitalization due to congestive heart failure, hypotension, pneumonia, chest pain and “possible infant death secondary to choking on e-cigarette cartridge.” While such reports do not indicate causation, they raise questions of biological plausibility that need to be addressed. Injuries also have been reported from explosion or overheating of the lithium batteries in e-cigarettes when the device is charged for long periods or if charged with an improper charger or a powerful electrical source. Reports include an 18-month-old girl who became seriously ill after drinking e-liquid in a refill container that was left in the child’s reach and was not sealed with a child-proof cap.

From September 2010 to February 2014, 2,405 calls were made to poison control centers related to e-cigarettes. E-cigarettes accounted for an increasing proportion of combined monthly e-cigarette and cigarette exposure calls, increasing from 0.3% in September 2010 to 41.7% in February 2014. E-cigarette exposures were reported mostly among children between 0 and 5 years of age (51.1%) and adults over 20 years of age (42.0%). Exposure types included ingestions (68.9%), inhalations (16.8%), eye exposures (8.5%), and skin exposures (5.9%). In 2014, a case report was published involving a 10-month-old boy who was poisoned by ingesting e-liquid from a cartridge reported to contain nicotine (18 mg/mL) and unknown concentrations of oil of wintergreen (methyl salicylate), glycerin, and propylene glycol.

Nicotine

Nicotine, whether inhaled, ingested, or in direct contact with the skin, can be particularly hazardous to certain populations, such as children, young people, pregnant women, nursing mothers, people with cardiovascular disease, and the elderly. Nicotine directly activates neuronal cholinergic receptors in autonomic ganglia, the adrenal gland, and central nervous system. Centrally, this action also enhances the release of other neurotransmitters, such as dopamine and serotonin, making it a very effective reinforcing and mood-altering substance, key elements in fostering nicotine’s addictive properties. Because nicotine is eliminated rapidly, it needs to be replaced frequently to maintain effects or to prevent withdrawal symptoms in users who are physically dependent. Peripheral effects include epinephrine release, vasoconstriction, increased heart rate and blood pressure, and combination of increased free radical production, vascular wall adhesiveness, and a reduction of fibrinolytic activity in the plasma that may contribute to premature atherosclerosis. Like other broadly neuroactive substances, chronic nicotine exposure during youth and adolescence may have lasting consequences on brain development.

The efficiency of nicotine delivery by e-cigarettes is variable and incompletely understood. Studies measuring levels of plasma nicotine and/or craving have shown disparate results ranging from no
nicotine delivery to levels similar to traditional smoking. The authors of a recent published analysis of the nicotine content of e-liquid bottles indicated that some products pose a potential danger as they can contain up to 720 mg of nicotine. This amount is several times the fatal dose of nicotine (and larger bottles are available online). The authors state further that the minimum lethal oral dose of nicotine when acutely ingested is 40 to 60 mg in children (e.g., as occurs with oral intake of tobacco from a tobacco cigarette ingested by a child) or 0.8 to 1.0 mg/kg of body weight in adult non-smokers.

Currently, no standards exist to specify how much nicotine e-cigarettes deliver, how consistently they deliver it, or if they are packaged safely. Without safety protections, standards for product consistency, or truth-in-labeling requirements, two e-cigarettes produced on the same production line can be dramatically different. Researchers have identified instances of poor quality control and significant variability in nicotine content when testing certain e-cigarette cartridges. This potential variability in nicotine content could be misleading to consumers who believe that they are consuming one level of nicotine but instead may be consuming higher levels in certain instances.

Other Chemicals and Particulates

The aerosol emitted from e-cigarettes results only from what is exhaled by users. E-cigarettes do not generate sidestream aerosol analogous to sidestream smoke from conventional cigarettes. Researchers have detected the presence of volatile organic compounds (VOCs), tobacco-related carcinogens, metals, and other chemicals in e-cigarette aerosol. Some of the chemicals, particularly some flavoring agents, were found to be cytotoxic to human and rat cells, particularly human embryonic cells.

