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Cochrane Database of Systematic Reviews | Systematic review - Intervention

Electronic cigarettes for smoking cessation

Published: 08/2016 | Date of last search: 01/2016 | Assessed as up to date: 01/2016 | See what's changed

Hartmann-Boyce J | McRobbie H | Bullen C | Begh R | Stead LF | Hajek P | Authors' declarations of interest

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Objectives

This review of studies aimed to find out whether electronic cigarettes help smokers stop smoking, and whether it is safe to use electronic cigarettes to do this.

Main findings

- **Electronic cigarettes compared to placebo:** Electronic cigarettes may increase the proportion of people who abstain from smoking for at least six months (low certainty evidence).
- **Electronic cigarettes compared to nicotine patches:** It is uncertain how effective electronic cigarettes are compared to nicotine patches (very low certainty evidence).
- **Adverse effects:** There may be little if any difference in the frequency of adverse events for electronic cigarettes compared to placebo electronic cigarettes or nicotine patches. The most frequently reported adverse events were mouth and throat irritation. None of the included studies reported serious adverse events considered related to using electronic cigarettes (low certainty evidence).

Summary of findings

Electronic cigarettes (EC) for smoking cessation

Population: Current smokers at enrolment into trials, motivated or unmotivated to quit
Intervention: Nicotine-containing electronic cigarettes
Comparison: Placebo electronic cigarettes or nicotine replacement therapy (nicotine patches)

View: Relative effect or Visual overview

Outcomes	Plain language statements	Absolute Effect: With control	Absolute Effect: With EC	Certainty of the evidence (GRADE)
Smoking cessation: Nicotine electronic cigarettes versus Placebo electronic cigarettes Follow-up: 6-12 months	*May increase the proportion of people who abstain from smoking for at least six months.*	40 per 1000	93 per 1000 Difference: 53 more people per 1000 (95% CI: 2 to 171 more people)	⊕⊕◯◯ Low certainty
Smoking cessation: Nicotine electronic cigarettes versus Nicotine patches Follow-up: 6 months	*It is uncertain how effective nicotine electronic cigarettes are compared to nicotine patches.*	58 per 1000	73 per 1000 Difference: 15 more people per 1000 (95% CI: 19 less to 77 more people)	⊕◯◯◯ Very low certainty

See more

Background

Electronic cigarettes (ECs) are electronic devices that produce an aerosol (or 'vapour') that the user inhales. This vapour typically contains nicotine without most of the toxins smokers inhale with cigarette smoke. Electronic cigarettes have become popular with smokers who want to reduce the risks of smoking. This review aimed to find out whether electronic cigarettes help smokers stop smoking, and whether it is safe to use electronic cigarettes to do this. See more detail about electronic cigarettes.

What this review is based on

Cochrane Reviews are based on systematic and robust selection of relevant studies. We included 24 studies in this review. See what studies we searched for and what we found.

Authors' conclusions

Electronic cigarettes may help people to quit smoking for at least six months compared with placebo. However, it is uncertain how effective electronic cigarettes are compared to nicotine patches, and the long-term safety of electronic cigarettes is unknown. The most commonly reported adverse effects of electronic cigarettes are irritation of the mouth and throat.

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Background

Throughout this review, we discuss two types of cigarettes: electronic and conventional tobacco cigarettes. To avoid confusion, all mention of smoking, smoking cessation, cigarette use, smoke intake, etc., concern conventional cigarettes. When the text concerns electronic cigarettes we use the abbreviation 'ECs'. EC users are sometimes described as vapers, and EC use as vaping. We refer to ECs that do not contain nicotine as placebo ECs.

Description of the condition

Stopping smoking is associated with large health benefits. Despite most smokers wanting to quit, many find it difficult to succeed in the long term. Almost half who try to quit without support will not manage to stop for even a week, and fewer than five per cent remain abstinent at one year after quitting (Hughes 2004).
Considering the other factors that contribute to tobacco dependence, there is interest in developing smoking cessation products that would not only help relieve the unpleasant effects of nicotine withdrawal but would also act as an effective substitute for smoking behaviour and the rituals and sensations that accompany smoking, without the health risks associated with the inhalation of tobacco smoke.

Description of the intervention

ECs are electronic vaporizing devices that have in common the ability to heat a liquid, usually comprising propylene glycol and glycerol, with or without nicotine and flavours, and stored in disposable or refillable cartridges or a reservoir, into an aerosol for inhalation. The commonly-used term for this aerosol is vapour, which we use throughout the review. ECs are currently being promoted by retailers to use instead of cigarettes when in smoke-free environments, and to replace conventional cigarettes with a safer alternative.

Why it is important to do this review

Since ECs appeared on the market in 2006 there has been a steady growth in sales, with some commentators reporting that ECs are a threat to the sales of cigarettes (Herzog 2013). This growth in sales is reflected in population survey data from high-income countries that show an increased awareness and use of ECs over time (ASH 2016; Agaku 2014; Ayers 2011; Gallus 2014; West 2016). Data from lower-income countries also suggest high levels of EC use and awareness (Jiang 2016; Palipudi 2016).
Smokers, healthcare providers and regulators are interested to know if these devices can help smokers quit and if it is safe to use them to do so. In particular, healthcare providers have an urgent need to know what advice they should give to people who smoke. The largest health gains are achieved from stopping smoking completely, as opposed to reducing cigarette consumption, and as such this review focuses on the effectiveness of ECs in aiding smoking cessation.

Objectives

To evaluate the safety and effect of using electronic cigarettes (ECs) to help people who smoke achieve long-term smoking abstinence.

Methods

Criteria for considering studies for this review

Types of studies

Randomized trials in which smokers are randomized to ECs or to a control condition, and which measure abstinence rates at six months or longer, to determine the effectiveness of ECs in aiding smoking cessation and reduction.
We anticipated that the search would return few randomized trials and so we also considered the results from cohort follow-up studies with six months' or longer follow-up. In this and the previous version of the review, we include those observational cohort studies which survey existing smokers at baseline, some of whom are already dual users of EC and cigarettes. As discussed in further detail below, these studies are heavily confounded due to the nature of their design. In anticipation of further high-quality studies becoming available, we will exclude this study design for effectiveness outcomes in the next update of this review, and will only include those observational studies where an intervention has been provided.
For adverse events and biomarkers, we included randomized cross-over trials and cohort follow-up studies with follow-up of greater than a week.
We included studies regardless of their publication status or language of publication.

Types of participants

People defined as current smokers at enrolment into the studies. Participants can be motivated or unmotivated to quit.

Types of interventions

We compare ECs with placebo ECs, ECs versus alternative smoking cessation aids, including nicotine replacement therapy or no intervention, and ECs added to standard smoking cessation treatment (behavioural or pharmacological or both) with standard treatment alone. As relatively few controlled trials are currently available (some are underway), we also include uncontrolled studies which evaluate ECs (see types of studies above).

Types of outcome measures

Cessation at the longest follow-up point, which was at least six months from the start of the intervention, measured on an intention-to-treat basis using the strictest definition of abstinence, preferring biochemically-validated results where reported. We collected any data on adverse events at one week or longer, serious and non-serious, from the included studies, including changes in relevant biomarkers.

Methods for identifying studies

For a detailed description of the strategies that were used to find studies that meet the selection criteria for this review, see: Methods for identifying studies (in *Additional details*).

Methods for collecting and analysing data

For a detailed description of the methods used to select studies, extract data from included studies, assess the risk of bias, and synthesize the findings of the included studies, see:
See: Methods for collecting and analysing data (in *Additional details*).

Results

Results of the search

Our searches resulted in 24 studies for inclusion in this review. Below, **Table 1** presents more detail about what we searched for and found. Figure X illustrates our inclusion and exclusion process in a study flow diagram. Then, in a series of tables and figures, we present the characteristics of included, excluded, and ongoing studies, as well as our judgements about risk of bias. (See Additional details for a list of all results tables and figures.)

Table 1 *What review authors searched for and found*

Results

Results of the search

Our searches resulted in 24 studies for inclusion in this review. Below, **Table 1** presents more detail about what we searched for and found. Figure X illustrates our inclusion and exclusion process in a study flow diagram. Then, in a series of tables and figures, we present the characteristics of included, excluded, and ongoing studies, as well as our judgements about risk of bias. (See Additional details for a list of all results tables and figures.)

Table 1 *What review authors searched for and found*

	What the review authors searched for	What the review authors found
Study designs	Randomized trials in which smokers are randomized to ECs or to a control condition. Cohort follow-up studies with six months' or longer follow-up. Observational cohort studies which survey existing smokers at baseline. For adverse events and biomarkers, randomized cross-over trials and cohort follow-up studies with follow-up of greater than a week.	24 completed studies (3 randomized trials and 21 cohort studies). 27 ongoing studies.
Interventions	ECs with placebo ECs ECs versus alternative smoking cessation aids, including nicotine replacement therapy or no intervention ECs added to standard smoking cessation treatment (behavioural or pharmacological or both) with standard treatment alone.	Two randomized trials compared EC with placebo (non-nicotine) EC and one of those also compared EC with nicotine patches. Both used early EC models with low nicotine content and poor battery life.
Participants	People defined as current smokers at enrolment into the studies. Participants can be motivated or unmotivated to quit.	People defined as current smokers at enrolment into trials, motivated or unmotivated to quit.
Settings	Any setting	Belgium, USA, UK, New Zealand, Italy, France, UK, Switzerland, South Africa. Mixed settings (community, laboratory, cancer centre, web-based, research unit, outpatient clinic, inpatients, telephone survey).
Outcomes	Cessation at the longest follow-up point, which was at least six months from the start of the intervention, measured on an intention-to-treat basis using the strictest definition of abstinence, preferring biochemically-validated results where reported. Any data on adverse events at one week or longer, serious and non-serious, from the included studies, including changes in relevant biomarkers.	The trial with both placebo EC and nicotine patches as comparisons reported cessation at 6 months, any adverse event reported by participants, and the proportion of serious adverse events. The second trial reported cessation at 12 months, and adverse events thought to be related to EC. Fourteen cohort studies reported abstinence at six months or longer. Seven cohort studies provided information on adverse events only.

ECs: Electronic cigarettes **Placebo ECs:** non-nicotine electronic cigarettes

Open in figure viewer

Figure x. Study flow diagram of searches conducted for this update: An overview of the number of studies that were screened for this version of the review and reasons for excluding studies

Table x. Characteristics of included studies: Relevant information about the methods, participants, interventions, and outcome measures for each study included in this review

Table x. Characteristics of excluded studies: Reasons for excluding specific studies that might appear to be relevant for this review

Table x. Characteristics of ongoing studies: Information about the methods, participants, interventions, and outcome measures of studies for which results have not yet been reported

Table x. Risk of bias of included studies: The review authors' judgements about the risk of specific types of systematic errors (bias) and - the basis for those judgements - for each included study

Figure x. Risk of bias summary: An overview of the review authors' judgements about the risk of specific types of systematic errors (bias) for all of the included studies

Effects of interventions

Summary of findings: This table presents the effects of electronic cigarettes compared to nicotine patches and to placebo

Overview of analyses (with forestplots)

Cessation

In the trial comparing EC to patch (Bullen 2013) there was little difference in six-month CO (carbon monoxide)-validated continuous abstinence between the treatment arms (7.3%, 5.8% and 4.1%, in the nicotine EC, patch and placebo EC arms respectively). We made two comparisons. The first compares abstinence rates between nicotine and placebo EC (7.3% versus 4.1%, risk ratio (RR) 1.77, 95% confidence interval (CI) 0.54 to 5.77; 362 participants; Analysis 1.1). The second compares abstinence rates between the nicotine EC and patch arms (7.3% versus 5.8%, RR 1.26, 95% CI 0.68 to 2.34; 584 participants; Analysis 2.1). Fewer than half of all participants across all groups accessed support (39.8%, 35.9%, and 35.6% in the nicotine EC, patch and placebo EC arms respectively).

In the other randomized trial (Caponnetto 2013a) one-year abstinence rates (at least six months of not smoking and CO-validated) were higher in the two nicotine EC arms (13% and 9%) compared with the placebo EC group (4%). In our analysis we combined the two nicotine EC arms and compared these with the placebo group: 11% versus 4%, RR 2.75, 95% CI 0.97 to 7.76; 300 participants (Analysis 1.1).

We combined data from the two studies comparing abstinence rates in nicotine versus placebo EC groups. There was no significant statistical heterogeneity between the studies ($Chi^2 = 0.30$, $P = 0.58$; $I^2 = 0\%$). The pooled results indicate that use of a nicotine-containing EC may increase the proportion of people who abstain from smoking for at least six months compared to placebo EC use (RR 2.29, 95% CI 1.05 to 4.96, low certainty evidence; Analysis 1.1, Summary of findings).

The included cohort studies (Summary of findings) share a serious limitation. As these studies only recruited current smokers, they excluded those people from the same population who tried ECs and stopped smoking (e.g. if 100 smokers tried ECs and 50 stopped smoking, these studies would only recruit the 50 who continued to smoke). Following up 'treatment failures' is likely to show a low treatment effect, even for treatments that are highly effective. To assess the effects of ECs on smoking, participants need to be recruited prior to initiating EC use. In future versions of this review, we will no longer include this group of studies.

Adverse events

None of the randomized trials or cohort studies reported any serious adverse events that were considered to be plausibly related to EC use.

Of the people available for six-month follow-up in the ASCEND trial (Bullen 2013), 44.4% of participants in the nicotine EC arm reported any adverse events, compared with 44.7% and 45.6% in the patch and placebo EC arms respectively. Based on this trial, there may be little if any difference in the proportion of people who experienced adverse events for nicotine versus placebo EC (RR 0.97, 95% CI 0.71 to 1.34, low certainty evidence; Analysis 1.2, Summary of findings) or for nicotine EC versus patch (RR 0.99, 95% CI 0.81 to 1.12, low certainty evidence; Analysis 2.2, Summary of findings).

