E-Cigarettes and Smoking Cessation
A primer for oncology clinicians

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BACKGROUND: Electronic cigarettes (e-cigarettes) are a psychosocial phenomenon of the 21st century with serious implications to public and individual health. The significant increase of their popularity and use has raised concerns in the healthcare community regarding their potential benefits and harm, particularly their use as a smoking cessation methodology.

OBJECTIVES: Current knowledge is presented about e-cigarettes, including the clinical implications of their use, and associated controversies are analyzed. In addition, practice recommendations and communication guidance are provided.

METHODS: An integrative review was performed.

FINDINGS: The long-term effect of e-cigarettes on individual and public health is unknown. Evidence from short-term studies, although limited, shows that e-cigarette use is less harmful than smoking. However, the evidence does not support the use of e-cigarettes as a smoking cessation methodology. Such recommendation remains a judgment call for the clinician based on each individual case.

Patients with cancer who continue smoking cigarettes after their diagnosis have an increased risk of negative health outcomes, such as complications from therapy, relapse, reduced quality of life, increased risk of death, and increased risk of new malignancies (Daniels et al., 2009; Gajdos et al., 2012; Underwood et al., 2012; Warren, Kasza, Reid, Cummings, & Marshal, 2013). The science has shown a causative association between smoking and adenocarcinoma of the lung, hepatocellular carcinoma, and colorectal cancer (U.S. Department of Health and Human Services [USDHHS], 2014). Compared to nonsmokers, smokers’ risk of death from all cancers is almost three times higher (Jha et al., 2013).

Most people with cancer who continue smoking after diagnosis understand the significance of smoking cessation, and most wish to quit. Many have tried to quit using different methods, including pharmacologic and psychological therapies (Duffy, Louzon, & Gritz, 2012; Park et al., 2012). Among adult cancer survivors who were regular smokers at diagnosis, 65% continued smoking after treatment completion (Jha et al., 2013).

The use of electronic cigarettes (e-cigarettes) is increasing among patients with cancer who smoke regularly. Many patients with cancer use e-cigarettes as a substitute for cigarettes or in addition to cigarettes. These patients report using e-cigarettes to manage nicotine cravings, reduce daily cigarette consumption, and to quit smoking (Borderud, Lin, Burkhalter, Sheffer, & Ostroff, 2014).

The tobacco industry dominates the e-cigarette market and promotes them as a healthier alternative to smoking and as a cessation method (Grana, Ling, Benowitz, & Glantz, 2014). The U.S. Food and Drug Administration (FDA) does not regulate or offer guidelines for e-cigarette manufacturing, marketing, or sales. In addition, information on e-cigarette safety and efficacy as a smoking cessation method is lacking. The current article attempts to answer whether e-cigarettes are efficacious as a strategy for smoking cessation in general and for patients with cancer in particular. The authors present what is known about e-cigarettes, point to what is still unknown, and offer clinicians an overview of the topic, practice recommendations, and communication strategies with patients who smoke cigarettes, use e-cigarettes, or are considering their use.

Background
E-cigarettes entered the U.S. and European markets in 2007 (Grana, Benowitz, & Glantz, 2014). E-cigarettes are battery-powered devices that
aerosolize nicotine. Many e-cigarettes are designed to emulate the look and the hand-to-mouth behavior of cigarette smoking. Generally, an e-cigarette consists of a battery, an atomizer with a heating coil, and liquid (e-liquid). Usually, e-liquid contains nicotine, water, and propylene glycol or glycerin solution. Most e-cigarettes also contain a flashing diode that mimics the look of a lit cigarette (Farsalinos, Romagna, Tsiapras, Kyrzopoulos, & Vourdris, 2014).

Battery voltage and differences in circuitry result in considerable variability in the e-cigarette heat level and vapor concentration, which affects the delivery of nicotine and other ingredients (Cheng, 2014). Adjusting battery wattage or the inhaled airflow modifies the amount of vapor and chemical density in each puff. Certain models are disposable, have a rechargeable battery, or have a refillable e-liquid tank. E-cigarettes with high nicotine content, multi-flavor disposable e-cigarettes, and vaporizers designed for liquid nicotine also have been introduced to the market (Grana, Benowitz, & Glantz, 2014).