The particle size distribution and number of particles delivered by e-cigarettes is similar to that of conventional cigarettes, with most of the particles in the ultrafine range (modes around 100 to 200 nanometers). The particle delivery appears to depend on nicotine level in the e-liquid, with more particles delivered in e-cigarettes with higher nicotine content; the presence of flavors does not seem to be a factor. Users exhale some of these particles, which exposes bystanders to “passive vaping.” Based on available data, it is plausible that e-cigarette aerosol could be inhaled deep into the lungs similar to tobacco smoke.

Chronic Toxicity

Data are limited on chronic use of these products; thus it is too soon to know if e-cigarettes will cause long-term harm. At a minimum, current research shows that e-cigarette aerosol is certainly not merely “water vapor” as is often claimed in product marketing. Overall, e-cigarettes that have been tested show much lower levels of most toxicants (but not particles) than conventional cigarettes. The thresholds for long-term human toxicity of potential toxicants in e-cigarette aerosol are not known, and the possibility of health risks to primary users of the products and those exposed passively to the product emissions must be considered.

The FDA website states that the safety and efficacy of e-cigarette products have not been fully studied, and that consumers of e-cigarettes have no way of knowing whether e-cigarettes are safe for their intended use, how much nicotine or other potentially harmful chemicals are being inhaled during use, or if there are any benefits associated with using these products.
EFFECT ON SMOKING CESSATION

Many e-cigarette consumers have strong, but to date unsubstantiated, beliefs that e-cigarettes are a safe and effective way for quitting cigarette use; many start using e-cigarettes because of those unsubstantiated beliefs. It is reasonable to assume that, if existing smokers switched completely from conventional cigarettes (with no other changes in use patterns) to e-cigarettes, there would be a lower disease burden associated with product use. However, available evidence (although limited) points to high levels of dual use of e-cigarettes with conventional cigarettes, no proven cessation benefits, and rapidly increasing youth initiation with e-cigarettes. Furthermore, high rates of dual use may result in greater total public health burden and possibly increased individual risk if a smoker maintains an even low-level tobacco cigarette addiction for many years instead of quitting.

Data are accumulating but conflicting regarding the potential benefits of e-cigarettes as a useful tobacco cessation tool, compared with other established nicotine replacement products (e.g., “gums,” lozenges, patches). Variation among e-cigarette products and vaping techniques may affect nicotine delivery, which in turn may affect their utility as a nicotine replacement intervention. Studies of adult smokers contradict claims that e-cigarettes are effective cessation aids. Pooled results of five population-based studies of smokers showed that smokers who used e-cigarettes were about one-third less likely to quit smoking than those who did not use e-cigarettes. Whether e-cigarette use prevents attempts to quit or whether people who choose to use e-cigarettes are more highly dependent and therefore have a harder time quitting remains to be determined. A randomized trial comparing e-cigarettes to the nicotine patch showed that in the context of low level behavioral support, the quit rate for those using e-cigarettes was low and similar to those using a nicotine patch. The number of cigarette smokers who actually quit tobacco product use with e-cigarettes is low. To date, no e-cigarette manufacturer has submitted the requisite applications for FDA approval of these products for smoking cessation.

Some vocal supporters of e-cigarettes have embraced the strategy of harm reduction as an approach to risky behavior that prioritizes the minimization of damage rather than elimination of the behavior. The debate over e-cigarettes has centered on whether e-cigarettes could be useful as a harm-reduction strategy in established adult cigarette smokers. E-cigarettes have been argued to be the most promising product for tobacco harm reduction to date, because, besides delivering nicotine vapor without the combustion products that are responsible for nearly all of the damaging effects from smoking, they also replace some of the rituals associated with smoking behavior. However, the behavior of vaping can become associated with its own behavioral rituals. Although the use of e-cigarettes could potentially reduce harm associated with smoking if their use were to replace the use of conventional cigarettes, some studies suggest that current smokers who use these products do not reduce use of conventional cigarettes and may delay cessation. Studies suggest further that e-cigarettes may contribute to nicotine addiction and are unlikely to discourage conventional cigarette smoking.