Discussion

Key findings and certainty of the evidence

As with the previous version of this review, a meta-analysis that pooled the results of two randomized trials

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Difference between protocol and review *(in About this review)*

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Table x. Characteristics of excluded studies
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Table x. Risk of bias of included studies
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Table x. GRADE evidence profile

Analyses with forest plots

Overview of analyses with forest plots
Analysis 1.1. Nicotine EC vs placebo EC (outcome: smoking cessation)
Analysis 1.2 . Nicotine EC vs placebo EC (outcome: adverse
Analysis 2.1 . Nicotine EC vs Nicotine replacement therapy (outcome: smoking cessation)
Analysis 2.2. Nicotine EC vs Nicotine replacement therapy (outcome: adverse events)

Appendices

Appendix 1 Summary of proportion of participants abstinent from smoking at follow-up: cohort studies

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Electronic cigarettes for smoking cessation

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Information for decision-makers

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For patients and the public

What are electronic cigarettes?
Electronic cigarettes (ECs) are known by a variety of names, including vape pens, e-hookahs, mods, tank systems, and e-cigs. ECs are electronic devices that use a battery to aerosolize a liquid, usually containing nicotine, flavouring, and other additives, which is inhaled through a mouthpiece.

Who can use electronic cigarettes?
Smokers report using ECs to reduce the risks of smoking or to help them quit smoking. The regulation of e-cigarettes varies by country. Because nicotine is highly addictive and can harm the developing adolescent brain, young people are discouraged from using ECs.

What other options are there?
Options to help people quit smoking include behavioural counselling, nicotine replacement therapy, and other medications. See: Other options (below).

How do people experience the intervention?
ECs replicate the experience of smoking, delivering a mist with nicotine instead of smoke. They may be perceived as cleaner. Some smokers may experience them as a bit harsher on the back of the throat, and some may experience that cravings return sooner than with smoking.

Is there anything else someone should know before using the intervention?
It is unknown whether ECs are harmful to others exposed to second-hand aerosol. There may be restrictions on where ECs can be used.

For clinical decisions

Indications and contraindications
Although electronic cigarettes (ECs) are promoted to help people quit smoking, their safety and effectiveness are uncertain. Smokers may therefore want to consider other options (see below).

Young people are discouraged from using ECs, because nicotine is highly addictive and might harm the developing adolescent brain.

Nicotine replacement products, rather than ECs, should be considered to manage nicotine withdrawal symptoms in hospitalized smokers.

Delivery
There are hundreds of different brands and models of ECs available. There is also wide variation in the composition of the fluid in the cartridge or in the EC reservoir (nicotine content, flavours, and other components). ECs may deliver very low amounts of nicotine to new users. However, even in the absence of good nicotine delivery, they can alleviate the urge to smoke.

There are differences between smoking a cigarette and smoking ECs. Smoking ECs too much at a time or smoking them for too long can lead to throat irritation and soreness. Nicotine absorption occurs more slowly with ECs than with smoking tobacco cigarettes, so smokers may need to get used to waiting longer to get a nicotine fix.

Cautions
The effects of long-term use of ECs, EC cessation, and interventions to help people quit using ECs are unknown.

Counselling patients
These points might be covered in response to questions by smokers about using ECs to help them quit smoking:

- The main findings of this review regarding the safety and effectiveness of ECs
- More detail about ECs
- Using ECs is probably less harmful than smoking conventional cigarettes, but we do not know how safe they are for users or those around them. The health consequences of vapor exposure are unknown, and inhaling EC flavourings might adversely affect respiratory function.
- There are other options that can help them to stop smoking (see below).

For policy decisions

Policy options
Policy options for electronic cigarettes (ECs) include: requiring disclosure of ingredients, regulating nicotine levels, regulating the composition of fluids (e.g. banning flavours with high toxicity), regulating disposal of devices and fluids, restrictions on advertising, requiring product warnings, taxation policies, restrictions on where ECs can be used, and banning ECs altogether.

Policy options targeted at preventing use of ECs by children and young people include requiring child-resistant packaging, restricting flavours with high youth appeal, restricting advertising targeted at young people, and restricting sale of ECs to young people.

Equity considerations
Use of ECs likely costs less than smoking. Therefore, to the extent that ECs are found to be safe and effective, affordability might not be a barrier to shifting from tobacco to ECs.

Economic considerations
There are many EC producers, including tobacco manufacturers, promoting ECs through advertising and social media. In addition to considering taxation policies and the cost of ECs relative to tobacco cigarettes, consideration needs to be given to how the cost of ECs might affect uptake by non-smokers, particularly young people.

Monitoring and evaluation
The impacts of policies aimed at encouraging or discouraging smokers to use ECs or to prevent youth from using ECs are uncertain. The effects of implementing such policies should be evaluated.

Because the safety and effectiveness of ECs is uncertain, rigorous evaluation is needed to inform future policy decisions. In the most recent update of this review, 15 ongoing randomised trials with follow-up of six months or longer were found.

Other options

Cochrane Reviews of other options to help people quit smoking

Mobile phone–based interventions for smoking cessation
Robyn Whittaker, Hayden McRobbie, Chris Bullen, Anthony Rodgers, Yulong Gu | 10 Apr 2016

Aversive smoking for smoking cessation
Peter Hajek, Lindsay F Stead | 23 Jul 2001

Telephone counselling for smoking cessation
Lindsay F Stead, Jamie Hartmann–Boyce, Rafael Perera, Tim Lancaster | 12 Aug 2013

Hypnotherapy for smoking cessation
Jo Barnes, Christine Y Dong, Hayden McRobbie, Natalie Walker, Monaz Mehta, Lindsay F Stead | 6 Oct 2010

Antidepressants for smoking cessation
John R Hughes, Lindsay F Stead, Jamie Hartmann–Boyce, Kate Cahill, Tim Lancaster | 8 Jan 2014

Nicotine replacement therapy for smoking cessation
Lindsay F Stead, Rafael Perera, Chris Bullen, David Mant, Jamie Hartmann–Boyce, Kate Cahill, Tim Lancaster | 14 Nov 2012

Print–based self–help interventions for smoking cessation
Jamie Hartmann–Boyce, Tim Lancaster, Lindsay F Stead | 3 Jun 2014

Relapse prevention interventions for smoking cessation
Peter Hajek, Lindsay F Stead, Robert West, Martin Jarvis, Jamie Hartmann–Boyce, Tim Lancaster | 20 Aug 2013

Other related Cochrane Reviews

Interventions to reduce harm from continued tobacco use
Nicola Lindson–Hawley, Jamie Hartmann–Boyce, Thomas R Fanshawe, Rachna Begh, Amanda Farley, Tim Lancaster | 13 Oct 2016

Physician advice for smoking cessation
Lindsay F Stead, Diana Buitrago, Nataly Preciado, Guillermo Sanchez, Jamie Hartmann–Boyce, Tim Lancaster | 31 May 2013

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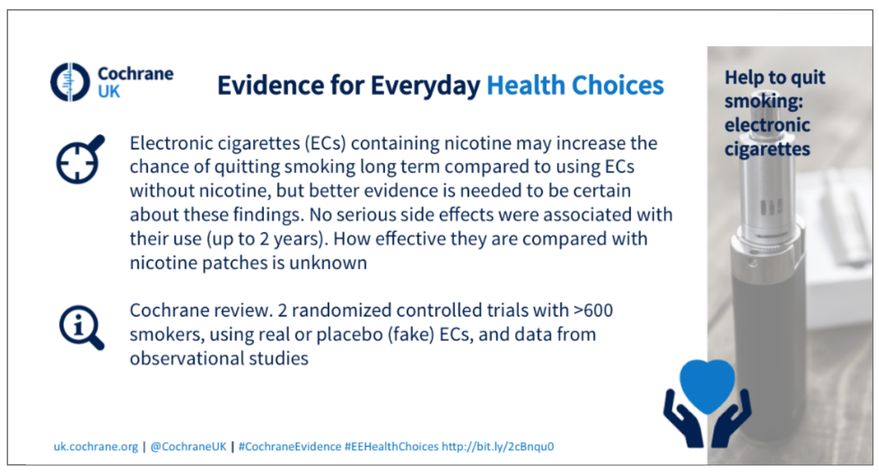
Blogshot



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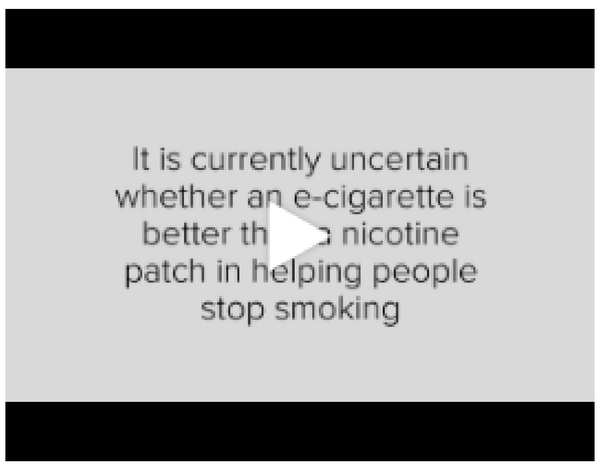
Vlogshot (Animated «slide show»)



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Press release

13. September, 2016. The conclusions of this updated Review are unchanged since the last review was published two years ago: electronic cigarettes may help smokers stop their smoking, and the included studies did not find any serious side effects associated with their use for up to two years. **See entire press release, with additional media coverage:** http://www.cochrane.org/news/conclusions-about-effects-electronic-cigarettes-remain-same

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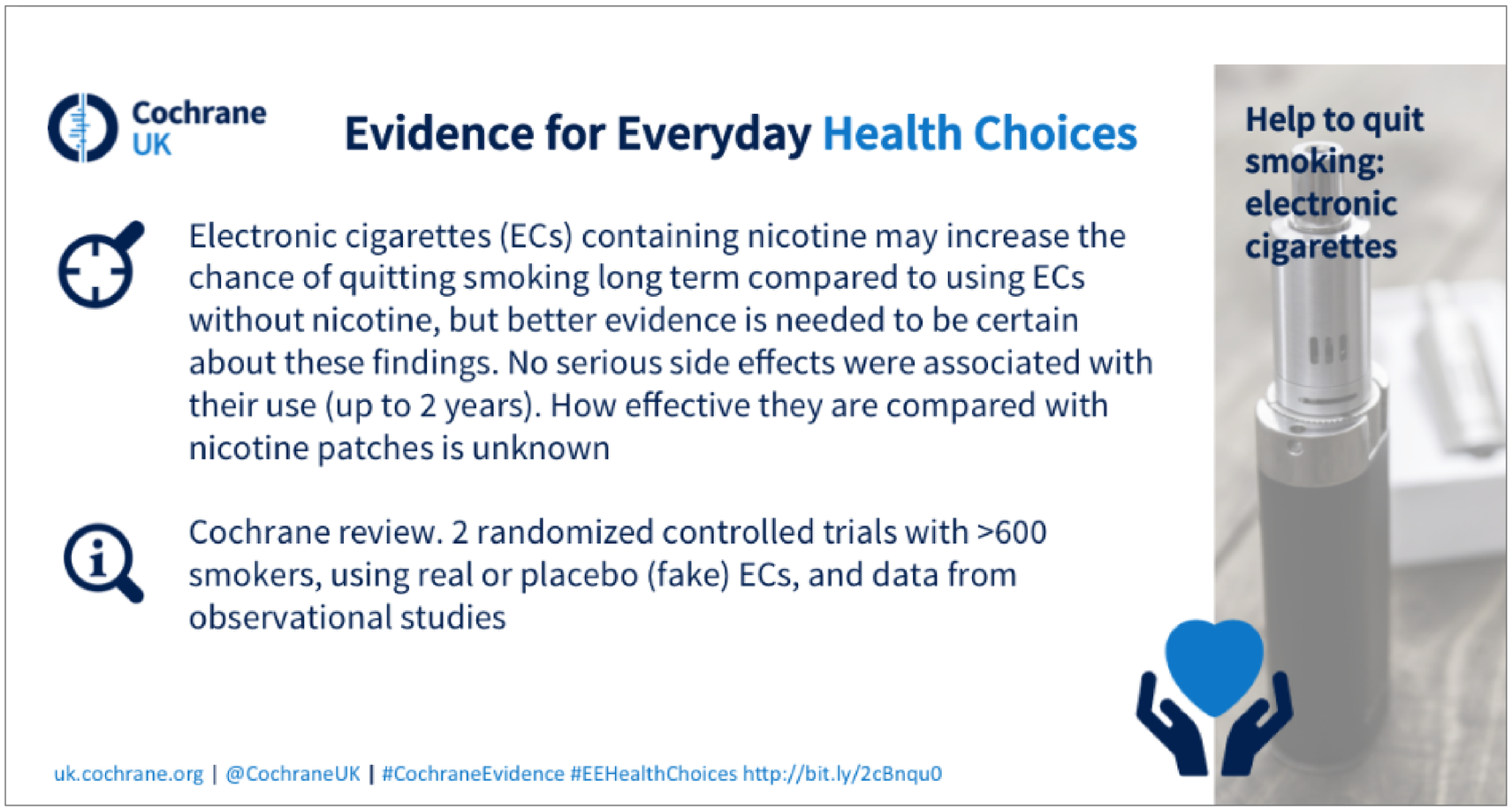

