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Electronic cigarettes for smoking cessation (Review)

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Electronic cigarettes for smoking cessation.
Cochrane Database of Systematic Reviews 2026, Issue 8. Art. No.: CD010216.
DOI: 10.1002/14651858.CD010216.pub11.

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Electronic cigarettes for smoking cessation

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Editorial group: Cochrane Central Editorial Service.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 8, 2026.

Citation: Lindson N, Livingstone-Banks J, Butler AR, McRobbie H, Bullen CR, Hajek P, Wu AD, Begh R, Theodoulou A, Ma C, Notley C, Rigotti NA, Turner T, Fanshawe T, Hartmann-Boyce J. Electronic cigarettes for smoking cessation. *Cochrane Database of Systematic Reviews* 2026, Issue 8. Art. No.: CD010216. DOI: 10.1002/14651858.CD010216.pub11.

ABSTRACT

Rationale

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

Objectives

To examine the safety, tolerability, and effectiveness of EC for helping people who smoke tobacco achieve long-term smoking abstinence, in comparison to non-nicotine EC, other smoking cessation treatments, and no treatment.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and PsycINFO to 1 January 2026, reference-checked, and contacted study authors.

Eligibility criteria

We included randomised controlled trials (RCTs) randomising people who smoked to an EC or control condition. Studies had to measure an eligible outcome.

Outcomes

Critical outcomes were abstinence from smoking after at least six months, adverse events (AEs), and serious adverse events (SAEs). Important outcomes were biomarkers, toxicants/carcinogens, long-term study product use and long-term patterns of EC and combustible cigarette use.

Risk of bias

We used the RoB 1 tool to assess risk of bias for each study and GRADE to assess evidence certainty.

Synthesis methods

We followed standard Cochrane methods for screening and data extraction. Where appropriate, we pooled data using random-effects models to calculate risk ratios (RRs) with 95% confidence intervals (CI) for dichotomous outcomes apart from SAEs. For SAEs, we calculated risk differences (RD) and 95% CI. For continuous outcomes, we calculated mean differences (MD) or standardised mean differences (SMD) with 95% CIs.

Included studies

We included 80 completed RCTs, representing 29,861 participants. Nine of these RCTs were new to this update. We rated 12 included studies as being at low risk of bias, 41 at high risk, and the remainder at unclear risk overall.

Synthesis of results

Nicotine EC result in increased quit rates compared to nicotine replacement therapy (NRT) (high-certainty evidence) (RR 1.61, 95% CI 1.23 to 2.12; I^2 = 55%; 11 studies, 4114 participants). In absolute terms, this might translate to an additional four quitters per 100 (95% CI 1 to 7 more). The proportion of participants experiencing AEs may be similar between groups (low-certainty evidence, limited by imprecision and inconsistency) (RR 0.95, 95% CI 0.72 to 1.24; I^2 = 72%; 8 studies, 3107 participants) and the proportion of participants experiencing SAEs is probably similar between groups (moderate-certainty evidence, limited by imprecision) (RD 0.01, 95% CI −0.01 to 0.02; I^2 = 0%; 10 studies, 4045 participants).

Nicotine EC probably result in increased quit rates compared to non-nicotine EC (moderate-certainty evidence, limited by imprecision) (RR 1.34, 95% CI 1.05 to 1.69; I^2 = 0%; 7 studies, 1918 participants). In absolute terms, this might lead to an additional two quitters per 100 (95% CI 0 to 4 more). There is probably little to no difference in the proportion of participants experiencing AEs between these groups (moderate-certainty evidence, limited by imprecision) (RR 1.01, 95% CI 0.95 to 1.08; I^2 = 0%; 6 studies, 909 participants) and there may be similar proportions of SAEs (RD 0.00, 95% CI −0.01 to 0.01; I^2 = 0%; 11 studies, 1786 participants; low-certainty evidence downgraded due to very serious imprecision).

Compared to behavioural support only or no support, quit rates may be higher for participants randomised to nicotine EC (low-certainty evidence due to risk of bias) (RR 1.75, 95% CI 1.39 to 2.20; I^2 = 13%; 11 studies, 7214 participants). In absolute terms, this represents an additional two quitters per 100 (95% CI 2 to 6 more). There was some evidence that people randomised to nicotine EC may be more likely to experience (non-serious) AEs (RR 1.22, 95% CI 1.00 to 1.49; I^2 = 58%; 11 studies, 2801 participants; very low-certainty evidence due to imprecision and risk of bias), but the evidence is uncertain. There was insufficient evidence to determine whether rates of SAEs differed between groups (RD 0.00, 95% CI −0.00 to 0.01; I^2 = 0%; 18 studies, 5032 participants; very low-certainty evidence downgraded due to imprecision and risk of bias).

Authors' conclusions

There is high-certainty evidence that nicotine EC increase quit rates compared to NRT, and moderate-certainty evidence that they probably increase quit rates compared to EC without nicotine. Evidence comparing nicotine EC with behavioural support or no support also suggests benefit, but is less certain due to risk of bias inherent in the study designs.

Overall incidence of SAEs was low across all study arms and there is now moderate-certainty evidence that SAE rates are similar when comparing nicotine EC with NRT. There was also no evidence of a difference in AEs between nicotine and non-nicotine EC nor between nicotine EC and NRT, but low-certainty evidence for increased AEs compared with behavioural support/no support. We did not detect evidence of serious short-term harm from nicotine EC, but longer, larger trials are needed to fully evaluate safety. The included studies tested regulated nicotine-containing EC; illicit products and/or products containing other active substances (e.g. tetrahydrocannabinol (THC)) may have different harm profiles.

The main limitation of the evidence base remains imprecision for some comparisons. Further RCTs are underway. To ensure the review continues to provide up-to-date information, this is a living systematic review. We run and screen searches monthly, with the review updated when relevant new evidence becomes available. Please refer to the *Cochrane Database of Systematic Reviews* for the most recent version of this review.

Funding

Cancer Research UK (PICCTR-2024/100012). The addition of new outcomes relating to vaping and smoking at six months or more was supported by the National Cancer Institute of the National Institutes of Health (NIH) and FDA Center for Tobacco Products (CTP) under Award Number 2U54CA229974. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or the Food and Drug Administration. The funders were not involved in the decision to submit for publication.

Registration

Protocol (2012) available via DOI: 10.1002/14651858.CD010216 (updates to 2012 protocol available via https://osf.io/upgjc/overview.

PLAIN LANGUAGE SUMMARY

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

Key messages

- Nicotine electronic cigarettes (e-cigarettes) can help people to stop smoking for at least six months. They work better than nicotine replacement therapy, and probably better than e-cigarettes without nicotine.
- E-cigarettes may work better than no support, or behavioural support alone, and may not be associated with serious unwanted effects.
- However, we still need more evidence, particularly about the effects of newer types of e-cigarettes that have better nicotine delivery than older types, as better nicotine delivery might help more people quit smoking.

What are e-cigarettes?

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

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

What did we want to find out?

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

What did we do?

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

We were interested in:

· how many people stopped smoking for at least six months; and

· how many people had unwanted effects, reported after at least one week of use.

What did we find?

We found 80 studies including 29,861 adults who smoked. Most studies took place in the USA (40 studies) and the UK (16). Most studies compared nicotine e-cigarettes with:

- nicotine replacement therapy (e.g. patches or gum);
- medicines to help people stop smoking (varenicline and cytisine);
- e-cigarettes without nicotine;
- heated tobacco (products that heat tobacco to a high enough temperature to release vapour, without burning it or producing smoke; these differ from e-cigarettes because they heat tobacco leaf/sheet);
- oral nicotine pouches (pouches that contain no tobacco but release nicotine when kept in the mouth);
- other types of nicotine-containing e-cigarettes (e.g. pod devices, newer devices);
- advice or counselling (behavioural support); or
- no support for stopping smoking.

What are the results of our review?

- More people stop smoking for at least six months with e-cigarettes than with nicotine replacement therapy (11 studies; 4114 people);

- People may be more likely to stop smoking for at least six months with e-cigarettes with nicotine than e-cigarettes without nicotine (7 studies, 1918 people);
- Nicotine e-cigarettes may help more people to stop smoking than behavioural support only or no support (11 studies, 7214 people);
- For every 100 people using nicotine e-cigarettes to stop smoking, 8 to 10 might successfully stop, compared with only 6 of 100 people using nicotine-replacement therapy, 6 of 100 using e-cigarettes without nicotine, or 5 of 100 people having no support or behavioural support only;
- We are uncertain if there is a difference between how many unwanted effects occur using nicotine e-cigarettes compared with nicotine replacement therapy, no support or behavioural support only (although non-serious unwanted effects were more common in groups receiving nicotine e-cigarettes compared to no support or only behavioural support);
- Studies comparing nicotine e-cigarettes to nicotine replacement therapy reported low numbers of unwanted effects, including serious unwanted effects. Compared to nicotine e-cigarettes, there is probably no difference in how many:
  - serious unwanted effects occur in people using nicotine replacement therapy;
  - non-serious unwanted effects occur in people using non-nicotine e-cigarettes.

What are the limitations of the evidence?

- We are confident in the evidence that nicotine e-cigarettes help more people to stop smoking than nicotine replacement therapy, but we need more evidence about e-cigarettes without nicotine.
- Studies comparing nicotine e-cigarettes with behavioural or no support also showed higher quit rates in people using nicotine e-cigarettes, but we are more uncertain of the data because the people in the studies were aware of each treatment they were getting.
- Most of our results for the unwanted effects could change when more evidence becomes available, as there were often few cases of effects reported with unclear results.

How up to date is the evidence?

This review updates our previous review published in 2025. We will update it again when new evidence becomes available. The evidence is up to date to 1 January 2026.

SUMMARY OF FINDINGS

Summary of findings 1. Nicotine EC compared to NRT for smoking cessation

Nicotine EC compared to NRT for smoking cessation

Patient or population: people who smoke cigarettes, aged 18 or older
Setting: various settings
Intervention: nicotine EC
Comparison: NRT

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Events with NRT	Events with Nicotine EC				
Smoking cessation at 6+ months Preferentially assessed with biochemical validation	Study population 6 per 100	 10 per 100 (7 to 13)	RR 1.61 (1.23 to 2.12)	4114 (11 RCTs)	⊕⊕⊕⊕ HIGH	-
Adverse events at 1+ weeks Assessed by self-report	Study population 41 per 100	 39 per 100 (30 to 51)	RR 0.95 (0.72 to 1.24)	3107 (8 RCTs)	⊕⊕⊖⊖ LOW[a]	-
Serious adverse events at 1+ weeks Assessed via self-report and medical records	Study population 6 per 100	 7 per 100 (5 to 8)	RD 0.01 (-0.01 to 0.02)	4045 (10 RCTs)	⊕⊕⊕⊖ MODERATE[b]	-

***The estimated number of events in the intervention group** (and its 95% CI) is based on the assumed number of events in the comparison group and the **relative effect** of the intervention (and its 95% CI). For cessation, the assumed number of events in the control group is based on assumed quit rates for NRT assuming receipt of limited behavioural stop-smoking support (as per [1]). The assumed risk for adverse events and serious adverse events is a weighted mean average of quit rates across control groups in contributing studies.

CI: confidence interval; **EC**: electronic cigarette; **NRT**: nicotine replacement therapy; **RCT:** randomised controlled trial; **RD:** risk difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level due to imprecision; CIs consistent with benefit and harm. Also downgraded one level due to inconsistency (I^2 = 72%)
[b]Downgraded one level due to imprecision; fewer than 300 events

Summary of findings 2. Nicotine EC compared to non-nicotine EC for smoking cessation

Nicotine EC compared to non-nicotine EC for smoking cessation

Patient or population: people who smoke cigarettes, aged 18 or older
Setting: various settings
Intervention: nicotine EC
Comparison: non-nicotine EC

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Events with non-nicotine EC	Events with nicotine EC				
Smoking cessation at 6+ months Preferentially assessed with biochemical validation	Study population		RR 1.34 (1.05 to 1.69)	1918 (7 RCTs)	⊕⊕⊕⊖ MODERATE[a,b]	-
	6 per 100	8 per 100 (6 to 10)				
Adverse events at 1+ week Assessed via self-report	Study population		RR 1.01 (0.95 to 1.08)	909 (6 RCTs)	⊕⊕⊕⊖ MODERATE[b]	-
	46 per 100	46 per 100 (44 to 50)				
Serious adverse events at 1+ week Assessed via self-report and medical records	Study population		RD 0.00 (-0.01 to 0.01)	1786 (11 RCTs)	⊕⊕⊖⊖ LOW[c]	-
	2 per 100	2 per 100 (1 to 3)				

***The estimated number of events in the intervention group** (and its 95% CI) is based on the assumed number of events in the comparison group and the **relative effect** of the intervention (and its 95% CI). For cessation, the assumed number of events in the control group is based on assumed quit rates for NRT assuming receipt of limited behavioural stop-smoking support (as per [1]). The assumed risk for adverse events and serious adverse events is a weighted mean average of quit rates across control groups in contributing studies.

CI: confidence interval; **EC**: electronic cigarette; **RCT:** randomised controlled trial; **RD:** risk difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.

[a]Not downgraded for risk of bias. One of seven studies considered high risk of bias; removing this study increased the direction of the effect in favour of the intervention.
[b]Downgraded one level due to imprecision: confidence intervals encompass both harm and no difference.
[c]Downgraded two levels due to imprecision; < 100 events overall

Summary of findings 3. Nicotine EC compared to behavioural support only/no support for smoking cessation

Nicotine EC compared to behavioural support only/no support for smoking cessation

Patient or population: people who smoke cigarettes, aged 18 or older
Setting: various settings
Intervention: nicotine EC
Comparison: behavioural support only/no support

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Events with behavioural support only/no support	Events with nicotine EC				
Smoking cessation at 6+ months Preferentially assessed using biochemical validation	Study population 5 per 100	9 per 100 (7 to 11)	RR 1.75 (1.39 to 2.20)	7214 (11 RCTs)	⊕⊕⊖⊖ LOW[a]	-
Adverse events at 1+ weeks Assessed via self-report	Study population 43 per 100	52 per 100 (43 to 64)	RR 1.22 (1.00 to 1.49)	2801 (11 RCTs)	⊕⊖⊖⊖ VERY LOW[a,b]	-
Serious adverse events at 1+ weeks Assessed via self-report and medical records	Study population 3 per 100	3 per 100 (3 to 4)	RR 0.00 (-0.00 to 0.01)	5032 (18 RCTs)	⊕⊖⊖⊖ VERY LOW[a,c]	-

***The estimated number of events in the intervention group** (and its 95% CI) is based on the assumed number of events in the comparison group and the **relative effect** of the intervention (and its 95% CI). For cessation, the assumed number of events in the control group is based on assumed quit rates assuming receipt of limited behavioural stop-smoking support (as per [1]). The assumed risk for adverse events and serious adverse events is a weighted mean average of quit rates across control groups in contributing studies.

CI: confidence interval; **EC**: electronic cigarette; **MA:** meta-analysis; **RCT:** randomised controlled trial; **RD:** risk difference; **RR:** risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.

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[a]Downgraded two levels due to risk of bias. Due to lack of blinding and differential support between arms, this domain was judged to be at high risk of bias.
[b]Downgraded one level due to imprecision. Confidence intervals incorporated no clinically significant difference and clinically significant harm.
[c]Downgraded one level due to imprecision. Fewer than 300 events

BACKGROUND

Throughout this review, we discuss (1) combustible cigarettes and (2) electronic cigarettes. Electronic cigarettes are hand-held and produce an aerosol for inhalation, formed by heating a liquid using a battery-powered heating coil. In this review, all mention of smoking, smoking cessation, cigarette use, smoke intake, etc. concerns combustible tobacco cigarettes. When the text concerns electronic cigarettes, we use the abbreviation 'EC'. EC users are sometimes described as 'vapers', and EC use as 'vaping'. We refer to EC that do not contain nicotine as non-nicotine EC; these can also be conceptualised as placebo EC, but we are using the term non-nicotine EC, as they can be conceptualised as an intervention in themselves. As nicotine is the primary addictive substance in cigarettes, this review does not address the use of vaping devices to inhale substances other than nicotine, such as cannabis.

Description of the condition

Stopping smoking tobacco is associated with large health benefits. Despite most people who smoke 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 one year after quitting [2].

Nicotine replacement therapy medications increase the chances of quitting through providing nicotine as a substitute medication, to help alleviate withdrawal symptoms, but even with such support, long-term quit rates remain low [3, 4, 5, 6, 7, 8]. One of the limitations of traditional nicotine replacement therapies (NRT) is that, apart from providing nicotine more slowly and at lower levels than smoking, none adequately addresses the sensory, behavioural, and/or social aspects of smoking that people who have smoked miss when they stop (e.g. holding a cigarette in their hands, taking a puff, their enjoyment of smoking, and feeling part of a group). EC may offer a way to overcome these limitations [9], and they have become a popular consumer choice for smoking cessation support where regulations allow [10].

There is no doubt that people can become dependent on tobacco, and many find it difficult to stop smoking, primarily because of nicotine and its actions on the brain's reward system [11]. However, developing dependence on tobacco smoking is a complex biopsychosocial process [12, 13]. Other tobacco chemicals, such as acetaldehyde and monoamine oxidase (MAO) inhibitors, seem to potentiate the effects of nicotine [13]. In addition, sensory and behavioural cues provide additional reinforcement of smoking behaviour [14, 15] and may over time become almost as rewarding as nicotine. There are several lines of evidence to support this. Firstly, people who smoke appear to have a preference for cigarette smoke compared to other forms of nicotine delivery. This is partly related to the speed of nicotine delivery through smoke inhalation. However, even when nicotine is administered intravenously, it does not provide the same level of satisfaction or reward as smoking [15, 16]. Secondly, the local sensory effects of smoking (e.g. the ‘scratch’ in the back of the throat) may be important for enjoyment and reward. Numbing the sensations of cigarette smoke by anaesthetising the upper and lower respiratory tract leads to less enjoyment of smoking [17]. Conversely, products that mimic the sensory effects of smoking on the mouth and throat (such as citric acid, black pepper, and ascorbic acid) reduce craving and some withdrawal symptoms, at least in the short term [18, 19, 20]. Thirdly, very low nicotine content cigarettes (VLNC), which have less nicotine (e.g. 0.08 mg) than the 1 mg in regular cigarettes, and so have negligible or no central effects, have also been investigated for their role in aiding smoking cessation [21]. Despite delivering low levels of nicotine, VLNC are satisfying over the initial few days of abstinence from nicotine [15, 22, 23, 24]. They also reduce tobacco withdrawal symptoms, including urges to smoke and low mood [15, 25, 26, 27, 28], and have been shown to improve long-term continuous abstinence rates [29]. Social aspects of smoking, such as feeling part of a like-minded group, or including smoking behaviour as part of one's social identity, are also elements of cigarette smoking that some people who smoke report to be drivers of cigarette use [30].

Considering the other factors that contribute to tobacco dependence, there is interest in developing smoking cessation products that not only help relieve the unpleasant effects of nicotine withdrawal, but that also act as effective substitutes for smoking behaviour and the rituals and sensations that accompany smoking, without the health risks associated with the inhalation of tobacco smoke. The only pharmaceutical treatment with some of these characteristics is the nicotine inhalator. However, this product does not have greater cessation efficacy than other NRT products [1, 31]. This may, in part, be due to the considerable effort (e.g. 20 minutes of continuous puffing) needed to provide nicotine blood concentrations consistent with other NRT products [32]. Adherence to correct use of the inhalator is low compared to other types of NRT [31]. It is therefore possible that any advantage of sensorimotor replacement is diminished by low nicotine delivery and limited similarities between inhalator use and the sensations of smoking [33].

Description of the intervention and how it might work

The liquid used in EC, usually comprising propylene glycol and glycerol, with or without nicotine and flavours, is stored in disposable or refillable cartridges or a reservoir or 'pod'. The commonly used term for this aerosol is vapour, which we use throughout this review. EC are marketed as consumer products in some jurisdictions, although banned in others. Although routes are in place for licencing them as medicine or medical devices in some areas, no country yet has a licenced medicinal EC.

EC provide sensations similar to smoking a cigarette. The vapour looks like tobacco smoke, but is only visible when the user exhales after drawing on the mouthpiece, not when the device is being held. In qualitative studies, users report a sense of shared identity with other users, similar to a tobacco-smoking identity, and also report pleasure and enjoyment of use, suggesting that EC may be viewed less as medical cessation aids but rather as acceptable alternatives to tobacco smoking [30, 34].

There are many different brands and models of EC available. Variation exists both in the device ('product') and consumable (liquid). There is a wide variation in the composition of EC liquids (e.g. nicotine content; flavours) [35, 36], with some users choosing to mix their own liquids [37]. Initial studies showed that early models of EC delivered very low amounts of nicotine to naïve users [33, 38, 39]. Later studies, that have measured nicotine pharmacokinetics in both experienced and naïve EC users, have found that some EC users can achieve blood nicotine levels similar to those achieved with smoking, albeit more slowly, and that their ability to do so often improves over time [40, 41, 42, 43, 44].

Early in their development, EC were designed to look like cigarettes and used disposable cartridges. These models were often called 'cig-a-likes'. The nicotine delivery from these products was low [45]. The later refillable, or 'tank', products have a larger battery and a transparent container that users fill with a liquid of their choice, and usually provide faster and more efficient nicotine delivery, allowing a wider choice of flavours and nicotine concentrations. They have more typically been used by experienced vapers, who reportedly managed to switch to vaping completely [46, 47, 48, 49, 50]. More recently, smaller 'pod' devices that use nicotine salt solutions have become available. This nicotine formulation reduces irritant effects and allows the delivery of higher nicotine levels that closely mimic the pharmacokinetic profile of nicotine delivery from cigarettes, despite the low battery power of the devices [51]. In qualitative studies, pod devices have been highly rated by users in terms of satisfaction, usability (simple to use), affordability, and availability [52]. The nicotine salts used in pods allow for high nicotine delivery; this may increase the likelihood that adults who smoke are able to transition completely from conventional cigarettes [53]. Average nicotine concentrations in EC sold in the United States increased overall from 2013 to 2018, for all flavour categories, and for rechargeable EC [54]. The EU Tobacco Products Directive [55] does not allow sales of liquids with nicotine content higher than 20 mg/mL, and so the US version of the Juul pod device (59 mg/nl nicotine) is not legally available within the EU [56, 57]. Most recently, there has been rapid growth in the use of disposable and single-use devices [58, 59]. These are available in a range of attractive flavours, generally have a high nicotine content, are low cost, and have a closed system that is designed to be disposed of following use. Disposable EC are receiving increased regulatory attention, and have recently been banned in the UK, as well as other countries [60].

