



Electronic cigarettes: not evidence-based cessation

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Despite extensive efforts, smoking remains a modern-day epidemic with profound health consequences. In 1984, Dr. C. Everett Koop, the Surgeon General of the US at that time, presented an important speech on the hazards of smoking. In his speech he stated “*The ultimate goal should be a smoke-free society by the year 2000.*” Unfortunately, we did not achieved that goal. Shortly after the target date for a smoke-free society as proposed by Dr. Koop, a new product was successfully introduced to the world, electronic cigarettes, or e-cigarettes, with the plan to provide a healthier alternative to smoking burnt tobacco. Unlike combustible cigarettes, e-cigarettes are battery-operated and use a heating element to heat an e-liquid releasing a chemical-filled aerosol. E-cigarettes also include e-pens, e-pipes, e-hookah, and e-cigars and are collectively known as electronic nicotine delivery systems (ENDS).

The first patent for a smokeless tobacco cigarette was filed in 1963 by the inventor Herbert Gilbert but it was not until the early 2000s when the world learned the commercial potential of e-cigarettes. E-cigarettes were successfully invented by Hon Lik, a Chinese pharmacist whose father died of lung cancer, with the goal of delivering nicotine with a smoke-free vapour. The assumption was that by eliminating the toxic chemicals found in combustible tobacco, these products would have less impact on smokers’ health and minimize the health-related consequences. After first being patented and then introduced into the Chinese market in 2003 these products appeared on the market in the US and UK 4 years later. E-cigarettes have quickly grown into a billion-dollar industry. In 2018 Americans will spend 4 billion dollars on e-cigarettes compared with 12 billion dollars in annual sales of burnt tobacco and is projected to outsell burnt tobacco products within the next

5 to 10 years (1). Currently in the US, e-cigarettes are the fastest growing patent class followed by 3-D printing and artificial intelligence (2).

Our relationship with smoking is complex. Historically smoking has been a symbol of cool (James Dean), a symbol of aspiration (Winston Churchill) and associated with genius (Albert Einstein). But once one starts smoking, despite the known detrimental health effects, quitting is not easy. In fact, it takes an average of 30 quit attempts over a smokers’ lifetime before quitting successfully (3). As Mark Twain once said, “Giving up smoking is the easiest thing in the world. I know because I’ve done it thousands of times.” In Ontario, Canada, the cessation rate, the proportion of smokers who remain abstinent for 12 months, is only 1.9% and has remained unchanged for several years (4).

In addition to being marketed as a safe alternative to burnt tobacco, e-cigarettes are marketed as an effective smoking cessation product without sufficient data to support these claims. Currently, the medical community is divided on its opinion about the use of e-cigarettes as a smoking cessation device. The scientific evidence that e-cigarettes are a useful aid for smoking cessation remains limited. In this review, we examined the current literature for evidence that could support or deny these claims to determine whether e-cigarettes can be a useful aid in combatting smoking addiction.

While some research shows e-cigarettes to be useful in quit attempts (5-7), results from a US national survey conducted of 729 current and former smokers showed that smokers are unsatisfied with the new devices and return to smoking tobacco cigarettes or maintain dual use of e-cigarettes and conventional cigarettes (8). The dissatisfaction may in part be due to the design evolution

of e-cigarettes. First-generation e-cigarettes were aptly named “cig-a-likes” because they closely resembled traditional cigarettes and were smoked the same way. First generation e-cigarette users would inhale the way they would with a traditional cigarette. This inhalation activated the atomizer to heat the e-liquid in the cartridge and convert the liquid to a vapor. Inhaling this vapor through the mouthpiece delivered nicotine to the lungs, and the user exhaled vapor that looks much like a cloud of cigarette smoke. As the technology has advanced, e-cigarettes have taken on new shapes. Current e-cigarettes have evolved into personal devices where users are able to tailor their devices to suit their personal smoking preferences. E-cigarette users, or “vapers”, are now able to adjust the strength and temperature of their devices. The variety of e-liquids available means that there is a flavor to suit anyone’s tastes and preferences. E-cigarettes have quickly evolved from a smoking alternative to a cloud-chasing, flavour phenomenon. Overall, these third-generation devices are highly modifiable and, in order to accommodate the modifications, have become much bulkier where the smoking style is highly unique.