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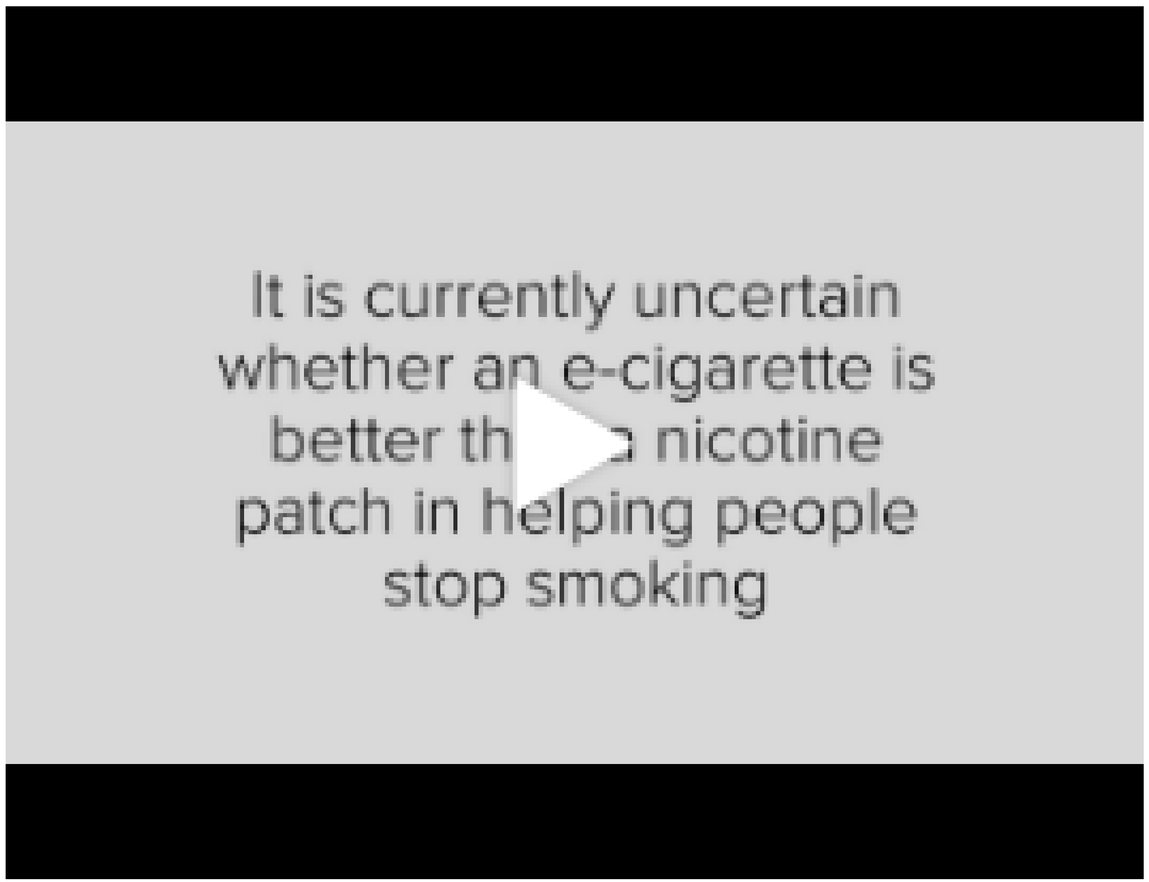

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Conclusions about the effects of electronic cigarettes remain the same

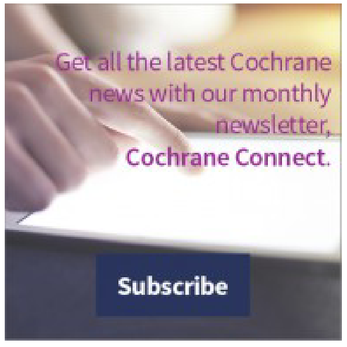
An updated Cochrane Review provides an independent, rigorous assessment of the best available evidence to date about electronic cigarettes for quitting smoking.

Scroll to the bottom of this article for a round-up of media coverage

The conclusions of this updated Review are unchanged since the last review was published two years ago: **electronic cigarettes** may help smokers stop their smoking, and the included studies did not find any serious side effects associated with their use for up to two years.

Many studies are now underway which may help us understand more about their effects in the future.

The first Cochrane Review, published in the Cochrane Library in December 2014, showed that electronic cigarettes may be an aid to smokers in stopping their smoking. The updated Review did not find any new randomized controlled trials (RCTs) with long-term outcomes looking at the effectiveness of electronic cigarettes in helping people to stop smoking. However, this is an active area of research, with a large number of ongoing studies that will add to the evidence in the next few years.



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Electronic cigarettes for smoking cessation

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About this review

Jump to: Publishing information | Article metrics | Authorship | Declarations | History

Publishing information

DOI: 10.1002/14651858.CD010216.pub3
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Cochrane Editorial Group: Cochrane Tobacco Addiction Group
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Altmetric:

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Picked up by 115 news outlets
Blogged by 9
Referenced in 2 policy sources
Tweeted by 216
On 14 Facebook pages
Referenced in 3 Wikipedia pages
Mentioned in 1 Google+ posts
Reddited by 1
On 1 videos

72 readers on Mendeley
1 readers on CiteULike

Authorship

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Chris Bullen
Rachna Begh
Lindsay F Stead
Peter Hajek

Authors' contributions
All authors contributed to the writing of this review.
JHB, HM and LS extracted data, with discrepancies and disagreements referred to PH.
As principal investigator of one of the included trials, CB was not involved with data extraction or assessment of study quality.

Declarations

Authors' declarations of interest
Within the last three years HM has received honoraria for speaking at research symposia and received benefits in kind and travel support from, and has provided consultancy to, the manufacturers of smoking cessation medications.

Within the last three years PH has provided consultancy for and received research funding from GSK, Pfizer, Novartis and other manufacturers of smoking cessation medications.

Two authors (HM, CB) have additional declarations:
CB and HM were investigators on a study of ECs from an EC manufacturer (Ruyan Group, Beijing and Hong Kong). Ruyan supplied the ECs used in the trial and contracted with Health NZ Ltd. to undertake the study. Health New Zealand Ltd funded The University of Auckland to conduct the trial, independently of Ruyan Group (Holdings) Ltd. The trial design conduct, analysis and interpretation of results were conducted independently of the sponsors.
CB and HM were investigators on the ASCEND EC trial funded by the Health Research Council of New Zealand that used product supplied at no charge from PGM international, a retailer of ECs.

JHB, RB and LS have no conflicts of interest to declare.

Acknowledgements
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Sources of support
Internal support
- Queen Mary University of London, UK.
  provides salary, office space and library resources for HM and PH
- The University of Auckland, New Zealand
  provides salary, office space and library resources for CB

External support
- No sources of support supplied

History

Version history

Title	Stage	Authors	Version	Publication Date
Electronic cigarettes for smoking cessation	Review	Jamie Hartmann-Boyce, Hayden McRobbie, Chris Bullen, Rachna Begh, Lindsay F Stead, Peter Hajek	https://doi.org/10.1002/14651858.CD010216.pub3	13 September 2016
Electronic cigarettes for smoking cessation and reduction	Review	Hayden McRobbie, Chris Bullen, Jamie Hartmann-Boyce, Peter Hajek	https://doi.org/10.1002/14651858.CD010216.pub2	17 December 2014
Electronic cigarettes for smoking cessation and reduction	Protocol	Hayden McRobbie, Chris Bullen, Peter Hajek	https://doi.org/10.1002/14651858.CD010216	14 November 2012

Search history

Date	Event	Description
23 June 2016	New search has been performed	Update search run January 2016, 11 new included studies added. Reduction removed as outcome, now covered in Harm Reduction review.
23 June 2016	New citation required but conclusions have not changed	11 new included studies added; no changes to conclusions.

What's changed

Date	Event	Description
14 December 2016	Amended	Clarification on outcome data from Adriaens - no changes to conclusions

Difference between protocol and review
Originally, the protocol did not specify a minimum follow–up period for data on adverse events. The Methods section has been changed to clarify that we will exclude follow–up data at less than a week.

The original version of this review included reduction as a secondary outcome. The 2016 update removed reduction as an outcome, to bring the review into line with other reviews of cessation treatments produced by the Cochrane Tobacco Addiction Group and to prevent substantial overlap with the update of the group's review of interventions for harm reduction (Stead 2007, update forthcoming).

Keywords

Medical Subject Headings (MeSH) Keywords
*Electronic Nicotine Delivery Systems [adverse effects, instrumentation];
*Smoking Prevention;
Cohort Studies;
Nicotine [administration & dosage];
Nicotinic Agonists [administration & dosage];
Publication Bias;
Randomized Controlled Trials as Topic;
Smoking [epidemiology];
Smoking Cessation [*methods];
Tobacco Use Cessation Products;

Medical Subject Headings Check Words:
Humans;
Middle Aged;

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Authorship

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Cochrane Database of Systematic Reviews | Systematic review - Intervention

Electronic cigarettes for smoking cessation

Published: 08/2016 | Date of last search: 01/2016 | Assessed as up to date: 01/2016 | See what's changed

Hartmann-Boyce J | McRobbie H | Bullen C | Begh R | Stead LF | Hajek P | Authors' declarations of interest

Altmetric score 16 More about this review

Hear from the author

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Background
Objectives
Methods
Results
Discussion
Authors' conclusion
References

Additional details
Methods details
Study characteristics
Risk of bias
Evidence tables
Analyses with forest plots
Appendices

Objectives

This review aimed to find out whether electronic cigarettes help smokers stop smoking, and whether it is safe to use electronic cigarettes to do this.

Main findings

- **Electronic cigarettes compared to placebo:** Electronic cigarettes may increase the proportion of people who abstain from smoking for at least six months (low certainty evidence).
- **Electronic cigarettes compared to nicotine patches:** It is uncertain how effective electronic cigarettes are compared to nicotine patches (very low certainty evidence).
- **Adverse effects:** There may be little if any difference in the frequency of adverse events for electronic cigarettes compared to placebo electronic cigarettes or nicotine patches. The most frequently reported adverse events were mouth and throat irritation. None of the included studies reported serious adverse events considered related to using electronic cigarettes (low certainty evidence).

Summary of findings

Electronic cigarettes (EC) for smoking cessation

Population: Current smokers at enrolment into trials, motivated or unmotivated to quit
Intervention: Nicotine-containing electronic cigarettes
Comparison: Placebo electronic cigarettes or nicotine replacement therapy (nicotine patches)

View: Relative effect or Visual overview

Outcomes	Plain language statements	Absolute Effect With control	Absolute Effect With EC	Certainty of the evidence GRADE
Smoking cessation: Nicotine electronic cigarettes versus Placebo electronic cigarettes Follow-up: 6-12 months	*May increase the proportion of people who abstain from smoking for at least six months.*	40 per 1000	93 per 1000 Difference: 53 more people per 1000 (95% CI: 2 to 171 more people)	⊕⊕◯◯ Low certainty
Smoking cessation: Nicotine electronic cigarettes versus Nicotine patches Follow-up: 6 months	*It is uncertain how effective nicotine electronic cigarettes are compared to nicotine patches.*	58 per 1000	73 per 1000 Difference: 15 more people per 1000 (95% CI: 19 less to 77 more people)	⊕◯◯◯ Very low certainty
Adverse events Follow-up: 6-24 months	*May be little if any difference in the frequency of adverse events for electronic cigarettes compared to placebo ECs or nicotine patches.*	One RCT provided data on the proportion of participants experiencing any adverse events. The proportion of participants in the study arms experiencing adverse events was similar (nicotine EC (electronic cigarettes) vs placebo EC: RR 0.97, 95% CI 0.71 to 1.34, 298 participants; nicotine EC vs nicotine patch: RR 0.99, 95% CI 0.81 to 1.22, 456 participants). The second RCT reported no statistically significant difference in the frequency of adverse events at three- or 12-month follow-up between the nicotine EC and placebo EC groups, and showed that in all groups the frequency of adverse events (with the exception of throat irritation) decreased over time.		⊕⊕◯◯ Low certainty

EC: Electronic cigarette **CI:** confidence interval **RR:** risk ratio **RCT:** randomized controlled trial

See less

Background

Electronic cigarettes (ECs) are electronic devices that produce an aerosol (or 'vapour') that the user inhales. This vapour typically contains nicotine without most of the toxins smokers inhale with cigarette smoke. Electronic cigarettes have become popular with smokers who want to reduce the risks of smoking. This review aimed to find out whether electronic cigarettes help smokers stop smoking, and whether it is safe to use electronic cigarettes to do this. See more detail about electronic cigarettes.

What this review is based on

Cochrane Reviews are based on systematic and robust selection of relevant studies. We included 24 studies in this review. See what studies we searched for and what we found.

Authors' conclusions

Electronic cigarettes may help people to quit smoking for at least six months compared with placebo. However, it is uncertain how effective electronic cigarettes are compared to nicotine patches, and the long-term safety of electronic cigarettes is unknown. The most commonly reported adverse effects of electronic cigarettes are irritation of the mouth and throat.

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Full text | Additional details

See also: Information for decision-makers
See also: Related systematic reviews
See also: Messages for media

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More detail about electronic cigarettes

What are electronic cigarettes?

Electronic cigarettes (ECs) are known by a variety of names, including vape pens, e-hookahs, mods, tank systems, and e-cigs. ECs are electronic devices that use a battery to aerosolize a liquid, usually containing nicotine, flavouring, and other additives, which is inhaled through a mouthpiece.

Image credit

Who can use electronic cigarettes?

Smokers report using ECs to reduce the risks of smoking or to help them quit smoking. The regulation of e-cigarettes varies by country. Because nicotine is highly addictive and can harm the developing adolescent brain, young people are discouraged from using ECs.

What other options are there?

Options to help people quit smoking include behavioural counselling, nicotine replacement therapy, and other medications. See: Information for decision makers - Other options.

How do people experience the intervention?

ECs replicate the experience of smoking, delivering a mist with nicotine instead of smoke. They may be perceived as cleaner. Some smokers may experience them as a bit harsher on the back of the throat, and some may experience that cravings return sooner than with smoking.

Is there anything else someone should know before using the intervention?

It is unknown whether ECs are harmful to others exposed to second-hand aerosol. There may be restrictions on where ECs can be used.

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What studies we searched for

We searched for studies published up to January 2016. We searched for randomized trials in which current smokers (motivated or unmotivated to quit) were randomized to EC or a control condition, and which measured abstinence rates at six months or longer. As the field of EC research is new, we also searched for cohort follow-up studies with at least six months follow-up.

What we found

We included 24 studies (three randomized trials, two of which were eligible for our cessation meta-analysis, and 21 cohort studies). Eleven of these studies are new for this version of the review. Two randomized trials compared EC with placebo (non-nicotine) EC, with a combined sample size of 662 participants. One trial included minimal telephone support and one recruited smokers not intending to quit. Both used early EC models with low nicotine content and poor battery life.

We identified 27 ongoing studies.

(For more detail, see Methods in the full text of this review.)

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(This prototype can't link to a web page)

About Cochrane Reviews

What is a systematic review?

A systematic review attempts to identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question. Researchers conducting systematic reviews use explicit, systematic methods that are selected with a view aimed at minimizing bias, to produce more reliable findings to inform decision making.

What is a Cochrane Review?

A Cochrane Review is a systematic review of research in health care and health policy that is published in the *Cochrane Database of Systematic Reviews*.