Different device types may differ significantly in their efficacy in helping people who smoke to quit, as they differ in delivery of nicotine. Nicotine itself, when delivered through mechanisms and doses similar to that delivered in traditional NRT, is not considered harmful [1]. The safety profile of the different types of nicotine EC may be similar as they use the same constituents, although within the generic range of EC types there is some evidence to suggest EC providing less nicotine may pose higher risks. This is because low-nicotine delivery devices need to be puffed at higher intensity to provide users with the nicotine levels they seek, and more intensive puffing is accompanied by increased inhalation of potential toxicants [61, 62, 63].

There is no one agreed classification system for EC devices, and product development has moved so quickly that the definitions used within trials of the devices tested may no longer necessarily be fit for purpose. In this review, the definitions used are based on those drawn from the included trials. We currently label different types of EC as 'cartridges' for devices with disposable cartridges and – typically, but not always – low nicotine delivery (e.g. cig-a-likes); refillable EC for devices that people fill with their own choice of liquids; pods for small devices with disposable pods that commonly use nicotine salts; and disposable for closed system devices designed to be disposed of after use.

Why it is important to do this review

Regulatory approaches being used for EC currently vary widely, from no regulation to partial and complete bans [64]. Within the USA, for example, the Food and Drug Administration (FDA) has classified EC as tobacco products, and laws include prohibition of EC use indoors, a requirement for retailers to have a licence to sell, and prohibition of sales to minors. Laws prohibiting sales to minors apply nationwide, but other laws vary by state [65]. The European Union includes EC in their Tobacco Products Directive, except where therapeutic claims are made or in instances where they contain over 20 mg/nl of nicotine [55].

Categorical statements about the toxicity of EC are not possible because of the large number of devices and liquids available and the frequent addition of new products to the market. In 2019, cases of severe lung injury associated with EC use were reported in the USA and, by February 2020, there were around 2800 hospitalised cases and 68 deaths [66]. This illness, which was termed E-cigarette or Vaping-Associated Lung Injury (EVALI), caused concern throughout the world [67] and a negative change in people's perception of the risks of EC use compared to smoking [68]. These cases were somewhat at odds with data from trials and cohort studies, and it was later found that these injuries were related to use of tetrahydrocannabinol (THC)-containing products adulterated with vitamin E acetate [69, 70].

Amongst those brands of nicotine EC that have been tested, levels of toxicants have been found to be substantially lower than in cigarettes [64, 71]. Long-term effects beyond 12 months are unclear, although based on what is known about liquid and vapour constituents and patterns of use, a report from the UK's Royal College of Physicians has concluded that using an EC is likely to be considerably safer than smoking [72]. The US National Academies of Sciences, Engineering, and Medicine (NASEM) concluded that EC are likely to be far less harmful than continuing to smoke cigarettes, with the caveat that the long-term health effects of EC use are not yet known [73].

Despite general acknowledgement that EC use exposes the user to fewer toxicants and at lower levels than smoking cigarettes [64, 73, 74, 75], in some countries and settings there remains hesitancy in making these products available to people who smoke as a harm reduction tool or smoking cessation aid ([76]). Concerns include the issue that the long-term effects of EC use on health are not yet known, the possible harms of second-hand EC vapour inhalation, the lack of quality control measures, and that EC may undermine smoke-free legislation if used in smoke-free spaces [64]. Of concern is also the involvement of the tobacco industry and that EC may be a gateway to smoking initiation or nicotine dependence amongst nicotine-naïve users, or may prolong continued dual use of tobacco amongst people who smoke cigarettes [64], and some research has investigated this [77]. A report from the US Preventive Services Taskforce concluded "that the current evidence is insufficient to assess the balance of benefits and harms of electronic cigarettes (e-cigarettes) for tobacco cessation in adults" [78]. However, others suggest that potential benefits outweigh potential disadvantages [49, 64, 71, 73, 74, 75].

People who smoke, healthcare providers, and regulators are interested in knowing if EC can help people to quit and if it is safe to use them to do so. In particular, healthcare providers have an urgent need to know what they should recommend to people to help them to stop smoking. The largest health gains are achieved from stopping smoking completely, as opposed to reducing cigarette consumption and, as such, this review focusses on the effectiveness of EC in aiding complete smoking cessation.

This review was first published in 2014, and updated in 2016, 2020, 2021, 2022, 2024, January 2025 and November 2025. We published an update to the protocol in 2023 and 2025 (see https://osf.io/upgjc/overview).

Following publication of the 2020 update of this review, we are maintaining it as a living systematic review [79]. This means we are continually running searches and incorporating new evidence into the review. For more information about the living systematic review methods being used, see Supplementary material 8. A living systematic review approach is appropriate for this review for three reasons. Firstly, the review addresses an important public health issue: the role of EC in enabling people who smoke to stop smoking, with the potential for substantial ongoing individual and societal benefits, depending on the extent of effectiveness. Secondly, there remains uncertainty in the existing evidence; more studies are needed to confirm the degree of benefit for different comparisons and product types, and there is considerable uncertainty about adverse events and other markers of safety. Thirdly, we are aware of multiple ongoing trials that are likely to have an important impact on the conclusions of the review.

OBJECTIVES

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

METHODS

We followed the Methodological Expectations of Cochrane Intervention Reviews (MECIR) when conducting the review [80], and PRISMA 2020 for the reporting [81]. As this is a living review, methods are periodically updated between review updates to ensure that the review remains relevant and reliable.

Differences between protocol and review

Changes to the methods are prespecified via https://osf.io/upgjc/overview; differences in methods from the protocol and between review updates are documented in Supplementary material 10. Additional changes may be made to the methods for future updates, which will also be documented.

Criteria for considering studies for this review

Types of studies

We include randomised controlled trials (RCTs) and randomised cross-over trials in which people who smoke are randomised to EC or to a control condition. RCTs are the best available primary evidence to fulfil our objectives. In response to editorial feedback from Cochrane and because of the growth in the RCT evidence base, we no longer include single-arm studies where all participants receive EC (see September 2025 protocol update).

We include studies regardless of their publication status or language of publication.

Types of participants

Participants are people defined as currently smoking cigarettes at enrolment into the studies. Participants can be of any age, motivated or unmotivated to quit, and we include studies that recruited pregnant people.

Should a study meet all other criteria, but include only a subset of eligible participants (e.g. a study on people who currently smoke and people who formerly smoked), we would only include data on the subgroup of participants who met our inclusion criteria. If these data were not available, we would include the study if at least 80% of participants met our inclusion criteria and would test the exclusion of the study in a sensitivity analysis.

Types of interventions

Any type of EC or intervention intended to promote EC use for smoking cessation, including studies that do not measure smoking cessation but provide EC with the instruction that they be used as a complete substitute for cigarette use. EC may or may not contain nicotine.

Types of comparators

We compare nicotine EC with alternative smoking cessation aids (e.g. NRT), EC without nicotine, standard treatment alone, and no intervention. We also compare different types of EC (refillable, cartridge, nicotine salt, free-base), different nicotine doses, and different flavours. We also compare non-nicotine EC with NRT, behavioural support/no support and a combination of non-nicotine EC together with NRT versus NRT alone; additional comparisons include advice to use EC vs no advice to use EC, and combinations of nicotine EC with single comparators.

Outcome measures

Critical outcomes

- Cessation at the longest follow-up point, 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;
- Number of participants reporting any type of adverse event(s) at one week or longer (as defined by study authors);
- Number of participants reporting any type of serious adverse event(s) at one week or longer (as defined by study authors).

Important outcomes

- Changes in the following measures at longest follow-up (one week or longer):
  - Carbon monoxide (CO), measured through breath or blood;
  - Blood pressure;
  - Heart rate;
  - Blood oxygen saturation;
  - Lung function measures;
  - Known toxicants/carcinogens, measured through blood, urine or saliva (toxicant names and abbreviations are listed in Supplementary material 9).
- Number of people still using their allocated study product (EC or pharmacotherapy) at longest follow-up (at least six months). The product could be that provided by the study, or could be the same product type but bought independently by the participant.

- Number of people using different combinations of EC and combustible cigarettes at longest follow-up (at least six months), split into the following four separate outcomes:
  - Number of people using EC and no combustible tobacco;
  - Number of people using no combustible tobacco and no EC;
  - Number of people using both EC and combustible tobacco;
  - Number of people using combustible tobacco and no EC.

Studies had to set out to measure one of the critical or important outcomes above to be eligible for inclusion. If a study set out to measure an eligible outcome but did not measure and/or report results on this outcome, we would still include this study and flag its missing data in the results section.

We intended to include any measure of an association between withdrawal symptoms and smoking cessation at six months or longer, as long as withdrawal was measured using a validated scale designed explicitly to investigate smoking withdrawal or craving. We added this because British guidelines now specify that efforts should be made to provide EC in a way that will reduce symptoms of withdrawal in people who smoke [82]. However, no studies provided data on this.

Search methods for identification of studies

Electronic searches

Searches are conducted monthly. This update includes results from searches conducted up to 1 January 2026:

- Cochrane Tobacco Addiction Group Specialized Register (CRS-Web up to 1 February 2023);
- Cochrane Central Register of Controlled Trials (CENTRAL; 2025, Issue 12) via CRS-Web;
- MEDLINE (OVID SP; 1 January 2004 to 1 January 2026);
- Embase (OVID SP; 1 January 2004 to 1 January 2026);
- PsycINFO (OVID SP; 1 January 2004 to 1 January 2026);
- ClinicalTrials.gov (via CENTRAL; 2025, Issue 12);
- WHO International Clinical Trials Registry Platform (ICTRP: www.who.int/ictrp/en/, via CENTRAL; 2025, Issue 12).

We did not search the Cochrane Tobacco Addiction Group Specialized Register beyond 1 February 2023 as it ceased to be maintained. At the time of the last search, the Register included the results of searches of MEDLINE (via OVID) to update 20221222; Embase (via OVID) to week 202251; and PsycINFO (via OVID) to update 20221219. See the Tobacco Addiction Group website for full search strategies and a list of other resources searched.

For the first version of the review, we also searched CINAHL (EBSCO Host) (2004 to July 2014). We did not search this database from 2016 onwards, 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 2020 searches added further terms, including the MESH heading 'Electronic Nicotine Delivery Systems' and terms to limit by study design. In 2025, we updated our search strategies in line with our change to only include RCTs (see September 2025 protocol update). We use the Cochrane highly sensitive search strategy for identifying randomised controlled trials and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 4 (83). The current and previous search strategies are listed in Supplementary material 1. The search date parameters of the original searches were limited to 2004 to the present, as EC were not available before 2004.

As part of our monthly screening process, any new records related to our included studies are incorporated into our records for that study. We searched for post-publication amendments and examined any relevant retraction statements and errata for included studies (e.g. through PubMed and the Retraction Watch Database; retractionwatch.com/retraction-watch-database-user-guide/), as errata could reveal important limitations or even serious flaws in the included trials [83]. We are confident our search strategy will have caught any post-publication amendments currently published, including expressions of concern, errata, corrigenda and retractions.

Searching other resources

We searched the reference lists of eligible studies found in the literature search and contacted authors of known trials and other published EC studies. We also searched for abstracts from the Society for Research on Nicotine and Tobacco (SRNT) Annual Meetings up to the March 2025 Annual Meeting.

Data collection and analysis

Selection of studies

Two review authors (for this update from: ADW, ARB, CM, CN, JHB, NL, TT, TRF, RB) independently pre-screened all titles and abstracts obtained from the search, using a screening checklist, and then independently screened full-text versions of the potentially relevant papers for inclusion. We resolved any disagreements by discussion or with a third review author (from authors named above).

Data extraction and management

One review author extracted data on study characteristics (ARB), whereas two review authors (for this update: ARB, CM) independently extracted outcome data, effect modifiers, and the information needed to make risk of bias judgements. We used a pre-piloted data extraction form, and checked the form for inconsistencies. We resolved any disagreements by discussion or with a third review author (NL or JHB). We extracted data on the following:

- Author(s);
- Date and place of publication;
- Study dates;
- 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), number of people still using study products, and relevant biomarkers;

- EC and/or combustible tobacco use at longest follow-up;
- Data investigating the association between withdrawal and smoking cessation;
- Assessment of time points;
- Study funding source;
- Author declarations of interest;
- Risk of bias in the domains specified below;
- Additional comments.

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

There were no papers that required translation; should there be in the future, we would use online translation software in the first instance, and seek a translator to assist us where necessary.

For studies that received tobacco or EC industry funding, the study name is reported followed by an asterisk (*).

One review author (NL for this update) entered the data contributing to meta-analysis into RevMan Web software for analysis [84], and another checked them (JHB for this update).

Risk of bias assessment in included studies

Two review authors (for this update: ARB, CM) independently assessed the risk of bias for each included study, using the Cochrane risk of bias tool (RoB 1) [85]. We resolved any disagreements by discussion or with a third review author (NL or JHB). 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. For each study, we judged each domain to be at low, high or unclear risk of bias. We resolved disagreements by discussion or by consulting a third review author.

Specific considerations about judgements for individual domains in this review are outlined below:

- Blinding of participants and personnel: For studies that did not use blinding, we considered studies to be at low risk in this domain if the intervention was compared to an active control of similar intensity, as we judged performance bias to be unlikely in this circumstance. If studies were unblinded and the comparator group was a minimal-intervention control or of lower intensity than the intervention group, we considered the study to be at high risk of bias in this domain.
- Following the standard methods of the Cochrane Tobacco Addiction Group [86], we considered studies to be at low risk of detection bias (blinding of outcome assessment) if our primary outcome was objectively measured or if the intensity of the intervention was similar between groups, or both. For studies where cessation was measured, our judgement was based on whether cessation was biochemically verified. Where cessation was not measured, we judged this domain based on adverse or serious adverse events.
- Again, following the standard methods of the Cochrane Tobacco Addiction Group, we rated studies as being at high risk of attrition bias if loss to follow-up was greater than 50% overall or if there was a difference in follow-up rates of more than 20% between study arms.

We judged studies to be at high risk of bias overall if they were rated at high risk in at least one domain, and at low risk of bias overall if they were judged to be at low risk across all domains evaluated. We judged the remaining studies to be at unclear risk of bias overall.

Measures of treatment effect

We analysed dichotomous data by calculating the risk ratio (RR) with a 95% confidence interval (CI), for each outcome for each individual study for all outcomes except SAEs. For example, for cessation, we calculated the RR as (number of events in intervention condition/intervention denominator)/(number of events in control condition/control denominator), using data at the longest follow-up period reported. For the first time in this update, we calculated risk differences for our SAEs outcome. As SAEs are rare, there are studies that report zero events in both arms. In meta-analyses calculating risk ratios, studies are excluded if zero is recorded in both arms. By using risk difference (RD) as the effect estimate, we were able to include all relevant studies in our analyses of SAEs, which increased the precision of our estimates (see September 2025 protocol update).

We analysed continuous data (other measures of tobacco exposure) by comparing the difference between the mean change from baseline to follow-up in the intervention and comparator groups, or by comparing absolute data at follow-up where insufficient data were available on mean change. Outcomes are reported as mean differences (MD) with 95% CI.

Unit of analysis issues

In the case of trials with multiple arms, we did not combine data between arms, unless this was the way it was presented by study authors, or there was no evidence of difference between similar trial arms for the outcome of interest. We noted in our analyses where this was the case.

For all of our included studies, the unit of assignment was the individual. If cluster-randomised trials are eligible in the future, we will assess whether the study authors have adjusted for this clustering, and whether this had an impact on the overall result. When clustering appears to have had little impact on the results, we will use unadjusted quit-rate data; however, when clustering does appear to have an impact on results, we will adjust for this using the intraclass correlation (ICC).

For randomised cross-over trials, we reported results at the end of the first assignment period where available and where sufficiently long to meet our inclusion criteria for outcomes. For cross-over trials analysed as RRs, standard error and CI calculations followed the methods described in Zou (2007) [87]. For cross-over trials analysed as risk differences, standard error and CI calculations followed the 'Wald+2' method to adjust for zero counts described in Agresti & Min (2005) [88]. All other outcomes from randomised cross-over trials are reported narratively. We offer a narrative synthesis of comparative trials that are not reported with sufficient data for meta-analysis, using effect direction plots as described in the *Cochrane Handbook for Systematic Reviews of Interventions,* where possible [89].

Dealing with missing data

For smoking cessation, we use a conservative approach, as is standard for the Cochrane Tobacco Addiction Group, treating

participants with missing data as still smoking. We base the proportion of people affected by adverse events on the number of people available for follow-up, and not the number randomised. For all other outcomes, we also use complete-case data and do not attempt to impute missing values.

Reporting bias assessment

We generated funnel plots where 10 or more RCTs contributed to an outcome, as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* [89].

Synthesis methods

We provide a narrative summary of the included studies. We have grouped studies by comparison type and outcome to carry out syntheses.

Where appropriate, we pooled data from RCTs in meta-analyses. For dichotomous data, we used random-effects Mantel-Haenszel models to calculate the pooled RR (or RD) with a 95% CI, in accord with the standard methods of the Cochrane Tobacco Addiction Group for cessation studies. For continuous outcomes, we calculated mean differences or standardised mean differences (as appropriate for studies using different measures for the same construct), using the inverse variance approach (also with a 95% CI). We calculated confidence intervals using the Hartung-Knapp-Sidik-Jonkman method in analyses with at least three studies, and the heterogeneity was greater than zero. In analyses of two studies, or where the estimate of heterogeneity was zero, we used the Wald-type method.

We assessed the clinical and methodological diversity between studies to guide our decision about whether data should be pooled. We were also guided by the degree of statistical heterogeneity, assessed using the I^2 statistic [90], calculated using the DerSimonian and Laird estimator for dichotomous outcome analyses, and the Restricted Maximum Likelihood (REML) estimator for continuous outcome analyses. We considered a value greater than 50% as evidence of substantial heterogeneity. Where I^2 values exceeded 75%, we discussed whether it was appropriate to pool results, taking into account the direction of effects within the analysis (i.e. whether heterogeneity was indicative of a difference in the direction or the magnitude of the effect).

Where studies were not pooled, but we had numerical data, we still provided effect estimates for individual RCTs and generated forest plots. Where there was insufficient data to calculate effect estimates, we summarised the information available and presented this information in effect direction plots. This was also the case when data had been presented per type of AE, rather than for all types together.

Investigation of heterogeneity and subgroup analysis

We carried out the following subgrouping:

- For the cessation outcome of the EC versus NRT comparison, we included one study conducted on pregnant women in a separate subgroup as pregnancy affects nicotine metabolism, and thus its effectiveness as a smoking cessation intervention.
- For the cessation outcome of the EC versus NRT comparison, we split the studies by the type of NRT therapy provided in the control arm (combination NRT; single-form NRT; unclear), as there is evidence that combination NRT is more effective than single-form NRT for smoking cessation [91].
- For continuous outcomes, we subgrouped data based on whether absolute values or change scores were available.

We had planned to undertake subgroup analyses to investigate differences between studies, such as the following:

- Intensity of behavioural support used (as this could potentially influence our critical outcome: smoking cessation);
- Type of EC, e.g. cartridge; refillable; pod; disposable (as this could potentially influence all outcomes due to different delivery mechanisms);
- Instructions for EC use, e.g. study provision, length of provision, whether participants had a role in product choice (as this could potentially influence all outcomes, given variation in available devices and liquids);
- Type of participants (this could potentially influence all outcomes, depending on, e.g. pre-existing conditions, previous experience with EC).

However, there were too few studies in each subgroup to conduct these latter analyses. Should further studies become available in the future, we will follow this approach. In the absence of sufficient data for subgroup analyses on EC type, in the text we specify the type of nicotine EC when reporting pooled results for cessation.

Sensitivity analysis

We conducted sensitivity analyses to detect whether pooled results were sensitive to the removal of studies judged to be at high risk of bias overall, and to the removal of studies reporting funding by the tobacco and/or vaping industry. We did this for all outcomes.

Certainty of the evidence assessment

Following standard Cochrane methodology, we created summary of findings tables for our three main comparisons using [92]: nicotine EC versus NRT; nicotine EC versus non-nicotine EC; and nicotine EC versus behavioural support only/no support. We selected these comparisons a priori as being the most clinically relevant.

In the summary of findings tables, we present data on our primary outcomes (cessation at longest follow-up, at least six months from baseline, and adverse events and serious adverse events at one week or longer) for these main comparisons.

Following standard Cochrane methodology, we used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the certainty of the body of evidence for each outcome, and to draw conclusions about the certainty of evidence within the text of the review. GRADE assessments were carried out by JHB and NL.

Equity considerations

We did not plan to investigate health inequity in this review, as this is explored in a separate Cochrane review [93].

Consumer involvement

Panels (size range: five to 15 of people with diverse vaping and smoking experiences from different social backgrounds have reviewed the methods of this review and attended periodic

workshops to discuss the findings of review updates, how to disseminate these, outcomes measured, and any potential changes to review methods.

RESULTS

Description of studies

Results of the search

Our study selection process is illustrated in Figure 1. For this update, our bibliographic database searches identified 1902 non-duplicate records. We screened all records and retrieved the full-text papers of 102 potentially relevant articles. After screening and checking the full texts, we included nine new completed studies (Bonevski 2025 [94, 95, 96, 97]; Cioe 2025 [98, 99]; Courtney 2025 [100, 101, 102]; Cox 2022 [103, 104, 105, 106, 107]; NCT03277495 [108]; NCT03625986 [109, 110, 111, 112]; NCT05278065 [113]; Robinson 2025 [114, 115]; Walker 2023 [116, 117, 118, 119]), 43 new articles linked to studies already included, and seven new ongoing studies (see Supplementary material 5). Secondary study reports are linked to primary study papers in the reference section.