To date, two randomized controlled trials have shown that e-cigarettes are not effective smoking-cessation tools (9,10). The first study was conducted in New Zealand and recruited smokers who were motivated to quit through newspaper advertisements and found that e-cigarettes were not superior to the patch as a smoking cessation tool. Subjects (657 motivated smokers who met the inclusion criteria) were randomly assigned to receive nicotine e-cigarettes (with cartridges containing 10 to 16 mg of nicotine per milliliter), nicotine patches (21 mg patch, one daily), or placebo (non-nicotine e-cigarettes). There were no statistical differences in 6-month quit rates between the three groups; the verified quit rates were 7.3% with nicotine e-cigarettes, 4.1% with non-nicotine e-cigarettes, and 5.8% with nicotine patches (9). Overall the abstinence rates were low in this study, perhaps due to lack of counselling and support. The trial also showed that dual use of tobacco cigarettes and e-cigarettes persisted amongst one third of the subjects at 6 months; dual use also occurred among patch users but at a lower level (7%) (9).

The results of another randomized controlled trial recently published in the *NEJM* also suggest that e-cigarettes are not effective for smoking cessation (10). The purpose of this study was to determine whether usual care (i.e., counselling and support), the 7 Food and Drug Administration (FDA) approved cessation aids, e-cigarettes

provided by NJOY, or financial incentives promote smoking cessation among unselected smokers. In this study, 6,006 smokers working for major US companies were assigned to one of 5 study groups. Overall, the abstinence rates were very low at 0.1, 0.5, 1, 2, and 2.9 in the whole population but in the engaged population, that is smokers motivated to quit, the abstinence rates were 4–6 times higher. Interestingly, redeemable deposits plus free cessation aids were superior to free e-cigarettes ($P=0.008$) (10). This was no surprise as we know people can be highly motivated by monetary incentives. Free e-cigarettes were not superior to usual care ($P=0.20$) or to free cessation aids ($P=0.43$) (10).

Hajek *et al.* has recently shown that e-cigarettes were more effective for smoking cessation than nicotine-replacement therapy, when both products were accompanied by behavioral support in a randomized trial where motivated smokers had some free reign over the products they used (7). This one-year study showed that e-cigarettes improved abstinence rates from 9.9% with nicotine replacement alone *vs.* 18.0% in the e-cigarette group. However, the authors defined abstinence as a self-report of not smoking more than five cigarettes over a 26-week period. Biochemical confirmation of cessation was not assessed over time. Instead, a one-time measurement of exhaled carbon monoxide at 52 weeks was used to confirm smoking status. This is especially problematic since the study was not blinded. Positive expectations have limited effects on long-term abstinence but exhaled carbon monoxide normalizes within 24 hours of smoke exposure. Study participants may have stopped smoking prior to the scheduled time to meet the expectations of the investigators. Moreover, this study failed to address the potential detrimental health effects of e-cigarettes (11-13). Of note, a study in mice found that a 4-month inhalational exposure to nebulized e-cigarette liquid containing nicotine promoted distal airspace enlargement and airway hyperreactivity (14).

Three population-based, longitudinal studies have also not shown associations between e-cigarette use and smoking cessation (15-17). Vickerman *et al.* surveyed a large group of tobacco users, approximately 3,000 participants, seeking support from 6 state tobacco quitlines. Overall, 30.9% of callers had used e-cigarettes, and smoking cessation was the most frequently reported reason for e-cigarette use (51.3%) (15). Among motivated smokers accessing the quitline for support the results show that e-cigarette users were less likely to have quit traditional smoking at 7 months compared with nonusers of e-cigarettes (16.6% e-cigarettes *vs.* 31.3% nonusers) (15).

Similarly, Adkison *et al.* conducted a longitudinal, international study with 1-year follow-up that involved data collected from the International Tobacco Control Four-Country Survey (16). This study found that the majority of smokers, 85%, used e-cigarettes to help them quit smoking. However, the results from this study showed that e-cigarette users did not quit smoking more frequently than nonusers ($P=0.52$) (16).