Awareness and Prevalence

National surveys show that most e-cigarettes users report using the devices for smoking cessation (85%) or consumption reduction (75%). Additional reasons for use are that e-cigarettes are perceived as a healthier alternative to cigarettes (86%) and are legal to use in smoke-free areas (71%) (Gravenel et al., 2014; Regan, Promoff, Dube, & Arrazola, 2013; West, Beard, & Brown, 2012). According to the Centers for Disease Control and Prevention (CDC, 2015) National Health Information Survey, in 2010, 3.3% of the U.S. population had ever tried e-cigarettes compared with 12.6% of the population in 2014. In 2014, 4% of the U.S. population regularly used e-cigarettes. This includes 13% of all high school students (up from 5% in 2013) and 4% of all middle school students (up from 1% in 2013). Population-based studies suggest that the highest use rate is among current smokers, followed by former smokers, and then nonsmokers. Since 2010, e-cigarette use has increased in all of the aforementioned groups (Grana, Benowitz, & Glantz, 2014).

According to Borderud et al. (2014), the rate of patients with cancer who ever tried e-cigarettes increased from 10.6% in 2013 to 38.5% in 2014; this increase is greater than in the general population. Such increase is possibly related to more quit attempts and claims that e-cigarettes are a healthier alternative to cigarettes. Patients who used e-cigarettes were more likely to be diagnosed with thoracic and head or neck cancers (Borderud et al., 2014).

Chemical Content of E-Cigarettes

Nicotine

Nicotine addiction is the most prevalent drug problem in the world. Nicotine is a tertiary amine constructed of a pyridine and a pyrrolidine ring. Nicotine binds to acetylcholine receptors at the ganglia and neuromuscular junctions in the brain. It permeates through the buccal mucosa and the blood–brain barrier, and interacts with dopamine-producing cells, the cholinergic system, and hormonal systems (Dwyer, McQuon, & Leslie, 2009). Nicotine stimulates the GABAergic neurons. Consequently, these neurons become desensitized and cease dopamine inhibition. This prompts cravings and reinforces addiction to nicotine. The CYP2A6 gene is a member of the cytochrome P450 enzyme system, and is instrumental in nicotine metabolism by oxidizing nicotine to its inactive metabolite cotinine. Reduced metabolism phenotype results in higher nicotine levels in the blood, which reduces cravings. Conversely, lower nicotine levels from increased metabolism enhance cravings (Akradou, 2015).

Short-term exposure to nicotine at low concentrations produces tremors and increases in heart rate, respiration, and blood pressure. Alertness level also increases. Ocular exposure causes irritation and redness. Nicotine is linked to hypertension complications, stroke, coronary and peripheral vascular disease, delayed wound healing, peptic ulcer disease, and esophageal reflux (CDC, 2015).

Nicotine is not proven to cause cancer; it promotes the growth of cancer cells and the proliferation of endothelial cells, therefore suggesting a role in tumor progression (Catassi, Servent, Paleari, Casario, & Russo, 2008). Studies suggest that nicotine increases lung cancer cells’ resistance to cisplatin (Platinol®) and, by overexpressing the alpha 9 subunit of the nAChR (α9-nAChR), contributes to breast cancer carcinogenesis (Nishioka et al., 2014).

Propylene Glycol and Glycerol

Propylene glycol and glycerol are solvents for nicotine and flavorings in e-liquids, and create the vapor in e-cigarettes when heated by the coil. Propylene glycol (1,2-propanediol) is a colorless, odorless, and thick liquid used in the synthesis of other glycols and polyester resins. It is used in pharmaceuticals, brake and hydraulic fluids, antifreezes, flavorings, perfumes, and theatrical smoke. Glycerol (purified glycerin) is a clear, colorless, viscous, and sweet-tasting liquid organic compound. It is used in pharmaceuticals, cosmetics, and food preparation (Pisinger & Dossing, 2014).