Figure 1. PRISMA study selection flow diagram for 2026 update

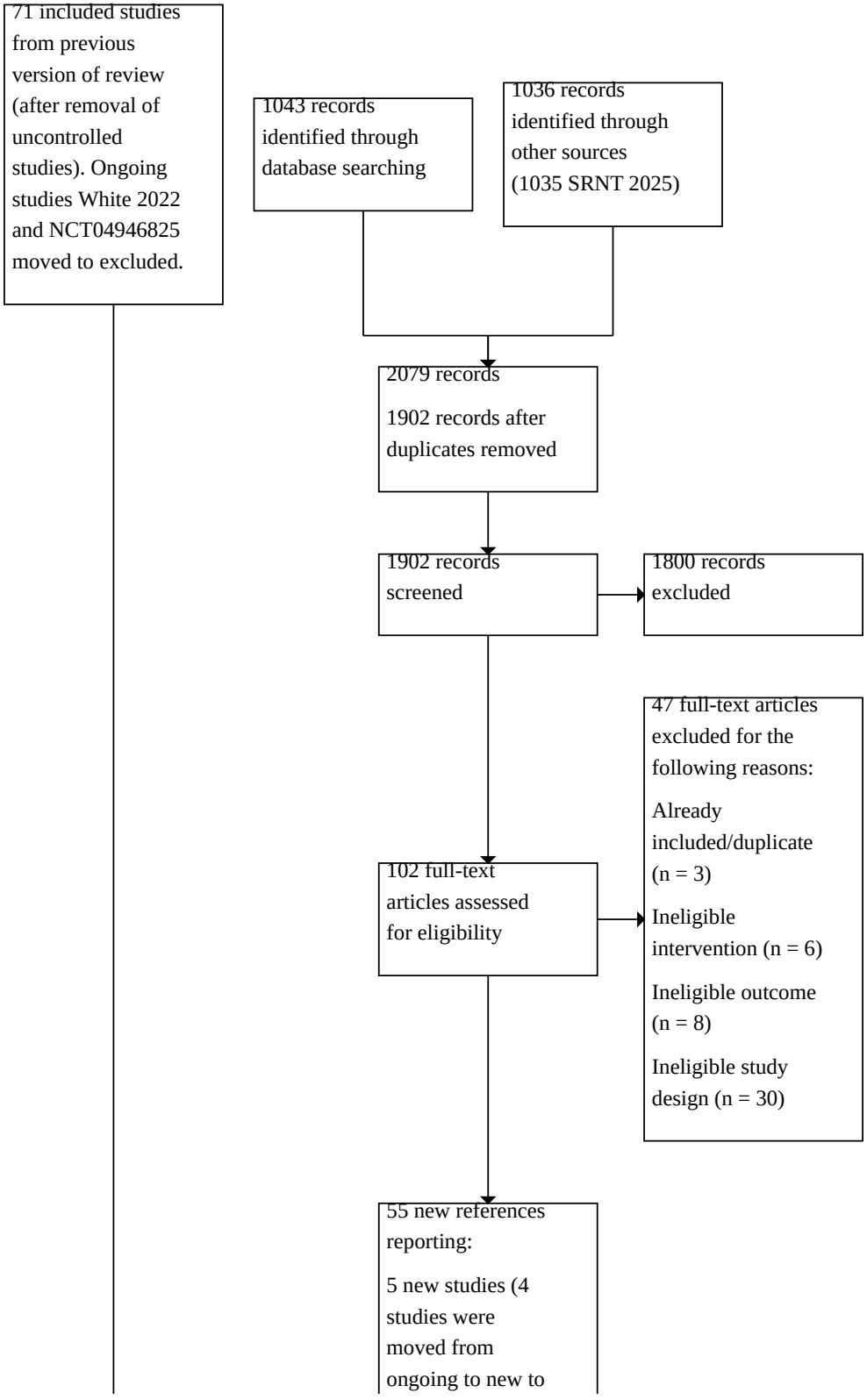
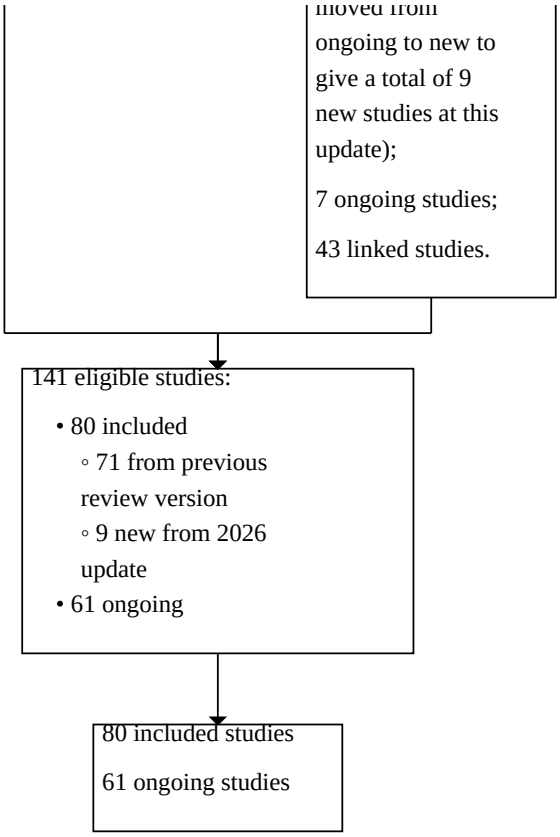


Figure 1. (Continued)



Included studies

In total, we included 80 studies. Key features of these included studies are summarised below and in Table 1. Further details on each included study can be found in the characteristics of included studies tables (Supplementary material 2). This update includes information on two new comparisons: nicotine EC vs cytisine (outcomes: smoking cessation, AEs, SAEs); and nicotine EC + cytisine vs cytisine (outcomes: smoking cessation, AEs, SAEs). This update includes information on four new outcomes: number of people using EC and no combustible tobacco; number of people using no combustible tobacco and no EC; number of people using both EC and combustible tobacco; and number of people using combustible tobacco and no EC. Data have been added to four existing comparisons: nicotine EC vs NRT (outcomes: cessation, continued EC use, AEs, SAEs); nicotine EC vs behavioural support only/no support (outcomes: cessation, AEs, SAEs, CO, NNAL, respiratory health); nicotine EC vs non-nicotine EC (outcomes: AEs, SAEs, CO, NNAL, respiratory and cardiac health (SBP)); and choice of EC flavour vs EC flavour assigned to match usual cigarette flavour (tobacco or menthol) (outcomes: AEs, SAEs, CO, cardiac health (heart rate, SBP)).

Participants

The 80 included studies represent 29,861 participants. Forty studies were conducted in the USA, 16 in the UK, six in Australia, five in Greece, three in Italy, two each in New Zealand and Canada, and one each in Belgium, Finland, the Netherlands, the Republic of Korea, Switzerland, and Turkey. All studies were conducted in adults who smoked. Twenty-three studies exclusively recruited participants who were not motivated to quit smoking; 29 studies exclusively recruited participants motivated or willing to quit; in five studies, participants had some motivation to quit; in two studies, participants had a limited interest in quitting; in two studies, participants were interested in reducing but not quitting; in one study, participants were willing to replace CC with EC; one study did not require participants to be motivated to quit, and motivation was not specified for the 17 other studies. Thirty-four studies recruited from specific population groups which included: thirteen studies that recruited participants based on a physical health condition (heart attack, cancer, HIV, periodontitis, awaiting surgery, smoking-related chronic disease, obesity); three studies that recruited participants with serious mental illness; three studies that recruited participants on treatment or having recently completed treatment for alcohol or other drug use; and three studies in dual users of EC and combustible cigarettes. One study recruited people accessing homeless centres or using supported temporary accommodation, and a further three recruited at-risk populations or those specifically within socially deprived areas. One study each recruited: people who self-identified as African-American; pregnant women; people who had recently made a failed attempt to quit smoking; people who had failed to quit with pharmacotherapy; people who found quitting difficult; people attending the emergency department; veterans; and veterans awaiting surgery.

Interventions and comparators

Three studies recruited dual users of combustible cigarettes and EC at baseline, and instructed them to continue using their own EC devices (Czoli 2019 [120]; Martinez 2021 [121, 122, 123, 124, 125, 126, 127]; Vickerman 2022 [128, 129, 130, 131]). One study recruited users of combustible cigarettes only and provided information on using EC, but did not provide them with EC (Elling 2023 [132, 133, 134]). The remaining studies all provided some form of nicotine EC.

In one study where nicotine EC was provided on their own, nicotine levels were judged to be so low as to be clinically comparable to non-nicotine EC (Lee 2019 [135, 136]); we include this study in non-nicotine EC comparisons. Thirteen studies compared nicotine EC with non-nicotine EC, 27 studies compared nicotine EC to behavioural support only or to no support, and 17 studies compared nicotine EC to NRT. Four studies compared high- versus low-nicotine EC devices (Caponnetto 2013* [137, 138, 139, 140, 141, 142, 143, 144]; Cobb 2021 [145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158]; Kanobe 2022* [159, 160, 161] Kimber 2021 [162]); four studies included comparisons based on flavours (Edmiston 2022* [163]; Higgins 2024 [164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174]; NCT03277495; Xu 2023* [175]); two studies directly compared device types (Kimber 2021; Yingst 2020 [176]); one study directly compared a free-based nicotine to a salt-based nicotine device (Russell 2021* [177]); and one compared higher versus lower wattage EC (NCT03113136 [178, 179, 180]). Results from these studies are reported by comparison in Synthesis of results. Further details on the intervention and comparator groups (where applicable) for each study can be found in the Supplementary material 2 table.

Where reported in the primary research publications, details of the devices tested can also be found in the characteristics of included studies tables (Supplementary material 2). Of the studies with sufficient data with which to judge, 27 used refillable devices, 20 used cartridge devices, two used both types, 14 used a pod device, three used disposable EC, two used standard research EC, one used high and low wattage EC, and one used a pre-filled tank EC. The remainder did not report device type.

Outcomes

Of the 80 included studies providing data for analyses:

- 34 reported data on abstinence at six months or longer;
- 35 reported data on adverse events (a further 18 studies provided data that did not contribute to meta-analyses);
- 48 reported data on serious adverse events;
- 28 reported data on carbon monoxide (a further nine studies provided data that did not contribute to meta-analyses);
- seven reported data on heart rate (a further four studies provided data that did not contribute to meta-analyses);
- nine reported data on blood pressure (a further five studies provided data that did not contribute to meta-analyses);
- three reported data on blood oxygen saturation;
- eight reported data on at least one known toxicant/carcinogen (a further three studies provided data that did not contribute to meta-analyses);
- 12 reported data on at least one measure of lung function (one further study provided data that did not contribute to meta-analyses);
- 10 reported data on study product use at six months or longer (one further study provided data that did not contribute to meta-analyses);
- 13 reported on one of our outcomes relating to EC and CC use (i.e. use of CC and EC, use of EC but not CC, use of CC but not EC, use of neither).

One study measured safety outcomes but did not report them in the text available at the time of writing; hence, this study currently does not contribute any data to this review (Skelton 2022 [181, 182, 183]).

Study types

All of our eighty studies were RCTs in accordance with our eligibility criteria, 34 of which contributed to cessation analyses. Seven studies used randomised cross-over designs.

Funding

Of the 75 studies that reported funding information, eight reported support from the tobacco or vaping industry, or that authors had received tobacco or vaping industry support outside the study being conducted, and 66 had no tobacco or EC industry funding or support. Below, we detail the industry funding from the eight studies that report tobacco or EC industry funding or support. Throughout the review, an asterisk (*) following the Study ID indicates studies that received tobacco or EC industry funding.

Caponnetto 2013* received funding from the Lega Italiana AntiFumo.

Caponnetto 2023* [184, 185, 186, 187] was funded by Philip Morris Product Société Anonyme.

Cravo 2016* [188, 189, 190, 191] was funded and supported by Fontem Ventures B.V. Imperial Brands plc (Imperial Tobacco plc) is the parent company of Fontem Ventures B.V., the manufacturer of the EC prototype used in their study.

Edmiston 2022* was funded by Altria Client Services LLC. Altria is the parent company of Philip Morris USA (producer of Marlboro cigarettes), John Middleton, Inc., U.S. Smokeless Tobacco Company, Inc., and Philip Morris Capital Corporation.

Kanobe 2022* was funded by RAI Services Company. The parent company is Reynolds American. Reynolds American manufacture and market a variety of tobacco products, including cigarettes (Newport, Camel, Pall Mall, Kent, Doral, Misty, Capri, and Natural American Spirit brands), EC (Vuse brand), and moist snuff (Grizzly and Kodiak brands).

Rose 2023* [192, 193, 194] was funded by the National Institute on Drug Abuse (NIDA). However, the lead author declared research support from Foundation for a Smoke-Free World (which has links to the tobacco industry), Philip Morris International, Altria, Embera Neuro Therapeutics, Inc., Otsuka Pharmaceutical, JUUL Labs, consulting with Revive Pharmaceuticals, and consulting and patent purchase agreements with Philip Morris International.

Russell 2021* was funded by the e-cigarette/alternative nicotine products industry.

Xu 2023* was funded by JUUL Labs, Inc.

Excluded studies

We list 37 studies excluded at the full-text stage across all updates of this review (this does not cover all studies ever excluded, but those that are most likely to require explanation), along with reasons for exclusion, in the characteristics of excluded studies table (Supplementary material 3). For this update specifically, the most common reason for exclusion was ineligible study design, but also included studies that did not include outcomes relevant to this review, studies with ineligible interventions and, finally, studies with duplicate references.

Two studies are listed as awaiting classification, as there is insufficient information to judge their eligibility (Supplementary material 4).

Risk of bias in included studies

Overall, we judged 12 studies to be at low risk of bias (Bullen 2013 [195, 196, 197, 198, 199, 200]; Cobb 2021; Courtney 2025; Eisenberg 2020 [201, 202, 203, 204, 205, 206, 207]; Hajek 2019 [208, 209, 210, 211, 212]; Hajek 2022 [213, 214, 215, 216, 217, 218]; Kerr 2020 [219, 220]; Lee 2018 [221, 222, 223, 224]; Lee 2019; Martinez 2021; Myers-Smith 2022 [225, 226]; Tuisku 2024 [227, 228]), 27 to be at unclear risk, and the remaining 41 at high risk of bias.

Details of the risk of bias judgements for each domain for each included study can be found in the characteristics of included studies tables (Supplementary material 2). Figure 2 and Figure 3 illustrate our judgements across included studies.

Figure 2. Risk of bias graph

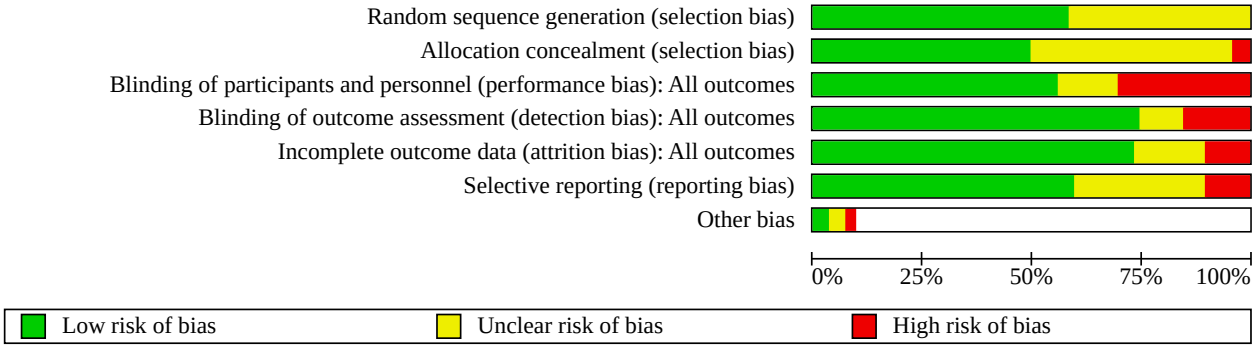


Figure 3. Risk of bias summary

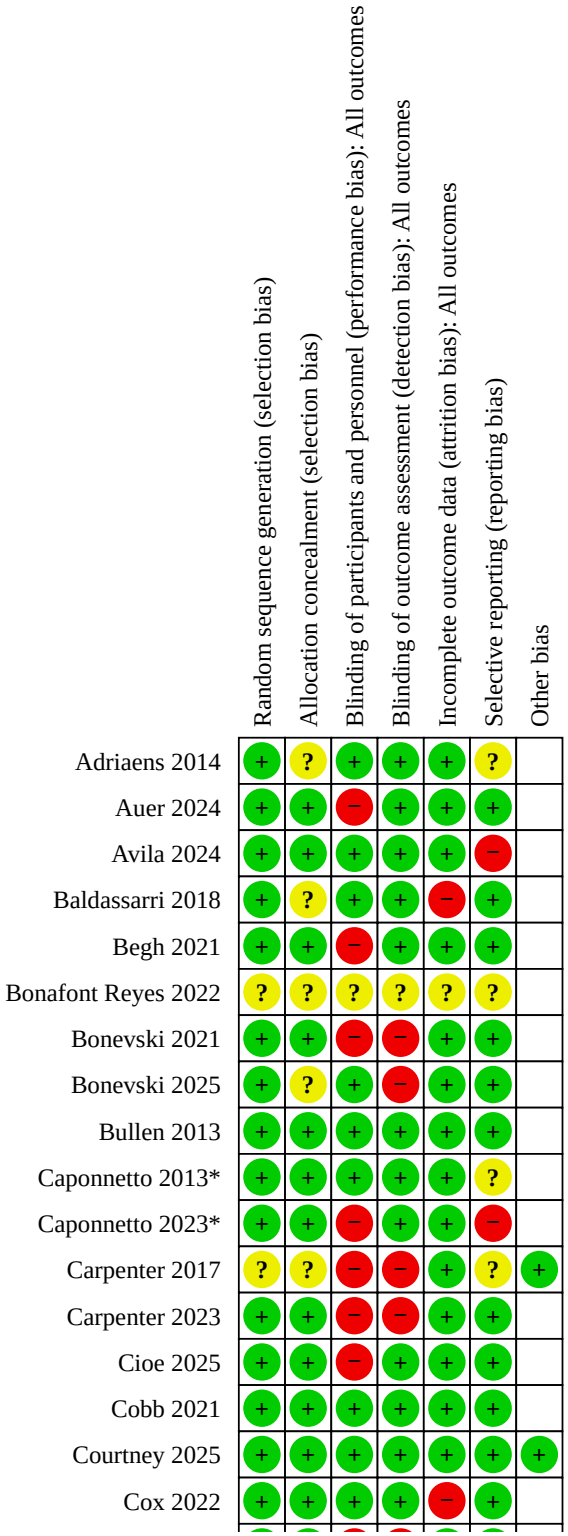


Figure 3. (Continued)

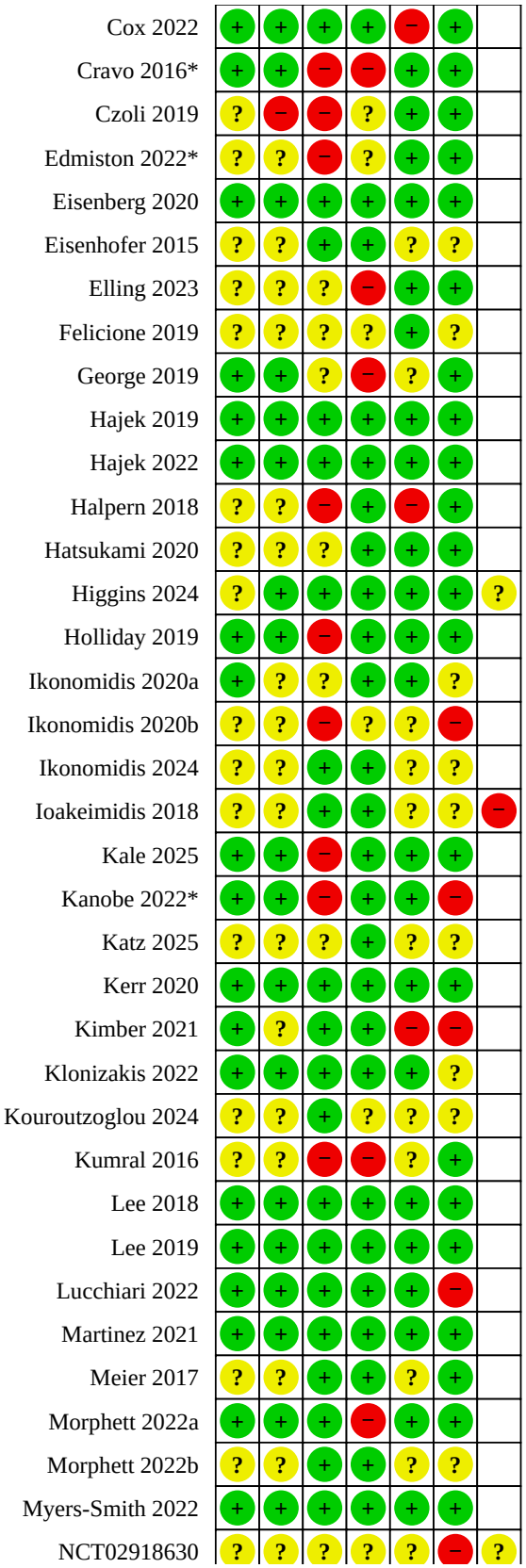
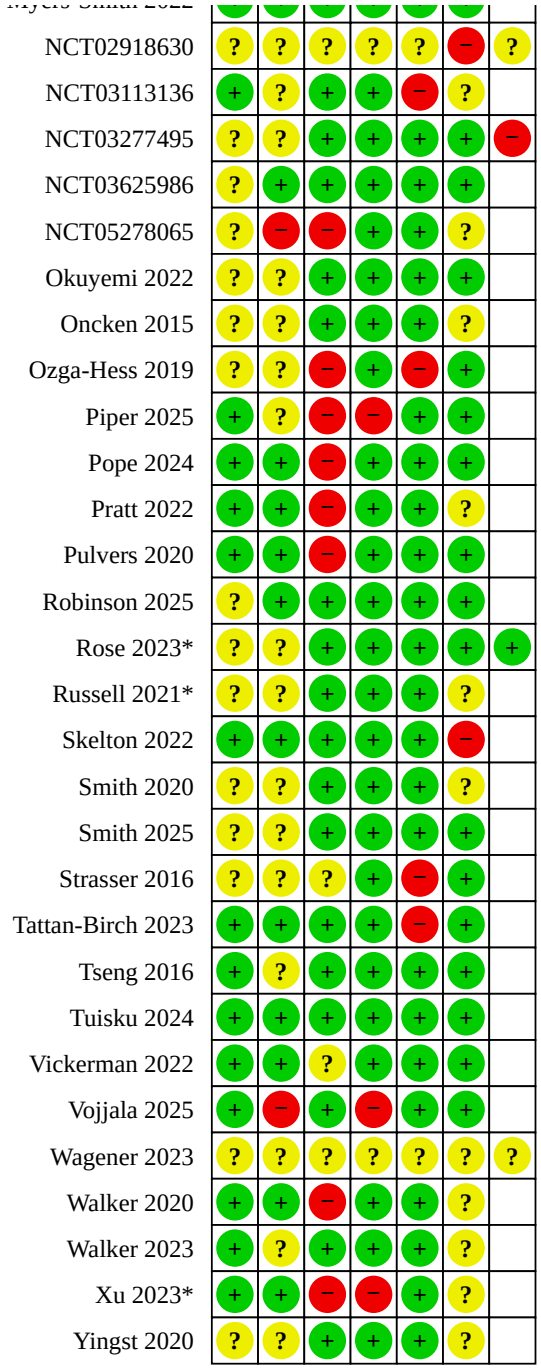


Figure 3. (Continued)



We judged no studies to be at high risk of selection bias for randomisation of allocation. We judged 47 studies to be at low risk, and 33 to be at unclear risk as there was insufficient information with which to judge. For allocation concealment, we rated three studies as being at high risk of bias, 40 at low risk, and 37 studies at unclear risk.

