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Electronic cigarettes for smoking cessation (Review)

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WILEY

[Intervention Review]

Electronic cigarettes for smoking cessation

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ABSTRACT

Background

Electronic cigarettes (ECs) are handheld electronic vaping devices which produce an aerosol by heating an e-liquid. People who smoke, healthcare providers and regulators want to know if ECs can help people quit smoking, and if they are safe to use for this purpose. This is a review update conducted as part of a living systematic review.

Objectives

To examine the safety, tolerability and effectiveness of using electronic cigarettes (ECs) to help people who smoke tobacco achieve long-term smoking abstinence, in comparison to non-nicotine EC, other smoking cessation treatments and no treatment.

Search methods

We searched the Cochrane Tobacco Addiction Group's Specialized Register to 1 February 2023, and Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and PsycINFO to 1 July 2023, and reference-checked and contacted study authors.

Selection criteria

We included trials in which people who smoke were randomized to an EC or control condition. We also included uncontrolled intervention studies in which all participants received an EC intervention as these studies have the potential to provide further information on harms and longer-term use. Studies had to report an eligible outcome.

Data collection and analysis

We followed standard Cochrane methods for screening and data extraction. Critical outcomes were abstinence from smoking after at least six months, adverse events (AEs), and serious adverse events (SAEs). We used a fixed-effect Mantel-Haenszel model to calculate risk ratios (RRs) with a 95% confidence interval (CI) for dichotomous outcomes. For continuous outcomes, we calculated mean differences. Where appropriate, we pooled data in pairwise and network meta-analyses (NMA).

Main results

We included 88 completed studies (10 new to this update), representing 27,235 participants, of which 47 were randomized controlled trials (RCTs). Of the included studies, we rated ten (all but one contributing to our main comparisons) at low risk of bias overall, 58 at high risk overall (including all non-randomized studies), and the remainder at unclear risk.

There is high certainty that nicotine EC increases quit rates compared to nicotine replacement therapy (NRT) (RR 1.59, 95% CI 1.29 to 1.93; $I^2 = 0\%$; 7 studies, 2544 participants). In absolute terms, this might translate to an additional four quitters per 100 (95% CI 2 to 6 more). There is moderate-certainty evidence (limited by imprecision) that the rate of occurrence of AEs is similar between groups (RR 1.03, 95% CI 0.91 to 1.17; $I^2 = 0\%$; 5 studies, 2052 participants). SAEs were rare, and there is insufficient evidence to determine whether rates differ between groups due to very serious imprecision (RR 1.20, 95% CI 0.90 to 1.60; $I^2 = 32\%$; 6 studies, 2761 participants; low-certainty evidence).

There is moderate-certainty evidence, limited by imprecision, that nicotine EC increases quit rates compared to non-nicotine EC (RR 1.46, 95% CI 1.09 to 1.96; $I^2 = 4\%$; 6 studies, 1613 participants). In absolute terms, this might lead to an additional three quitters per 100 (95% CI 1 to 7 more). There is moderate-certainty evidence of no difference in the rate of AEs between these groups (RR 1.01, 95% CI 0.91 to 1.11; $I^2 = 0\%$; 5 studies, 1840 participants). There is insufficient evidence to determine whether rates of SAEs differ between groups, due to very serious imprecision (RR 1.00, 95% CI 0.56 to 1.79; $I^2 = 0\%$; 9 studies, 1412 participants; low-certainty evidence).

Due to issues with risk of bias, there is low-certainty evidence that, compared to behavioural support only/no support, quit rates may be higher for participants randomized to nicotine EC (RR 1.88, 95% CI 1.56 to 2.25; $I^2 = 0\%$; 9 studies, 5024 participants). In absolute terms, this represents an additional four quitters per 100 (95% CI 2 to 5 more). There was some evidence that (non-serious) AEs may be more common in people randomized to nicotine EC (RR 1.22, 95% CI 1.12 to 1.32; $I^2 = 41\%$, low-certainty evidence; 4 studies, 765 participants) and, again, insufficient evidence to determine whether rates of SAEs differed between groups (RR 0.89, 95% CI 0.59 to 1.34; $I^2 = 23\%$; 10 studies, 3263 participants; very low-certainty evidence).

Results from the NMA were consistent with those from pairwise meta-analyses for all critical outcomes, and there was no indication of inconsistency within the networks.

Data from non-randomized studies were consistent with RCT data. The most commonly reported AEs were throat/mouth irritation, headache, cough, and nausea, which tended to dissipate with continued EC use. Very few studies reported data on other outcomes or comparisons, hence, evidence for these is limited, with CIs often encompassing both clinically significant harm and benefit.

Authors' conclusions

There is high-certainty evidence that ECs with nicotine increase quit rates compared to NRT and moderate-certainty evidence that they increase quit rates compared to ECs without nicotine. Evidence comparing nicotine EC with usual care/no treatment also suggests benefit, but is less certain due to risk of bias inherent in the study design. Confidence intervals were for the most part wide for data on AEs, SAEs and other safety markers, with no difference in AEs between nicotine and non-nicotine ECs nor between nicotine ECs and NRT. Overall incidence of SAEs was low across all study arms. We did not detect evidence of serious harm from nicotine EC, but the longest follow-up was two years and the number of studies was small.