The vaporizing process emits formaldehyde (Kosmider et al., 2014). The average quantity of formaldehyde in vapor from high-voltage (i.e., 5 volts) e-cigarettes is greater than the average quantity of formaldehyde emitted from cigarettes (Jensen, Lou, Pankow, Strongin, & Peyton, 2015). Exposure to high levels of formaldehyde is linked to nasopharyngeal cancer and cancers of the hematopoietic and lymphatic systems, particularly myeloid leukemia. Formaldehyde can cause pulmonary edema, dyspnea, bronchitis, arrhythmia and tachycardia, and asthma-like allergies (Kosmider et al., 2014; World Health Organization [WHO], 2014). Formaldehyde is classified as a group 1 carcinogen by the International Agency for Research on Cancer (FDA, 2010).
Tobacco-Specific Nitrosamines

Tobacco-specific nitrosamines (TSNAs) are carcinogens that are found only in tobacco and tobacco smoke. TSNAs are formed during tobacco processing. Tobacco smoke nicotine reacts with ambient nitrous acid and form TSNAs. TSNAs are implicated as causes of oral cancer, lung cancer, esophageal cancer, and pancreatic cancer (Cheng, 2014).

Farsalinos et al. (2014) studied 21 e-liquid refills and found TSNAs in all of them. Goniewicz, Kuma, Gawron, Knysak, and Kosmider (2013) identified TSNAs in the vapor of almost all e-cigarettes studied. Other vapor studies (Cheah, Chong, Tan, Morshed, & Yee, 2012; Czogala et al., 2013; Kim & Shin, 2013) found TSNAs at very low levels. In some cases, the levels (8.2 ng/g) were similar to levels found in nicotine replacement therapies (NRTs), which are considered safe. Conversely, Winston or Marlboro Light brands contain 3,365 ng/g and 4,808 ng/g TSNAs, respectively.

Flavorings

E-liquids contain a variety of natural and artificial flavoring agents. Most are used in food products. Tierney, Karpinski, Brown, Luo, and Pankow (2016) examined the amount of flavor chemicals in 30 e-liquids, including popular flavors such as cherry, cotton candy, chocolate, vanilla, and coffee. Six of the 24 identified flavoring compounds were aldehydes, including diacetyl (butanedione or butane-2,3-dione). Allen et al. (2015) found diacetyl in 47 of 51 flavors studied. Diacetyl is a respiratory irritant that often causes bronchiolitis obliterans (Van Rooy et al., 2009). Menthol is often added to tobacco cigarettes and e-liquids. Menthol effects include altered perception of tobacco smoke by cooling, smoothing, and slight numbing. Nicotine addiction increases through menthol’s desensitization ability. In addition, menthol increases the flux of nitrosamine across the porcine esophagus and negatively affects fibroblast cells (Willershausen et al., 2014).

Volatile Organic Compounds

Volatile organic compounds (VOCs) are emitted as gas from solid or liquid compounds widely used in paint thinners, varnishes, and cleaning products. VOCs include a variety of chemicals, many of which are hazardous and cause headaches, bronchial irritation, nausea, damage to liver and kidneys, and even cancer (Goniewicz et al., 2014). Compared to cigarette smoke, vapor from e-cigarettes contains far fewer VOCs. An analysis of vapor from 12 e-cigarette brands by Goniewicz et al. (2014) revealed the presence of toluene (0.2 to 6.3 mcg per one e-cigarette) and p,m-xylene (0.1 to 0.2 mcg per one e-cigarette) in all samples, and benzene, chlorobenzene, ethylbenzene, o-xylene, styrene, 1,3-dichlorobenzene, 1,4-dichlorobenzene, 1,2-dichlorobenzene, and naphthalene in some samples; all are VOCs. Other studies showed similar results (Schripp, Markewitz, Uhde, & Saltzhammer, 2013; Trehy et al., 2012; Zhang, Sumner, & Chen, 2013).

“Those who used e-cigarettes were more likely to be diagnosed with thoracic and head or neck cancers.”

Particles and Ultrafine Particles

According to the U.S. Environmental Protection Agency (2014), particle size determines health risk. Inhaled particles, size 10 microns or less, can adversely affect the respiratory system. Ultrafine particles (UPs) are particles less than 0.1 micron (100 nm) in size. The median size of particles generated from tobacco cigarette smoke is 200-400 nm. Smaller particles reach farther in the respiratory system than larger ones. UPs migrate deeper in the respiratory system and reach the alveolar sacs. UPs can reach the liver, kidney, heart, and brain (Williams, Villarreal, Bozhilov, Lin, & Talbot, 2013).