Types of Cochrane Review

- **Intervention reviews** assess the benefits and harms of interventions used in healthcare and health policy.
- **Diagnostic test accuracy reviews** assess how well a diagnostic test performs in diagnosing and detecting a particular disease.
- **Methodology reviews** address issues relevant to how systematic reviews and clinical trials are conducted and reported.
- **Qualitative reviews** synthesize qualitative evidence to address questions on aspects other than effectiveness.
- **Prognosis reviews** address the probable course or future outcome(s) of people with a health problem.

Cochrane Review methods

Cochrane Reviews base their findings on the results of studies that meet certain quality criteria, since the most reliable studies will provide the best evidence for making decisions about health care. Authors of Cochrane

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Summary of Findings

Interactive table: http://bit.ly/isof-e-cigarettes-test

Electronic cigarettes (EC) for smoking cessation

Population: Current smokers at enrolment into trials, motivated or unmotivated to quit
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EC: Electronic cigarette **CI:** confidence interval **RR:** risk ratio **RCT:** randomized controlled trial

(in this example, both comparisons are in same table. Normally would be one table per comparison)

Electronic cigarettes (EC) for smoking cessation

Population: Current smokers at enrolment into trials, motivated or unmotivated to quit

Intervention: Nicotine-containing electronic cigarettes

Comparison: Placebo electronic cigarettes or nicotine replacement therapy (nicotine patches)

View: Visual overview

Outcomes	Relative effect (95% CI) Nº of participants & studies	Certainty of the evidence GRADE
Smoking cessation: nicotine EC versus placebo EC Follow-up: 6-12 months	RR 2.29 (1.05 to 4.96) Based on data from 662 people in 2 studies	⊕⊕◯◯ Low certainty
Smoking cessation: nicotine EC versus nicotine replacement therapy Follow-up: 6 months	RR 1.26 (0.68 to 2.34) Based on data from 584 people in 1 study	⊕◯◯◯ Very low certainty
Adverse events Follow-up: 6-24 months	-	⊕⊕◯◯ Low certainty

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Smoking cessation: nicotine EC versus nicotine replacement therapy Follow-up: 6 months	15 more people per 1000	⊕◯◯◯ Very low certainty
Adverse events Follow-up: 6-24 months		⊕⊕◯◯ Low certainty

EC: Electronic cigarette **CI:** confidence interval **RR:** risk ratio **RCT:** randomized controlled trial

Authors' reasons for 'Low certainty' judgment:

- ***Indirectness:*** The electronic cigarette used in Bullen 2013 was not very effective at delivering nicotine.
- ***Imprecision:*** Only two included studies, small number of events (< 300) in each arm.

For more detail, see Evidence Profile

See also GRADE definitions for certainty of evidence

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Authors' reasons for 'Very low certainty' judgment:

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For more detail, see Evidence Profile

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Authors' reasons for 'Low certainty' judgment:

- ***Risk of bias:*** 11/13 included studies (cohort studies) judged to be at high risk of bias.
- ***Imprecision:*** Only one trial provided data for nicotine EC versus nicotine replacement therapy.

For more detail, see Evidence Profile

See also GRADE definitions for certainty of evidence

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GRADE Working Group grades of evidence:

⊕⊕⊕⊕ **High:** This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different* is low.

⊕⊕⊕○ **Moderate:** This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different* is moderate.

⊕⊕○○ **Low:** This research provides some indication of the likely effect. However, the likelihood that it will be substantially different* is high.

⊕○○○ **Very low:** This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different* is very high.

* **Substantially different** = a large enough difference that it might affect a decision

More information about GRADE: http://www.gradeworkinggroup.org/

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Figure x. GRADE evidence profile

Patient or population: Current smokers at enrolment into trials, motivated or unmotivated to quit
Intervention: Nicotine-containing electronic cigarettes
Comparison: Placebo electronic cigarettes or nicotine replacement therapy

Quality assessment							Illustrative comparative risks* (95% CI)				
Number of participants (studies)	Design	Risk of bias	Inconsis-tency	Indirectness	Imprecision	Other consider-ations	Assumed risk[1] Control	Corresponding risk Electronic cigarettes	Relative effect	Certainty of the evidence (GRADE)	Importance
Nicotine EC versus placebo EC[2]: Cessation (assessed with exhaled CO; Follow-up: 6-12 months)											
662 (2 studies)[3]	RCTs	Not serious	Not serious	Serious[4]	Serious[5]	None	40 per 1000	93 per 1000 (42 to 201)	RR 2.29 (1.05 to 4.96)	⊕⊕◯◯ Low[4,5]	CRITICAL
Nicotine EC versus nicotine replacement therapy: Cessation (assessed with exhaled CO; Follow-up: 6 months)											
584 (1 study)[3]	RCT	Not serious	Not serious	Serious[4]	Serious[6]	None	58 per 1000	73 per 1000 (42 to 201)	RR 1.26 (0.68 to 2.34)	⊕◯◯◯ Very low[4,6]	CRITICAL
Adverse events (AEs) (Follow-up: 6-24 months)											
1201 (2 RCTs, 9 cohort studies)	RCTs Cohort studies	Serious[7]	Not serious	Not serious	Serious[8]	None	Summary data not available. No studies reported serious AEs considered related to EC use. One RCT provided data on the proportion of participants experiencing any adverse events. The proportion of participants in the study arms experiencing adverse events was similar (ECs vs placebo EC: RR 0.97, 95% CI 0.71 to 1.34 (298 participants); ECs vs patch: RR 0.99, 95% CI 0.81 to 1.22 (456 participants)). The second RCT reported no statistically significant difference in the frequency of AEs at three- or 12-month follow-up between the EC and placebo EC groups. Cohort studies found mouth and throat irritation, dissipating over time, to be the most frequently reported AEs in EC users.			⊕⊕◯◯ Low[7,8]	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **RCT:** randomized controlled trial.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

GRADE Working Group grades of evidence:

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** Substantially different = a large enough difference that it might affect a decision

[1] 'Assumed risk' calculated as risk in control groups.
[2] 'Placebo EC' refers to ECs which do not contain nicotine.
[3] Only RCTs reported here. Some cohort data also available (see full review) but only RCTs provide efficacy data
[4] Downgraded one level due to indirectness. The electronic cigarette used in Bullen 2013 was not very effective at delivering nicotine.
[5] Downgraded one level due to imprecision. Only two included studies, small number of events (< 300) in each arm.
[6] Downgraded two levels due to imprecision. Only one included study, with small number of events in each arm.
[7] Downgraded due to risk of bias. 11/13 included studies (cohort studies) judged to be at high risk of bias.
[8] Downgraded due to imprecision. Only one trial provided data for nicotine EC versus nicotine replacement therapy.

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Methods for identifying studies

Electronic searches

We searched the following databases in January 2016:

- Cochrane Tobacco Addiction Group Specialized Register
- Cochrane Central Register of Controlled Trials (CENTRAL) (the Cochrane Library, 2016, Issue 1)
- MEDLINE (OVID SP) (2004 to 2016 January week 2, & MEDLINE in process/In data review Feb 1 2016)
- Embase (OVID SP) (2004 to 2016 week 5)
- PsycINFO (OVID SP) (2004 to 2016 January week 4)

For the first version of the review we also searched CINAHL (EBSCO Host) (2004 to July 2014). We did not search this database for this review update as it did not contribute additional search results to the first version of the review.

The search terms were broad and included e-cig$ OR elect$ cigar$ OR electronic nicotine. The search for the 2016 update added the terms vape or vaper or vapers or vaping. The search date parameters are limited to 2004 to the present, because ECs were not available before 2004.

Searching other resources

We searched the reference lists of studies found in the literature search and the metaRegister of controlled trials database (www.isrctn.com/page/mrct). We also contacted authors of known trials and other published EC studies.

MEDLINE search strategy

1. e-cig$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
2. electr$ cigar$.mp.
3. electronic nicotine.mp.
4. (vape or vaper or vapers or vaping).ti,ab.
5. 1 OR 2 OR 3 OR 4

Identical terms used for other databases.

Line 4 added to search strategy for 2016 update.

Methods for collecting and analysing data

Selection of studies
Two review authors (from JHB, HM, LS or RB) independently prescreened all titles and abstracts obtained from the search, using a screening checklist. Where there was disagreement, we obtained the full-text version and resolved the disagreement by discussion or by referral to a third review author (PH).
Two review authors (from JHB, HM and RB) obtained and independently screened full-text versions of the potentially relevant papers for inclusion. We resolved any disagreements by discussion or with a third review author (PH).

Data extraction and management
Two review authors (from JHB, HM or LS) extracted data from the included studies, and checked them against each other. A third review author (PH) was available to review and resolve any discrepancies. We extracted data on:
- Author
- Date and place of publication
- Study design
- Inclusion and exclusion criteria
- Setting
- Summary of study participant characteristics
- Summary of intervention and control conditions
- Number of participants in each arm
- Smoking cessation outcomes
- Type of biochemical validation (if any)
- Adverse events (AEs), serious adverse events (SAEs), and relevant biomarkers
- Assessment time points
- Risk of bias in the domains specified below
- Additional comments

We adopted a broad focus to detect a variety of adverse events.

One review author then entered the data into Review Manager 5 software for analyses, and another checked them.

Assessment of risk of bias in included studies
Two review authors (JHB and HM or LS) independently assessed the risk of bias for each included study, following the approach recommended in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). This approach uses a domain-based evaluation that addresses seven different areas: random sequence generation; allocation concealment; blinding of participants and providers; blinding of outcome assessment; incomplete outcome data; selective outcome reporting; and other potential sources of bias. We assigned a grade (low, high, or unclear) for risk of bias for each domain. We resolved disagreements by discussion or by consulting a third author (PH).

Measures of treatment effect
We analyzed dichotomous data by calculating the risk ratio (RR), using the longest follow-up data reported. For cessation, we calculated the RR as ((number of events in intervention condition/intervention denominator) / (number of events in control condition/control denominator)) with a 95% confidence interval (CI).
We analyzed continuous data (other measures of tobacco exposure) by comparing the difference between the mean change from baseline to the longest follow-up point in the intervention and control groups.

Unit of analysis issues
We extracted data on smoking outcomes only from RCTs in which individuals were the unit of randomization.
In the case of trials with multiple arms, we combined all relevant experimental intervention groups of the study into a single group, and combined all relevant control intervention groups into a single control group.
We offer a narrative synthesis of data from cohort studies.

Dealing with missing data
For smoking cessation, we used a conservative approach as is standard for the Cochrane Tobacco Addiction Group, treating participants with missing data as still smoking. We based the proportion of people affected by adverse events on the number of people available for follow-up, and not the number randomized.

Assessment of heterogeneity
We assessed the clinical and methodological diversity between studies to guide our decision as to whether data should be pooled. We were also guided by the degree of statistical heterogeneity, assessed by calculating the I^2 statistic (Higgins 2003); we considered a value greater than 50% as evidence of substantial heterogeneity.
Assessment of reporting biases
Reporting bias is best assessed using funnel plots, where 10 or more RCTs contribute to an outcome. However, there are currently insufficient studies to support this approach.

Data synthesis
We provide a narrative summary of the included studies. Where appropriate, we have pooled data from these studies in meta-analyses. For dichotomous data, we used a fixed-effect Mantel-Haenszel model to calculate the risk ratio with a 95% confidence interval, in accord with the standard methods of the Cochrane Tobacco Addiction Group for cessation studies.

We had planned to calculate the summary estimates for continuous outcomes (e.g. biomarkers of tobacco exposure) using the inverse variance approach (also with a 95% CI). However, there were insufficient data with which to do so.

For adverse events, we originally planned to enter the most commonly-reported adverse events into meta-analyses to determine if there were any significant differences between the EC and control groups. We also originally planned to include data from cross-over trials in a meta-analysis using paired data obtained from reports. However, there were again insufficient data with which to do so, and hence we have summarized adverse event data narratively.

Subgroup analysis and investigation of heterogeneity
We had planned to undertake subgroup analyses to investigate differences between studies, such as:
- Intensity of behavioural support used;
- Type of control group (e.g. placebo EC, NRT);
- Type of participants (e.g. experience of EC use).

However, there were too few studies to conduct such analyses. Should further studies become available in future, we will follow this approach.

Sensitivity analysis
We had planned to undertake sensitivity analyses to assess the effect of removing studies judged to be at high risk of bias. However, there were too few studies to conduct such analyses. Should further studies become available in subsequent updates, we will adopt this approach.

Summary of findings table
Following standard Cochrane methodology, we created a 'Summary of findings' table for both outcomes. For cessation, the 'Summary of findings' table only includes data from randomized controlled trials. Also following standard Cochrane methodology, we used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome, and to draw conclusions about the quality of evidence within the text of the review.