For performance bias, we rated 45 studies to be at low risk, 24 at high risk, and 11 at unclear risk. For detection bias, we rated 60 as low risk, 12 as high risk, and eight as unclear risk. In the high-risk studies, blinding was not used and different levels of support were provided; this alone, or in conjunction with the outcome measures being used (subjective rather than objective measures), meant that we thought there was a high risk of bias being introduced.

We judged most studies (59 out of 80) to be at low risk of attrition bias. We rated eight studies with substantial loss to follow-up as being at high risk of attrition bias. Thirteen studies did not provide sufficient data on which to judge, and hence we judged them to be at unclear risk.

Of the 80 studies, we considered 48 to be at low risk of reporting bias, as all prespecified or expected outcomes were reported. We rated eight as being at high risk, as data were not available as specified in the original protocols (note, in some cases these are recent studies, and judgement on these may change as more publications emerge). We judged 24 to be at unclear risk, due to insufficient information with which to make a judgement.

We considered Ioakeimidis 2018 [229] to be at high risk of other bias; data were from a conference poster and the associated abstract, and quit rates in the intervention arm differed between the two sources. We considered NCT03277495 to be at high risk of bias as the prespecified study design differed from the final study design and this change was not justified. We considered three further studies to be at unclear risk, and three studies to be at low risk in this domain.

Synthesis of results

Data on our outcomes of interest are summarised below and in our Summary of findings 1, Summary of findings 2, and Summary of findings 3. Forest plots are available through 'analysis' links; for some outcomes, benefit is plotted on the right; for others it is plotted on the left. This is due to direction of effect, e.g. an increase in cessation is a benefit, whereas an increase in a carcinogen is not. Axes are labelled accordingly.

Direct comparisons between nicotine EC and other pharmacotherapies

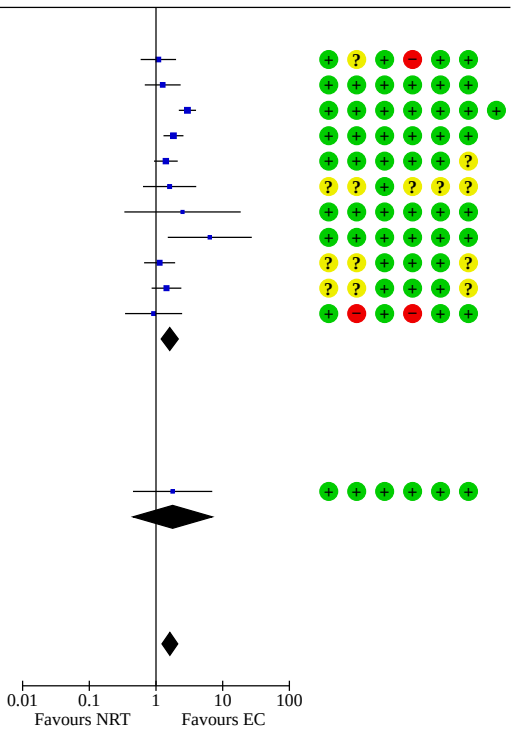
Comparisons reported here include nicotine EC versus NRT, nicotine EC versus varenicline, nicotine EC versus cytisine and EC versus combination therapy such as NRT plus bupropion, and non-nicotine EC plus varenicline.

Cessation

Pooled data from eleven studies (two cartridges, five refillable, one pod, one disposable, one with a mixture of refillable and pod devices, one not specified), six of which were rated as being at low risk of bias (Bullen 2013; Courtney 2025; Hajek 2019; Hajek 2022; Lee 2018; Myers-Smith 2022), three as unclear (Klonizakis 2022 [230, 231, 232, 233, 234]; Kouroutzoglou 2024 [235]; Russell 2021*) and two as high risk (Bonevski 2025; Vojjala 2025 [236, 237, 238, 239, 240, 241]), showed increased quit rates in people randomised to nicotine EC when compared with NRT (RR 1.61, 95% CI 1.23 to 2.12; I^2 = 55%; 4114 participants; Figure 4). The certainty of evidence is high and has not been downgraded. One study included in this analysis, Hajek 2022, was conducted in pregnant women. There was no evidence of a subgroup difference between this study and studies in participants not selected on the basis of pregnancy (P = 0.89, I^2 for subgroup differences = 0%). Follow-up time was based on the end of pregnancy, and our analysis included only those participants with follow-up of at least six months. We also subgrouped studies based on whether single-form or combination NRT was provided in the comparator arm. Four of the studies provided combination NRT, i.e. patch and another form (Bonevski 2025; Hajek 2019; Myers-Smith 2022; Vojjala 2025); five provided single-form NRT (Bullen 2013; Courtney 2025; Hajek 2022; Kouroutzoglou 2024; Lee 2018); and in two studies the NRT provided was unclear (Klonizakis 2022; Russell 2021*).

Figure 4. Analysis 1.1: EC vs NRT – Smoking cessation

Study or Subgroup	EC Events	EC Total	NRT Events	NRT Total	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Not selected on pregnancy						
Bonevski 2025	19	179	18	184	9.3%	1.09 [0.59 , 2.00]
Bullen 2013	21	289	17	295	9.2%	1.26 [0.68 , 2.34]
Courtney 2025	148	524	50	524	14.9%	2.96 [2.20 , 3.98]
Hajek 2019	79	438	44	446	14.0%	1.83 [1.30 , 2.58]
Klonizakis 2022	36	84	25	82	12.7%	1.41 [0.93 , 2.12]
Kouroutzoglou 2024	8	19	5	19	5.7%	1.60 [0.64 , 4.01]
Lee 2018	5	20	1	10	1.6%	2.50 [0.34 , 18.63]
Myers-Smith 2022	13	68	2	67	2.8%	6.40 [1.50 , 27.30]
Russell 2021*[a]	34	140	15	70	10.5%	1.13 [0.66 , 1.94]
Russell 2021*[b]	44	145	15	71	10.9%	1.44 [0.86 , 2.40]
Vojjala 2025	7	63	7	58	5.2%	0.92 [0.34 , 2.47]
Subtotal (HKSJ[c])		**1969**		**1826**	**96.9%**	**1.61 [1.20 , 2.16]**
Total events:	414		199			
Test for overall effect: T = 3.59, df = 10 (P = 0.005)						
Heterogeneity: Tau² (DL[d]) = 0.11; Chi² = 24.57, df = 10 (P = 0.006); I² = 59%						
1.1.2 Pregnant population						
Hajek 2022[e]	6	169	3	150	3.1%	1.78 [0.45 , 6.97]
Subtotal		**169**		**150**	**3.1%**	**1.78 [0.45 , 6.97]**
Total events:	6		3			
Test for overall effect: Z = 0.82 (P = 0.41)						
Heterogeneity: Not applicable						
Total (HKSJ[c])		**2138**		**1976**	**100.0%**	**1.61 [1.23 , 2.12]**
Total events:	420		202			
Test for overall effect: T = 3.88, df = 11 (P = 0.003)						
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.89), I² = 0%						
Heterogeneity: Tau² (DL[d]) = 0.10; Chi² = 24.57, df = 11 (P = 0.01); I² = 55%						



Footnotes

[a]FBNPs EC arm; control group split to avoid double-counting
[b]NSP EC arm; control group split to avoid double-counting
[c]CI calculated by Hartung-Knapp-Sidik-Jonkman (HKSJ) method.
[d]Tau² calculated by DerSimonian and Laird method.
[e]This is a subset of data from participants followed up for 6 months or longer

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

Subgroup and sensitivity analyses

There was little evidence of subgroup differences (P = 0.11, I^2 for subgroup differences = 55.1%) when all three groups were included and compared in the analysis, and no evidence of a subgroup difference (P = 0.52, I^2 for subgroup differences = 0%) when only the combination and single-form groups were compared. Results were not sensitive to the exclusion of the one study that received industry funding (Russell 2021*) or the two studies at high risk of bias; for each sensitivity analysis, the point estimates were 1.72 and 1.74 respectively, and the CIs remained consistent with those from the main analysis.

Narrative summary of unpooled studies

One study, Ioakeimidis 2018, available as a conference presentation only and considered at high risk of bias due to inconsistencies in the data reported, favoured varenicline for quitting compared with nicotine EC (cartridge) (RR 0.31, 95% CI 0.11 to 0.82; 54 participants; Analysis 2.1). In another study, Tuisku 2024 (refillable; low risk of bias), more people quit when randomised to receive a combination of non-nicotine EC plus varenicline compared with nicotine EC (RR 0.73, 95% CI 0.53 to 1.01; 305 participants; Analysis 3.1), though the CI included the potential for no difference. Ioakeimidis 2018 and Tuisku 2024 were not pooled as, in the latter, a non-nicotine EC was provided alongside varenicline, and evidence suggests non-nicotine EC is more effective than no treatment.

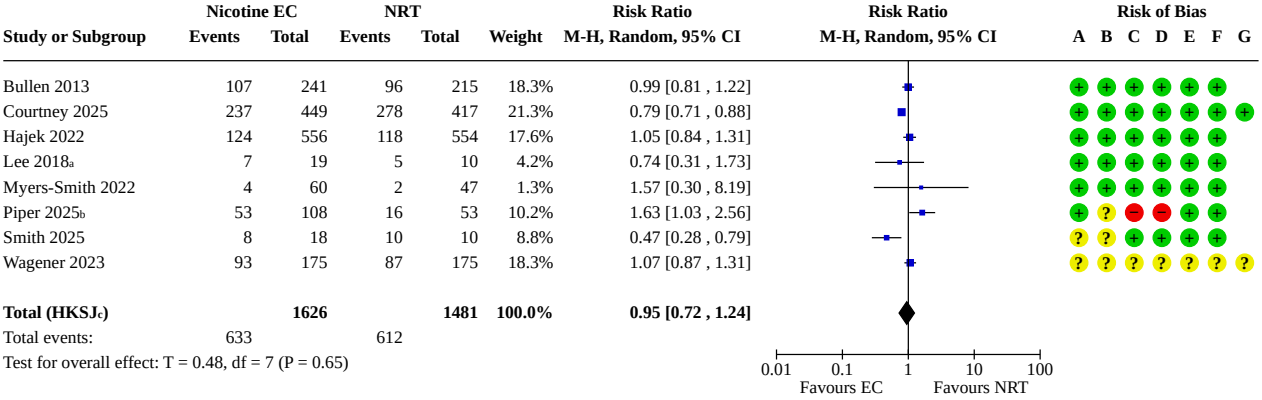
One study, Walker 2023 (pod; unclear risk of bias) investigated the effectiveness of nicotine EC versus cytisine and showed increased quit rates in people randomised to use nicotine EC (RR 1.56, 95% CI 1.06 to 2.30; 508 participants; Analysis 4.1).

One study, Kouroutzoglou 2024 (device type not specified; unclear risk of bias), available as a conference presentation only and considered at unclear risk of bias, did not find a difference in quit rates between nicotine EC and combination NRT plus bupropion (RR 0.89, 95% CI 0.44 to 1.81; 38 participants; Analysis 5.1).

Adverse events

Pooled data from eight studies (five considered as being at low risk of bias (Bullen 2013; Courtney 2025; Hajek 2022; Lee 2018; Myers-Smith 2022), two at unclear risk (Smith 2025 [242, 243, 244]; Wagener 2023 [245, 246]), and one at high risk (Piper 2025 [247, 248, 249, 250, 251, 252, 253]) showed that there is probably no difference in the number of participants reporting adverse events (AEs) between nicotine EC and NRT arms (RR 0.95, 95% CI 0.72 to 1.24; I^2 = 72%; 3107 participants; Figure 5).

Figure 5. Analysis 1.3: EC vs NRT - Adverse events



Heterogeneity: Tau² (DLd) = 0.04; Chi² = 24.82, df = 7 (P = 0.0008); I² = 72%

Footnotes

aData at 4 weeks post-operation; time from baseline not defined and likely to differ between participants

bIntervention arm contains data from EC + placebo patch and EC + no patch study arms

cCI calculated by Hartung-Knapp-Sidik-Jonkman (HKSJ) method.

dTau² calculated by DerSimonian and Laird method.

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

Sensitivity analyses

Removing the one study at high risk of bias (Piper 2025) did not change the interpretation of the effect (Table 2). However, the certainty of evidence for this outcome was deemed to be low. We downgraded one level due to imprecision, as the CIs were consistent with both benefit and harm and one level due to inconsistency, as a result of the substantial statistical heterogeneity detected. None of the studies contributing data to this analysis received funding from the vaping or tobacco industries.

Narrative summary of unpooled studies

Hajek 2019 (low risk of bias) and Bonafont Reyes 2022 [254] (unclear risk of bias) did not contribute data to this meta-analysis due to the way in which events were recorded. In Hajek 2019's prespecified adverse reactions of interest, nausea was more frequent in the NRT group, throat/mouth irritation was more frequent in the nicotine EC group, and there was little difference in other reactions. Bonafont Reyes 2022 recruited participants with chronic obstructive pulmonary disease (COPD) and reported "a trend towards decreased dyspnoea and COPD symptoms ... in the EC arm compared to the NRT arm", but did not provide further detail. See Supplementary material 11 for more detail.

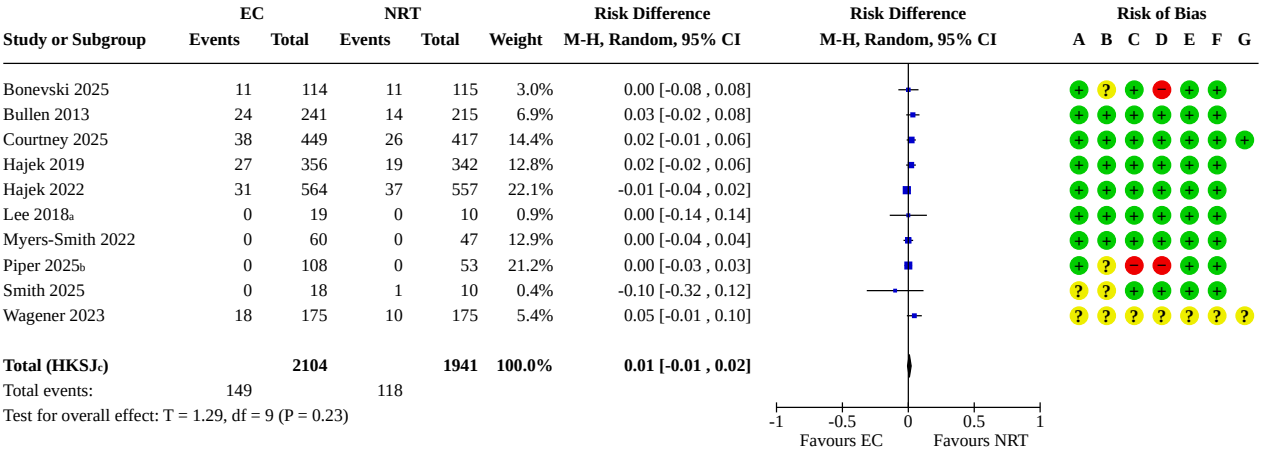
Neither study comparing EC with varenicline provided data in a way that could be entered into a meta-analysis. In Ioakeimidis 2018 (high risk of bias), reports of sleep disorders were evenly distributed between groups, and nausea was more common in the varenicline arm than in the nicotine EC arm (see Supplementary material 11 for more detail). Tuisku 2024 (low risk of bias) reported more AEs leading to discontinuation of study treatment in the non-nicotine EC plus varenicline arm (27, 17.6%) compared with the EC arm (15, 9.9%).

In Walker 2023 (unclear risk of bias), there was no clear evidence of a difference in the number of participants reporting AEs in the nicotine EC arm versus the cytisine arm, with CI encompassing the possibility of higher rates of AEs in the nicotine EC arm or the cytisine arm (RR 1.01, 95% CI 0.84 to 1.20; 508 participants; Analysis 4.2).

Serious adverse events

Ten studies comparing nicotine EC with NRT provided data on serious adverse events (SAEs). Six were deemed to be at low risk of bias (Bullen 2013; Courtney 2025 Hajek 2019; Hajek 2022; Lee 2018; Myers-Smith 2022), two at unclear risk (Smith 2025; Wagener 2023), and two at high risk (Bonevski 2021 [255, 256, 257]; Piper 2025). In some studies, no events occurred in either arm. Pooled results showed no clear evidence of a difference in the risk of SAEs between the nicotine EC arms and the NRT arms. There is moderate-certainty evidence for this outcome, downgraded one level due to imprecision, as there were fewer than 300 events (RD 0.01, 95% CI −0.01 to 0.02; I^2 = 0%; 4045 participants; Figure 6).

Figure 6. Analysis 1.4: EC vs NRT – Serious adverse events



Heterogeneity: Tau² (DLd) = 0.00; Chi² = 7.70, df = 9 (P = 0.56); I² = 0%

Footnotes

aData at 4 weeks post-operation; time from baseline not defined and likely to differ between participants

bIntervention arm contains data from EC + placebo patch and EC + no patch study arms

cCI calculated by Hartung-Knapp-Sidik-Jonkman (HKSJ) method.

dTau² calculated by DerSimonian and Laird method.

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

Sensitivity analyses

Removing the two studies deemed to be at high risk of bias did not change the interpretation of the effect (Table 2). None of the studies contributing data to this analysis received funding from the vaping or tobacco industries. In Hajek 2022 (conducted in pregnant women), the authors reported no evidence of a difference in birth outcomes overall. However, low birthweight (< 2500 g) was less frequent in the EC than the NRT arm (14.8% versus 9.6%; RR 0.65, 95% CI 0.47 to 0.90).

Narrative summary of unpooled studies

No SAEs occurred in Ioakeimidis 2018 (nicotine EC vs. varenicline; high risk of bias; Analysis 2.2). In Tuisku 2024 (low risk of bias), two people reported SAEs in the nicotine EC arm and none in the non-nicotine EC plus varenicline arm (RD 0.01, 95% CI -0.01 to 0.04; 305 participants; Analysis 3.2).

In Walker 2023 (unclear risk of bias), eight participants reported SAEs in each study arm, with no clear evidence of a difference in risk between nicotine EC and cytisine (RD 0.01, 95% CI -0.02 to 0.04; 508 participants; Analysis 4.3).

Carbon monoxide (CO)

Pooled data from five studies (Hatsukami 2020 [258, 259]; Kerr 2020; Klonizakis 2022; Lee 2018; Smith 2025), none of which received tobacco/vaping industry funding and none of which were considered as being at high risk of bias, compared nicotine EC with NRT. CO levels (in ppm) decreased more in those randomised to nicotine EC; however, the CIs incorporated the possibility of no meaningful between-group difference (MD −1.98, 95% CI −3.78 to −0.18; I^2 = 0%; 385 participants; Analysis 1.5). A sixth, small study (Eisenhofer 2015 [260]; n = 11; unclear risk of bias) was reported as a conference abstract and hence had limited data available. At three weeks, this study showed that both EC and NRT groups had "significantly reduced" CO, but between-group differences were not reported.

Heart rate, blood pressure, and oxygen saturation

Pooled data from two studies comparing nicotine EC with NRT (166 participants; one study judged to be at unclear risk of bias (Hatsukami 2020; cig-a-like) and one at low risk (Kerr 2020), neither in receipt of vaping/tobacco industry funding), showed no clear evidence of a clinically meaningful difference in heart rate (MD 0.53, 95% CI −1.76 to 2.83; I^2 = 0%; 166 participants; Analysis 1.6), systolic blood pressure (MD −1.62, 95% CI −3.59 to 0.36; I^2 = 0%; 166 participants; Analysis 1.7), or blood oxygen saturation (MD −0.14, 95% CI −0.59 to 0.30; I^2 = 0%; 165 participants; Analysis 1.8), although CIs were wide.

Toxicants

Only Hatsukami 2020 (unclear risk of bias, no tobacco/vaping industry funding, n = 111) contributed data for these outcomes. For 3-HPMA, 2-HPMA, and HMPMA, point estimates favoured EC but CIs included no difference (Analysis 1.10; Analysis 1.11; Analysis 1.12). There was no evidence of a difference for NNAL (nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1- butanol) but CIs were again wide (Analysis 1.9). For PheT, CEMA, and AAMA (Analysis 1.13; Analysis 1.14; Analysis 1.15), point estimates favoured NRT but CIs included no difference.

Lung function

Lee 2018 and Kerr 2020 (both low risk of bias; no tobacco/vaping industry funding, comparison with NRT) measured change in FEV1 (forced expiratory volume) and FEV1/FVC (forced vital capacity) (both low risk of bias; n = 81). High statistical heterogeneity (I^2 = 89%) precluded pooling for FEV1 (Analysis 1.16). The point estimate for Lee 2018 favoured EC and for Kerr 2020 favoured NRT; for Kerr 2020, the CIs included no difference. There was no evidence of a difference for FEV1/FVC, but there was moderate unexplained statistical heterogeneity and, again, CIs were wide (MD 10.15, 95% CI −24.36 to 44.67; I^2 = 51%; 81 participants; Analysis 1.17). For PEF (peak expiratory flow), only one study contributed to this analysis (Kerr 2020, n = 55). The point estimate favoured NRT but CIs were wide and included no difference (MD -3.00, 95% CI -27.09 to 21.09; Analysis 1.18).

Study product use

Five studies (none at high risk of bias; one, Russell 2021*, with vaping industry funding) reported study product use at six months or longer, but statistical heterogeneity precluded pooling (I^2 = 95%). Whereas Russell 2021* (unclear risk of bias) and Lee 2018 (cig-a-like; low risk of bias) found no difference between the EC and NRT arms, in the other three studies, people in the EC arm were more likely to continue to use the study product they had been allocated than those in the NRT arm (Analysis 1.19).

Long-term nicotine EC and combustible cigarette use

Five studies comparing nicotine EC to NRT (none industry-funded, one at high risk of bias, remainder at low risk of bias) reported at least one of these outcomes (as seen in Analysis 1.20; Analysis 1.21; Analysis 1.22; Analysis 1.23). Use of EC without combustible tobacco was higher in those randomised to EC arms (RR 4.40, 95% CI 1.27 to 15.28; I^2 = 78%; 2776 participants; Analysis 1.20); statistical heterogeneity was high but driven by magnitude rather than direction of effect. Abstinence from both nicotine EC and combustible tobacco was lower in EC arms (RR 0.49, 95% CI 0.26 to 0.91; I^2 = 31%; 2776 participants; Analysis 1.21). Three of the four studies (all low risk of bias) reporting on concurrent use of EC and combustible tobacco found higher rates in the EC arm; the fourth found higher rates in the NRT arm. Statistical heterogeneity precluded pooling (Analysis 1.22). The four studies reporting on combustible tobacco use with no EC use found lower rates in the EC compared to NRT arms (RR 0.76, 95% CI 0.58 to 1.01; I^2 = 83%; 4 studies, 2543 participants; Analysis 1.23), but CI incorporated the possibility of no effect and statistical heterogeneity was high (driven by magnitude rather than direction of effect).

No other studies comparing nicotine EC with pharmacotherapies have reported these outcomes.