Metal particles, silicate particles, and UPs are found in e-cigarette vapor, some in higher concentrations than cigarettes, including tin, silver, iron, nickel, aluminum, and silicate, and nanoparticles of tin, chromium, and nickel. Exposure to such particles and UPs exacerbates respiratory diseases (i.e., asthma and chronic obstructive pulmonary disease) and constrict arteries, which can trigger myocardial infarction (Fuoco, Buonanno, Stabile, & Vigo, 2014; Pisinger & Dossing, 2014; Williams et al., 2013).

Adverse Health Effects

Pulmonary Effects

Schripp et al. (2013) warned about the impact of inhaled e-cigarette vapor on the lungs. E-cigarettes cause dry cough, irritation of the pharynx, and irritation of the upper and lower respiratory system (Tsikrika et al., 2014). Research shows that short e-cigarette use (less than five minutes) causes similar symptoms seen in smoking, including decreased fractional exhaled nitric oxide and a significant rise in dynamic airway resistance. A smoking-related decrease in fractional exhaled nitric oxide retards lung function. This presents concerns for people with chronic lung diseases, such as asthma, emphysema, and chronic bronchitis. Because e-cigarettes are used, on average, for more than five minutes during a typical day, the potential clinical impact is greater (Vardavas et al., 2012). Other studies (Palamidas et al., 2014; Tsikrika et al., 2014) found that use of e-cigarettes causes a significant increase in airway...
resistance, a decrease in airway conductance, and elevated levels of exhaled carbon monoxide.

Cardiovascular Effects
Studies have found that e-cigarette use increases heart rate, elevates diastolic blood pressure, and reduces saturation (Czogala et al., 2013; Tsikrika et al., 2014; vakali et al., 2014). Hypertension is a known cardiovascular risk factor and, in patients with a cardiovascular disease, increased heart rate is a predictor of mortality (lipi et al., 2014). Data indicate that typical patterns of e-cigarette use are associated with absorption of large amounts of nicotine by the body, producing plasma concentration levels similar to smoking. This increases the risk of cardiac arrhythmias and hypertension (lipi et al., 2014).

Other Health Effects
The long-term effects of e-cigarette use on cancer risk are unknown. However, e-cigarette use exposes the user to known carcinogens, such as formaldehyde, that makes a user's lifetime risk of cancer as much as 15 times greater than the risk from prolonged smoking (Jensen et al., 2015). E-cigarettes present potential harm, particularly to the seriously ill, such as patients with oncologic, pulmonary, or cardiac diseases. Methicillin-resistant Staphylococcus aureus (MRSA) exposed to e-cigarette vapor produces defense mechanism acids, thereby increasing its virulence and impeding the body's capability to destroy bacteria (alexander, Enany, Hwang, Sladewski, & Nizet, 2014).

Public Health Concerns
Secondhand Vapor
Exhaled vapor contains propylene glycol, glycerol, flavorings, and nicotine. It also may contain acetone, formaldehyde, acetaldehyde, propanol, diacetin, and triacetine. Concentrations of these chemicals are small and unlikely to present danger to public health. The majority of the chemicals (more than 4,000) present in tobacco smoke are not found in e-cigarettes, vapor, or e-liquids (Schrripp et al., 2013). However, passive exposure to vaporized particles, nicotine, and cancer-causing substances have adverse health effects (Schaufnagel, 2015). Chromium, not present in cigarette smoke, and nickel at much higher levels than cigarette smoke, were found in e-cigarette vapor. In addition, lower concentrations of lead and zinc were detected in secondhand vapor compared to cigarettes (Saffari et al., 2014).

A comparison study by Flouris et al. (2012) evaluated respiratory effects from secondhand smoke and secondhand vapor after one hour of exposure. Although significant adverse effects from secondhand cigarette smoke were observed, such as increase in white blood cell, lymphocyte, and granulocyte counts, no adverse effects from secondhand vapor were noted (Flouris et al., 2012). E-cigarette vapor half-life is 11 seconds, whereas the half-life of cigarette smoke is 20 minutes. Therefore, the risk from e-cigarette vapor exposure is considerably lower than exposure to secondhand smoke, and exposure to secondhand vapor from e-cigarettes poses negligible risk to public health (Bertholon et al., 2013). Other studies present similar conclusions (Burystyn, 2014; Czogala et al., 2013).