Figure x. Study flow diagram of searches conducted for this update

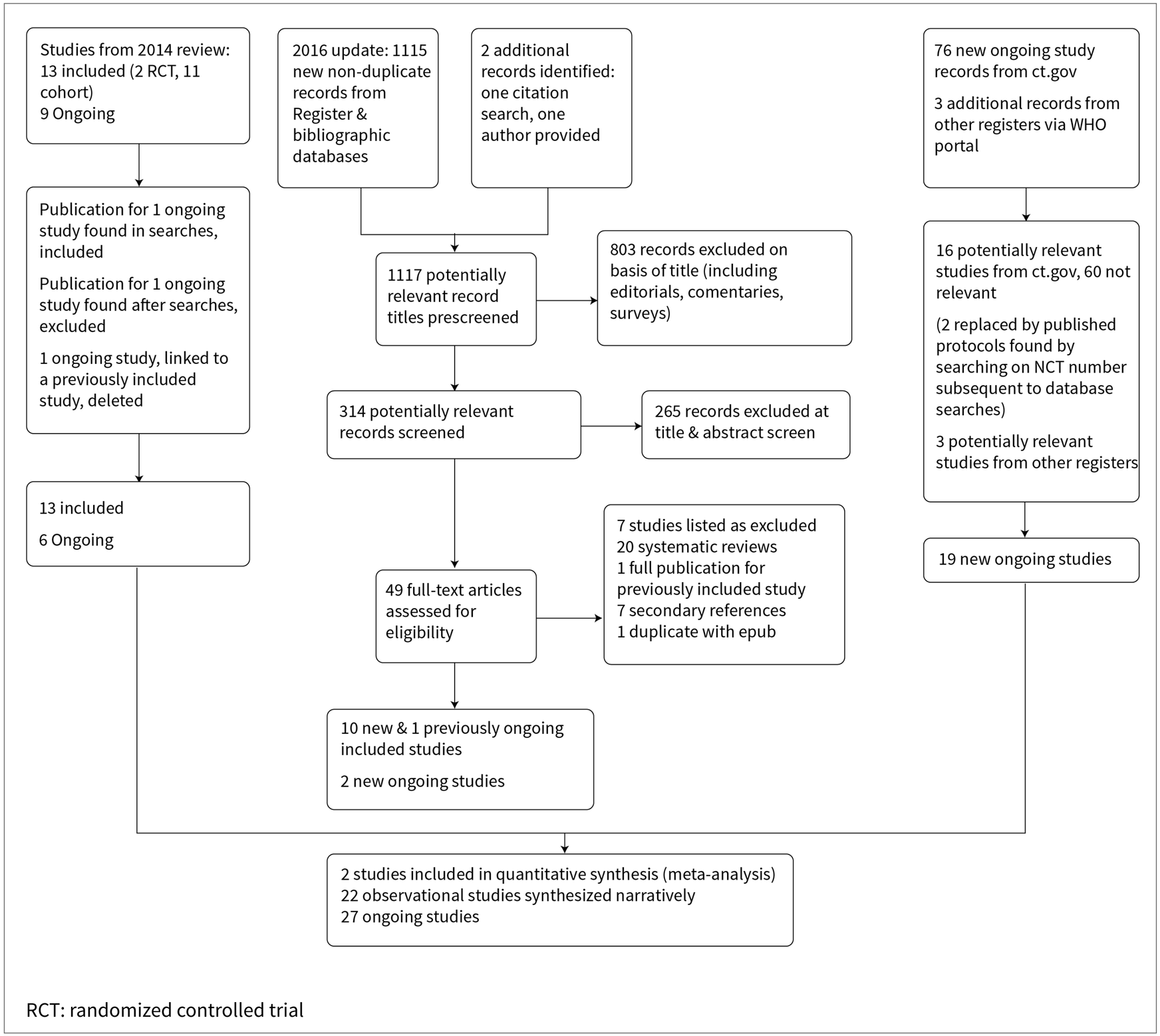

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Figure x. Risk of bias summary

: re view authors' judgements about each risk of bias item for each included study

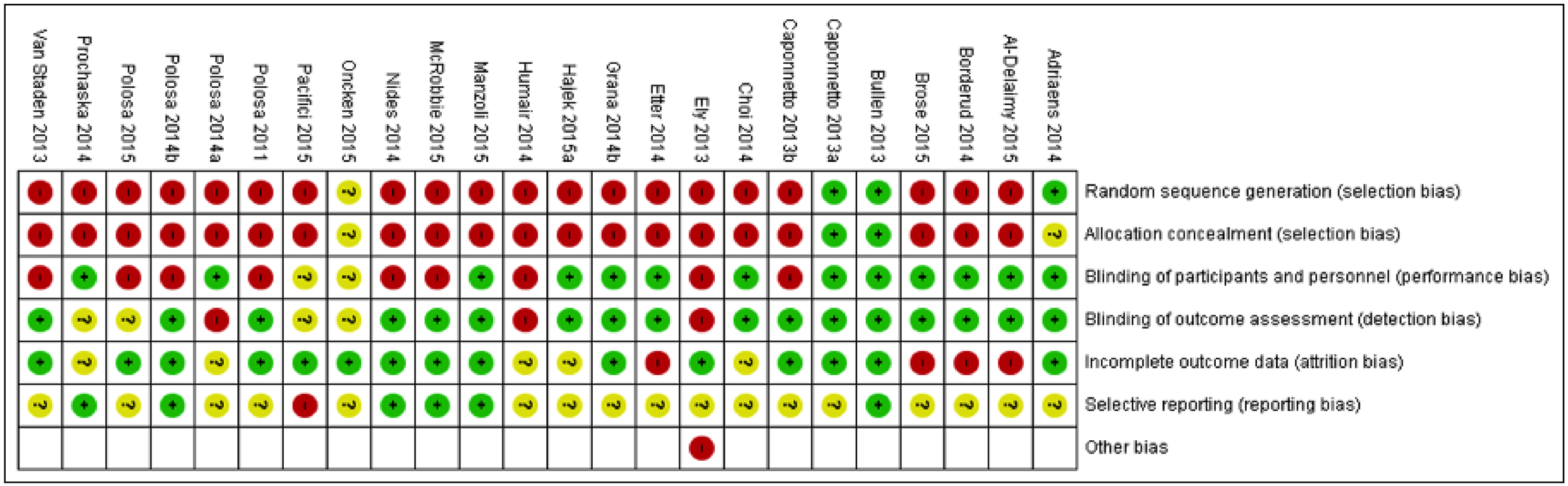

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Table x. What review authors searched for and found

	What the review authors searched for	What the review authors found
Study designs	Randomized trials in which smokers are randomized to ECs or to a control condition. Cohort follow-up studies with six months' or longer follow-up. Observational cohort studies which survey existing smokers at baseline. For adverse events and biomarkers, randomized cross-over trials and cohort follow-up studies with follow-up of greater than a week.	24 completed studies (3 randomized trials and 21 cohort studies). 27 ongoing studies.
Interventions	ECs with placebo ECs ECs versus alternative smoking cessation aids, including nicotine replacement therapy or no intervention ECs added to standard smoking cessation treatment (behavioural or pharmacological or both) with standard treatment alone.	Two randomized trials compared EC with placebo (non-nicotine) EC. One trial included minimal telephone support and one recruited smokers not intending to quit, and both used early EC models with low nicotine content and poor battery life.
Participants	People defined as current smokers at enrolment into the studies. Participants can be motivated or unmotivated to quit.	People defined as current smokers at enrolment into trials, motivated or unmotivated to quit.
Settings	Any setting	Belgium, USA, UK, New Zealand, Italy, France, UK, Switzerland, South Africa. Mixed settings (community, laboratory, cancer centre, web-based, research unit, outpatient clinic, inpatients, telephone survey).
Outcomes	Cessation at the longest follow-up point, which was at least six months from the start of the intervention, measured on an intention-to-treat basis using the strictest definition of abstinence, preferring biochemically-validated results where reported. Any data on adverse events at one week or longer, serious and non-serious, from the included studies, including changes in relevant biomarkers.	No studies reported serious AEs considered related to EC use. One randomized trial provided data on the proportion of participants experiencing any adverse events. Cohort studies found mouth and throat irritation, dissipating over time, to be the most frequently reported AEs in EC users.

Difference between protocol and review

Originally, the protocol did not specify a minimum follow–up period for data on adverse events. The Methods section has been changed to clarify that we will exclude follow–up data at less than a week.

The original version of this review included reduction as a secondary outcome. The 2016 update removed reduction as an outcome, to bring the review into line with other reviews of cessation treatments produced by the Cochrane Tobacco Addiction Group and to prevent substantial overlap with the update of the group's review of interventions for harm reduction (Stead 2007, update forthcoming).

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Characteristics of excluded studies

Study	Reason for exclusion
Adkison 2013	Although this study uses a prospective cohort design, no data on EC use were collected at baseline, with EC use data only being available at follow-up
Battista 2013	Short-term EC use only
Biener 2015	Cohort study, but EC use evaluated retrospectively only
Brown 2014a	Cross-sectional survey
Bullen 2010	Short-term EC use only
Chausse 2015	Ineligible study design
Chorti 2012	Short-term EC use only
Czogala 2012	Short-term EC use only
Dawkins 2012	Short-term EC use only
Dawkins 2013a	Short-term EC use only

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Characteristics of ongoing studies

Caponnetto 2014

Study name	Smoking cessation and reduction In schizophrenia (the SCARIS study)
Methods	3-arm prospective 12m randomized controlled trial investigating efficacy and safety of EC ***Setting:*** psychiatric and smoking cessation centres, Italy ***Recruitment:*** local newspapers and radio/television advertisements
Participants	153 participants, schizophrenic in stable phase of illness, smoked at least 10 cpd over previous 5 years, aged 18 - 65, in good general health, not currently attempting to quit smoke or wishing to do so in next 6m ***Excluded if:*** use smokeless tobacco or NRT; pregnant or breastfeeding; current or recent (1 yr) history of drug or alcohol abuse; other significant co-morbidities
Interventions	12-wk supply of: 1) EC, high nicotine (24 mg) 2) EC, no nicotine (0 mg, with tobacco aroma)
Outcomes	Follow-up visits at 4, 8, 12, 24 and 52 wks ***Outcome measures:*** • Smoking cessation • Smoking reduction (≥ 50% from baseline) • Adverse events • Quality of life • Neurocognitive functioning • Participant perceptions and satisfactions with products
Starting date	September 2014
Contact	Pasquale Caponnetto, p.caponnetto@unict.it

Fraser 2015

Study name	An open-label randomized pragmatic policy trial examining effectiveness of short-term use of Nicotine Replacement Therapy (NRT) vs short- or long-term use of NRT vs short- or long-term use of NRT or electronic nicotine delivery systems for smoking cessation in cigarette smokers
Methods	Phase 3 blinded RCT ***Setting:*** Australia ***Recruitment:*** commercial market research panel
Participants	***Target sample size:*** 1600 Current daily smokers (at least 6 cpd), can read and understand English, agree to try samples of nicotine products, willing to complete surveys, 18 years or older Excl. if currently treated for serious medical condition, pregnant or planning to become pregnant or breastfeed in next 12m
Interventions	a) Factsheet explaining relative harm of NRT compared to smoking, free sample of NRT, participant chooses preferences, has free for 3 wks then offered at subsidised rate for further 6m b) As (a) but with additional information provided c) As (a) but additional information on electronic cigarettes and emphasis on cessation, and may select electronic cigarettes as well as NRT
Outcomes	6 and 12m, self-report Continuous abstinence, NRT and EC use, interest in quitting smoking and in quitting NRT, cigarette consumption, product orders and use, quit attempts
Starting date	February 2014
Contact	Coral Gartner, c.gartner@uq.edu.au

ISRCTN60477608

Study name	The efficacy of e-cigarettes compared with nicotine replacement therapy, when used within the UK stop smoking service
Methods	Multicentre pragmatic randomized controlled trial to examine the efficacy of e-cigarettes compared with nicotine replacement therapy ***Setting:*** UK stop-smoking service ***Recruitment:*** participants attending UK stop-smoking service
Participants	***Target:*** 886 participants Aged 18 or older, current smoker accessing stop-smoking service, able to read/write/understand English
Interventions	Smokers who want help to quit smoking will be individually randomized to receive usual care (UC; a choice of NRT combined with usual care behavioural support provided by a Stop Smoking Service) or EC with the same behavioural support
Outcomes	***Primary:*** CO-validated sustained abstinence rates at 52 wks post–TQD ***Secondary:*** sustainable abstinence at 4 and 24 wks, 7-day PP abstinence at 4, 24 and 52 wks, smoking reduction, treatment ratings, adverse reactions, cost efficacy
Starting date	April 2015
Contact	Anna Phillips, a.phillips@qmul.ac.uk

KCT0001277

Study name	Effect of an electronic cigarette for smoking reduction and cessation in Korean male smokers: a randomized, controlled study
Methods	Parallel single-blinded randomized controlled trial ***Setting:*** Hospital, Korea ***Recruitment:*** not specified
Participants	Sample size not stated Men, 18 or older, at least 10 cpd for past year, smoked for at least 3 years, motivated to quit or reduce cigarette consumption. Excl. if history of serious disease or quit attempt in past 12m using NRT
Interventions	1) 50-min education sessions on smoking cessation and the use of smoking-cessation aids, instructed to visit the medical office each month for evaluation and counselling by a health practitioner who was unaffiliated with the study. Participants supplied with eGo-CTM EC from Ovale in 12-wk supply 2) As (1) but instead of EC given nicotine gum in 12-wk supply
Outcomes	***Primary:*** continuous abstinence at 12 and 24 wks ***Secondary:*** 7-day PP abstinence at 12 and 24 wks, cpd, adverse events
Starting date	May 2012
Contact	Yoo-Seok Cheong, Dankook University Hospital

Lopez 2016

Study name	Randomized controlled trial methods for novel tobacco products evaluation
Methods	Randomized parallel-assignment double-blind trial ***Setting:*** USA (2 sites) ***Recruitment:*** message boards, radio, print, web-based advertising
Participants	***Estimated enrolment:*** 520 Inclusion criteria: Age 21 - 65, smoke > 9 cpd for at least 1 yr, smoke regular filtered cigarettes or machine-rolled cigarettes with filter, CO > 9 ppm, no 'serious quit attempt' in past month, not planning to quit in next 6m, interested in reducing cig consumption ***Exclude if:*** pregnant or nursing, unstable or significant medical condition, use of non-cigarette nicotine in past 7 days, uncontrolled mental illness or substance abuse
Interventions	For 24 wks: 1) Cigarette substitute (plastic tube, does not provide drug delivery) 2) EC with no nicotine (EGO EC) 3) As (2) but 8 mg/ml nicotine 4) As (2) but 36 mg/ml nicotine
Outcomes	Urinary NNAL and cotinine at 24 wks, biomarkers of oxidative stress, glutathione and 8 Isoprostanes
Starting date	June 2015
Contact	Thomas Eissenberg, Virginia Commonwealth University

Lucchiari 2016

Study name	Benefits of tobacco free cigarette among heavy smokers undergoing a lung cancer screening program: a randomized controlled study
Methods	Randomized parallel-assignment double-blind trial ***Setting:*** Early lung cancer detection programme (Cosmos II) at European Institute of Oncology ***Recruitment:*** volunteers participating in screening programme
Participants	***Estimated enrolment:*** 210 Inclusion criteria: Smokers > 10 cpd for > 10 years, motivated to reduce smoking, not already in cessation treatment ***Exclusion criteria:*** 1. Symptomatic CVD 2. Symptomatic severe respiratory disease 3. Regular psychotropic medication use 4. Current or past history of alcohol abuse 5. Use of smokeless tobacco or NRT 6. Participation in another antismoking programme in the current year
Interventions	All participants receive smoking cessation programme including a motivational interview and 3 months low-intensity distance counselling 1) EC and activity tracker 2) Nicotine-free EC and activity tracker 3) Activity tracker
Outcomes	At 6 and 12m ***Primary:*** pulmonary health ***Secondary:*** psychological well-being, cpd, CO, daily activity, cough-related QoL, lifestyle
Starting date	September 2014
Contact	Marianna Masiero, University of Milan