Available evidence indicates that a substantial portion of e-cigarette users of all ages use cigarettes at the same time. This “dual use” pattern raises the concern that e-cigarettes are being used as a “bridge product”, bridging smokers from one cigarette to the next by satisfying their nicotine addiction in places where smoking is not allowed rather than as a means to quit smoking entirely, raising concerns that the beneficial public health impact of e-cigarettes could be minimal. This pattern suggests that e-cigarettes are being used to perpetuate nicotine addiction rather than break it. Also, individuals who chose to continue smoking conventional cigarettes (in any quantity) retain cardiovascular disease and cancer risks, as these risks are affected more by smoking duration than intensity. Dual use of both e-cigarettes and conventional cigarettes also carries the risk of...
secondhand smoke exposure, which can worsen respiratory problems in others, particularly those with asthma.

According to the WHO, the efficacy of e-cigarettes in aiding smoking cessation has not been demonstrated scientifically and those concerned are advised strongly not to use e-cigarettes until a reputable national regulatory body has found them to be safe and effective.17

REGULATION OF E-CIGARETTES

In June 2009, President Obama signed the Family Smoking Prevention and Tobacco Control Act into law, which granted the FDA authority to regulate all tobacco products. This Act specifically directed the FDA to regulate cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco; it also authorized the agency to extend its authority to other categories of tobacco products, including cigars and e-cigarettes.

In April 2011, the FDA stated that it would regulate e-cigarettes as “tobacco products” and not as “drug-delivery devices.”18 This decision resulted from a federal court ruling that blocked the FDA from regulating e-cigarettes as drug-delivery devices due to a specific interpretation of the Family Smoking Prevention and Tobacco Control Act. Under that law, any product that contains nicotine from tobacco and makes no claims to be therapeutic must be regulated as a tobacco product. Concerns have been raised that this ruling allows for the sale of unregulated refined nicotine directly to consumers, unless and until the FDA takes further action.

With the authority vested in the Family Smoking Prevention and Tobacco Control Act, the FDA proposed a new rule in April 2014, which would extend the agency’s tobacco authority to cover “additional tobacco products.”19 Products that would be “deemed” to be subject to FDA regulation are those that meet the statutory definition of a tobacco product, including currently unregulated marketed products, such as e-cigarettes, cigars, pipe tobacco, nicotine gels, waterpipe (or hookah) tobacco, and dissolvable tobacco products.

Consistent with currently regulated tobacco products, under the proposed rule, makers of e-cigarettes would, among other requirements, register with the FDA and report product and ingredient listings; only market new tobacco products after FDA review; only make direct and implied claims of reduced risk if the FDA were to confirm that scientific evidence supports the claim and that marketing the product will benefit public health as a whole; and not distribute free samples. Additional provisions that would apply to newly “deemed” tobacco products include minimum age and identification restrictions to prevent sales to underage youth; requirements to include health warnings; and prohibition of vending machine sales, unless in a facility that never admits youth.

Critics of the proposed rule contend that the FDA did not go far enough, particularly with respect to the use of flavorings. While some states and localities have enacted regulations affecting the sale, marketing, and use of e-cigarettes to minors, these regulations can be circumvented by purchasing these products on the Internet. Easy access to these products (e.g., online or via kiosks in shopping malls), in addition to their wide array of cartridge flavors (such as coffee, mint, candy, and fruit flavors), may make them particularly appealing to adolescents. Critics further contend that prospects for manufacturers and marketers of e-cigarettes would likely be enhanced if clean indoor air laws designed to curb the risks of secondary cigarette smoke exposure do not include prohibitions on vaping in indoor environments. Regulation of e-liquids, including requirements for labeling and child-proof caps, also must be taken into consideration.
Absent federal law, the sale, use, and taxation of these products is being addressed by states and localities. Thirty-four state laws address e-cigarettes either explicitly or as part of language applying to tobacco-derived or nicotine-containing products. Twenty-eight of these state laws (all of which have been adopted since 2009) explicitly apply to e-cigarettes; 22 states regulate youth access to e-cigarettes; 12 states explicitly apply smoke-free air provisions to e-cigarettes; and 1 state, Minnesota, has imposed an excise tax on e-cigarettes.