Variations in suction volume, puff duration, and vapor production among e-cigarette brands, and the continuously growing number of new e-liquids, makes full analysis very difficult. Based on the existing evidence, it is reasonable to determine that, compared with cigarettes, public health effects of e-cigarette use are small. However, prolonged exposure in closed quarters presents a health risk. Additional research is needed (Parsalinos & Polosa, 2014).

Renormalization of Smoking
Changing the culture about cigarette smoking has been a decades-long campaign. The Public Health Cigarette Smoking Act of 1970 banned radio and television advertising of tobacco products, including cigarettes (CDC, 2007). The ban has been instrumental in making smoking less glamorous, particularly for younger people. Among the many drivers reducing smoking prevalence are the recognition of cigarette smoking as an addiction and a cause of cancer. According to the USDHHS (2015), smoking prevalence among middle and high school students has declined from 28% in 1996 to 8% in 2014.

E-cigarette use is allowed in most public places. If the behavior of smoking—inhaling fumes from a burning substance—is accepted as a societal norm, it may result in a gradual reversal of smoking bans. It may also reduce the amount of people who are attempting to quit because of the influence of societal pressure. The WHO (2014) report raises concerns about smoking renormalization by suggesting that nonsmokers, particularly children, use nicotine at a higher rate than anticipated if e-cigarettes were not available.

The report suggests that, once addicted to nicotine, users of e-cigarettes will switch to cigarette smoking. The report stresses that the renormalization effect causes the behavior of smoking to seem attractive, therefore perpetuating the smoking epidemic and nicotine addiction.

Fairchild, Bayer, and Colgrove (2014) suggested that e-cigarette marketing methods, which replicate effective cigarette marketing methods of the 20th century, pose a threat to the successful public health campaign to remove smoking as a cultural norm. In 2014, e-cigarette advertising reached 70% of all middle and high school students (CDC, 2016). E-cigarette use can prompt relapse among former smokers and discourage other smokers from attempting to quit, thereby increasing tobacco consumption and related health issues (Dutra, Stanton, & Glantz, 2014). E-cigarettes increase cravings for tobacco cigarettes, whereas tobacco cigarettes do not stimulate urges for e-cigarettes (Dutra et al., 2014).
Dual Use
Borderud et al. (2014) found dual use of e-cigarettes and tobacco cigarettes to be the predominant pattern. In May 2015, the CDC warned about serious health consequences resulting from excessive exposure to nicotine for people who practice dual use. Dual use is associated with increased nicotine dependence (Wills, Knight, Williams, Pagano, & Sargent, 2014). Among adolescents, 61%–81% of e-cigarette users practice dual use (Grana, Benowitz, & Glantz, 2014). Use of e-cigarettes is associated with higher odds of cigarette smoking. Clinicians must identify dual use as an additional source of nicotine (Dutra et al., 2014).

Smoking duration and intensity (number of cigarettes) determine the risk for cancers (i.e., lung, pancreatic, and esophageal). Mortality rates for lung cancer are correlated with the number of years a patient has smoked and the number of cigarettes smoked daily. Risk of death from lung cancer increases with added years of smoking; smoking more cigarettes daily, but for fewer years, poses less risk of lung cancer than smoking fewer cigarettes daily but for more years (Thun et al., 2013). Using e-cigarettes to decrease the number of daily smoked cigarettes without complete abstinence may reduce some of the cancer risk. However, related to the importance of duration, the effect on risk is not proportional to the reduced number of tobacco cigarettes.

The Gateway Hypothesis
The Gateway Hypothesis (GH) has been discussed extensively in relation to drug use. The concept has reemerged in connection with e-cigarettes. Concerns have been raised that, along with the renormalization of smoking, e-cigarette use is a gateway to cigarette smoking (Limb, 2013; West & Brown, 2014). Schraufnagel (2015) suggests that e-cigarettes are a gateway to nicotine addiction.