NCT01842828

Study name	Spain-UK-Czech E-cigarette Study (SUKCES)
Methods	Randomized controlled trial, open-label pilot study ***Setting:*** smoking cessation clinics in London, Madrid and Prague ***Recuitment:*** via smoking cessation clinics
Participants	220 smokers seeking help to quit ***Inclusion criteria:*** 18 or older, want help to quit ***Exclusion criteria:*** pregnant or breastfeeding; enrolled in other research; currently using EC
Interventions	1) standard care plus 4 wks EC supply 2) standard care only
Outcomes	• CO-validated continuous abstinence at 4 and 24 wks post-TQD • Withdrawal symptoms at 1 and 4 wks post-TQD • EC use • EC taste and satisfaction compared to conventional cigarettes • Adverse events
Starting date	December 2013
Contact	Peter Hajek, p.hajek@qmul.ac.uk

NCT01989923

Study name	Smoking cessation in women with gynaecological conditions
Methods	Randomized controlled trial, open-label feasibility study ***Setting:*** hospital clinic, USA ***Recruitment:*** in clinic
Participants	30 women smokers with cervical dysplasia ***Inclusion criteria:*** women smokers of at least 10 cpd over past year, diagnosis of cervical dysplasia, cervical cancer, and lower genital tract dysplasia and cancer, aged 18 - 65 ***Exclusion criteria:*** previous diagnoses or treatment for cancer (except for non-melanoma skin cancer); stroke, heart disease, heart attack, or irregular heart beat; pregnancy and lactation; plan to continue to use other nicotine as well as study products; uncontrolled hypertension; using other stop-smoking medication; taking prescription medicine for depression or asthma
Interventions	1) NRT patch (21 mg for first 3 wks, 14 mg for 2nd 3 wks) plus nicotine gum (2 mg) or lozenges (2 mg) for 6 wks 2) EC device ('Blu' Cig) with refills to last 6 wks, number provided based on packs smoked a day x 1.5 Strength of EC reduced at 3 wks Both groups receive identical cessation counselling
Outcomes	At 6 and 12 wks via survey: • Cpd • PP abstinence at 7 and 30 days • Smoking cessation • Participants' attitudes and beliefs towards treatments • Adherence
Starting date	June 2013
Contact	Laura A Beebe, laura-beebe@ouhsc.edu

NCT02004171

Study name	Electronic cigarettes or nicotine inhaler for smoking cessation
Methods	Randomized controlled trial, open-label safety/efficacy study ***Setting and recruitment:*** not specified, USA
Participants	40 participants ***Inclusion criteria:*** 18 - 60 years old, meet DSM-IV criteria for nicotine dependence, seeking treatment for smoking cessation, smoking at least 15 cpd ***Exclusion criteria:*** DSM-IV diagnosis of schizophrenia, schizoaffective disorder, or bipolar disorder; current diagnosis of major depressive disorder; current diagnosis for other psychiatric disorders that may require intervention over course of study; receiving treatment for nicotine dependence; pregnancy, lactation, or chance of pregnancy; unstable medical condition; substance abuse diagnosis; use of cannabis or alcohol on more than 20 days in past 30 days; suicide risk
Interventions	4 wks: 1) ECs (2nd generation) with 24 mg nicotine cartridges, 1 - 2 cartridges daily 2) Nicotine inhaler with 10 mg cartridges, max 16 cartridges per day
Outcomes	Over 4 wks: • cpd • Withdrawal • Benefits from smoking cessation (breathing, sense of taste and smell, physical fitness) • Adverse events • BMI
Starting date	December 2013
Contact	Barney Vaughan, vaughan@nyspi.columbia.edu

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Characteristics of included studies

Key features of the included studies

EC brands and nicotine doses used in the studies varied: elusion brand EC (first-generation technology) with cartridges containing 16 mg nicotine, or 21 mg/24-hour nicotine patches; 'Categoria' brand EC (model 401, which is no longer produced) with disposable cartridges containing 7.2 mg nicotine; Joyetech e-GO-C second-generation EC, the Kanger T2-CC second-generation EC, 'Twisp eGo' 18 mg/ml nicotine, among others. Modes of delivery of ECs were similarly varied: couriered to participants, mailed voucher to exchange for nicotine replacement therapy at a pharmacy, dispensed during visits to clinics, among others. Supportive interventions were varied and included weekly behavioral support and phone- or text-based behavioral support.

Sort tables by: comparison | study design

Randomised controlled trials

	Participants					
Study /setting	**Inclusion criteria**	**Exclusion criteria**	**Enrolled**	**Interventions**	**Controls**	**Outcomes**
Adriaens 2014* Community and laboratory Belgium	Smoker for at least 3 years, smoking at least 10 factory-made cpd, not intending to quit in the near future but willing to try a less unhealthy alternative	Diabetes, severe allergies, asthma or other respiratory diseases, psychiatric problems, dependence on chemicals other than nicotine, pregnancy, breast feeding, hypertension, CV disease, currently using any kind of smoking cessation therapy, prior use of EC	Tot al N: 48 provided data (51 consented, 50 attended any lab sessions, 2 further withdrawals) Randomized to: EC1 16, EC2 17, control 17 56% women, mean age 44, mean cpd 19, mean FTCD 5.79, all unwilling to quit with no baseline EC use	Two intervention groups (EC1 and EC2) provided with 2nd-generation EC and instructed to use EC or smoke ad libitum (EC1 group provided with Joyetech eGO-C, EC2 group provided with Kanger T2-CC) and provided guidance on EC use	6 bottles for 2 months at week 8 (half offered EC1, half offered EC2); no guidance on use	***Cessation*** (definition not provided, validated with eCO 5 ppm or less) ***Adverse events and biomarkers*** (eCO, salivary cotinine measured during lab sessions) ***Others:*** craving and withdrawal symptoms via lab sessions, "benefits and complaints", mood, EC usage
Bullen 2013 Research Unit New Zealand	18 years of age or older; smoked 10 or more cpd over past year; wanted to stop smoking	Pregnant and breastfeeding women, people using cessation medicines or using other support to quit, heart attack, stroke, severe angina in the last 2 weeks, poorly-controlled medical disorder, allergies, other chemical dependence	Total N: 657 62% women, mean age 42, ⅓ NZ Maori, smoking 18 cpd, mean FTND score 5.5	Randomized 4:4:1 to NEC, PATCH or PEC use for 13 weeks (from 1 week prior to TQD) NEC: Elusion brand 16 mg cartridges; sent product via courier	PEC: As per EC but 0 mg cartridges All participants referred to Quit-line and received an invitation to access phone- or text-based support. This was accessed by <10% PATCH: 21 mg/24-hour patch; sent voucher to exchange for NRT at pharmacy (dispensing costs covered)	Sustained (≤ 5 cigarettes allowed) validated (exhaled breath CO < 10 ppm) abstinence at 6 months ≥ 50% self-reported reduction in baseline cigarettes at 6 months Participants reporting any adverse events Proportion of AEs that were serious Proportion of unrelated AEs
Caponnetto 2013a Outpatient clinic Italy	Smoked at least 10 cpd for past 5 years; age 18-70; in good health; not currently or intending to quit smoking in the next 30 days	Symptomatic cardiovascular or respiratory disease; regular psychotropic medicine use; current or past history of alcohol abuse; use of smokeless tobacco or NRT; pregnant or breast feeding.	Total N: 300 36% women, mean age 44 (SD 12.5), mean cpd 20 (IQR: 15-25) No participants discontinued intervention	EC presented as a healthier alternative to tobacco smoke and could be freely used, ad libitum (up to 4 cartridges per day) for 12 weeks, as a tobacco substitute EC used: 'Categoria' (model 401) with disposable cartridges: Grp A: 12 weeks of 7.2 mg capsules ('Original') Grp B: 6 weeks 7.2 mg ('Original') then 6 weeks 5.4 mg ('Categoria')	Grp C: 12 weeks of 0 mg ('Original')	Abstinence at 12 months (complete self-reported abstinence from tobacco smoking since previous visit at 6 months, confirmed with CO < 7 ppm at 12 months) ≥ 50% reduction in AEs thought to be related to tobacco smoking and EC at baseline and at each study visit (7 follow-up visits over 12 weeks, plus at 24 and 52 weeks)

Observational studies

		Participants				
Study	**Design/Setting**	**Inclusion criteria**	**Exclusion criteria**	**Enrolled**	**Exposure**	**Outcomes**
Al-Delaimy 2015	Prospective cohort study	State residents aged 18-59 who had smoked at least 100 cigarettes during their lifetime and smoked cigarettes "at least some days" at baseline	Not stated	Total N: 1000 adult smokers (for this review, only include 236 ever EC users and 306 'will never use EC' respondents) 52.2% women; 30% 18-44 years old, 70% 45-59; 10% Hispanic, 73% non-Hispanic white, 18% other; 83.6% daily smoker, 43% intended to quit smoking in next 6m	At baseline asked to indicate if they had used, might use, or would never use EC. Defined EC as "devices that look like cigarettes and contain nicotine but do not produce tobacco smoke; some brands are The Safe Cig, Green Smoke, and Blu."	Self-reported prolonged abstinence for 1m or longer, assessed via phone at 12m
Borderud 2014	Prospective cohort study	Smokers (smoked cigarettes or used other tobacco products within past 30 days) accepting cessation programme	Not stated	Total N: 1074. 781 eligible for 6-12m follow-up; 56.5% women, mean age 56, mean cpd 13, mean FTND 3.7. At baseline, 26.5% (285/1074) had used EC within last 30 days, 92% dual users	All participants offered "multicomponent, evidence-based behavioral and pharmacologic treatment for tobacco dependence"; plans differed by individual but offered up to 5 sessions of phone or in-person counselling	Self-reported 7-day PP abstinence Gone at least 1 day without smoking CPD
Brose 2015	Prospective cohort study	Smoked in the past year	Not stated	Total N: 4064, 1769 followed up 50% women, mean age 43.4, mean cpd 12.9, 23% used EC at baseline, 46.3% attempted to quit in past year Of those using EC at baseline, majority used 'first generation' EC that were cigarette-like in appearance	EC use at baseline and 12m follow-up	Reported being 'ex-smoker' at 12m follow-up Quit attempts 50% reduction in cpd
Caponnetto 2013b	Prospective cohort study	Smoked ≥ 20 cpd for at least the past 10 years; diagnosis of schizophrenia	Alcohol and illicit drug use, recent myocardial infarction, angina pectoris, high blood pressure diabetes mellitus, severe allergies	Total N: 14 57% women, mean age 44.6 (SD 12.5), mean pack years smoked 28.8 (SD 12.9)	EC ('Categoria' brand) with an initial 4-week supply of 7.4 mg nicotine cartridges. Instructed to use ad libitum up to 4 cartridges per day. EC cartridges supplied at months 1, 2, and 3 No instruction on cessation or reduction was provided.	Cigarette consumption, CO, AEs and positive and negative symptoms of schizophrenia were measured Sustained reduction of ≥ 50% for at least 30 days at 12 months 30-day point prevalence CO-validated abstinence at 12 months Adverse events
Choi 2014	Longitudinal survey (data from the Minnesota Adolescent Community Cohort) Telephone survey USA	Participants who completed the survey between October 2010 and March 2011 and provided follow-up data 1 year later	Not stated	Total N: 346 (No further details provided)	Observational; no specific intervention. No data on nicotine content of ECs are provided	Self-reported smoking cessation at 1-year follow-up (not otherwise defined)
Ely 2013	Prospective cohort study Single family practice USA	Want to quit or switch from tobacco cigarettes to ECs	Not stated	Letters sent to 640 patients, 48 chose to participate and 44 completed the programme, 4 were lost to follow-up; Of the 44 participants, 66% women, all non-Hispanic/white, aged 20 - 75 (30% were age 51 - 60), 57% had a high school education or less	The 6-month smoking cessation programme was based on The '5 A's' model and transtheoretical model. Options for treatment were discussed with each participant at the start of the programme. All used an EC, with 16 using bupropion and 2 using varenicline as well Participants were provided with written information on "blu cig" and "smoke tip" ECs, regarding cost, availability, nicotine dosage options	Abstinence from smoking and EC use Abstinence from smoking but not EC use ≥ 50% reduction of baseline cigarette consumption (still using ECs)
Etter 2014	Longitudinal Internet survey Open to all nationalities; of respondents, 34% US, 24% France, 8% UK, 6% Switzerland, 28% other countries	Aged 18 years and older	Not stated	***One-month survey*** Total N: 477, mean age 42, 41% women, 59% had a diploma giving access to university, 28% daily or occasional smokers, 76% daily EC users. 50/477 occasional or daily smokers at baseline ***One-year survey*** Total N: 367, mean age 43, 42% women, 59% had a diploma giving access to university, 24% daily or occasional smokers, 79% daily EC users. 35/367 occasional or daily smokers at baseline	Observational; no specific intervention. Participants that had completed a baseline questionnaire were emailed one month and one year later and asked to provide follow-up data on EC use and smoking behaviour	From among those that were smoking cigarettes at baseline 7-day PP abstinence from smoking at 12 months Smoking consumption (change from baseline) at 12 months

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Table x. Risk of bias of included studies

Adriaens 2014

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	Low risk	Block randomization was performed by using a randomization tool available on the website www.randomizer.org (But high for abstinence outcome as non-randomized for our purposes)
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	Low risk	Unblinded but as this review only includes data on objective measurements and not cessation judged unlikely to affect outcomes.
Blinding of outcome assessment (detection bias)	Low risk	Unblinded but as this review only includes data on objective measurements and not cessation judged unlikely to affect outcomes.
Incomplete outcome data (attrition bias)	Low risk	36 out of 48 completed follow-up (11/16 in EC1 group, 12/17 in EC2 group, 13/17 in control group)
Selective reporting (reporting bias)	Unclear risk	Outcome reporting somewhat non-traditional; for example, collecting complaints but not explicitly adverse events, and incidence of AEs not reported. Unable to find prospectively registered protocol
Other bias	Unclear risk	