Six of nine e-cigarette companies that were surveyed in a 2014 Congressional report indicated support for some form of regulation, such as restrictions on the sale and marketing of e-cigarettes to children and teenagers; a ban of the usage of television to market e-cigarettes; a prohibition on characterizing flavors; restricting online sales; and regulation of e-cigarettes at the point of sale. Specific actions and recommendations from the WHO and other health organizations have been published recently to inform policymaking on such issues.

Relevant AMA Policy

AMA policy supports FDA regulatory authority of all tobacco products and nicotine delivery systems. At the June 2014 Annual Meeting, the HOD amended Policy H-495.973 to oppose the exemption of any non-pharmaceutical nicotine and tobacco products from FDA regulation. Specifically, the policy calls for tighter restrictions on the sale and marketing of e-cigarettes including:

- legislation and/or regulation addressing the minimum purchase age, locations of permissible use, the use of secure, child- and tamper-proof packaging and design, advertising and promotion activities, and sponsorship of e-cigarettes;
- transparency and disclosure concerning the design, content of, and emission from e-cigarettes;
- restrictions on the use of characterizing flavors that may enhance the appeal of such products to minors, and the development of strategies to prevent marketing to, and use of, e-cigarettes by minors; and
- the prohibition of claims of reduced risk and/or the marketing of e-cigarettes as tobacco cessation tools until such time that credible evidence is developed that supports such claims.

AMA Policy H-490.909 “Use of Electronic Cigarettes (e-cigarettes) in Smoking Cessation Programs” urges that: (1) e-cigarettes be classified as (nicotine) drug delivery devices and should be subject to FDA regulation with appropriate standards for identity, strength, purity, packaging, and labeling with instructions and contraindications for use, including age of the user; (2) state legislatures prohibit the sales of e-cigarettes and all other nicotine devices that are not FDA-approved; and (3) as currently marketed, e-cigarettes be included in smoke free laws but separately defined from tobacco products.

AMA Policy H-495.988(1), “FDA Regulation of Tobacco Products,” calls upon the AMA to reaffirm its position that all tobacco products (including but not limited to, cigarettes, smokeless tobacco, chewing tobacco, and hookah/water pipe tobacco) are harmful to health and that there is no such thing as a safe cigarette.

THE PHYSICIAN’S ROLE

Considering the expanding awareness and use of e-cigarettes among adolescents and adults, it is likely physicians will need to consider how best to counsel patients about these products. Although it is not possible to endorse a product that is not yet regulated for quality, consistency, efficacy, and
safety, it is possible that e-cigarettes could be a potential aid in the battle against smoking and
tobacco addiction. However, genuine uncertainty exists about the therapeutic merits of e-cigarettes
or their role as a harm reduction strategy. Physicians should be sensitive that when patients ask
about e-cigarettes they are likely asking for help to quit smoking, which provides an opportunity
for discussing this important topic. If patients ask about e-cigarettes, they should be informed of the
need for more research to determine the safety and efficacy of these products.

Physicians may consider expanding their social history questions to ask, “Do you vape (or do you
use electronic cigarettes)?” rather than asking only, “Do you smoke?” Subsequent advice would
then be tailored to the individual being counseled. For nonsmokers, the physician message should
clearly be, “Don’t start. E-cigarettes are not a safe alternative to smoking conventional tobacco.”
For an individual who has never smoked cigarettes but has tried e-cigarettes (and is thus at risk for
trying traditional cigarettes), physicians should emphasize the potential for nicotine addiction
introduced by these devices and caution them on the unknown risks of these unregulated products.
For current smokers interested in quitting smoking, e-cigarettes are unproven aids for smoking
cessation. It is important to emphasize the potential hazard associated with dual use, as some
patients may choose to use e-cigarettes in venues where they can’t smoke (e.g., in a workplace or
some other environment).