E-cigarettes serve as starter products for non-tobacco users and their trial can result in nicotine addiction (Henningfield & Zaatari, 2010; Pepper et al., 2013). A South Korean student survey (N = 75,643) found that 9% used e-cigarettes, and the majority of users (99%) smoked tobacco cigarettes as well. The researchers noted that e-cigarettes are a new conduit for nicotine addiction (Lee, Grana, & Glantz, 2014). In addition, a survey at baseline and at six months of ninth-graders (N = 2,530) who used e-cigarettes found that e-cigarette use was strongly associated with smoking (odds ratio = 2.65, 95% confidence interval [16.4%, 28.9%]). The strong association implies possible causation (Leventhal et al., 2015).

Studies that examined concomitant smokeless tobacco and cigarette smoking among adolescents revealed a progression to cigarette smoking and more failed quit attempts. Concerns that e-cigarettes present a similar catalyst or gateway are valid and relevant.

TABLE 1.
STUDIES OF E-CIGARETTE EFFICACY AS A SMOKING CESSATION METHODOLOGY

<table>
<thead>
<tr>
<th>STUDY</th>
<th>TYPE</th>
<th>N</th>
<th>FINDINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adkison et al., 2013; Grana, Popova, &amp; Ling, 2014</td>
<td>Longitudinal</td>
<td>6,000</td>
<td>E-cigarette use by smokers was not correlated with a larger cessation rate, or with reduced number of smoked cigarettes.</td>
</tr>
<tr>
<td>Al-Delaimy et al., 2015</td>
<td>Population-based</td>
<td>1,000</td>
<td>Cigarette smokers who never used e-cigarettes have greater likelihood to decrease tobacco cigarette consumption and stop smoking. Smokers who used e-cigarettes have greater risk for inability to succeed in cessation.</td>
</tr>
<tr>
<td>Biener &amp; Hargraves, 2015</td>
<td>Longitudinal</td>
<td>695</td>
<td>Regular use of e-cigarettes for more than 30 days was correlated with successful smoking cessation.</td>
</tr>
<tr>
<td>Borderud et al., 2014</td>
<td>Observational</td>
<td>1,074</td>
<td>E-cigarettes are not an effective smoking cessation method for patients with cancer to reduce the number of smoked cigarettes.</td>
</tr>
<tr>
<td>Bronse et al., 2015</td>
<td>Longitudinal</td>
<td>4,064</td>
<td>Daily use of e-cigarettes is associated with increases in rates of attempting to stop smoking, but not with smoking cessation.</td>
</tr>
<tr>
<td>Brown et al., 2014</td>
<td>Population-based</td>
<td>5,863</td>
<td>Smokers who attempted to quit without professional support and used e-cigarettes were 60% more likely to succeed, compared with smokers that relied on self-control or over-the-counter NRTs.</td>
</tr>
<tr>
<td>Bullen et al., 2013; Farsalinos &amp; Polosa, 2014</td>
<td>RCT</td>
<td>657</td>
<td>By comparing nicotine e-cigarettes, non-nicotine e-cigarettes, and nicotine patches as methods of cessation, intent-to-treat analysis at six months revealed that all three methods produced similar results.</td>
</tr>
<tr>
<td>Grana, Benowitz, &amp; Glantz, 2014</td>
<td>Meta-analysis</td>
<td>1,700</td>
<td>E-cigarettes were linked to much lower probability of smoking cessation.</td>
</tr>
<tr>
<td>McRobbie et al., 2014</td>
<td>Systematic review of RCTs</td>
<td>662</td>
<td>Smokers who used e-cigarettes had increased odds for smoking cessation compared to placebo users.</td>
</tr>
<tr>
<td>Suffin et al., 2015</td>
<td>Prospective</td>
<td>271</td>
<td>Trying e-cigarettes did not deter future smoking and possibly contributed to smoking continuation.</td>
</tr>
</tbody>
</table>

NRT—nicotine replacement therapy; RCT—randomized, controlled trial.
addition, the high rate of dual use presents greater individual risk as well as greater public health risk (Galanti, Rosendahl, & Wickholm, 2008; Post, Gilljam, Rosendahl, Bremberg, & Galanti, 2010).

The GH has become a predictive model rather than a descriptive one. The model does not entail a gateway from a soft substance to a hard substance, but from nicotine to nicotine. It does not concentrate on risky behavior as a starter for riskier behavior, but emphasizes the potential move from nicotine to much more nicotine.