Al-Delaimy 2015

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	High risk	Observational study
Allocation concealment (selection bias)	High risk	Observational study
Blinding of participants and personnel (performance bias)	Low risk	Although there is no blinding, the study design and lack of intervention or contact with researchers mean that there is unlikely to be significantly impact on performance
Blinding of outcome assessment (detection bias)	Low risk	Telephone report, unblinded, but given nature of the study differential misreport seems unlikely
Incomplete outcome data (attrition bias)	High risk	Greater loss to follow-up for 'will never use' than users
Selective reporting (reporting bias)	Unclear risk	Unable to determine prespecified outcomes
Other bias	Unclear risk	

Borderud 2014

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	High risk	Observational study
Allocation concealment (selection bias)	High risk	Observational study
Blinding of participants and personnel (performance bias)	Low risk	Although there is no blinding, the study design means that there is unlikely to be significantly impact on performance
Blinding of outcome assessment (detection bias)	Low risk	Self-report only but differential misreport across EC conditions judged to be unlikely
Incomplete outcome data (attrition bias)	High risk	Large number of participants (285) lost to follow-up (of eligible, 59.5% followed up). A further 82 deceased "significantly higher percentage of E-cigarette users dropped out of tobacco treatment and were lost to follow-up than non–E-cigarette users". Complete-case analysis not significant, ITT analysis significant.
Selective reporting (reporting bias)	Unclear risk	Unable to determine prespecified outcomes
Other bias	Unclear risk	

Brose 2015

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	High risk	Observational study
Allocation concealment (selection bias)	High risk	Observational study
Blinding of participants and personnel (performance bias)	Low risk	Although there is no blinding, the study design and lack of intervention or contact with researchers mean that there is unlikely to be significantly impact on performance
Blinding of outcome assessment (detection bias)	Low risk	Online survey, differential misreport seems unlikely
Incomplete outcome data (attrition bias)	High risk	43.3% (1759) followed up. 1687 used in analyses due to missing data or baseline pipe or cigar smoking. 1473 used in quit attempt analysis (further missing data)
Selective reporting (reporting bias)	Unclear risk	Unable to determine prespecified outcomes
Other bias	Unclear risk	

Bullen 2013

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	Low risk	Computerised block randomization
Allocation concealment (selection bias)	Low risk	Computerised via study statistician
Blinding of participants and personnel (performance bias)	Low risk	NEC and PEC were blind to treatment condition in relation to one another. No blinding for NEC/PEC vs PATCH conditions, but as NEC and PATCH were both active treatments performance bias judged unlikely
Blinding of outcome assessment (detection bias)	Low risk	Biochemical validation used
Incomplete outcome data (attrition bias)	Low risk	LTFU 22% (all considered smokers). Patch group had a higher LTFU and withdrawal than EC (loss to follow-up 17% NEC, 27% patches, 22% PEC). However, minimal difference in per-protocol and ITT analyses
Selective reporting (reporting bias)	Unclear risk	All prespecified outcomes reported
Other bias	Unclear risk	

Caponnetto 2013a

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	Low risk	Computer-generated, block size 15 (5:5:5 ratio)
Allocation concealment (selection bias)	Low risk	Randomization carried out by pharmacy, who did not have direct contact with the participants
Blinding of participants and personnel (performance bias)	Low risk	Double-blind. "Blinding was ensured by the identical external appearance of the cartridges. The hospital pharmacy was in charge of randomization and packaging of the cigarettes"
Blinding of outcome assessment (detection bias)	Low risk	Biochemical validation used
Incomplete outcome data (attrition bias)	Low risk	211 (70.3%) and 183 (61%) attended 6- and 12-month follow-up (at 12m, 35% lost in 7.2 group; 37% lost in 5.4 group; 45% lost in no-nicotine group)
Selective reporting (reporting bias)	Unclear risk	Unclear if original intention was to combine groups A+B or not. In sample size calculation they compared A+B with C, but results are not reported in this way
Other bias	Unclear risk	

Caponnetto 2013b

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	High risk	Prospective cohort; no randomization
Allocation concealment (selection bias)	High risk	Not randomized
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Low risk	Biochemical validation used
Incomplete outcome data (attrition bias)	Low risk	0/14 lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Unable to determine prespecified outcomes
Other bias	Unclear risk	

Choi 2014

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	High risk	Prospective cohort
Allocation concealment (selection bias)	High risk	Not randomized
Blinding of participants and personnel (performance bias)	Low risk	Although there is no blinding, the study design and lack of intervention or contact with researchers mean that there is unlikely to be significantly impact on performance
Blinding of outcome assessment (detection bias)	Low risk	Although there is no blinding, the study design and lack of intervention or contact with researchers mean that there is unlikely to be significantly impact on detection
Incomplete outcome data (attrition bias)	Unclear risk	Unable to determine attrition bias
Selective reporting (reporting bias)	Unclear risk	Unable to determine prespecified outcomes
Other bias	Unclear risk	

Ely 2013

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	High risk	Prospective cohort
Allocation concealment (selection bias)	High risk	Not randomized
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	High risk	No blinding
Incomplete outcome data (attrition bias)	Low risk	4/48 lost to follow-up
Selective reporting (reporting bias)	Unclear risk	Unable to determine prespecified outcomes
Other bias	High risk	No definition of abstinence provided Not clear if 'completed programme' was at 6 months.

Etter 2014

Bias	Author's judgement	Support for judgment
Random sequence generation (selection bias)	High risk	Prospective cohort
Allocation concealment (selection bias)	High risk	Not randomized
Blinding of participants and personnel (performance bias)	Low risk	Although there is no blinding, the study design and lack of intervention or contact with researchers mean that there is unlikely to be significantly impact on performance
Blinding of outcome assessment (detection bias)	Low risk	Although there is no blinding, the study design and lack of intervention or contact with researchers mean that there is unlikely to be significantly impact on detection
Incomplete outcome data (attrition bias)	High risk	28% (N = 367) for those who answered the baseline survey (N = 1329) provided data at 1-year follow-up
Selective reporting (reporting bias)	Unclear risk	Unable to determine prespecified outcomes
Other bias	Unclear risk	

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Table x. Overview of analyses

Comparison 1 Nicotine EC vs Placebo

	Analysis	Outcome or subgroup	Studies	Participants	Statistical method	Effect estimate
1.1	Forest plot ↓	Smoking cessation	2	662	Risk Ratio (M-H, Fixed, 95% CI)	2.29 [1.05, 4.96]
1.2	Forest plot ↓	Proportion of participants reporting adverse events	1	298	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.71,1.34]

Comparison 2 Nicotine EC vs Replacement therapy

	Analysis	Outcome or subgroup	Studies	Participants	Statistical method	Effect estimate
2.1	Forest plot ↓	Smoking cessation	1	584	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.68, 2.34]
2.2	Forest plot ↓	Proportion of participants reporting adverse events	1	456	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.81,1.22]

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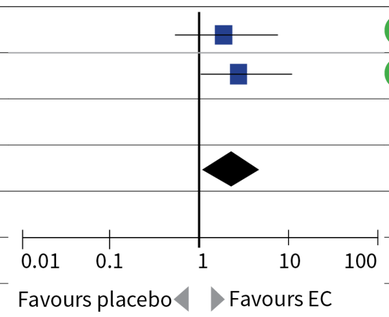
Overview of analyses

Comparison 1 Nicotine EC vs Placebo

Analysis	Outcome or subgroup	Studies	Participants	Statistical method	Effect estimate
Analysis 1.1	Smoking cessation	2	662	Risk Ratio (M-H, Fixed, 95% CI)	2.29 [1.05, 4.96]

	Experimental		Control			Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	*Events*	*Total*	*Events*	*Total*	*Weight*	*M.H, Fixed, 95% CI*	*M.H, Fixed, 95% CI*	*A B C D E F G*
Bullen 2013	21	289	3	73	47.3%	1.77 [0.54, 5.77]		+ + + + + +
Caponnetto 2013a	22	200	4	100	52.7%	2.75 [0.97, 7,76]		+ + + + + ?
Total (95% CI)		**489**		**173**	**100.0%**	**2.29** [1.05, 4.96]		
Total events	43		7					
Heterogeneity:	Chi²=0.30, df=1 (P=0.58); I²=0%							
Test for overall effect:	Z=2.09 (P=0.04)							



Risk of bias legend

A Random sequence generation (selection bias)
B Allocation concealment (selection bias)
C Blinding of participants and personnel (performance bias)
D Blinding of outcome assessment (detection bias
E Incomplete outcome data (attrition bias)
F Selective reporting (reporting bias)
G Other bias

Close ↑

Analysis 1.2	Proportion of participants reporting adverse events	1	298	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.71,1.34]

Comparison 2 Nicotine EC vs nicotine replacement therapy

Analysis	Outcome or subgroup	Studies	Participants	Statistical method	Effect estimate
Analysis 2.1	Smoking cessation	1	584	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.68, 2.34]
Analysis 2.2	Proportion of participants reporting adverse events	1	456	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.81,1.22]

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Overview of analyses

Comparison 1 Nicotine EC vs Placebo

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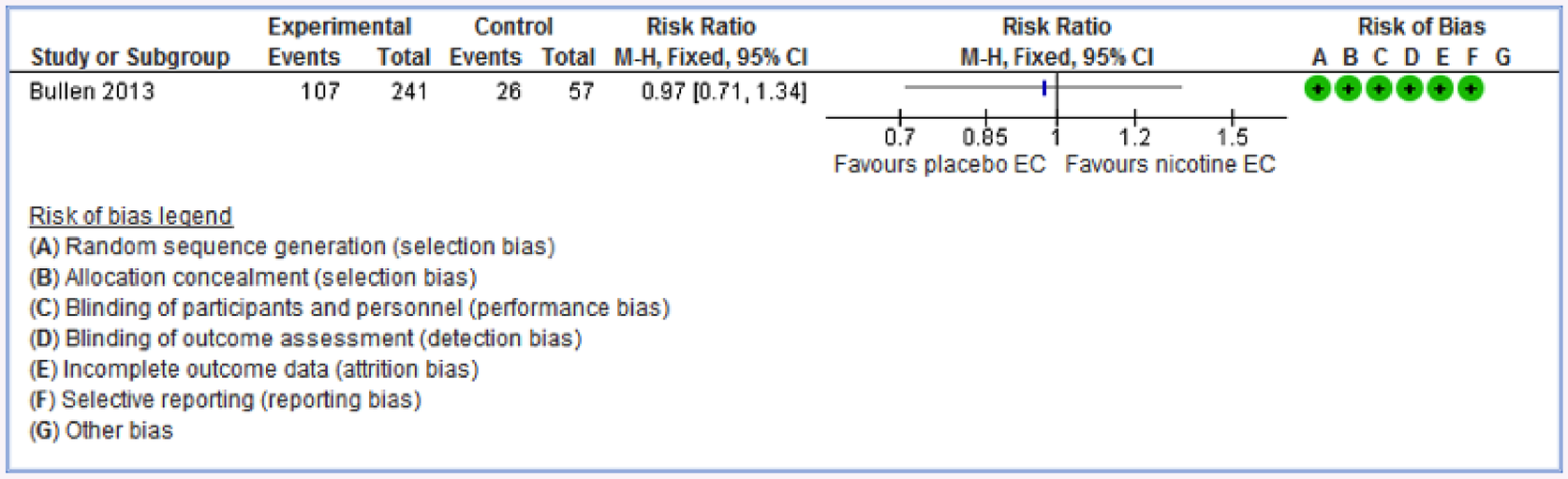

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Comparison 2 Nicotine EC vs nicotine replacement therapy

Analysis	Outcome or subgroup	Studies	Participants	Statistical method	Effect estimate
Analysis 2.1	Smoking cessation	1	584	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.68, 2.34]
Analysis 2.2	Proportion of participants reporting adverse events	1	456	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.81,1.22]

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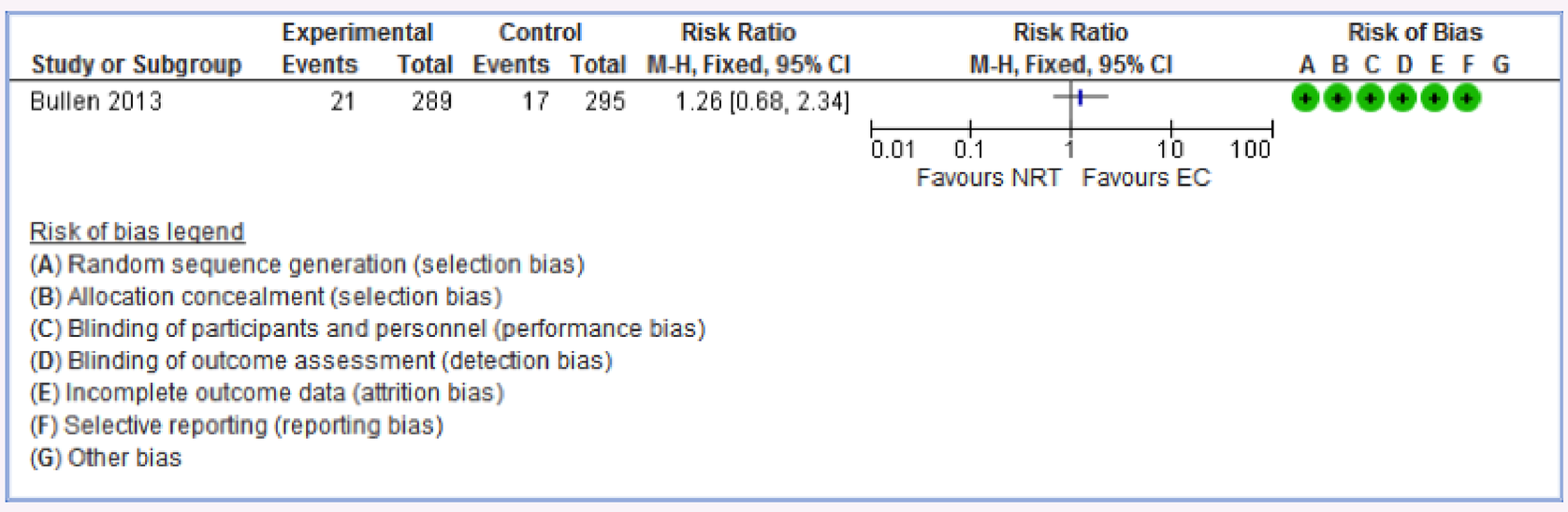