Nicotine EC versus other tobacco/nicotine products used for stopping combustible tobacco use

Nicotine EC vs heated tobacco

Two studies (Caponnetto 2023*: n = 220; tobacco/vaping industry-funded; Ikonomidis 2024 [261, 262]: n = 100), compared nicotine EC with heated tobacco. We considered Caponnetto 2023* to be at high risk of bias due to a lack of blinding alongside strong participant product preferences; Ikonomidis 2024 was at unclear risk. Caponnetto 2023* reported on AEs, SAEs, CO, and VO_2 max as a measure of lung function, heart rate, and blood pressure at 12 weeks follow-up. Ikonomidis 2024 reported CO levels at one month. The effect estimate demonstrated no clear evidence of a difference in AEs between the nicotine EC and heated tobacco group (RR 0.86, 95% CI 0.68 to 1.10; 220 participants; Analysis 6.1). There were no SAEs reported in either arm, resulting in a risk difference (RD) of 0.00 (95% CI -0.02 to 0.02; 220 participants; Analysis 6.2). There was no clear evidence of a between-group difference in CO levels (MD 1.00, 95% CI −1.04 to 3.03; I^2 = 6%; 2 studies, 267 participants; Analysis 6.3). When Caponnetto 2023* was removed in a sensitivity analysis, the direction of the effect estimate changed (MD -20); however, the interpretation of the CI remained the same (95% CI -3.23 to 2.83). There was also no clear between-group difference in VO_2 max (MD 6.20, 95% CI -2.01 to 14.41; 211 participants; Analysis 6.4). The following was reported in Caponnetto 2023* on heart rate and blood pressure, and is reported in Supplementary material 13 and Supplementary material 14: “No significant changes in the mean resting heart rate, blood pressure, and BMI during product use were observed between and within study groups.”

Nicotine EC vs oral nicotine pouches

One study (Avila 2024 [263, 264, 265]; n = 26; high risk of bias) compared nicotine EC with oral nicotine pouches (ONPs). This study, at high risk of bias because of potential selective reporting as urine and blood samples were not analysed, reported on SAEs and CO. No SAEs were reported in either study arm (RD 0.00, 95% CI -0.14 to 0.14; 26 participants; Analysis 7.1), and reduction in CO was greater in the EC arm than in the ONP arm, though the CI included the potential for greater reductions in CO with nicotine pouches (MD -12.44, 95% CI -28.82 to 3.94; 26 participants; Analysis 7.2). Avila 2024 reported participants in the ONP arm were more likely than those in the EC arm to report cough (ONP: 5/12; EC: 3/14) and shortness of breath (ONP: 3/12; EC: 1/14), though the frequency of cough and shortness of breath decreased and was similar between arms by week four (Supplementary material 11).

Nicotine EC versus non-nicotine EC, behavioural support or no support

Of note, for the nicotine EC versus behavioural/no support comparison, all contributing studies were deemed as being at high risk of performance bias (and thus high risk of bias overall), as it is impossible to blind behavioural interventions.

Cessation

Versus non-nicotine

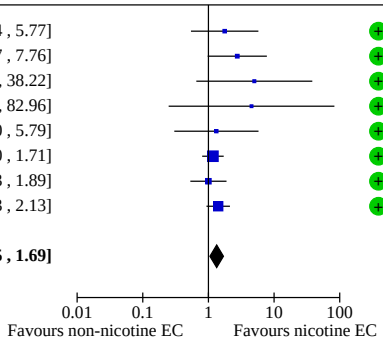
At six months or longer, quit rates were higher in nicotine EC groups than in comparator groups. Compared to EC without nicotine (placebo EC), pooled results showed nicotine EC probably produced higher quit rates (RR 1.34, 95% CI 1.05 to 1.69; I^2 = 0%; 1918 participants; Figure 7; five studies of cartridge and two studies of refillable devices). There is moderate-certainty evidence that nicotine EC probably increases quit rates compared to non-nicotine EC. The certainty has been downgraded one level due to imprecision, as there are fewer than 300 events overall. It has not been downgraded for risk of bias: removing the one study considered at high risk of bias increased the direction of the effect in favour of nicotine EC. The interpretation of the effect remained the same when we removed the one study at high risk of bias (Lucchiari 2022 [266, 267, 268, 269, 270, 271, 272]) and when we removed the one study with tobacco/vaping industry funding (Caponnetto 2013*).

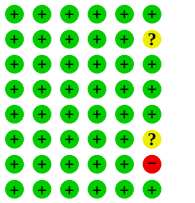
Figure 7. Analysis 8.1: Nicotine EC vs non-nicotine EC – Smoking cessation

Study or Subgroup	Nicotine EC Events	Nicotine EC Total	Non-nicotine EC Events	Non-nicotine EC Total	Weight	Risk Ratio M-H, Random, 95% CI
Bullen 2013	21	289	3	73	4.0%	1.77 [0.54 , 5.77]
Caponnetto 2013*	22	200	4	100	5.2%	2.75 [0.97 , 7.76]
Cobb 2021[a]	10	130	1	65	1.4%	5.00 [0.65 , 38.22]
Cobb 2021[b]	4	130	0	65	0.7%	4.53 [0.25 , 82.96]
Eisenberg 2020	4	128	3	127	2.6%	1.32 [0.30 , 5.79]
Klonizakis 2022	36	84	30	82	39.3%	1.17 [0.80 , 1.71]
Lucchiari 2022	15	70	15	70	13.9%	1.00 [0.53 , 1.89]
Tuisku 2024	42	152	30	153	33.0%	1.41 [0.93 , 2.13]
Total (Wald[c])		**1183**		**735**	**100.0%**	**1.34 [1.05 , 1.69]**
Total events:	154		86			

Test for overall effect: Z = 2.40 (P = 0.02)

Heterogeneity: Tau² (DL[d]) = 0.00; Chi² = 6.04, df = 7 (P = 0.54); I² = 0%





Footnotes

[a]36 mg/mL arm; control group split to avoid double-counting
[b]8 mg/mL arm; control group split to avoid double-counting
[c]CI calculated by Wald-type method.
[d]Tau² calculated by DerSimonian and Laird method.

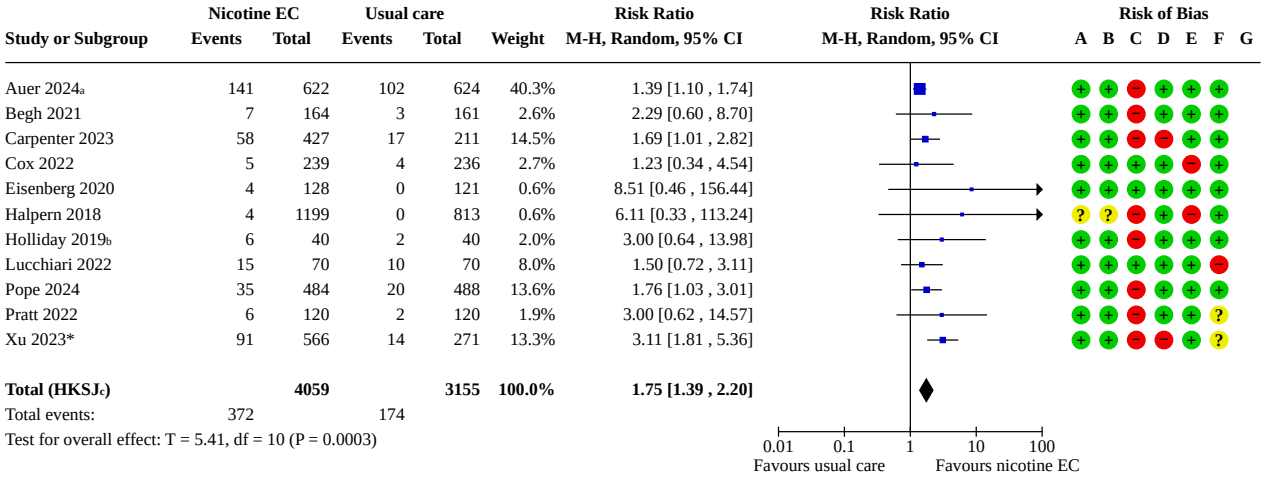
Risk of bias legend

(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

Versus behavioural support or no support

The effect may be more pronounced when comparing nicotine EC to behavioural support only or to no support (RR 1.75, 95% CI 1.39 to 2.20; I^2 = 13%; 7214 participants; Figure 8; 11 studies (five refillable, three cartridges, three pods)). As noted above, as this involved unblinded comparisons with unequal levels of support, we judged all data contributing to this outcome to be at high risk of bias and, hence, the certainty of the evidence was low, downgraded two levels due to risk of bias. One of the studies contributing data to this comparison reported tobacco/vaping industry funding (Xu 2023*). The removal of this study in a sensitivity analysis did not change the interpretation of the effect (Table 2).

Figure 8. Analysis 9.1: EC vs behavioural support only/no support – smoking cessation



Heterogeneity: Tau² (DLd) = 0.02; Chi² = 11.45, df = 10 (P = 0.32); I² = 13%

Footnotes

aAs NRT was not provided by the study, we classed this comparator arm as "behavioural support only."

bAlthough participants were given a choice of nicotine concentration including 0 mg, none of the participants chose the non-nicotine e-liquid

cCI calculated by Hartung-Knapp-Sidik-Jonkman (HKSJ) method.

dTau² calculated by DerSimonian and Laird method.

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

Pulvers 2020 [273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286] (pod device; high risk of bias) measured cessation at six months in the intervention group only, using self-report. As they did not measure cessation at six months in the comparator group, we could not include these data in our meta-analysis.

Adverse events

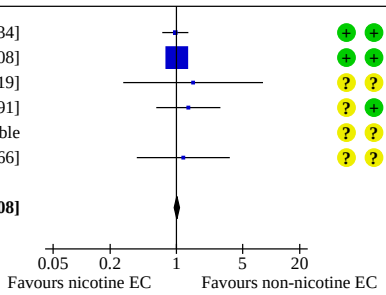
Versus non-nicotine

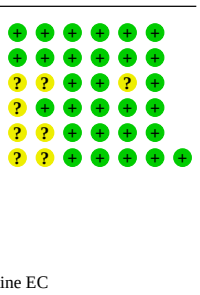
Pooled data from six studies (none at high risk of bias, one reporting tobacco/vaping industry funding) showed that there is probably no difference in the number of participants experiencing adverse events when comparing nicotine EC to non-nicotine EC (RR 1.01, 95% CI 0.95 to 1.08; I^2 = 0%; 909 participants; Figure 9); this is moderate-certainty evidence, downgraded one level due to imprecision (as the CI encompasses both harm and no difference). Data from Robinson 2025 (unclear risk of bias) could only be added using generic inverse variance methods and, hence, we present this in a separate analysis (Analysis 8.19). This resulted in no difference in the RD and 95% CI, and thus did not alter the interpretation of the result. Removing the one study linked to industry funding from the main analysis also had no effect on the interpretation of the result (Table 2).

Figure 9. Analysis 8.2: Nicotine EC vs non-nicotine EC – Adverse events

Study or Subgroup	Nicotine EC Events	Nicotine EC Total	Non-nicotine EC Events	Non-nicotine EC Total	Weight	Risk Ratio M-H, Random, 95% CI
Bullen 2013	107	241	26	57	4.1%	0.97 [0.71 , 1.34]
Eisenberg 2020	120	128	118	127	94.8%	1.01 [0.94 , 1.08]
Meier 2017	3	24	2	24	0.1%	1.50 [0.27 , 8.19]
NCT03625986	11	35	8	34	0.7%	1.34 [0.61 , 2.91]
Okuyemi 2022	0	109	0	106		Not estimable
Rose 2023*[a]	4	11	4	13	0.3%	1.18 [0.38 , 3.66]
Total (Wald[b])		**548**		**361**	**100.0%**	**1.01 [0.95 , 1.08]**
Total events:	245		158			

Test for overall effect: Z = 0.32 (P = 0.75)





Heterogeneity: Tau² (DL[c]) = 0.00; Chi² = 1.02, df = 4 (P = 0.91); I² = 0%

Footnotes

[a]All participants receiving placebo patch

[b]CI calculated by Wald-type method.

[c]Tau² calculated by DerSimonian and Laird method.

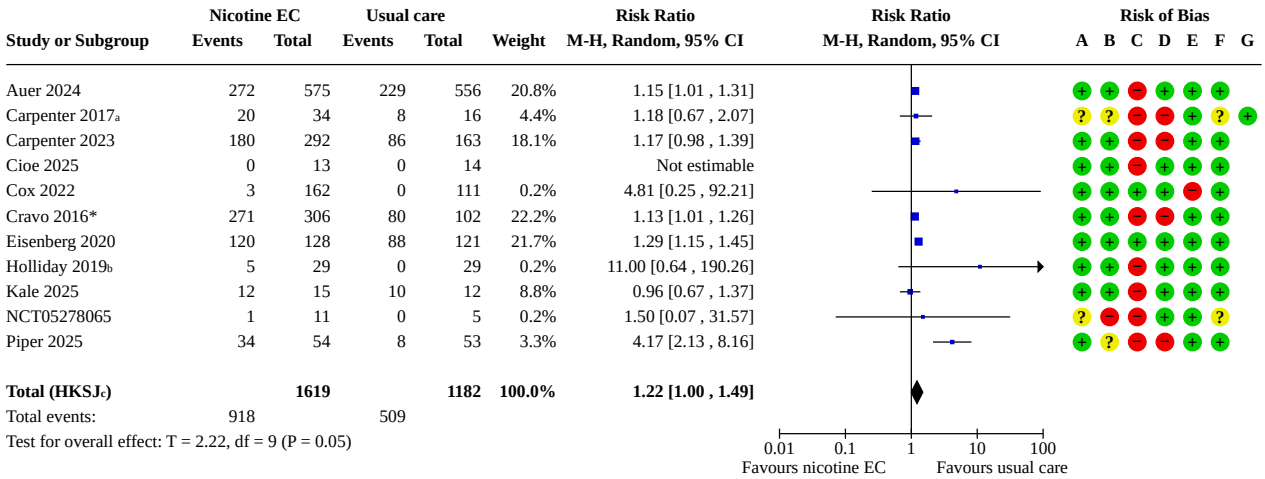
Risk of bias legend

(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

Versus behavioural support only or no support

When comparing nicotine EC to behavioural support only or to no support, evidence suggests more people in the groups randomised to nicotine EC may experience adverse events (RR 1.22, 95% CI 1.00 to 1.49; I^2 = 58%; 2801 participants; Figure 10). This was judged to be very low-certainty evidence downgraded two levels due to risk of bias and imprecision. Interpretation of the outcome was not sensitive to the inclusion of the one study with tobacco/vaping industry support (Cravo 2016*).

Figure 10. Analysis 9.2: EC vs behavioural support only/no support – adverse events



Heterogeneity: Tau² (DLd) = 0.02; Chi² = 21.65, df = 9 (P = 0.01); I² = 58%

Footnotes

aa24 mg EC arm included here; 16 mg data reported elsewhere

bParticipants offered choice of nicotine or no-nicotine EC; all chose nicotine-containing EC

cCI calculated by Hartung-Knapp-Sidik-Jonkman (HKSJ) method.

dTau² calculated by DerSimonian and Laird method.

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

Narrative summary of unpooled studies

A further 12 RCTs provided AE or related data for this comparison, but could not be included in the meta-analysis due to the way in which data were presented (see Supplementary material 11). In the studies comparing nicotine EC to non-nicotine EC, two found similar event rates across arms (Caponnetto 2013*, unclear risk of bias; Tuisku 2024, low risk of bias), and two reported more events in the nicotine EC arms (Felicione 2019 [287]; Tseng 2016 [288, 289, 290, 291]; unclear risk of bias). In a further study comparing nicotine to non-nicotine EC, events were reported by type, with an increase in some seen in the nicotine group and an increase in others seen in the non-nicotine group (Lucchiari 2022; high risk of bias). In the seven studies comparing nicotine EC to behavioural support only or traditional cigarettes, Kumral 2016 [292] (high risk of bias) found an increase in sinonasal symptoms in the group receiving nicotine EC compared to behavioural support only, and Ozga-Hess 2019 [293] (high risk of bias) found that throat irritation, cough, and dry mouth increased in the e-cigarette group relative to the traditional cigarette group. By contrast, Pulvers 2020 (high risk of bias) found a reduction in respiratory symptoms in the EC group compared to the traditional cigarette group, and Pope 2024 [294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308] (high risk of bias) found no clear difference in the number of participants reporting dry cough and throat and mouth irritation between the EC arm and the referral information arm. Begh 2021 [309, 310, 311, 312, 313] (high risk of bias) found an increase in throat irritation, palpitations, and dizziness in the EC group, but decreases in cough, headache, nausea, dry mouth, shortness of breath, and stomach pain. Edmiston 2022* (high risk of bias) did not break down AEs by group but reported that three participants experienced a non-serious AE definitely related to the study product. Pratt 2022 [314, 315, 316, 317, 318, 319, 320] (high risk of bias) reported no statistically significant between-group differences in AEs.

Serious adverse events

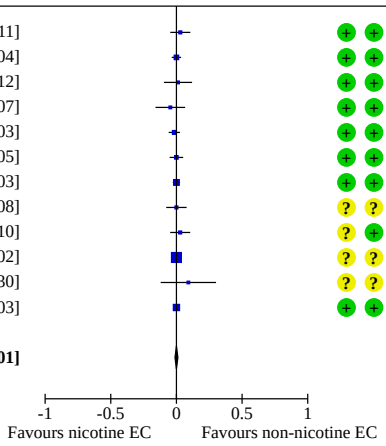
Versus non-nicotine EC

Twelve studies compared nicotine EC with non-nicotine EC and reported data on SAEs; in five of these no events occurred. The pooled analysis of eleven of the studies (four low risk of bias, five unclear, two high) found no clear evidence of a difference between groups (RD 0.00, 95% CI −0.01 to 0.01; I^2 = 0%; 1786 participants; Figure 11). The evidence was of low certainty; this was downgraded two levels due to imprecision, as there were fewer than 100 events overall. Data from Robinson 2025 (unclear risk of bias) could only be included using generic inverse variance methods and, hence, is represented in a second analysis, which resulted in no difference in the RD and 95% CI, and thus the interpretation of the result (Analysis 8.20). Two of the studies had links to industry funding (Caponnetto 2013*; Rose 2023*); removing them from the main analysis also made no change to the effect estimate or 95% CI. Removing the two studies at high risk of bias also made no change to the effect estimate or CI (George 2019 [321, 322]; Lucchiari 2022; Table 2).

Figure 11. Analysis 8.3: Nicotine EC vs non-nicotine EC – Serious adverse events

Study or Subgroup	Nicotine EC Events	Nicotine EC Total	Non-nicotine EC Events	Non-nicotine EC Total	Weight	Risk Difference M-H, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
Bullen 2013	24	241	4	57	2.1%	0.03 [-0.05 , 0.11]	+	+	+	+	+	+	
Caponnetto 2013*	0	72	0	45	9.5%	0.00 [-0.04 , 0.04]	+	+	+	+	+	?	
Cobb 2021[a]	8	86	3	37	1.0%	0.01 [-0.10 , 0.12]	+	+	+	+	+	+	
Cobb 2021[b]	5	81	4	37	0.9%	-0.05 [-0.16 , 0.07]	+	+	+	+	+	+	
Eisenberg 2020	3	128	5	127	6.5%	-0.02 [-0.06 , 0.03]	+	+	+	+	+	+	
George 2019	0	37	0	37	4.6%	0.00 [-0.05 , 0.05]	+	+	?	−	?	+	
Lucchiari 2022	0	70	0	70	15.8%	0.00 [-0.03 , 0.03]	+	+	+	+	+	−	
Meier 2017	0	24	0	24	2.0%	0.00 [-0.08 , 0.08]	?	?	+	+	?	+	
NCT03625986	1	35	0	34	2.1%	0.03 [-0.05 , 0.10]	?	+	+	+	+	+	
Okuyemi 2022	0	109	0	106	36.8%	0.00 [-0.02 , 0.02]	?	?	+	+	+	+	
Rose 2023*[c]	1	11	0	13	0.3%	0.09 [-0.12 , 0.30]	?	?	+	+	+	+	+
Tuisku 2024	2	152	2	153	18.4%	0.00 [-0.03 , 0.03]	+	+	+	+	+	+	
Total (Wald[d])		**1046**		**740**	**100.0%**	**0.00 [-0.01 , 0.01]**							
Total events:	44		18										

Test for overall effect: Z = 0.02 (P = 0.99)



Heterogeneity: Tau² (DL[e]) = 0.00; Chi² = 3.09, df = 11 (P = 0.99); I² = 0%

Footnotes

[a]36 mg/mL; control group split to avoid double counting
[b]8 mg/mL; control group split to avoid double counting
[c]All participants receiving placebo patch
[d]CI calculated by Wald-type method.
[e]Tau² calculated by DerSimonian and Laird method.

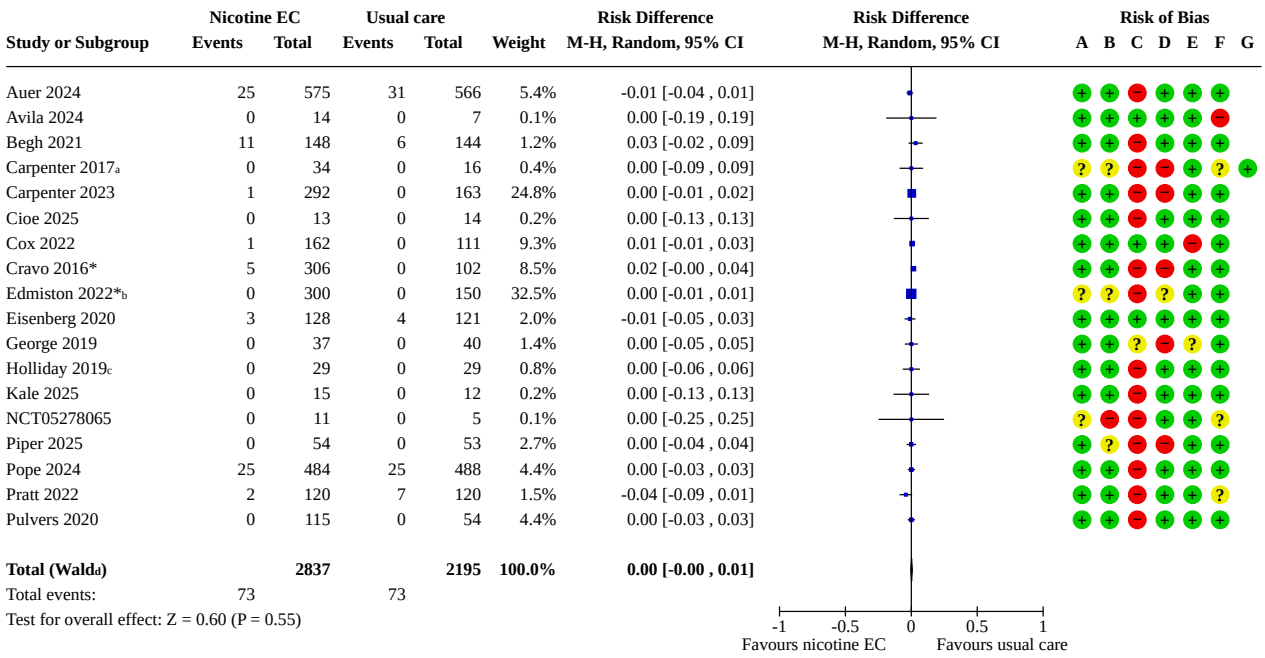
Risk of bias legend

(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

Versus behavioural support only or no support

Eighteen studies compared nicotine EC with behavioural support only or no support and reported data on SAEs; in ten of these, no events occurred. Pooled results from all the studies showed no clear evidence that the risk of SAEs was higher in either group (RD 0.00, 95% CI −0.00 to 0.01; I^2 = 0%; 5032 participants; Figure 12). Here, the certainty of evidence was very low; this was downgraded due to risk of bias and imprecision (fewer than 300 events). Removing the two studies with tobacco/vaping industry support (Edmiston 2022*; Cravo 2016*) did not affect the interpretation of the result (Table 2).