Nicotine acts as a gateway drug on the brain. This occurs regardless whether the nicotine source is from smoking, secondhand smoke, or e-cigarettes. E-cigarettes can facilitate a new phenomenon of nicotine addiction, much like the impact of cigarettes in the 20th century (Kandel & Kandel, 2014).

The Harm Reduction Debate
Harm reduction (HR) proponents believe that smoking is a part of the culture and a tobacco-free world is unrealistic. Some smokers may quit, but many will not. HR proponents say, therefore, that the healthcare community must strive to make smoking safer by using a substitute product instead of behavior modification to discontinue use (McNeill & Munafo, 2013). Because e-cigarettes do not contain many of the carcinogens and toxins produced by smoking, HR proponents suggest that e-cigarettes should be promoted as a better alternative to satisfy nicotine addiction cravings. Consequently, proponents say that millions of smokers may switch and eventually overcome their addiction to nicotine, therefore decreasing associated health issues and reducing healthcare costs (McNeill & Munafo, 2013).

The other side of the debate emphasizes the lack of sufficient scientific data about e-cigarette safety and its efficacy as a smoking cessation modality. Opponents assert that e-cigarettes do not present any health benefits, and the HR model will lead to compensatory use of e-cigarettes in which users inhale more vapor or use more e-cigarettes to compensate for the reduced nicotine (Berridge, 2014). Smokers who switch to e-cigarettes may modify their puffing behavior by taking longer and slower puffs, therefore increasing their nicotine intake.

Others worry that HR messages dilute and weaken the primary message—an end to nicotine addiction by smoking cessation. Smokers may stop smoking abruptly and fail or adopt e-cigarette use and continue nicotine addiction. The results of HR policies do not outweigh the risks, particularly when the number of smokers has been declining for the past four decades (Nitzkin, 2014).

E-Cigarettes and Smoking Cessation
The compounds in tobacco smoke are linked to many deleterious health effects, mainly cancer, cardiovascular diseases, and pulmonary diseases. Smoking just one to four cigarettes per day doubles the risk of dying from heart disease (Bjartveit & Tverdal, 2005). If e-cigarette use either increases or has a neutral effect on the prevalence of cigarette smoking, harm across the population may increase (Ebbert, Agunwamba, & Rutten, 2015). Smoking cessation must be evaluated against the potential increase of nicotine addiction overall (see Table 1).

Patients With Cancer
Smoking cessation after a cancer diagnosis is associated with many health benefits, including a better response to chemotherapy, reduced complication rates, improved quality of life, and potentially better prognosis (Karam-Hage, Cinciripini, & Gritz, 2014). Continued smoking among patients with advanced cancer is associated with greater pain severity and interruptions in activities of daily living related to pain (Ditre et al., 2011). Pain is often a barrier to smoking cessation and quit attempts among people with cancer (Aigner et al., 2015). Studies show that e-cigarettes can relieve some symptoms of withdrawal (Dawkins, Turner, Roberts, & Soar, 2013). Patients with cancer who wish to quit smoking consider e-cigarettes, particularly because such products are marketed as healthier alternatives to smoking. However, according to Borderud et al. (2014), e-cigarette use among patients with cancer is not efficacious as a smoking cessation method.

Current clinical guidelines do not recommend e-cigarettes for smoking cessation. The FDA has not approved e-cigarettes as a smoking cessation method, and the U.S. Preventive Services Task Force (2015) concluded that the current evidence on e-cigarettes for smoking cessation is insufficient. Although e-cigarettes may play a role in combating the overall smoking phenomenon, current findings do not suggest that e-cigarette use increases the smoking cessation rate. To promote the best outcomes of cancer therapy, oncology clinicians must consider the essentiality of smoking cessation for their patients. A growing number of researchers call for more studies involving e-cigarettes and patients with cancer (Barton, 2015; Borderud et al., 2014; Filton, 2015). Although only a few studies have focused on smoking cessation methods among people with cancer, there are several proven FDA-approved approaches to smoking cessation. Therefore, oncology clinicians should not recommend e-cigarettes to patients as a first-line therapy for smoking cessation. Instead, they should discuss what is currently known and unknown about the safety and efficacy of e-cigarettes and endorse FDA-approved therapies (Harrell, Simmons, Correa, Padya, & Brandon, 2014).

