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CASE AND COMMENTARY

How Should Physicians in Low- and Middle-Income Countries Regard Electronic Nicotine Delivery Systems to Facilitate Smoking Cessation?

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Abstract

Electronic nicotine delivery systems (ENDS) have been widely referred to as “safer,” “healthier,” and more “effective” smoking cessation aids, but little evidence supports such claims. New concerns about pulmonary injuries associated with ENDS suggest reasons for concern about these products’ health risks and potential for nicotine addiction. Nevertheless, multinational tobacco companies heavily market ENDS to retain customers with nicotine addiction, and global progress against tobacco use might slow as a result. The tobacco industry has managed to divide the tobacco control community by offering hope of harm reduction without actual evidence of ENDS’ effectiveness or long-term safety. Low- and middle-income countries need this evidence to assess ENDS’ value in mitigating tobacco use.

Case

Dr L, a family medicine physician in a middle-income country, sees Mr G, a 47-year-old man with moderately controlled hypertension and hyperlipidemia. Mr G has a 50-pack-per-year smoking history and has tried, without success, to quit. Over the last 3 months, he has cut his smoking from 2 packs to 5 or 6 cigarettes per day. Mr G explains enthusiastically to Dr L that he’s finally been able to reduce his regular cigarette use by using electronic (e-)cigarettes,¹ which, along with tobacco cigarettes, are heavily marketed in his neighborhood. “I’ve been told that e-cigarettes don’t contain the cancer-causing toxins in real cigarettes,² so I feel better about smoking these instead, and I love the flavors.”^{3,4}

Dr L has worked with many patients who struggle with smoking cessation and with family members who struggle with the consequences⁵ of having a family member who smokes. While some recent research suggests that e-cigarettes offer a better means of smoking cessation than other methods,^{6,7} significant uncertainty remains about the effects of long term e-cigarette use.⁸ “This is good progress. I know it’s hard because cigarettes are everywhere here,” said Dr L. Then, trying to clarify, he added, “Nicotine concentrations in e-cigarette oil blends can still be harmful,⁹ and there could be other carcinogens in these blends,⁴ so it’s important that you continue to try to wean yourself off the habit altogether.”¹⁰

Mr G looked crestfallen, and Dr L considered how best to respond.

Commentary

The US Food and Drug Administration (FDA) defines electronic nicotine delivery systems (ENDS) as noncombustible tobacco products including “vapes, vaporizers, vape pens, hookah pens, electronic cigarettes (e-cigarettes or e-cigs), and e-pipes,”¹¹ as well as devices with flavored nicotine-containing “pods” that attach to them. Use of these products has grown enormously since the 2003 invention of e-cigarettes by a Chinese pharmacist whose father died of lung cancer.¹² Manufacturers marketed these products first in China and subsequently in the United States, notably without any regulatory oversight.¹³ The Family Smoking Prevention and Tobacco Control Act, which established FDA regulatory authority over tobacco products, was not signed into law until 2009.¹⁴ Some in the public health community welcomed ENDS as a potential harm-reduction approach to the continued global tobacco epidemic, reasoning that any reduction in cigarette use should outweigh any potential risks of ENDS.¹⁵

In 2016, the FDA officially deemed that it had regulatory authority over the manufacture, import, packaging, labeling, advertising, promotion, sale, and distribution of ENDS.¹⁶ Of note is that the FDA has not approved ENDS for smoking cessation.¹⁷ A 2016 Cochrane review reported low-quality evidence supporting ENDS’ efficacy in aiding quitting.⁷ However, in 2018, Public Health England of the United Kingdom (UK) provided a summary of available evidence to support the clinical use of ENDS.¹⁸ Multinational tobacco companies and some experts have promoted these products with implied claims of their safety and cessation efficacy.¹⁹ In fact, recent findings suggest that US smokers use these products more than they do FDA-approved cessation aids (such as nicotine replacement, bupropion, and varenicline) to help them quit.²⁰

Despite the international marketing success of ENDS, consumers and clinicians should be cautious about these products' use. Evidence suggests that ENDS pose risks for human cardiac events,²¹ pulmonary toxicity,²² and cancer.²³ Recent studies have also shown increased exposure to toxic volatile organic compounds (carcinogens) among adolescent smokers²⁴ and have found potentially toxic metals in e-liquids.²⁵ Nicotine itself is a neurotoxin that poses a particular risk for the developing child and adolescent brain.²⁶ ENDS use is now considered an epidemic among young persons in the United States.²⁷ Therefore, clinicians should carefully evaluate the clinical utility and the risks of ENDS for those addicted to nicotine who use them long-term. Clinicians have a duty of care to be up-to-date on the literature on ENDS, including recent developments regarding safety and efficacy.

Counseling Mr G

Any practicing clinician who has advised a patient to quit smoking understands the extraordinary difficulty these patients face in overcoming nicotine addiction and other behavioral reinforcements that sustain tobacco use. Nonetheless, most experts agree that counseling and various approved cessation medications improve quitting success, especially when combined.²⁸

Mr G, a heavy smoker, is at significant risk for serious illness (especially for the many cancers caused by smoking), and he presents an ethical challenge for his primary care physician. Mr G has accessed ENDS in an effort to reduce the [harms of heavy smoking](#), and he has probably seen or heard advertising that reinforces his decision. Although there are approved medications and alternatives,¹⁷ these are likely to be more expensive than ENDS and are not always covered by health insurance. An ethical dilemma confronting Dr L is that ENDS are commercial products marketed by multinational tobacco companies as "healthier," even though they have not yet been fully vetted for cessation treatment. Dr L's dilemma is also emblematic of a wide gulf between different public health agencies' and professionals' positions on ENDS. The UK's National Health Service, for example, suggested that the risk of harm from ENDS is worth ignoring as it is a safer alternative to smoking,¹⁸ while others believe that the risk of sustained nicotine addiction and unproven claims about ENDS should be more strongly considered in the clinical treatment of tobacco use.