Figure 12. Analysis 9.3: EC vs behavioural support only/no support – serious adverse events



Heterogeneity: Tau² (DLe) = 0.00; Chi² = 9.50, df = 17 (P = 0.92); I² = 0%

Footnotes

aData from 24 mg arm (0 events in 16 mg arm as well)
bMenthol and tobacco flavour arms were combined
cParticipants offered choice of nicotine or no-nicotine EC; all chose nicotine-containing EC
dCI calculated by Wald-type method.
eTau² calculated by DerSimonian and Laird method.

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

Carbon monoxide

High statistical heterogeneity (I^2 = 76%) precluded pooling CO data from seven trials (n = 746, none considered to be at high risk of bias) comparing nicotine EC with non-nicotine EC (Analysis 8.4). Point estimates from five studies (one reporting links to industry funding; Rose 2023*) favoured nicotine EC and two (one reporting industry funding; Caponnetto 2013*) favoured non-nicotine EC, but in all cases, CIs were consistent with no clinically meaningful difference. Three further studies measured CO levels in those assigned to nicotine EC and those assigned to non-nicotine EC, but did not present data in a way that could be pooled: George 2019 (high risk of bias) did not compare data by group; Tseng 2016 (unclear risk of bias) reported no between-group differences but no analysable data; and Meier 2017 [323] (unclear risk of bias) found a slightly higher CO reading in those using nicotine EC, but the clinical and statistical significance of this difference was not clear (see Supplementary material 12 for more detail).

Pooled data from 14 studies comparing nicotine EC with behavioural support or no support resulted in a high I^2 value (93%); thus, pooled results are not presented here (see Analysis 9.4 for individual study data). None of these studies reported tobacco/vaping industry funding. Heterogeneity was primarily driven by magnitude rather than direction of effect, with results in 13 of 14 studies favouring nicotine EC. Five further trials reported data that could not be included in the meta-analysis. Of those studies comparing nicotine EC to combustible cigarettes, Cravo 2016* found that CO levels declined in the EC group and remained similar to baseline in the cigarette group, and George 2019 reported that the lowest tertile of CO at the end of study was amongst those with the best compliance with EC and least dual use. Czoli 2019 instructed baseline dual users to spend periods only using EC or only using traditional cigarettes; CO measured during sole EC use was lower than baseline and lower than during cigarette-only periods. NCT03113136 reported reduced CO levels in dual users of combustible tobacco and EC compared with exclusive combustible tobacco users. Further details can be found in Supplementary material 12.

Heart rate

Two trials (Caponnetto 2013*, Cobb 2021, n = 401; one industry-funded, neither at high risk of bias) provided data on heart rate and compared nicotine EC with non-nicotine EC. While the effect estimate indicated lower mean heart rate in the nicotine EC arm, the CI included the potential for no clinically significant between-group difference (MD −1.23, 95% CI −3.55 to 1.08; I^2 = 0%; 401 participants; Analysis 8.5). Removing the study with industry support did not affect the interpretation of the results (Table 2). Two RCTs (Hatsukami 2020; Katz 2025 [324, 325, 326, 327]) compared nicotine EC with no intervention and found no evidence of a clinically significant difference (MD 1.72, 95% CI −3.34 to 6.78; I^2 = 0%; 111 participants; Analysis 9.5).

A further three RCTs provided data on heart rate that could not be used to calculate effect estimates. George 2019 (high risk of bias) compared nicotine to non-nicotine EC and reported no difference in heart rate between arms; Cravo 2016* compared nicotine EC with combustible cigarettes and reported "no clinically significant changes." Cioe 2025 compared nicotine EC to behavioural support only and reported "no clinically significant changes" between groups. See Supplementary material 13 for further information.

Blood pressure

While the pooled effect estimate from three trials (Caponnetto 2013*; Cobb 2021, NCT03625986; one industry-funded, none at high risk of bias) indicated higher systolic blood pressure (BP) in the nicotine EC arm at follow-up, the CI included the potential for no clinically significant difference in BP between the nicotine EC and non-nicotine EC arms (MD 2.28, 95% CI −0.41 to 4.97; I^2 = 0%; 470 participants; Analysis 8.6). Removing the study with industry support did not affect the interpretation of the results (Table 2). Three studies (none reporting tobacco/vaping industry funding) compared nicotine EC to behavioural support only and reported data on systolic BP; there was a small difference favouring the EC arms, but the CI included the potential for no clinically significant difference (MD −2.23, 95% CI −5.38 to 0.92; I^2 = 4%; 319 participants; Analysis 9.6). Four further RCTs measured change in blood pressure but presented results in a way that could not be pooled. George 2019 (high risk of bias) compared nicotine EC and non-nicotine EC and combined data from both groups; BP declined over time. Cravo 2016* found "no clinically significant changes" when comparing nicotine EC to combustible cigarettes at two weeks. Katz 2025 assigned participants to nicotine EC and combustible cigarettes in consecutive two-week phases and reported lower diastolic BP after the EC phase than after the combustible cigarette phase. Cioe 2025 compared a nicotine EC group to a behavioural support only group and reported that systolic blood pressure was reduced in the EC group and stayed the same in the behavioural support group.

Oxygen saturation

Hatsukami 2020 compared nicotine EC to combustible cigarettes and found no clear evidence of a difference in blood oxygen saturation when comparing nicotine EC to cigarettes (MD 0.20, 95% CI -0.30 to 0.70; 89 participants; Analysis 9.7).

Toxicants

Three studies comparing nicotine EC with non-nicotine EC measured NNAL (Cobb 2021; NCT03625986; Okuyemi 2022 [328, 329]). None of the studies were at high risk of bias or were industry-funded. Pooling the studies resulted in high statistical heterogeneity (I^2 = 99%; Analysis 8.7) and so the pooled estimate is not presented here. Two of the studies found no clear evidence of a difference in NNAL values between groups, whereas one study found lower NNAL in the nicotine EC group. Six trials comparing nicotine EC to behavioural/no support measured change in NNAL and provided sufficient data to calculate summary effects (two industry-funded; Analysis 9.8). Four of the six studies found results favouring nicotine EC, but the final two indicated no difference; statistical heterogeneity was high (I^2 = 96%), so pooled results are not presented. One study comparing nicotine EC to no treatment described their findings narratively and stated that *"NNAL decreased more over time in the e-cigarette group ... the e-cigarette group had significantly lower NNAL at 4 weeks (estimate = 0.54; SE = 0.23; t = 2.37; P < 0.02), but the group difference was attenuated at 8 weeks (estimate = 0.42; SE = 0.23; t = 1.83; P < 0.07)"* (Pratt 2022). Czoli 2019, which was a cross-over trial, found NNAL and 1-HOP decreased when using nicotine EC compared to increasing when using traditional cigarettes (Supplementary material 15).

Two trials (Cravo 2016*; Hatsukami 2020) measuring change in 3-HPMA, reported decreased measures in the EC arm (SMD −0.46, 95% CI −0.66 to −0.26; I^2 = 0%; 474 participants, Analysis 9.9) versus the combustible cigarette arms. Removing Cravo 2016* due to industry funding did not affect the interpretation of the results (Table 2).

One trial (Hatsukami 2020; n = 90) found non-statistically significant lower levels of 2-HPMA, HMPMA, PhET, and AAMA in nicotine EC arms compared to control (Analysis 9.10; Analysis 9.11; Analysis 9.12; Analysis 9.14), but found no difference in CEMA (Analysis 9.13).

One trial (Cravo 2016*; high risk of bias) found reductions in S-PMA compared to the use of combustible cigarettes (MD -1371, 95% CI -1995.23 to -746.77; 384 participants; Analysis 9.15) and another trial found reductions in the biomarker of harm, MDA, compared to the use of combustible cigarettes (Supplementary material 15).

Lung function

Three trials comparing nicotine EC to non-nicotine EC measured FEV1 (Caponnetto 2013*; Cobb 2021; NCT03625986; unclear, low and unclear risk of bias respectively). The pooled analysis demonstrated no clear evidence of an effect (SMD −0.01, 95% CI −0.68 to 0.66; I^2 = 55%; 417 participants; Analysis 8.8) and a sensitivity analysis removing Caponnetto 2013* due to industry funding did not change the interpretation. Similarly, no difference was found between nicotine and non-nicotine EC for FEV1/FVC (Analysis 8.9), which was measured by only two of the previous trials (Caponnetto 2013*; Cobb 2021), and a sensitivity analysis, removing Caponnetto 2013*, did not change this. Cobb 2021 also measured FVC, PEF (peak expiratory flow) and FEF (forced expiratory flow 25-75) and found no evidence of difference between nicotine and non-nicotine EC (Analysis 8.10; Analysis 8.11; Analysis 8.12). In Caponnetto 2013*, FeNO increased more in the nicotine EC than the non-nicotine EC group (MD 2.35, 95% CI 1.78 to 2.92; 90 participants; Analysis 8.13).

For the comparison of nicotine EC versus behavioural support only/no support, pooled results from five studies (two industry-funded) found improvements in FEV1 but with CI including no difference (SMD 0.12, 95% CI −0.10 to 0.34; I^2 = 29%; 781 participants; Analysis 9.16). However, a sensitivity analysis removing the studies with

industry funding changed the point estimate to indicate no clear difference with similar CI (SMD -0.01, 95% CI -0.40 to 0.39). The two studies reporting FEV1/FVC (Edmiston 2022*; Katz 2025) favoured nicotine EC when pooled; however, the lower CI indicated the potential of no effect of either the intervention or comparator (MD 1.02, 95% CI −0.47 to 2.50; I^2 = 71%; 348 participants; Analysis 9.17) and removing the industry-funded study at high risk of bias led to a point estimate closer to the null and CI spanning benefit and harm of the intervention (MD 0.20, 95% CI -0.47 to 2.50). Data from two studies (Katz 2025; NCT05278065) provided a pooled estimate indicating no clear difference in FVC values between study arms (SMD 0.11, 95% CI −0.56 to 0.77; I^2 = 0%; 37 participants; Analysis 9.18). Pooled data from three studies (one reporting tobacco/vaping industry funding) showed no difference in FEF 25-75, with moderate statistical heterogeneity (MD −0.05, 95% CI −0.43 to 0.34; I^2 = 53%; 3 studies, 571 participants; Analysis 9.19). In a sensitivity analysis removing Cravo 2016*, the result was still consistent with no clear difference, though the point estimate was greater in magnitude (favouring behavioural/no support).

Data from one study (NCT05278065) showed no clear difference in PEF (MD 0.99, 95% CI -1.28 to 3.26; 16 participants; Analysis 9.20) or FeNo (MD 3.15, 95% CI -2.53 to 8.83; 16 participants; Analysis 9.22) between study arms. Another study, with industry funding (Cravo 2016*), showed no clear difference in PEF 25-75 (litres/minute) between groups (MD -7.10, 95% CI -29.14 to 14.94; 387 participants; Analysis 9.21).

Katz 2025, which randomised participants to nicotine EC or continued combustible cigarettes, measured changes in objective (spirometry, oscillometry), self-reported (CAT, SGRQ-C) lung function, and reported no significant differences (Supplementary material 16).

Study product use

Three trials (all low risk of bias; none industry-funded), comparing nicotine EC with non-nicotine EC, reported the number of participants still using EC at six months or longer. Slightly more participants were still using EC in the nicotine EC arms, but CI were wide and included no difference (RR 1.14, 95% CI 0.77 to 1.69; I^2 = 30%; 874 participants; Analysis 8.14).

Long-term nicotine EC and combustible cigarette use

Two studies (neither industry-funded, both low risk of bias) comparing nicotine EC to non-nicotine EC, reported at least one of these outcomes (as seen in Analysis 8.15; Analysis 8.16; Analysis 8.17; Analysis 8.18); all results were imprecise, with wide CI incorporating the possibility of effects in either direction. Use of EC with no combustible tobacco was higher in the non-nicotine EC arms, and statistical heterogeneity was moderate (RR 5.38, 95% CI 0.43 to 66.54; I^2 = 53%; 458 participants; Analysis 8.15). Use of neither EC nor combustible tobacco was higher in nicotine EC arms (RR 1.59, 95% CI 0.46 to 5.51; I^2 = 0%; 458 participants; Analysis 8.16) and concurrent use of EC and combustible tobacco was lower in the nicotine EC arms (RR 0.88, 95% CI 0.71 to 1.09; I^2 = 0%; 458 participants; Analysis 8.17). Only one study (Bullen 2013) reported on combustible tobacco use with no EC use; no clear difference was detected (RR 1.06, 95% CI 0.85 to 1.33; 298 participants; Analysis 8.18).

Three studies (none industry-funded, all high risk of bias due to the nature of the comparison) compared nicotine EC with behavioural support only/no support and reported on all four of these outcomes (as seen in Analysis 9.23; Analysis 9.24; Analysis 9.25; Analysis 9.26). Rates of EC use with no combustible tobacco use were higher in nicotine EC arms, though CI were wide, incorporating the possibility of effects in the opposite direction, and statistical heterogeneity was high (driven by magnitude rather than direction of effect) (RR 4.69, 95% CI 0.21 to 105.12; I^2 = 89%; 1784 participants; Analysis 9.23). Two studies found higher rates of no EC or combustible tobacco use in the EC arms, but the third found the opposite; statistical heterogeneity driven by direction of effect precluded meta-analysis. Rates of concurrent EC and combustible tobacco use were higher in EC arms (RR 4.45, 95% CI 3.54 to 5.61; I^2 = 0%; 1986 participants; Analysis 9.25). Combustible tobacco use with no EC use was lower in EC arms; high statistical heterogeneity was driven by magnitude rather than direction of effect (RR 0.46, 95% CI 0.30 to 0.72; I^2 = 81%; 2169 participants; Analysis 9.26).

Direct comparisons between different nicotine EC conditions

Comparisons based on nicotine dose

Six trials provided data comparing different doses of nicotine in EC (although other studies provided a range of doses, these were not randomly assigned). Only one study provided data on abstinence; in Cobb 2021 (cartridge; low risk of bias), quit rates were higher in the higher-dose arm but the 95% CI included no difference (RR 2.50, 95% CI 0.80 to 7.77; 260 participants; Analysis 10.1).

Three studies (all at high risk of bias) provided data on AEs, two of which provided data in such a way that the studies could not be pooled. Kimber 2021 reported "no changes over time or differences between condition", and Pratt 2022 reported "no statistically significant between group differences" (see Supplementary material 11). Kanobe 2022* found slightly more participants in the lower-dose group reported AEs; however, the 95% CI incorporated the null and also the possibility that more people experienced AEs in the higher-dose arm (RR 0.90, 95% CI 0.58 to 1.40; 68 participants; Analysis 10.2). Two studies comparing nicotine strength reported SAEs (Caponnetto 2013*,unclear risk of bias; Cobb 2021, low risk of bias), resulting in a pooled result of RD 0.01, 95% CI −0.03 to 0.05; I^2 = 0%; 239 participants (Analysis 10.3), with the CI incorporating no differences in the potential harm and benefit of the higher dose. Removing Caponnetto 2013* due to industry funding resulted in no change to the interpretation of the effect (Table 2).

Point estimates favoured higher-dose EC and the CI excluded no difference for CO (MD −0.92, 95% CI −1.71 to −0.13; I^2 = 0%; 3 studies, 348 participants; one in the high risk of bias study; Analysis 10.4) and FEV1/FVC (MD 0.91, 95% CI 0.18 to 1.64; I^2 = 0%; 2 studies, 350 participants; no high risk of bias studies; Analysis 10.10). Interpretation of Analysis 10.4 did not change when excluding the one study at high risk of bias (Kimber 2021), or the one study with tobacco/vaping industry funding (Caponnetto 2013*); excluding the same study from Analysis 10.10 maintained the same direction of effect, but the CI widened to cross the null. There were no clear differences between arms for heart rate, BP, other lung function measures, or NNAL (Analysis 10.5; Analysis 10.6; Analysis 10.13; Analysis 10.8; Analysis 10.9; Analysis 10.7; all included Caponnetto 2013* (unclear risk of bias) and Cobb 2021 (low risk of bias), except for Analysis 10.13 which included Caponnetto 2013* alone and Analysis 10.7, which included Cobb 2021 alone). The interpretation of the analyses including both studies remained the same when

Caponnetto 2013* was excluded due to industry funding. More participants in the higher-dose nicotine group were still using EC at six months or longer, but data were from one study and CIs were wide and included no difference (RR 1.27, 95% CI 0.95 to 1.68; 260 participants; Analysis 10.14). In Yingst 2020 (cross-over, comparing different doses and different devices; unclear risk of bias), exhaled CO and reported nausea did not differ between devices; self-reported dizziness was low overall but slightly higher in the higher-dose arm. Further details can be found in Supplementary material 11 and Supplementary material 12.

Cobb 2021 (no industry funding, low risk of bias, n = 167 for these outcomes) reported on three outcomes related to EC and combustible tobacco use at six months or longer. For all, CIs were wide and incorporated the possibility of no difference or an effect in the opposite direction. EC use with no combustible tobacco use was higher in the lower nicotine arm, as were no EC or combustible tobacco use and concurrent EC and combustible tobacco use (Analysis 10.15; Analysis 10.16; Analysis 10.17). Data were not available for combustible tobacco use in the absence of EC use.

Comparisons based on flavour

One study randomised participants to different flavour conditions (1. tobacco flavour only; 2. a choice of flavours) and followed up participants for six months or longer (Xu 2023*, industry-funded, high risk of bias, pod EC). Quit rates were lower in the choice compared to the tobacco arm, but the CIs were wide and incorporated no difference and a clinically significant increase relative to tobacco flavour (RR 0.80, 95% CI 0.54 to 1.16; 566 participants; Analysis 11.1). Xu 2023* also reported on product use at six months or longer; again, there was no clear evidence of a difference, but CIs were wide (RR 1.10, 95% CI 0.86 to 1.40; 522 participants; Analysis 11.6).

Higgins 2024 (unclear risk of bias) randomised participants to either tobacco-flavoured EC or choice of flavour, alongside very low nicotine content (VLNC) combustible cigarettes. This study did not find evidence of difference between groups in AEs (RR 1.01, 95% CI 0.88 to 1.15; 158 participants; Analysis 11.2), SAEs (RD -0.03, 95% CI -0.09 to 0.03; 158 participants; Analysis 11.3), CO (MD -4.52, 95% CI -11.06 to 2.02; 124 participants; Analysis 11.4) or NNAL (MD -0.09, 95% CI -1.26 to 1.08; 120 participants; Analysis 11.5).

Another study, NCT03277495 (63 participants; high risk of bias), randomised participants to either use EC in the flavour of cigarettes they would usually buy (i.e., tobacco or menthol) or EC in a choice of flavours (tobacco, menthol, blueberry, watermelon). There was no clear evidence of a difference between groups for any of the outcomes reported: AEs (Analysis 12.1); SAEs (Analysis 12.2); CO (Analysis 12.3); heart rate (Analysis 12.4); systolic blood pressure (Analysis 12.5), with 95% CI spanning both potential benefit and harm of either arm in all cases.

One study (Edmiston 2022*, 300 participants, high risk of bias, vaping/tobacco industry funding) randomised participants to different flavours (tobacco versus menthol) and provided SAE data in a way that could be used to compute RD, although no SAEs occurred in either arm (RD 0.00, 95% CI -0.01 to 0.01; 300 participants; Analysis 13.1). NNAL (MD -26.10, 95% CI -66.73 to 14.53; 232 participants; Analysis 13.2), FEV1/FVC (MD -0.67, 95% CI -2.34 to 1.00; 212 participants; Analysis 13.3), and FEV1 (MD -0.46, 95% CI -1.67 to 0.75; 212 participants; Analysis 13.4) were lower in the tobacco flavour group, but CIs were wide and included no difference. No other outcomes from this paper were eligible for inclusion in our review.

More information on flavour choices from the studies in this review can be found in companion publications [330, 331].

Comparisons based on device type

Two studies directly compared device types. Kimber 2021 (high risk of bias) compared cartridge to refillable ECs, whereas Yingst 2020 compared a cig-a-like EC to a refillable EC. Outcomes eligible for this review were AEs and CO. For AEs, Kimber 2021 reported *"no changes over time or differences between condition",* and Yingst 2020 found slightly higher levels of dizziness in the refillable group and the same levels of nausea between groups at three weeks post-baseline (see Supplementary material 11). Kimber 2021 found no difference between arms for CO, but CIs were wide (MD 0.70, 95% CI -4.98 to 6.38; 32 participants; Analysis 14.1), and Yingst 2020 found that, although CO was reduced in both the cig-a-like and refillable device groups, there was no clear difference in the magnitude of the change (see Supplementary material 12).

Nicotine salt versus free-based nicotine

One study (Russell 2021*, pod device; unclear risk of bias, tobacco/vaping industry funding) contributed data to this comparison. Quit rates (RR 1.25, 95% CI 0.85 to 1.83; 285 participants; Analysis 15.1) and study product use (RR 1.07, 95% CI 0.82 to 1.41; 227 participants; Analysis 15.2) were both similar between arms.

Higher versus lower wattage EC

One study (NCT03113136, high risk of bias, n = 267; device type not specified) compared a higher wattage EC with a lower wattage EC. Quit rates were similar between study arms, and the CI included the potential for benefit from either (RR 0.72, 95% CI 0.30 to 1.74; 267 participants; Analysis 16.1). The study did not find evidence of a difference in rates of AEs (RR 0.92, 95% CI 0.79 to 1.06; 267 participants; Analysis 16.2) or SAEs (RD -0.00, 95% CI -0.03 to 0.03; 267 participants; Analysis 16.3).