For those who are using e-cigarettes, it is important to state clearly that data are inconclusive
regarding the safety and efficacy of these products. While some physicians may choose to
acknowledge that e-cigarettes are probably less hazardous than conventional cigarettes in smokers
who are unable or unwilling to quit, physicians should emphasize that e-cigarette vapor is not
harmless water vapor. For some smokers, the use of e-cigarettes might be considered as an option
to help them quit smoking if they can commit to short-term use with an established quit date. It is
important to emphasize that there is not enough evidence for clinicians to counsel their patients
who use conventional cigarettes to use e-cigarettes as a primary smoking cessation aid. Due to the
novelty of these products, there also are no data to determine possible chronic health effects from
long term use of e-cigarettes.

A number of FDA-approved smoking cessation medications are available that have been
appropriately tested in clinical trials and are known to be safe and effective for smokers to reduce
their dependence on nicotine, including nicotine gum, nicotine skin patches, nicotine lozenges,
nicotine oral inhaled products, and nicotine nasal spray. Although controversial, some smoking
cessation experts see potential in e-cigarettes as a cessation tool, addressing behavioral and sensory
needs that other nicotine replacement products, such as transdermal patches and gum, do not. Data
are not available to compare e-cigarettes with counseling, nicotine replacement, or use of
bupropion or varenicline. Free help is available to all smokers who want to quit at 1-800-QUIT-
NOW or by visiting www.smokefree.gov.

With the growing use of e-cigarettes, physicians need to be alert for nicotine poisoning. They need
to educate patients and especially parents and other caregivers about this danger, and advocate for
measures that will help prevent potentially fatal liquid nicotine poisoning of infants and young
children. In the United States, the lack of regulatory oversight has resulted in inconsistent labeling,
insufficient or nonexistent child protective packaging for bottles of replacement liquid, and product
design and flavoring that may encourage children to explore and ingest these products.

DISCUSSION

Given the rapid increase in electronic cigarette use among both adults and adolescents, rigorous
surveillance of these products is particularly important, including their impact on the initiation and
cessation of conventional tobacco use and concurrent use with other conventional tobacco products. Due to the lack of rigorous chemical analyses and toxicological studies, as well as clinical trials on commercially available e-cigarettes, neither their value as therapeutic aids for smoking cessation nor their “safety” as cigarette replacements is established. At this time, the public health impact of wide distribution of these devices is unknown. Limited data exist on the safety or effectiveness of e-cigarettes; consumers have no way of knowing whether the purported therapeutic benefits or advantages of e-cigarettes over conventional cigarettes are real. There are no requirements for manufacturers of e-cigarettes to adhere to established consumer safety practices that list ingredients and produce consistent products with uniform concentrations and defined maximum doses of nicotine. Studies have demonstrated a lack of standards for e-cigarettes, mislabeled nicotine content, and wide variability in e-cigarette constituents and toxicants. The e-liquid aerosolized in e-cigarette devices is not uniform in ingredient content and concentration. Until e-cigarette regulations are introduced to standardize device content and characteristics, product variability will continue to limit claims of safety and reliability.

The potential benefits of e-cigarettes, including harm reduction and enhancing smoking cessation, have not been proven by long-term studies of significant numbers of e-cigarette users. E-cigarettes have not been proven to help people quit smoking; it is unclear whether e-cigarettes may be effective as smoking-cessation aids or whether they perpetuate nicotine addiction and thus interfere with smoking cessation. The value of e-cigarettes as a substitute for conventional cigarettes has been questioned because of high levels of dual use with conventional cigarettes; the hope that e-cigarettes will reduce harm by delivering “clean” nicotine will not be realized in continuing dual users. Used appropriately, e-cigarettes may have a valuable part to play in smoking cessation, but because the long-term safety of e-cigarettes is unclear, and the effects of secondhand exposure to vapors unknown, it is important to proceed cautiously to ensure that users and the general public are protected from harm. Given that smokers already have access to licensed nicotine-replacement therapy products, it is important to establish whether e-cigarettes are effective in aiding quitting. It is crucial to distinguish whether the use of e-cigarettes in a quit attempt improves the likelihood of success of that attempt, or whether the use of e-cigarettes for any purpose, such as aiding smoking reduction or recreation, promotes or suppresses attempts to stop smoking.

