Puffing to Persistent Smoking Cessation

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Nicotine e-cigarettes are a safe and effective way to help patients stop smoking. (J Am Board Fam Med 2024;37:354–356.)

Keywords: **E-Cigarettes, Tobacco Cessation, Tobacco Use**

Strength of Recommendation: B

Based on systematic review of randomized and non-randomized trials.

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Illustrative Case

A 34-year-old man who is currently unhoused and has a history of alcohol use disorder comes to see you to get help quitting smoking. He has smoked one pack of cigarettes daily for the last 10 years and could not tolerate a trial of varenicline. What can you recommend to help him stop smoking?

Clinical Context

An estimated 11.5% of US adults smoked cigarettes in 2021, with higher rates among individuals with lower annual household incomes, lack of insurance, and mental health comorbidities.[1] Despite decreases in smoking rates over the last decade, smoking remains the leading cause of preventable death in the US.[2] While quitting has major health benefits, fewer than 7.5% of those who try are able to quit.[3]

Two different aspects of smoking reinforce dependence. The first is the chemical response to nicotine and avoidance of withdrawal symptoms. Nicotine patches, gums, and lozenges are designed to replace this aspect of smoking for those trying to quit. The second aspect is sociobehavioral: cues such as the sensory experience of taking a puff, the social identification of "being a smoker," and the ritual nature of taking a smoke break. Electronic cigarettes (ECs), which mimic the sensations and experience of smoking, can replace some of these sociobehavioral cues for patients who currently smoke.

ECs have been available in the US since 2007,[4] and by 2018, 14.9% of US adults had ever used an EC.[5] There is a wide variety in the physical appearance and mode of combustion of ECs, as well as in the formulation of the e-liquid, which can contain various concentrations of nicotine, flavors, and other components. Although ECs have increased in popularity since their introduction,[6] the lack of standardization among products and concerns about long-term safety of nicotine ECs have limited their widespread use as harm reduction or smoking cessation aids.

A Cochrane review was designed to investigate whether nicotine ECs are safe and effective interventions for smoking cessation. The meta-analysis compared nicotine ECs to nicotine replacement treatment (NRT), non-nicotine ECs, or behavioral support only/no treatment.[7] This Cochrane review is being updated on a monthly basis to reflect most recent data on this rapidly evolving clinical topic.

Methods

This article was identified as a potential PURL through the standard systematic methodology.[15] An additional literature search was conducted by

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searching Dynamed and UpToDate with the terms *vaping* and *e-cigarettes* and *treatment for smoking cessation* to find additional literature to place this research into the context of current clinical practice.

Study Summary

This systematic review (78 studies, 40 of which were RCTs, including 22,052 participants) investigated the effectiveness and safety of nicotine e-cigarettes (ECs) as a smoking cessation tool. Included patients were cigarette smokers and either motivated or unmotivated to quit. Nicotine ECs were compared with nicotine replacement therapy (NRT), non-nicotine Ecs, or behavioral support alone. The primary outcomes were cessation of smoking using biochemically validated results at the longest follow-up point, minimum 6 months, and participant-reported adverse events at one week or longer.

The authors concluded with high certainty that use of nicotine ECs was associated with higher quit rates compared with NRT (6 studies, n = 2378; risk ratio [RR] 1.63, 95% CI 1.30-2.04,) and with moderate certainty that the rate of adverse events was similar between the 2 groups (4 studies, n = 1072; RR 1.02, 95% CI 0.88-1.19). When comparing nicotine ECs to non-nicotine ECs, there was moderate certainty that nicotine ECs led to higher quit rates (5 studies, n = 1447; RR 1.94, 95% CI 1.21-3.13), and moderate certainty of no difference in adverse events (5 studies, n = 1840; RR 1.01, 95% CI 0.91-1.11). Comparison of nicotine ECs to behavioral support alone was limited by risk of bias but, with low certainty, there were increases in quit rates with nicotine ECs (7 studies, n = 3126; RR 2.66, 95% CI 1.52 - 4.65) and more adverse events (4 studies, n = 765; RR 1.22, 95% CI 1.12-1.32) among EC users.

Overall, there was no evidence of serious harm associated with EC use, although follow-up time was relatively short (2 years or less) and sample sizes were small. The use of ECs could lead to an additional 4 quitters per 100 compared with NRT, an additional 7 quitters per 100 compared with non-nicotine EC, and an additional 2 quitters per 100 compared with behavioral support alone, without a significant increase in adverse events

What Is New

Nicotine ECs should be considered as a safe and effective intervention to help patients stop smoking. Use of nicotine ECs would be expected to lead to an additional 4 patients per 100 stopping smoking at 6 months of use, without a significant increase in adverse events.

Caveats

For many clinicians, the combination of varenicline and behavioral support is considered standard of care for smoking cessation. Varenicline is FDA-approved and is the first-line recommendation for smoking cessation made by organizations like the United States Preventive Services Task Force.[8] However, only 2 studies in the meta-analysis, both of which the study authors judged to have high risk of bias, compared nicotine ECs to varenicline. One found a lower quit rate among patients randomized to nicotine ECs compared with varenicline,[9] and the other found no difference in adverse events among patients using nicotine EC and varenicline compared with varenicline alone (with wide confidence intervals).[10] Thus, this meta-analysis may not be practice-changing in terms a of first-line choice for smoking cessation, but could inform second-line options for patients who are not candidates for or do not wish to take varenicline. ECs could also be seen as a practice-changing harm reduction measure for patients who are not yet ready to quit smoking.

The FDA does not regulate ECs and thus concentrations of nicotine vary widely among ECs. Recent EC devices have higher nicotine doses than in the past, yet given their novelty, are included in fewer studies. If nicotine content in ECs continues to increase, this could affect both outcomes of the study.

Some clinicians may be concerned about E-cigarette or Vaping-Associated Lung Injury (EVALI) when recommending ECs to patients. EVALI prevalence spiked in summer 2019 and rates have been decreasing since.[11] Analysis of EVALI epidemiology showed that contamination with vitamin E acetate[12] and use of THC-containing oils[13] were the primary risk factors for lung injury; the link between nicotine ECs and EVALI is much less clear.[14] The Cochrane study authors point out that generally speaking, nicotine ECs contain far fewer contaminants than cigarettes.

Studies included in this meta-analysis enrolled a diverse set of patients, including individuals with comorbid mental illnesses, homelessness, and substance use disorders, as well as patients who were not motivated to quit smoking. The study authors

point out that these groups generally have lower quit rates and less success with conventional smoking cessation methods, so if effective, ECs could be particularly useful as an unconventional approach to help these populations.

Challenges to Implementation

The FDA has classified nicotine ECs as tobacco products and has not authorized their medical use, meaning that clinicians cannot prescribe nicotine ECs to their patients, nor are nicotine ECs covered by insurance. Although the cost of ECs is generally lower than the cost of cigarettes, the burden of seeking out and paying for ECs falls entirely on patients. There are restrictions regarding the sales of ECs, however these are generally the same as those regarding sales of cigarettes.

Studies included in this meta-analysis measured rates of cessation and/or adverse effects at a minimum of 6 months, but the longest follow-up period was 2 years. Clinicians may feel wary about recommending ECs when the longer-term data are limited.

To see this article online, please go to: http://jabfm.org/content/37/2/354.full.

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