How should Dr L proceed? Both the physician and the patient in this case correctly understand that ENDS might have less carcinogenic potential than combustible tobacco products. Dr L also correctly understands that the overall

risks for long-term ENDS use are still unclear. ENDS will certainly sustain Mr G's nicotine addiction, which is dangerous for patients with cardiac risk factors such as hypertension and hyperlipidemia.²⁹ Moreover, Mr G continues to use cigarettes, for which there is no safe threshold of consumption.

Dr L wisely reinforces Mr G's progress in reducing his daily cigarette use, but, just as wisely, Dr L recognizes the need to assist Mr G in weaning himself completely from nicotine. In this case, there needs to be a mutually agreed-upon endpoint to Mr G's ENDS use. Just as with nicotine replacement therapy, Dr L needs to work with Mr G to set a date by which he completely ceases using any tobacco product, including ENDS. Reinforcing Mr G's intention to reduce his risk of tobacco-related disease will support his autonomy in this effort.

Considerations for Dr L

Guidelines. As part of efforts to end the tobacco epidemic,³⁰ the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC)—the first international health treaty³¹—provides guidance for cessation assistance at the national level. The FCTC recommends cessation supports and treatment of tobacco dependence as key components of a comprehensive, integrated tobacco control program. In particular, the FCTC guidelines call for development of national strategies for evidence-based clinical treatments that are free of conflicts of interest with “commercial and other vested interests of the tobacco industry.”³² Health professionals everywhere arguably have a duty to advocate for such evidence-based measures as part of quality-focused and equitable health care systems in their countries.

Conflicts of interest. Further muddying global perspectives on ENDS are efforts of a large multi-national tobacco company to promote the Foundation for a Smoke-Free World. Led by a former WHO deputy director,³³ this Foundation has dedicated millions of dollars to ending smoking,³³ which “means eliminating the use of cigarettes and other forms of combustible tobacco worldwide.”³⁴ While continuing to vigorously market cigarettes throughout the world,³⁵ the tobacco company now markets new heat-not-burn tobacco products in the United States in an attempt to keep its customers.³⁶ These products also have not been evaluated for safety or cessation efficacy.³⁶ The WHO correctly states that if the company “were truly committed to a smoke-free world, the company would support these [WHO FCTC] policies.” Instead, the company “engages in large scale lobbying and prolonged and expensive [litigation](#) against evidence-based tobacco control policies such as those found in the WHO FCTC.”³² The risk to public health

posed by this paradoxical effort cannot be underestimated. Spending millions of dollars on high-level lobbying annually³⁷ and obfuscating new product risks are effective tools to sustain profitability. The newfound commitment to a smoke-free world is likely to be more of the same.

Recommendations

Clinicians such as Dr L need to rely on evidence-based information about ENDS and also to be aware of multinational [tobacco industry initiatives](#) to preserve their market share and sustain demand for potentially deadly tobacco products. ENDS might have many more health risks than originally identified and should have already been subject to careful scientific scrutiny. Dr L should support this patient's commitment to reduce his tobacco use. He should recommend other proven cessation aids as alternatives to ENDS. Dr L can also meet with him more frequently and perhaps support his quit attempts with telephone contact and referrals to other cessation support services such as telephone quitlines.³⁸

Given the growing evidence of health risks of ENDS and the still-tenuous evidence that there are population benefits to using these largely unregulated products, there is no compelling ethical or clinical justification for clinicians to recommend vaping for smoking cessation. Clinicians should advise patients, as Dr L has, to eventually eliminate any form of nicotine delivery, regardless of their global locale. When deciding how to treat and advise Mr G, Dr L should be guided by fundamental ethical considerations of clinical care, as articulated by the WHO.

Most health practitioners want to do what is best for their patients. Non-maleficence ("first do no harm"), beneficence (doing good) and trust are fundamental ethical principles at the heart of clinical care. Health practitioners also seek to ensure that patients are given adequate information, are consenting to treatments and procedures voluntarily, and have the capacity to understand and appreciate the potential benefits and risks of the care they receive. Health practitioners seeking to provide the best possible care to their patients in the most ethical manner may find it difficult to balance the right to information with the need to avoid information overload.³⁹

Dr L should also incorporate procedural justice considerations by explaining how he made his recommendations and which values and evidence he used to inform these recommendations. In this way, he would ensure transparency of his decision making with his patient.

The advertising blitz and the subsequent rift over the utility of ENDS in a normally unified public health community will likely continue. ENDS use has

been firmly established in many high-income countries, even those with functional regulatory authorities.⁴⁰ In low- and middle-income countries (LMICs), however, clinicians and consumers need more information and more alternatives to assist smoking cessation rather than just accepting ENDS as an unproven cessation tool. LMICs suffer from information asymmetries regarding ENDS, as these products established consumer markets before clinical guidelines or regulatory regimes for them were established.⁴¹

New Problems for ENDS

In August 2019, reports of severe pulmonary injury associated with ENDS gave rise to more concerns about these products' use among public health authorities.⁴² An epidemic of these injuries caused a variety of jurisdictions to temporarily ban the sale of ENDS and to issue warnings not to use products that have been altered with any additives, especially cannabinoids.⁴³ Until more is known about the role of ENDS in these injuries, additional caution about recommending ENDS use should be exercised.⁴⁴

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