The main limitation of the evidence base remains imprecision due to the small number of RCTs, often with low event rates. Further RCTs are underway. To ensure the review continues to provide up-to-date information to decision-makers, this review is a living systematic review. We run searches monthly, with the review updated when relevant new evidence becomes available. Please refer to the *Cochrane Database of Systematic Reviews* for the review's current status.

PLAIN LANGUAGE SUMMARY

Can electronic cigarettes help people stop smoking, and do they have any unwanted effects when used for this purpose?

What are electronic cigarettes?

Electronic cigarettes (e-cigarettes) are handheld devices that work by heating a liquid that usually contains nicotine and flavourings. E-cigarettes allow users to inhale nicotine in a vapour rather than smoke. Because they do not burn tobacco, e-cigarettes do not expose users to the same levels of chemicals that can cause diseases in people who smoke conventional cigarettes.

Using an e-cigarette is commonly known as 'vaping'. Many people use e-cigarettes to help them to stop smoking tobacco. In this review we focus primarily on e-cigarettes containing nicotine.

Why we did this Cochrane Review

Stopping smoking lowers the risk of cancer, heart attacks and many other diseases. Many people find it difficult to stop smoking. We wanted to find out if using e-cigarettes could help people to stop smoking, and if people using them for this purpose experience any unwanted effects.

What did we do?

We searched for studies that looked at the use of e-cigarettes for stopping smoking.

We looked for randomized controlled trials, in which the treatments people received were decided at random. This type of study usually gives the most reliable evidence about treatment effects. We also looked for studies in which everyone received e-cigarette treatment. We also included studies that gave smokers e-cigarettes and monitored their health even if there was no randomised group, because such studies can contribute to our understanding of the health effects of using EC.

We were interested in finding out:

- how many people stopped smoking for at least six months; and
- how many people had unwanted effects, reported on after at least one week of use.

Search date: We included evidence published up to 1st July 2023.

What we found

We found 88 studies which included 27,235 adults who smoked. The studies compared e-cigarettes with:

- nicotine replacement therapy, such as patches or gum;
- varenicline (a medicine to help people stop smoking);
- e-cigarettes without nicotine;
- heated tobacco (products designed to heat tobacco to a high enough temperature to release vapour, without burning it or producing smoke; these differ from e-cigarettes because they heat tobacco leaf/sheet rather than a liquid);
- other types of nicotine-containing e-cigarettes (e.g. pod devices, newer devices);
- behavioural support, such as advice or counselling; or
- no support for stopping smoking.

Most studies took place in the USA (38 studies), the UK (19), and Italy (9).

What are the results of our review?

People are more likely to stop smoking for at least six months using nicotine e-cigarettes than using nicotine replacement therapy (7 studies, 2544 people), or e-cigarettes without nicotine (6 studies, 1613 people).

Nicotine e-cigarettes may help more people to stop smoking than no support or behavioural support only (9 studies, 5024 people).

For every 100 people using nicotine e-cigarettes to stop smoking, 8 to 10 might successfully stop, compared with only 6 of 100 people using nicotine-replacement therapy, 7 of 100 using e-cigarettes without nicotine, or 4 of 100 people having no support or behavioural support only.

We are uncertain if there is a difference between how many unwanted effects occur using nicotine e-cigarettes compared with nicotine replacement therapy, no support or behavioural support only. There was some evidence that non-serious unwanted effects were more common in groups receiving nicotine e-cigarettes compared to no support or behavioural support only. Low numbers of unwanted effects, including serious unwanted effects, were reported in studies comparing nicotine e-cigarettes to nicotine replacement therapy. There is probably no difference in how many non-serious unwanted effects occur in people using nicotine e-cigarettes compared to e-cigarettes without nicotine.

The unwanted effects reported most often with nicotine e-cigarettes were throat or mouth irritation, headache, cough and feeling sick. These appeared similar to those people experience when using NRT. These effects were reduced over time as people continued using nicotine e-cigarettes.

How reliable are these results?

Our results are based on few studies for most outcomes and, for some outcomes, the data varied widely.

We found evidence that nicotine e-cigarettes help more people to stop smoking than nicotine replacement therapy. Nicotine e-cigarettes probably help more people to stop smoking than e-cigarettes without nicotine, but more studies are still needed to confirm this.

Studies comparing nicotine e-cigarettes with behavioural or no support also showed higher quit rates in people using nicotine e-cigarettes, but provide less certain data because of issues with study design.

Most of our results for the unwanted effects could change when more evidence becomes available.

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Key messages

Nicotine e-cigarettes can help people to stop smoking for at least six months. Evidence shows they work better than nicotine replacement therapy, and probably better than e-cigarettes without nicotine.

They may work better than no support, or behavioural support alone, and they may not be associated with serious unwanted effects.

However, we still need more evidence, particularly about the effects of newer types of e-cigarettes that have better nicotine delivery than older types of e-cigarettes, as better nicotine delivery might help more people quit smoking.