Furthermore, in a paper by Grana *et al.*, they provided more evidence that e-cigarette use was not associated with higher rates of smoking cessation (17). This study involved a longitudinal analysis of a national sample of current US smokers to determine whether e-cigarette use predicted successful quitting or reduced cigarette consumption and found that the self-reported quit rate was not higher among smokers using e-cigarettes as a smoking cessation device. In fact, the results showed that e-cigarette users had lower quit rates and a lower reduction in cigarette consumption (17). Importantly, further analysis showed that intention to quit [OR, 5.59 (95% CI, 2.41–12.98); $P<0.001$] and cigarettes smoked per day [OR, 0.97 (95% CI, 0.94–0.99); $P=0.02$] significantly predicted quit status but past 30-day e-cigarette use did not [OR, 0.76 (95% CI, 0.36–1.60); $P=0.46$] (17).

Further doubts about the usefulness of e-cigarettes for facilitating smoking cessation were raised by the systematic review and meta-analysis performed by Kalkhoran *et al.* (18). The aim of this study was to assess the association between e-cigarette use and smoking cessation among adult cigarette smokers, irrespective of their motivation for using e-cigarettes. Surprisingly, this study found that e-cigarette use may lower the odds of an individual quitting smoking combustible tobacco products by 28% (18).

And finally, when looking at a targeted group, current smokers with cancer, 1,074 were referred to a tobacco cessation program and it was found that e-cigarette users were twice as likely to be smoking at follow-up (6 months) as compared with nonusers, after adjusting for nicotine dependence, quit attempts, and cancer diagnosis (19). In this study, e-cigarette users were more nicotine dependent than nonusers, had more prior quit attempts, and were more likely to be diagnosed with thoracic and head or neck cancers, possibly suggesting that this group of patients would have more difficulty quitting without a tapering dose of nicotine. In addition to the other studies presented, this raises doubts concerning the usefulness of e-cigarettes for facilitating smoking cessation among smokers in general or patients with cancer more specifically.

The studies summarized in this article are not without biases and limitations. Survey studies were not designed to

specifically address the effect of e-cigarettes on smoking cessation. Their uncontrolled nature and other potential confounding factors could limit the ability to see a treatment effect. As discussed previously, the largest randomized controlled trial was limited by its lack of blinding and failure to confirm the smoking status of its participants. Unfortunately, most of the studies were underpowered and the studies both supporting and opposing e-cigarettes as a smoking cessation tool were biased by what stage a person may be on the Transtheoretical Model of Behavior Change (20), the number of quit attempts, and the other smoking cessation techniques they were currently using or have used in the past. While there may be a subset of users that still needs to be identified where e-cigarettes may be effective at improving abstinence, overall, we currently lack evidence supporting the use of e-cigarettes as effective smoking cessation devices.

The health and economic effects of smoking cessation are well established as tobacco use is the leading preventable cause of disease globally. Despite extensive research, smoking cessation rates are still at unacceptably low levels. For example, Ontario's smoking cessation rate has remained for many years at 1.9% (4). When it comes to quitting, most smokers quit on their own without the aid of formal treatment (i.e., medication and counselling) (21).

Smokers' efforts to quit smoking may be undermined by the promotion of smoking cessation products because these products reduce their confidence in their ability to quit on their own by implying that quitting cannot be achieved successfully without the use of these aids (22). The truth is, the majority of smokers do not want to quit smoking and we need to figure out why. Sixty-five percent of smokers refused participation in the study by Zhu *et al.* (22). The same is true for vapers; the majority do not want to quit (23). Developing and promoting interventions to improve smokers' odds of success has been the focus of smoking cessation efforts for so long that the field has largely neglected to investigate how to get more smokers to try to quit and to try more frequently. Increasing the quit attempt rate is a key goal for tobacco control efforts and critical to further reducing smoking (4). E-cigarettes are not the answer to this complex problem, and we need to be very careful about the role these nicotine delivery devices have in our society.

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Footnote

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