Non-nicotine EC

Although non-nicotine EC served as a 'control group' in our primary analysis, due to its behavioural properties, it can also be considered an intervention. Comparisons included here are: non-nicotine EC versus NRT; non-nicotine EC versus behavioural support/no treatment; and non-nicotine EC as an adjunct to NRT. None of these studies reported data on change in heart rate, BP, oxygen saturation, toxicants, or lung function.

Cessation

Two studies (one cartridge, one refillable; neither at high risk of bias) compared non-nicotine EC with NRT (Klonizakis 2022; Lee 2019). The pooled estimate showed no clear evidence of a difference in quit rates between the two interventions (RR 0.99, 95% CI 0.64 to 1.54; I^2 = 36%; 314 participants; Analysis 17.1).

When comparing non-nicotine EC to behavioural or no support, pooled results from two studies (Eisenberg 2020; Lucchiari 2022; both cig-a-like; one at high risk of bias) found higher quit rates in participants randomised to non-nicotine EC, but the CI included the

possibility of no difference (RR 1.59, 95% CI 0.80 to 3.19; I^2 = 0%; 2 studies, 388 participants; Analysis 18.1).

When evaluating non-nicotine EC as an adjunct to NRT versus NRT, Walker 2020 [332, 333, 334] (refillable; high risk of bias) also found higher quit rates in participants randomised to non-nicotine EC, although again the CI included no difference (RR 1.67, 95% CI 0.50 to 5.53; 624 participants; Analysis 19.1).

Adverse events

Lee 2019 (low risk of bias) found that fewer participants receiving non-nicotine EC reported AEs than those receiving NRT, with the CI excluding no difference (RR 0.33, 95% CI 0.12 to 0.87; 132 participants; Analysis 17.2).

Eisenberg 2020 (low risk of bias) found a higher rate of adverse events in the non-nicotine EC arm than in the behavioural support only arm, with CI excluding no difference (RR 1.28, 95% CI 1.13 to 1.44; 248 participants; Analysis 18.2). Also comparing non-nicotine EC to behavioural support, Lucchiari 2022 (high risk of bias) reported that some AEs were lower in the non-nicotine EC arm, some higher, and others were reported at similar rates to the behavioural support arm (overall AE rates were not reported; see Supplementary material 11).

Walker 2020 (high risk of bias) found fewer AEs in participants receiving non-nicotine EC + NRT compared to NRT alone, with the CI excluding no difference (RR 0.70, 95% CI 0.53 to 0.91; 344 participants; Analysis 19.2).

Serious adverse events

For the non-nicotine EC versus NRT comparison, no SAEs were reported in either arm of Lee 2019 (low risk of bias; RR 0.00, 95% CI -0.03 to 0.03; 132 participants; Analysis 17.3).

Two studies reported on rates of SAEs when comparing non-nicotine EC with behavioural support (Lucchiari 2022, high risk of bias; Eisenberg 2020, low risk of bias), with no clear evidence of a difference between groups (RD 0.00, 95% CI −0.02 to 0.03; 388 participants; Analysis 18.3). Removing Lucchiari 2022 in a sensitivity analysis, shifted the RD slightly to 0.01, but the CI continued to bridge the null (95% CI -0.04 to 0.05; Table 2).

In Walker 2020 (high risk of bias), more SAEs occurred in the group randomised to non-nicotine EC + NRT than in the NRT-alone group, but the CI included no difference as well as the potential for a clinically significant difference in favour of the intervention (RD 0.02, 95% CI -0.01 to 0.06; 624 participants; Analysis 19.3).

Carbon monoxide

One study investigating the comparison between non-nicotine EC and NRT reported change in CO between baseline and six-month follow-up (Klonizakis 2022; unclear risk of bias). The point estimate favoured NRT; however, the CI encompassed both benefit and harm of the intervention (MD 2.00; 95% CI -0.50 to 4.50; 164 participants; Analysis 17.4).

Advice to use EC to stop smoking

Three studies did not provide EC, but instead provided participants with advice on how to use EC to stop smoking; none reported tobacco/vaping industry funding. Martinez 2021 (low risk of bias) and Elling 2023 (high risk of bias) both provided people received self-help smoking cessation interventions with information on how to use EC to stop smoking compared to a smoking cessation intervention, without the recommendation to use EC. However, Martinez 2021 specifically recruited people using both combustible cigarettes and EC (dual users) at baseline and Elling 2023 only required participants to be combustible cigarette users at baseline. Pooling smoking cessation rates from these two studies provided no clear evidence of a difference between the groups advised to use EC and those who did not receive that advice (RR 1.02, 95% CI 0.88 to 1.19; I^2 = 0%; 2652 participants; Analysis 20.1), and removing Elling 2023 in a sensitivity analysis resulted in no change to the interpretation of the effect.

In Vickerman 2022, more AEs occurred in the group receiving advice to use EC to stop smoking; however, the CI included no difference (RR 1.27, 95% CI 0.72 to 2.26; 52 participants; Analysis 20.2). No SAEs were reported in either study group in Vickerman 2022 (RR 0.00, 95% CI -0.07 to 0.07; 52 participants; Analysis 20.3).

Two studies (neither industry-funded, one at high risk of bias and one at low risk of bias) reported on concurrent use of EC and combustible tobacco at six months or longer. Statistical heterogeneity driven by direction of effect precluded synthesis (Analysis 20.6). Only Martinez 2021 (low risk of bias, no industry funding, n = 1259 for these analyses) reported on the other three outcomes; in all cases, CIs were wide and incorporated the possibility of effects in the opposite direction. EC use with no combustible tobacco use was higher in the arm receiving no advice related to EC (Analysis 20.4). Use of neither EC nor combustible tobacco was higher in the arm randomised to receive EC advice (Analysis 20.5). There was no evidence of a difference in the proportion reporting combustible tobacco use with no EC use (Analysis 20.7).

EC as an adjunct to other interventions

Nicotine EC and NRT

This section covers two comparisons: comparisons in which both arms received NRT and participants were randomised to nicotine EC or non-nicotine EC, and studies in which all participants received NRT and one arm was randomised to nicotine EC, in addition. No studies in this group reported data on heart rate, BP, oxygen, or toxicants.

Cessation

Two trials (Baldassarri 2018 [335, 336, 337]; Walker 2020; both at high risk of bias, both refillable, neither reporting tobacco/vaping industry funding), in which all participants received NRT, compared nicotine EC to non-nicotine EC. The pooled results favoured nicotine EC, with the CI excluding no difference (RR 1.77, 95% CI 1.07 to 2.94; I^2 = 0%; 1039 participants, Analysis 21.1).

Three studies (two high risk of bias, one unclear risk; two refillable, one cartridge; none reporting tobacco/vaping industry funding) compared nicotine EC + NRT to NRT alone. In two of these studies, participants in both groups received nicotine patches but, in Morphett 2022b [338, 339] (refillable; unclear risk of bias), participants in the NRT-only arm also received a short-acting form of NRT. Pooling results from all three studies resulted in high statistical heterogeneity, precluding meta-analysis (I^2 = 83%). This heterogeneity was driven by one study (Morphett 2022a [340, 341, 342]; high risk of bias). This study tested a cartridge device, and

historically, cartridge devices have had poorer nicotine delivery than refillables. Once this study was removed, heterogeneity disappeared (I^2 = 0%), but only two studies remained (Morphett 2022b; Walker 2020). In these two studies, pooled results showed more people quit in the refillable nicotine EC + NRT arm than in the NRT alone arm (RR 3.57, 95% CI 1.96 to 6.51; I^2 = 0%; 980 participants; Analysis 22.1). This effect persisted when the other study at high risk of bias, Walker 2020, was removed in a sensitivity analysis.

Adverse events

Three trials in which nicotine EC were compared to non-nicotine EC (both with NRT as an adjunct) reported data on AEs. Baldassarri 2018 (high risk of bias) reported results combined across groups but noted *"no significant differences by treatment group"* (Supplementary material 11). Pooled data from the other two studies (one at high risk of bias; one reporting tobacco/vaping industry funding: Rose 2023*) also showed no clear evidence of difference (RR 1.11, 95% CI 0.93 to 1.32; I^2 = 0%; 677 participants; Analysis 21.2). Sensitivity analyses, removing the study at high risk of bias (Walker 2020) and removing the industry-funded study (Rose 2023*), did not affect the interpretation of this result (Table 2).

The four trials comparing nicotine EC + NRT to NRT alone and contributing data on AEs were all at high risk of bias and none reported tobacco/vaping industry funding. Pooling results from all three studies resulted in high statistical heterogeneity, precluding meta-analysis (I^2 = 78%). Individual findings are presented in Analysis 22.2.

Serious adverse events

Pooled data from two studies (one high risk, one unclear; one reporting tobacco/vaping industry funding), comparing nicotine EC with non-nicotine EC as adjuncts to NRT, showed fewer SAEs in the nicotine EC group than in the non-nicotine EC group, but the CI included no difference (RD −0.02, 95% CI −0.04 to 0.01; I^2 = 0%; 1069 participants; Analysis 21.3). Removing the study at high risk of bias (Walker 2020) or with industry funding (Rose 2023*) had no effect on interpretation.

Five studies (all high risk of bias; none reporting tobacco/vaping industry funding) provided data on SAEs and compared nicotine EC + NRT to NRT alone. The pooled estimate suggested no clear difference in SAE rates between groups (RD 0.00, 95% CI −0.00 to 0.00; I^2 = 0%; 2352 participants; Analysis 22.3).

Carbon monoxide

Pooled data from two studies (one high risk of bias, one unclear; one reporting tobacco/vaping industry funding), comparing nicotine and non-nicotine EC as adjuncts to NRT, found a greater reduction in CO in the nicotine EC group. However, the CI included the potential for greater reduction from the non-nicotine EC arm (MD -4.62, 95% CI -12.07 to 2.82; 70 participants; Analysis 21.4) between groups and there was substantial statistical heterogeneity (I^2 = 77%). We have pooled these studies despite the high I^2 as the individual study effects both showed a benefit of nicotine EC, with the difference being in the magnitude of effect. Removing the study at high risk of bias (Baldassarri 2018) left only Rose 2023*, with the following effect estimate: MD -9.10, 95% CI -15.83 to -2.37; whereas removing the study with industry funding (Rose 2023*) left only Baldassarri 2018, with the following effect estimate: MD -1.40, 95% CI -4.26 to 1.46.

Walker 2020 (high risk of bias; comparing nicotine EC + NRT, non-nicotine EC + NRT, and NRT alone) measured change in CO levels but did not report data in a way that could be pooled. CO declined over time, with the greatest reduction seen in the nicotine EC group (see Supplementary material 12).

Lung function

Baldassarri 2018 (high risk of bias), compared nicotine EC to non-nicotine EC, with both groups receiving NRT. They found no between-group differences in FeNO, FEV1, or FVC (Analysis 21.5; Analysis 21.6; Analysis 21.7); CIs were wide for all outcomes.

Study product use

For these comparisons, only Baldassarri 2018 (high risk of bias), provided data that could be entered into meta-analysis for the product use outcome. There was no difference between the nicotine EC + NRT and non-nicotine EC + NRT arms in product use, but only nine participants contributed data (RR 1.25, 95% CI 0.29 to 5.35; Analysis 21.8).

Walker 2020 (high risk of bias) provided some data for this outcome; however, it could not be meta-analysed as we were unable to calculate the total number of participants using *any* study product for the EC + nicotine patch arms (i.e., patch, EC or both at six months). Rather, the numbers of participants using EC, patch or both were reported separately for each category, and are reported in Supplementary material 17.

Long-term nicotine EC and combustible cigarette use

Two studies (neither industry-funded, both high risk of bias) compared nicotine EC to non-nicotine EC in participants instructed to use NRT and reported on concurrent use of EC and combustible tobacco at six months or longer. Rates were lower in those assigned to nicotine EC (RR 0.55, 95% CI 0.11 to 2.74; I^2 = 63%; 708 participants; Analysis 21.11). Only Baldassarri 2018 (not industry-funded, high risk of bias, n = 22) reported on other outcomes within this comparison and outcome group; in all cases, CIs were wide, incorporating effects in the opposite direction. EC use with no combustible tobacco use, no EC or combustible tobacco use, and combustible tobacco use with no EC use were higher in those randomised to higher nicotine EC (Analysis 21.9; Analysis 21.10; Analysis 21.12).

Nicotine EC and varenicline

One study, Tattan-Birch 2023 [343, 344] (high risk of bias, 92 participants), evaluated nicotine EC and varenicline compared to varenicline alone. The study terminated early due to varenicline supply issues (an international recall), and the only data eligible for inclusion in this review related to AEs and SAEs. There was no evidence of a difference in AEs, though the CI was wide (RR 1.18, 95% CI 0.84 to 1.67; Analysis 23.1). No SAEs occurred in either study arm (RD 0.00; 95% CI -0.04 to 0.04; Analysis 23.2).

Nicotine EC and cytisine

Walker 2023 (pod; unclear risk of bias) compared a group randomised to both nicotine EC and cytisine and a group randomised to cytisine only. Smoking cessation rates were higher in the nicotine EC + cytisine arm; however, the CI also incorporated

the possibility of no difference between the groups (RR 1.39, 95% CI 0.96 to 2.01; 597 participants; Analysis 24.1). Walker 2023 also measured AEs and SAEs; in both cases, the cytisine only group had fewer people reporting that they had experienced AEs, but the CI incorporated the null (AEs: RR 1.16, 95% CI 1.00 to 1.35; 597 participants; Analysis 24.2; SAEs: RD 0.02, 95% CI -0.01 to 0.05; 597 participants; Analysis 24.3).

Nicotine EC and very low nicotine content cigarettes

Higgins 2024 (unclear risk of bias) tested nicotine EC as an adjunct to very low nicotine content (VLNC) combustible cigarettes compared with VLNC alone. There was no evidence of a difference in AEs (RR 0.97, 95% CI 0.88 to 1.07; 243 participants; Analysis 25.1) or SAEs (RD -0.01, 95% CI -0.06 to 0.04; 243 participants; Analysis 25.2). This study reported four SAEs that were "related, probably related or possibly related" to the study arm intervention. One event occurred in the EC + VLNC arm (hypertension), and the three events in the normal nicotine combustible cigarettes arm were OASIS score increase (measuring anxiety severity and impairment), irritability, and hypertension. There was decreased CO in the nicotine EC + VLNC arm compared with VLNC alone (MD -7.15, 95% CI -13.07 to -1.23; 132 participants; Analysis 25.3). Whereas for both the heart rate (MD -3.30, 95% CI -6.88 to 0.28; 136 participants; Analysis 25.4) and systolic blood pressure (MD -1.30; 95% CI -5.94 to 3.34; 136 participants; Analysis 25.5) outcomes the data favoured the EC + VLNC arm, the CI also incorporated the possibility of no difference and potential harm. There was no evidence of a difference in blood oxygen saturation (MD 0.00, 95% CI -0.46 to 0.46; 136 participants; Analysis 25.6) and NNAL (MD 0.29, 95% CI -1.83 to 2.41; 110 participants; Analysis 25.7) between-study arms.

Reporting biases

Six analyses contained sufficient data for us to create funnel plots, five of which showed some evidence of asymmetry (EC vs NRT - smoking cessation, Figure 13; EC vs NRT - SAEs, Figure 14; nicotine EC vs non-nicotine EC - SAEs, Figure 15; nicotine EC vs behavioural/no support - smoking cessation, Figure 16; nicotine EC vs behavioural/no support - AEs, Figure 17). However, whilst each plot contained 10 studies or more, the number of studies contributing to each plot is still considered low and so these plots should be interpreted with caution and not considered diagnostic. A funnel plot for the SAE outcome in the nicotine EC versus behavioural/no support comparison showed no evidence of asymmetry (Figure 18).

Figure 13. Comparison: Nicotine EC vs NRT. Outcome: smoking cessation

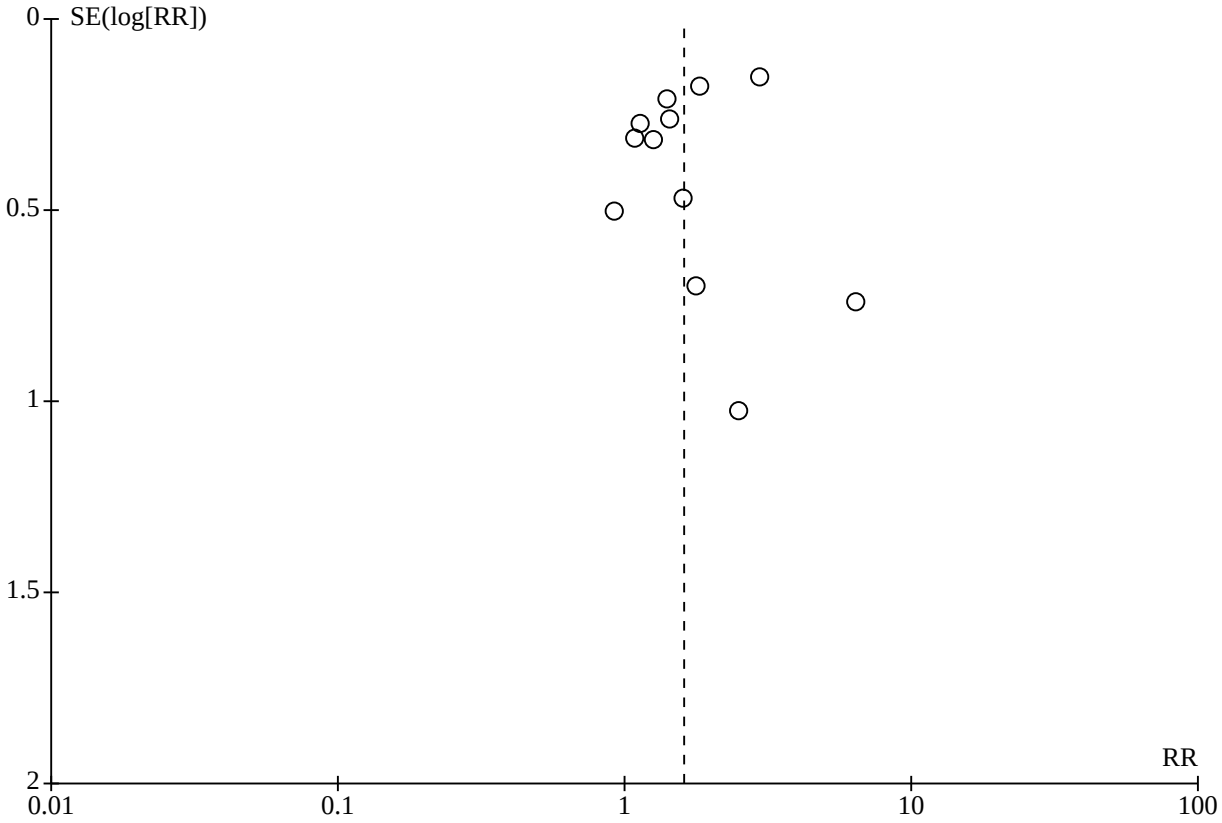


Figure 14. Comparison: Nicotine EC vs NRT. Outcome: SAEs

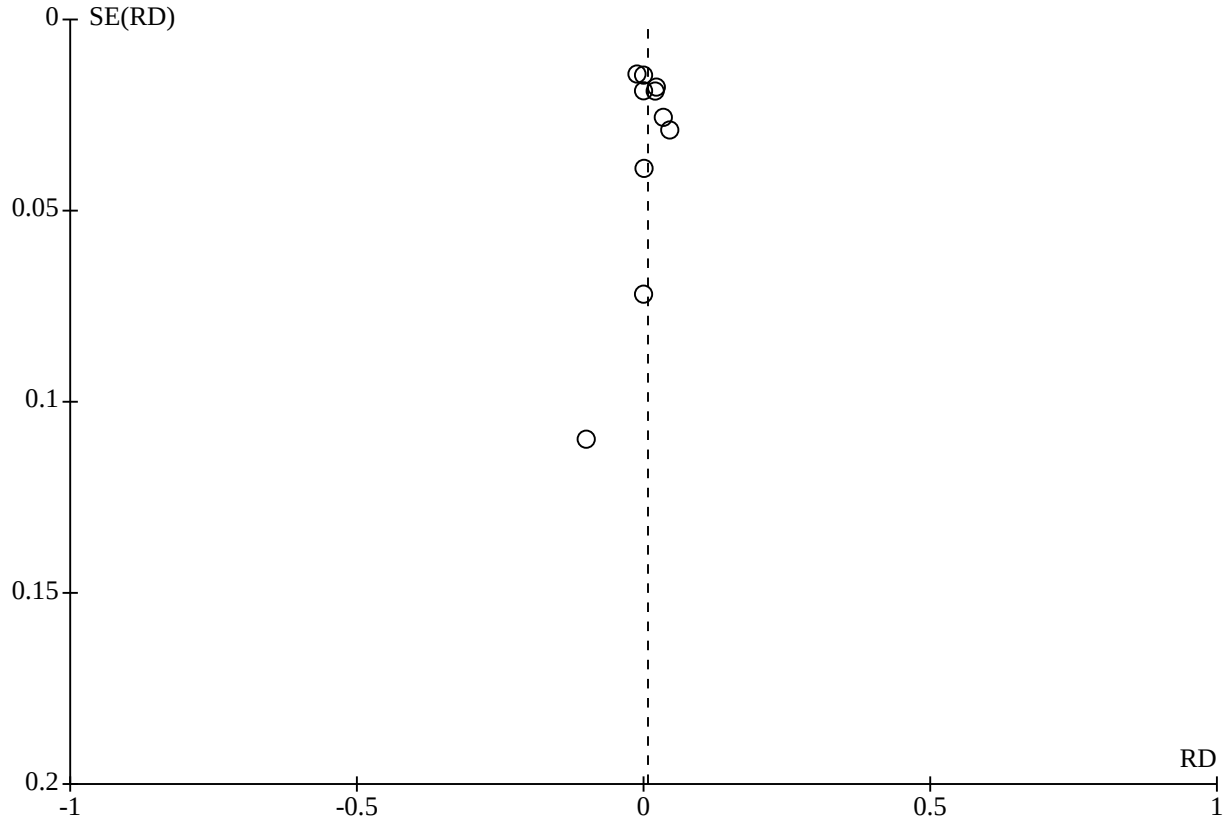


Figure 15. Comparison: Nicotine EC vs non-nicotine EC. Outcome: SAEs

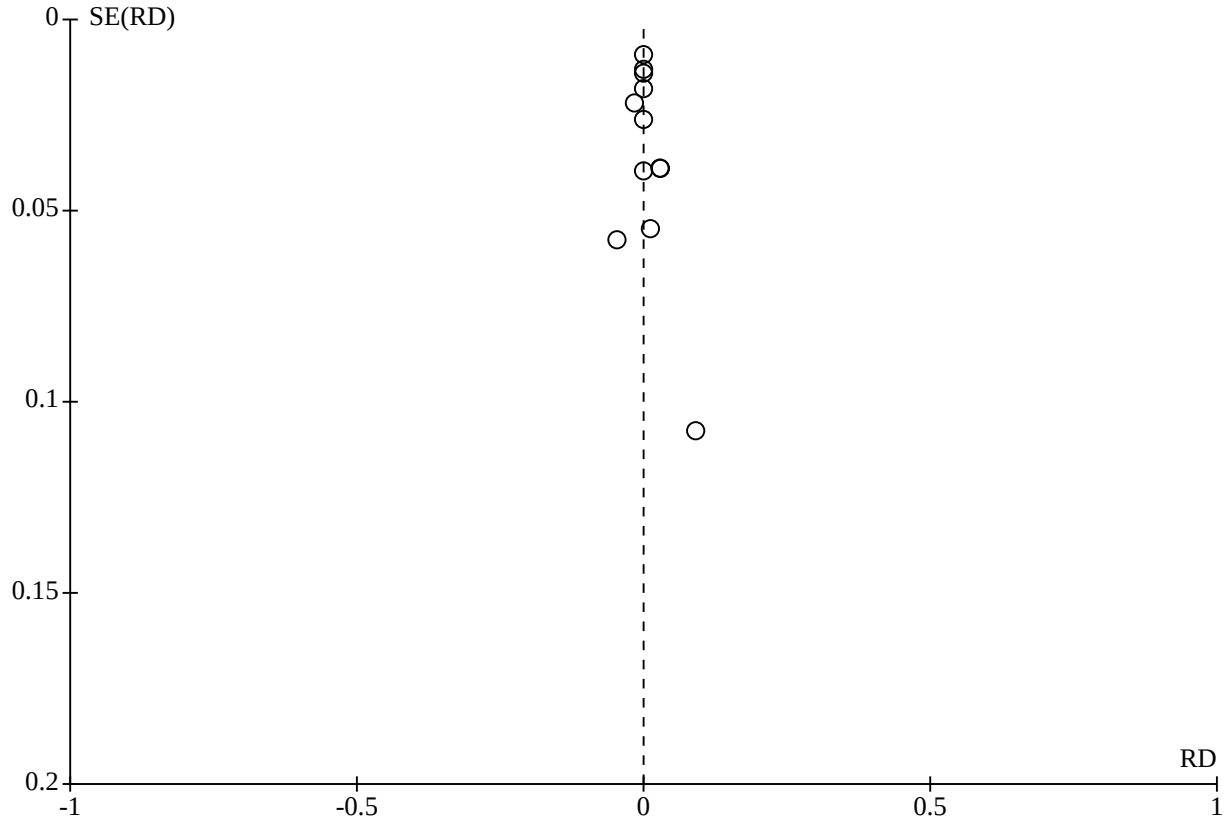


Figure 16. Comparison: Nicotine EC vs behavioural/no support. Outcome: smoking cessation