Because e-cigarettes deliver fewer total chemicals and fewer carcinogens than conventional tobacco-burning cigarettes, they are sometimes considered less hazardous products. However, e-cigarette cartridge fluids and their emissions are not yet well characterized and may vary among products. E-cigarettes have the potential to cause acute adverse health effects. Injuries and illness have resulted from e-cigarette use, which may be related to lack of basic safeguards in the product design and manufacturing process, as well as the contents of the solution. There is a real danger to infants and young children from e-liquid. Adverse health effects for people exposed to e-cigarette emissions cannot be excluded; research is needed to determine whether the vapor produced by e-cigarettes is harmful to bystanders.

Without more research, consumers currently don’t know the potential risks of e-cigarettes when used as intended, how much nicotine or other potentially harmful chemicals are being inhaled during use, or whether there are any relative benefits associated with using these products. It is important to assess e-cigarette toxicant exposure and individual risk as well as health effects of e-cigarettes as they are actually used to ensure safety of all ages and populations. The first priority is to characterize the safety profile of these products, including in long-term users. If these products are demonstrated to be safe, their efficacy as smoking cessation aids should then be tested in appropriately designed clinical trials. Ideally, these studies would have been conducted prior to marketing of these products.
Data on the impact of e-cigarettes on adolescents are particularly limited. Young adulthood marks a critical developmental period, one that often coincides with both the initiation and establishment of regular tobacco use. Available data suggest that youth awareness of e-cigarettes is high and use is increasing rapidly. The extent to which e-cigarette use in youth will result in nicotine dependence and subsequent use of other tobacco products is unknown. Avoiding preventable contact with a highly concentrated nicotine solution remains important; this can be achieved by specific labeling of all products, child-proof packaging, and proper consumer education.

Increases in the use and acceptance of e-cigarettes by consumers depend not only on explicit marketing such as via advertising, but on cultural attitudes and beliefs about potential harms. If the risk of using these products is perceived to be low, the likelihood of use increases. Just as cultural glamorization of cigarette smoking led to increased use in the mid-twentieth century United States (and in the Third World thereafter), and just as glamorous views of smoking as incorporated in movies, television shows, and other mass media have served to inhibit prevention efforts to reverse statistics on incidence and prevalence of cigarette smoking, glamorization of vaping as a behavior portrayed as enjoyable and safe, compared to smoking, contributes to societal shifts in attitudes and behaviors associated with these products. Smoking is now perceived by a majority of Americans as an unseemly activity, with negative attitudes attached to exposing others to the smells and health risks of a smoker’s cigarette smoke. Vaping can be portrayed as more “respectful of others” and healthy if second-hand exposure is perceived to be irrelevant as a harm.

A number of states and localities have taken action to address the sale and use of these products, but only federal regulation can ensure that all ages and populations are protected. The FDA is encouraged to act swiftly to assert jurisdiction over e-cigarettes and to issue regulations regarding their manufacture and prohibiting their marketing and sale, particularly to youth and current nonsmokers. While most adolescents using e-cigarettes are dual users, up to a third of them have never smoked a conventional cigarette, indicating that some youth are starting use of the addictive drug nicotine with e-cigarettes.