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Overview of analyses

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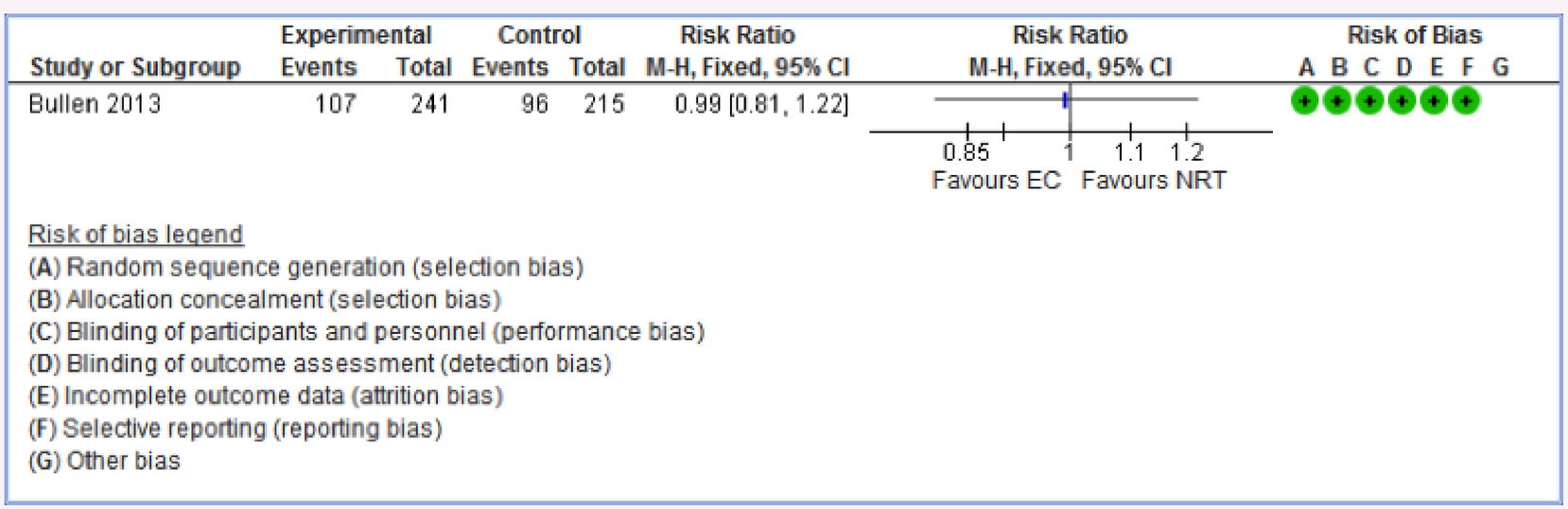

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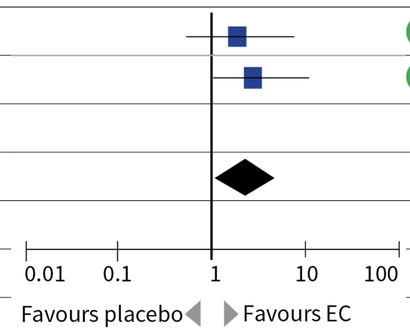
Analysis 1.1. Nicotine EC vs placebo EC (outcome: smoking cessation)

	Experimental		Control			Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	*Events*	*Total*	*Events*	*Total*	*Weight*	*M.H, Fixed, 95% CI*	*M.H, Fixed, 95% CI*	*A B C D E F G*
Bullen 2013	21	289	3	73	47.3%	1.77 [0.54, 5.77]		+ + + + + +
Caponnetto 2013a	22	200	4	100	52.7%	2.75 [0.97, 7,76]		+ + + + + ?
Total (95% CI)		**489**		**173**	**100.0%**	**2.29** [1.05, 4.96]		
Total events	43		7					
Heterogeneity:	Chi²=0.30, df=1 (P=0.58); I²=0%							
Test for overall effect:	Z=2.09 (P=0.04)							



Risk of bias legend

A Random sequence generation (selection bias)
B Allocation concealment (selection bias)
C Blinding of participants and personnel (performance bias)
D Blinding of outcome assessment (detection bias
E Incomplete outcome data (attrition bias)
F Selective reporting (reporting bias)
G Other bias

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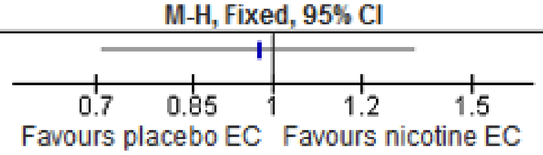
Analysis 1.2. Nicotine EC vs placebo EC (outcome: adverse events)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Risk Ratio M-H, Fixed, 95% CI	Risk of Bias A	B	C	D	E	F	G
Bullen 2013	107	241	26	57	0.97 [0.71, 1.34]	+	+	+	+	+	+	



Risk of bias legend
(A) Random sequence generation (selection bias)
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(F) Selective reporting (reporting bias)
(G) Other bias

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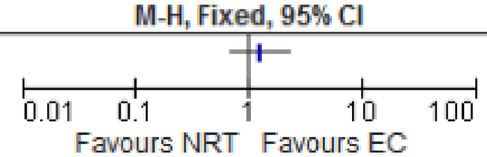
Analysis 2.1. Nicotine EC vs Nicotine replacement therapy (outcome: smoking cessation)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Risk Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
Bullen 2013	21	289	17	295	1.26 [0.68, 2.34]	+ + + + + +



Risk of bias legend
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(G) Other bias

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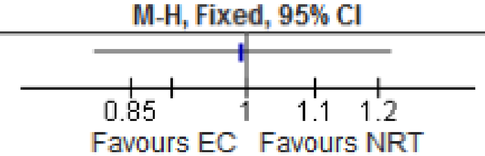
Analysis 2.2. Nicotine EC vs Nicotine replacement therapy (outcome: adverse events)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Risk Ratio M-H, Fixed, 95% CI	Risk of Bias A B C D E F G
Bullen 2013	107	241	96	215	0.99 [0.81, 1.22]	+ + + + + +



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(F) Selective reporting (reporting bias)
(G) Other bias

Effects of interventions

1 ***Comparison 1.*** *Nictotine EC versus placebo EC*

Key characteristics of included studies 1

Summary of findings 1

Cessation:

Table x. Analysis 1.1. Nicotine EC versus placebo EC: Cessation
Figure x. Nicotine EC versus placebo EC: Cessation

Text that would go here: summary of effect for this comparison on outcome. The following is dummy text. (Text that would go here: summary of effect for this comparison on outcome. The following is dummy text In the trial comparing EC to patch (Bullen 2013) there was little difference in six-month CO (carbon monoxide)-validated continuous abstinence between the treatment arms (7.3%, 5.8% and 4.1%, in the nicotine EC,

Adverse events:

Table x. Analysis 1.2. Nicotine EC versus placebo EC: Adverse events
Figure x. Nicotine EC versus placebo EC: Adverse events

(Text that would go here: summary of effect for this comparison on outcome. The following is dummy text. (Text that would go here: summary of effect for this comparison on outcome. The following is dummy text In the trial comparing EC to patch (Bullen 2013) there was little difference in six-month CO (carbon monoxide)-validated continuous abstinence between the treatment arms (7.3%, 5.8% and 4.1%, in the nicotine EC, patch and placebo EC arms respectively). We made two comparisons. The first compares abstinence rates

2 ***Comparison 2.*** *Nictotine EC versus nicotine replacement therapy*

Key characteristics of included studies 2

Summary of findings

Cessation:

Table x. Analysis 2.1. Nicotine EC versus nicotine replacement therapy: Cessation
Figure x. Nicotine EC versus nicotine replacement therapy: Cessation

(Text that would go here: summary of effect for this comparison on outcome. The following is dummy text. (Text that would go here: summary of effect for this comparison on outcome. The following is dummy text In the trial comparing EC to patch (Bullen 2013) there was little difference in six-month CO (carbon monoxide)-validated continuous abstinence between the treatment arms (7.3%, 5.8% and 4.1%, in the nicotine EC, patch and placebo EC arms respectively). We made two comparisons. The first compares abstinence rates between

Adverse events:

Table x. Analysis 2.2. Nicotine EC versus nicotine replacement therapy: Adverse events
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Appendix 1. Summary of proportion of participants abstinent from smoking at follow-up: cohort studies

Study	Smokers motivated or unmotivated to quit?	Intervention vs relevan t Control	% abstinent				
Cohort studies			**6-month**	**12-month**	**18-month**	**24-month**	**Notes**
Adriaens 2014 [1]	Unmotivated to quit	Nicotine EC	19.6% (10/51)				Data from 8 month follow-up
Al-Delaimy 2015	Not defined. 43% intended to quit in next 6m	Had ever used nicotine EC at baseline		5% (12/236)			Compared to 10.5% in never users
Borderud 2014	Motivated to quit	Used EC in past 30 days at baseline		14.5%			Average follow-up 10 months . Compared to 30% in non EC users. Denominators for both groups not known, but ITT analysis
Caponnetto 2013b	Unmotivated to quit	Nicotine EC		14% (2/14)			
Ely 2013	Motivated to quit	Nicotine EC [2]	44% (21/48)				
Manzoli 2015	Not defined	Nicotine EC		16% (51/319)			Compared to 15% non-users at baseline
Pacific i 2015	Unmotivated to quit	Nicotine EC		53% (18/34)			
Polosa 2011	Unmotivated to quit	Nicotine EC	23% (9/40)		15% (6/40)	13% (5/40)	
Polosa 2014b	Unmotivated to quit	Nicotine EC	36% (18/50)				
Polosa 2015	Not defined	Nicotine EC	42% (30/71)	41% (29/71)			
Cohort studies not allowing inclusion of non-responders			**6-month**	**12-month**	**18-month**	**24-month**	**Notes**
Brose 2015	Not defined. 46% attempted to quit in past 1 yr	Daily EC users at baseline		8% (7/86)			Compared to 9.5% non-daily EC users and 12.9% non-users

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For patients and the public

What are electronic cigarettes?

Electronic cigarettes (ECs) are known by a variety of names, including vape pens, e-hookahs, mods, tank systems, and e-cigs. ECs are electronic devices that use a battery to aerosolize a liquid, usually containing nicotine, flavouring, and other additives, which is inhaled through a mouthpiece.

Image credit

Who can use electronic cigarettes?

Smokers report using ECs to reduce the risks of smoking or to help them quit smoking. The regulation of e-cigarettes varies by country. Because nicotine is highly addictive and can harm the developing adolescent brain, young people are discouraged from using ECs.

What other options are there?

Options to help people quit smoking include behavioural counselling, nicotine replacement therapy, and other medications. See: Information for decision makers - Other options.

How do people experience the intervention?

ECs replicate the experience of smoking, delivering a mist with nicotine instead of smoke. They may be perceived as cleaner. Some smokers may experience them as a bit harsher on the back of the throat, and some may experience that cravings return sooner than with smoking.

Is there anything else someone should know before using the intervention?

It is unknown whether ECs are harmful to others exposed to second-hand aerosol. There may be restrictions on where ECs can be used.

For clinical decisions

Indications and contraindications

Although electronic cigarettes (ECs) are promoted to help people quit smoking, their safety and effectiveness are uncertain. Smokers may therefore want to consider other options.

Young people are discouraged from using ECs, because nicotine is highly addictive and might harm the developing adolescent brain.

Nicotine replacement products, rather than ECs, should be considered to manage nicotine withdrawal symptoms in hospitalized smokers.

Delivery

There are hundreds of different brands and models of ECs available. There is also wide variation in the composition of the fluid in the cartridge or in the EC reservoir (nicotine content, flavours, and other components). ECs may deliver very low amounts of nicotine to new users. However, even in the absence of good nicotine delivery, they can alleviate the urge to smoke.

There are differences between smoking a cigarette and smoking ECs. Smoking ECs too much at a time or smoking them for too long can lead to throat irritation and soreness. Nicotine absorption occurs more slowly with ECs than with smoking tobacco cigarettes, so smokers may need to get used to waiting longer to get a nicotine fix.

Cautions

The effects of long-term use of ECs, EC cessation, and interventions to help people quit using ECs are unknown.

Counselling patients

These points might be covered in response to questions by smokers about using ECs to help them quit smoking:

- The Main findings of this review regarding the safety and effectiveness of ECs
- More detail about ECs
- Using ECs is probably less harmful than smoking conventional cigarettes, but we do not know how safe they are for users or those around them. The health consequences of vapor exposure are unknown, and inhaling EC flavourings might adversely affect respiratory function.
- There are other options that can help them to stop smoking

For policy decisions

Policy options

Policy options for electronic cigarettes (ECs) include: requiring disclosure of ingredients, regulating nicotine levels, regulating the composition of fluids (e.g. banning flavours with high toxicity), regulating disposal of devices and fluids, restrictions on advertising, requiring product warnings, taxation policies, restrictions on where ECs can be used, and banning ECs altogether.

Policy options targeted at preventing use of ECs by children and young people include requiring child-resistant packaging, restricting flavours with high youth appeal, restricting advertising targeted at young people, and restricting sale of ECs to young people.

Equity considerations

Use of ECs likely costs less than smoking. Therefore, to the extent that ECs are found to be safe and effective, affordability might not be a barrier to shifting from tobacco to ECs.

Economic considerations

There are many EC producers, including tobacco manufacturers, promoting ECs through advertising and social media. In addition to considering taxation policies and the cost of ECs relative to tobacco cigarettes, consideration needs to be given to how the cost of ECs might affect uptake by non-smokers, particularly young people.

Monitoring and evaluation

The impacts of policies aimed at encouraging or discouraging smokers to use ECs or to prevent youth from using ECs are uncertain. The effects of implementing such policies should be evaluated.

Because the safety and effectiveness of ECs is uncertain, rigorous evaluation is needed to inform future policy decisions. In the most recent update of this review, 15 ongoing randomised trials with follow-up of six months or longer were found.

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Sorry, in this sketch, links to external websites don't work.
But there **is** an *interactive Summary of Findings* for this review at this link address:
bit.ly/isof-e-cigarettes-test

Open a browser window (Chrome works best) and type in the url manually.

If you were looking for more information about GRADE:
www.gradeworkinggroup.org

We didn’t create content for the link you clicked on in this sketch.

Please describe **what you clicked on** and **what you would expect to find here** if this was an actual visit to a live web site.

Clicking on language links would take you translations of the summary.

We have not created those pages in this prototype.