Because of forceful marketing drives, more patients will raise questions about e-cigarettes. Because of the importance of smoking cessation for people with cancer, oncology clinicians should...
undertake a proactive approach. Patients with cancer who use or plan to use e-cigarettes, despite clinicians’ advice to the contrary, must be monitored for negative effects of e-cigarette use (Brandon et al., 2015).

Implications for Practice
Knowledge about the short-term effects of e-cigarettes is insufficient, and knowledge about their long-term safety is practically nonexistent. The lack of industry standards and/or government regulations renders generalizations about e-cigarettes inadequate. The need for extensive research is urgent. E-cigarettes may support smoking cessation, but definitive evidence about their efficacy is required. E-cigarettes may provide a less damaging source of nicotine than cigarettes, but data of decreased harm with long-term use are presently not available (Franck, Budlovsky, Windle, Filion, & Eisenberg, 2014).

Clinicians must document their patients’ e-cigarette use in addition to cigarette smoking, and educate their patients about e-cigarettes. A list of resources for patient education is available in Figure 1. A patient who smokes and who enquires about e-cigarettes is potentially signaling a willingness for cessation. Clinicians must take advantage of such an opportunity to help the patient quit and should explain e-cigarettes compared to cognitive-behavioral therapy, approved NRTs (e.g., patch, gum, inhaler), and non-nicotine medications, such as varenicline (Chantix®) or bupropion (Zyban®) (Grana, Ling, Benowitz, & Glantz, 2014). Smoking cessation guidelines contain scientifically proven information on how to help patients quit smoking (Larzelere & Williams, 2012).

A small body of evidence infers that e-cigarettes are a potential tool in the smoking cessation toolbox; an exact role has yet to be established. Some clinicians may presume that e-cigarettes are a lesser health risk and, therefore, feel comfortable recommending e-cigarette use to their patients. Since conclusive evidence and regulations are lacking, evaluation of the risk/benefit ratio for each patient before an e-cigarette recommendation is essential because some patients may benefit from e-cigarettes as a smoking cessation modality. Therefore, clinicians may consider e-cigarette use for patients on a case-by-case basis within the context of a plan of care. The growing popularity and use of e-cigarettes is certain to increase patient inquiries about their efficacy, cancer risk, effect of secondhand exposure, and short-term and long-term health risks. This compels clinicians to be up-to-date on the latest research and recommendations.

Conclusion
Smoking has been the leading cause of preventable deaths in the United States (CDC, 2015). Several factors, including anti-smoking campaigns, education, and tobacco control policies, successfully reduced the number of smokers from 43% of the U.S. population in 1964 to 18% in 2014. The USDHHS (2014) recommends continuation of current policies while implementing new ones to decrease the possible harm from emerging nicotine delivery products, such as e-cigarettes. A growing body of researchers suggests that e-cigarettes should be taxed and regulated as tobacco products until evidence for their benefits is presented (Mainous, Tanner, Mainous, & Talbert, 2015; Trenblay et al., 2015; Voigt, 2015).

In March 2016, the U.S. Department of Transportation banned e-cigarette use on all flights. Passengers are allowed to carry e-cigarettes with them onto planes, but are not allowed to charge their batteries during flight. In May 2016, the FDA extended its authority to all tobacco products, including e-cigarettes. The new rules prohibit e-cigarette sales to minors, prohibit distribution of free samples, and prohibit sales of e-cigarettes in vending machines. According to the new rules, if an e-cigarette contains nicotine, the following warning label must be placed on all packaging and advertising materials: “WARNING: This product contains nicotine. Nicotine is an addictive chemical” (FDA, 2016).

Policy statements from the American College of Physicians, the American Heart Association, the American Society of Clinical Oncology, and the American Thoracic Society acknowledge that e-cigarettes present health risks, the necessity for extensive research, and urgent need for regulation. Potential benefits must be evaluated in totality, taking into consideration the effect on the general population and on patients with chronic diseases. The aforementioned societies do not endorse e-cigarettes as a cessation tool in the smoking cessation toolbox; an exact role has yet to be established.
method (Bhatnagar et al., 2014; Brandon et al., 2015; Crowley, 2015; Schraufnagel et al., 2014). Until scientific data are produced, a recommendation to use or not to use e-cigarettes remains a judgment call for clinicians.

**REFERENCES**


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