The use of e-cigarettes could re-normalize smoking, promote experimentation among young people who otherwise may not have tried smoking, or lead to dual-use together with conventional cigarettes and thereby deter some smokers from quitting. To minimize the potential negative impacts on prevention and cessation, and the undermining of existing tobacco control measures, e-cigarette use should be prohibited where tobacco cigarette use is prohibited and the products should be subject to the same sales and marketing restrictions as tobacco cigarettes. The sale of characterizing flavors should be eliminated in e-cigarettes and all other tobacco products with no exemptions. Evidence-based policies and regulations are needed that protect the entire population (children and adults, smokers and nonsmokers) in the context of how the e-cigarette industry is marketing and promoting these products. Therapeutic claims should be prohibited until such time that e-cigarette companies provide evidence that, as actually used, e-cigarettes improve cessation success. Until such evidence is provided and evaluated thoroughly, the continued marketing and use of these products constitutes an uncontrolled experiment on the U.S. population.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following recommendations be adopted, and the remainder of the report be filed.

1. That Policy H-495.973 FDA to Extend Regulatory Jurisdiction Over All Non-Pharmaceutical Nicotine and Tobacco Products be amended by addition and deletion to read as follows:
Our AMA supports:

1. supports the U.S. Food and Drug Administration’s (FDA) proposed rule that would implement its deeming authority allowing the agency to extend FDA regulation of tobacco products to pipes, cigars, hookahs, e-cigarettes and all other non-pharmaceutical tobacco/nicotine products not currently covered by the Federal Food, Drug, and Cosmetic Act and its amendments, as amended by the Family Smoking Prevention and Tobacco Control Act.

2. supports legislation and/or regulation addressing the of electronic cigarettes and all other non-pharmaceutical tobacco/nicotine products that:
   (a) establishes a minimum legal purchasing age of 18; locations of permissible use;
   (b) prohibits use in all places that tobacco cigarette use is prohibited, including in hospitals and other places in which health care is delivered;
   (c) applies the same marketing and sales restrictions that are applied to tobacco cigarettes, including prohibitions on television advertising, product placement in television and films, and the use of celebrity spokespeople;
   (d) prohibits product claims of reduced risk or effectiveness as tobacco cessation tools, until such time that credible evidence is available, evaluated, and supported by the FDA;
   (e) requires the use of secure, child- and tamper-proof packaging and design, and safety labeling on containers of replacement fluids (e-liquids) used in e-cigarettes, advertising and promotion activities, and sponsorship of e-cigarettes and all other non-pharmaceutical tobacco/nicotine products;
   (f) establishes manufacturing and product (including e-liquids) standards for identity, strength, purity, packaging, and labeling with instructions and contraindications for use;
   (g) requires transparency and disclosure concerning the product design, contents of, and emissions; and from e-cigarettes and all other non-pharmaceutical tobacco/nicotine products;
   (h) restricts the use of characterizing flavors that may enhance the appeal of such products to youth minors, and the development of strategies to prevent marketing to, and use of, e-cigarettes and all other non-pharmaceutical tobacco/nicotine products by minors; and (j) the prohibition of claims of reduced risk and/or the marketing of e-cigarettes as tobacco cessation tools until such time that credible evidence is developed that supports such claims. (Modify HOD Policy)

2. Our AMA urges physicians to:
   (a) educate themselves about e-cigarettes, be prepared to counsel patients about the use of these products and the potential for nicotine addiction and the potential hazards of dual use with conventional cigarettes, and be sensitive to the possibility that when patients ask about e-cigarettes, they may be asking for help to quit smoking;
   (b) consider expanding clinical interviews to inquire about “vaping” or the use of e-cigarettes;
   (c) promote the use FDA-approved smoking cessation tools and resources for their patients and caregivers; and
   (d) advise patients who use e-cigarettes to take measures to assure the safety of children in the home who could be exposed to risks of nicotine overdose via ingestion of replacement e-cigarette liquid that is capped or stored improperly. (New HOD Policy)
3. That our AMA encourage further clinical and epidemiological research on e-cigarettes
   (New HOD Policy)

4. That Policy H-490.909 Use of Electronic Cigarettes (e-cigarettes) in Smoking Cessation
   Programs be rescinded. (Rescind HOD Policy)

Fiscal Note: Less than $500
REFERENCES