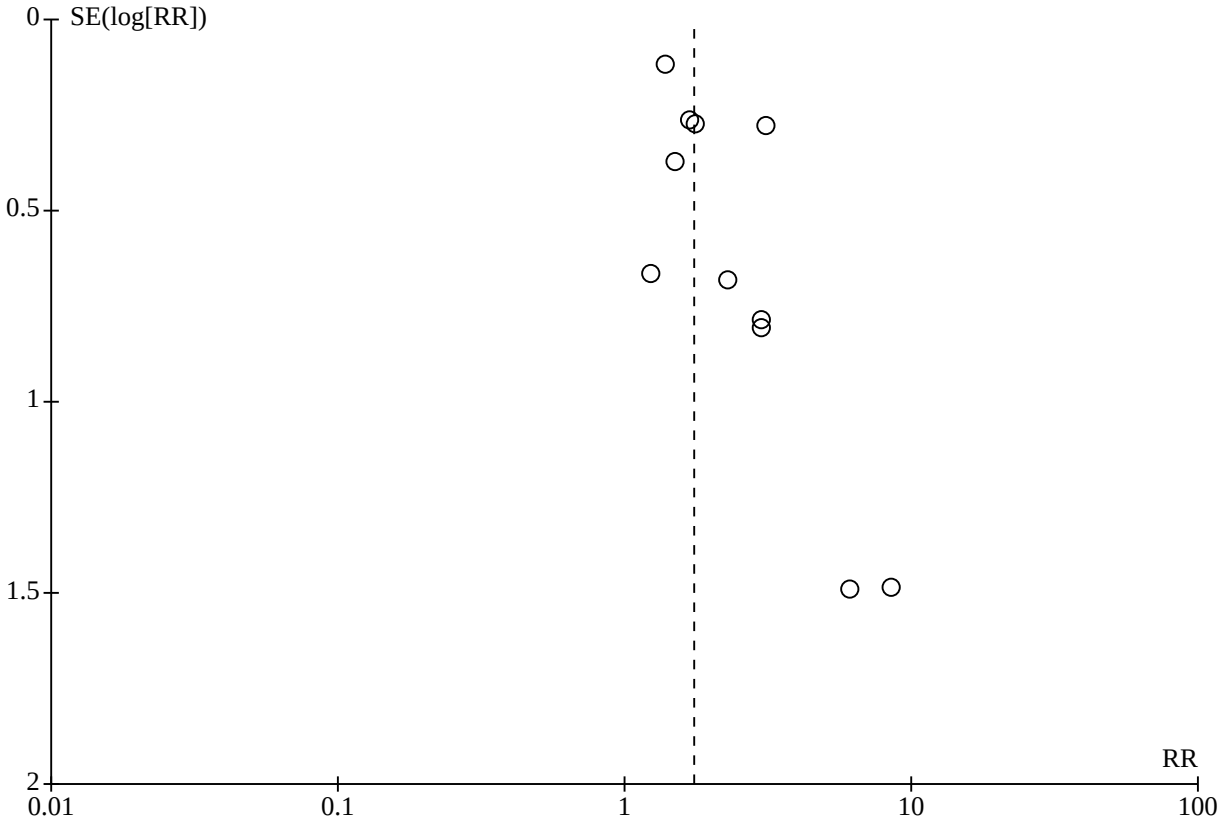


Figure 17. Comparison: Nicotine EC vs behavioural/no support. Outcome: AEs

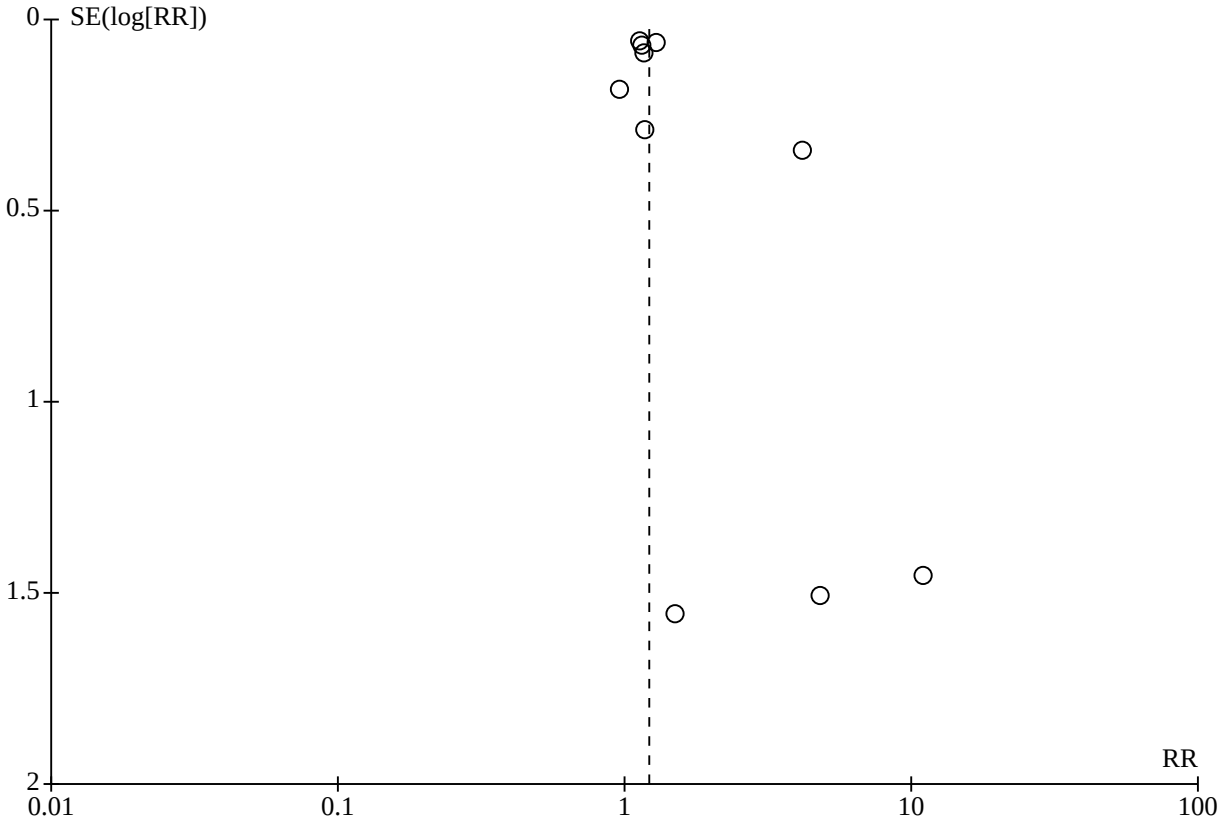
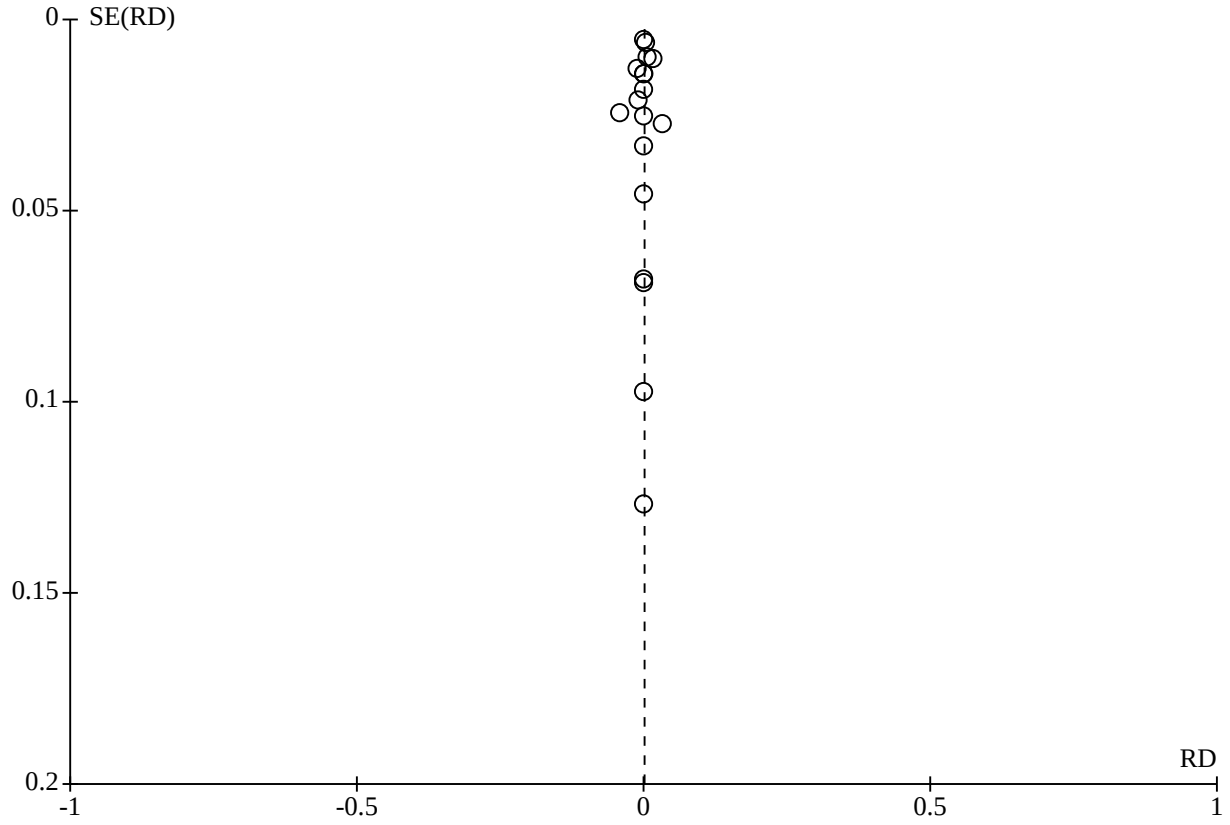


Figure 18. Comparison: Nicotine EC vs behavioural/no support. Outcome: SAEs



DISCUSSION

Summary of main results

This update includes 80 RCTs, with nine of these studies published since the last version (November 2025) of the review. Our three main comparisons, nicotine EC compared to NRT, nicotine EC compared to non-nicotine EC, and nicotine EC compared to behavioural support only/no support, continue to show increased quit rates in people assigned to nicotine EC arms. This conclusion has high certainty for the comparison with NRT, moderate certainty for the comparison with non-nicotine EC, and low certainty for the comparison with behavioural support only/no support (Summary of findings 1; Summary of findings 2; Summary of findings 3). In absolute terms, pooled data suggest an additional one to seven people for every 100 users of the intervention would quit smoking with nicotine EC compared to NRT, an additional zero to four people for every 100 would quit smoking with nicotine EC compared to non-nicotine EC, and an additional two to six people for every 100 would quit smoking with nicotine EC compared to behavioural support only or no support for smoking cessation.

There remains moderate certainty of no evidence of a difference in rates of adverse events (AEs) with nicotine EC compared to non-nicotine EC. Evidence of no difference in rates of AEs with nicotine EC compared to NRT has been downgraded from moderate to low certainty since the last iteration of the review as inconsistency between relevant studies increased. Evidence on AEs and SAEs was of low to very low certainty across all other comparisons, due to a paucity of data, apart from in the case of the SAE outcome for the EC versus NRT comparison where there is now moderate certainty of no difference in SAEs between groups as the number of events has increased so that the outcome is only downgraded once due to imprecision. Notably, many of the studies that measured SAEs reported no such events in either study arm. For nicotine EC compared to non-nicotine EC, pooled data suggest no evidence of a difference in the number of people experiencing AEs or SAEs. Conversely, data from comparisons between nicotine EC and behavioural support alone or no support suggest an additional nine people per 100 assigned to nicotine EC may experience AEs (compared with 43 per hundred assigned to receive behavioural or no support), but with no evidence of a difference in SAEs; this evidence was of very low certainty in both cases. Only one study (Higgins 2024) reported any SAEs that were "related, probably related or possibly related" to the study product in an EC arm. However, participants in this arm also received very low nicotine content (VLNC) combustible cigarettes.

Beyond AEs and SAEs, we consider data on a range of safety- and health-related outcomes, including CO and other toxicants, lung function, BP, heart rate, and oxygen levels. Data on all of these outcome measures were limited; for most outcomes within most comparisons, only one or two studies currently contributed data. A companion paper (up to date to January 2022) provides more data on the measured toxicants, analysing studies based on actual use of EC and combustible cigarettes [345]. Consistent with findings from this review, the companion paper found that most measured toxicants were lower in people exclusively using EC than those exclusively smoking or those both smoking and using EC.

Most measured toxicants were lower in people using both EC and smoking compared to smoking only.

We also consider longer-term use of study products and vaping and smoking behaviours at six months or longer. Data on these are sparse and imprecise; data on longer-term use of study products is discussed further in a companion publication [346].

Limitations of the evidence included in the review

We consider the certainty of the evidence as it relates to primary outcomes for our three main comparisons: nicotine EC versus NRT; nicotine EC versus non-nicotine EC; nicotine EC versus behavioural support only/no support (Summary of findings 1; Summary of findings 2; Summary of findings 3).

Risk of bias did not impact on the certainty of evidence for comparisons between nicotine and non-nicotine EC, or between nicotine EC and NRT. However, risk of bias decreased our certainty in the effect estimates for our nicotine EC versus behavioural support only/no support comparison as, due to the nature of the comparison, blinding was not possible and different levels of support could lead to bias.

All but two of our primary outcomes for our main comparisons were downgraded for imprecision, due to wide confidence intervals and few events. At this update, one outcome (AEs for the EC versus NRT comparison) was also downgraded due to inconsistency, as the I^2 of 72% indicated substantial statistical heterogeneity.

Six of our outcomes had 10 or more studies contributing to meta-analysis and, therefore, we were able to generate funnel plots. The funnel plot for the nicotine EC versus behavioural/no support comparison (SAE outcome) did not show any evidence of asymmetry (Figure 18). There was some evidence of asymmetry in the other plots (Figure 13; Figure 14; Figure 15; Figure 16; Figure 17), However, whilst each plot contained 10 studies or more, the number of studies contributing to each plot is still considered low and so these plots should be interpreted with caution and not considered diagnostic. Apparent asymmetry may be explained either by some level of publication bias (e.g. smaller studies that show no benefit of nicotine EC remaining unpublished), or by heterogeneity between studies in either the intervention effect or the underlying outcome event rate. Therefore, we did not downgrade the certainty of the evidence for publication bias; however, we will continue to monitor these plots as the evidence is updated.

This field of research and EC devices themselves continue to evolve rapidly. This is the sixth update conducted as part of our 'living systematic review' approach, which will proceed until at least 2027, meaning we can continue to rapidly incorporate new evidence (see Supplementary material 8).

This update incorporates new data from 1 April 2025 to 1 January 2026. Subsequent monthly searches will keep the evidence in this review current. Although studies predominantly came from the USA and UK, this review covers data from 13 countries. Geographical range in studies may be particularly important, due to the marked differences in EC regulation between countries; for example, studies conducted in countries that limit nicotine dose in EC, or allow only certain EC devices to be tested, may observe less pronounced effects on quitting. This review includes studies on some under-researched populations, including people not motivated to quit smoking, people with substance misuse disorders, people with serious mental health conditions, people living in socially deprived areas and people experiencing homelessness. Quit rates in these groups are traditionally lower, but these groups may particularly stand to benefit from EC if they are effective because, in absolute terms, conventional cessation methods are often not as effective for them.

As well as the rapid pace of research in this field, evolutions in EC technology pose a challenge when considering the applicability of our evidence to the present. We had downgraded the certainty of our data in the 2016 update, as the devices tested in the trials were first-generation 'cig-a-like' devices which did not deliver nicotine well, meaning the studies may have yielded more conservative estimates than would be seen with newer models, as newer devices and models have tended towards improved nicotine delivery. Nicotine delivery is also relevant to the comparator NRT arms tested; use of both a shorter- and a longer-acting form of NRT show the highest success, and it is important that, where possible, this be the comparator chosen for such trials [91]. We no longer downgrade the evidence on this basis as studies with newer device types are now included, although there will always be a time lag between current devices and the research evidence available. As further data emerge, we hope to be able to formally test for differences in subgroup analyses, and in head-to-head comparisons of different device types. A companion paper explores available data on flavours in more detail, but is up-to-date until February 2024 and so not as up-to-date as this review [330; 331]. The AEs described continue to look similar, regardless of the brand of EC used or nicotine content, with placebo and nicotine-containing EC showing similar numbers and types of AEs in direct comparisons. They also reflect what is reported in survey data [48, 347].

The structure of our analyses follows the standard practice of the Cochrane Tobacco Addiction Group, i.e. evaluating outcomes on an intention-to-treat basis, meaning our pooled results represent the effect of *offering an EC intervention.* This is different from evaluating the per-protocol effect, or the effect only on those who use the EC to quit smoking entirely, or continue to smoke whilst also using EC. Although pragmatic and hopefully of use to those designing and delivering interventions, we acknowledge that our intention-to-treat approach limits the ability to use the data presented here to draw conclusions about biomarkers in subgroups of participants based on subsequent EC use/smoking profiles. A companion publication, up to date to January 2022, attempts to address this deficit [345].

Cessation

All three comparisons found effect estimates favouring nicotine EC for smoking cessation. For nicotine EC versus NRT, we continue to judge the evidence to be of high certainty, meaning we are very confident that the true effect lies close to the estimate of the effect. For nicotine EC versus non-nicotine EC, we continue to judge the evidence to be of moderate certainty, meaning we think the true effect is likely to be close to the estimate of effect. For nicotine EC versus behavioural support only/no support, we continue to judge the evidence to be of low certainty, meaning we have limited confidence in the effect estimate. Nicotine EC versus non-nicotine EC comparisons isolate the effect of nicotine as provided by an EC, and nicotine EC versus NRT comparisons isolate the effect of the sensorimotor elements provided by an EC. Both of these

comparisons find a benefit of nicotine EC for smoking cessation. Therefore, it might logically follow that the comparison between nicotine EC and behavioural support only/no support would find a benefit in favour of nicotine EC, since this comparison would capture both pharmacological and sensorimotor mechanisms of effect. This increases our confidence in the effect of nicotine EC when compared to behavioural support alone or to no support. NRT has also been shown to be more effective than behavioural support alone, further supporting the likelihood that nicotine EC would be more effective than behavioural support alone [1].

Adverse and serious adverse events

Moderate-certainty evidence does not show a difference in SAEs for the nicotine EC compared to NRT comparison or in AEs for the nicotine EC compared to non-nicotine EC comparison. For all other outcomes in this category, evidence is of low or very low certainty. Imprecision remains a key issue for these outcomes. None of the analyses signalled serious harm but, unlike our cessation analyses, many of the CIs encompassed the possibility of both clinically significant harm and clinically significant benefit, and longer-term health effects are unknown. This uncertainty should reduce as more studies become available.

Limitations of the review processes

We consider the review process we used to be robust. For the outcome assessment, we followed the standard methods used for Cochrane Tobacco Addiction Review Group cessation reviews. Our search strategy included CENTRAL, which incorporates findings from trial registries, and we were able to capture a number of ongoing studies. However, there may be unpublished data that our searches did not uncover. We also considered participants lost to follow-up as continuing to smoke, which is standard practice in this field. There are concerns that frequently updating meta-analyses can lead to issues with multiple testing; we followed Cochrane guidance in conducting this living systematic review and hence do not adjust for multiple testing [79].

Six of our review authors are authors of the included studies. These authors were not involved in the decisions about inclusion of their studies, or in risk of bias assessment for these studies; this approach is standard across all Cochrane reviews (regardless of subject area) and has been approved by the Cochrane editorial office as sufficient to avoid bias.

Our review includes studies funded by the tobacco/vaping industry – Cochrane guidelines (not tobacco addiction-specific) mandate that studies be included regardless of funder, in order that the reviews remain transparent and rigorous. As noted throughout the results section, we removed studies with tobacco or vaping industry funding for sensitivity analyses; our conclusions were unchanged when we did this. This means that studies funded by tobacco or vaping industries *did not influence* our conclusions. We do not receive any funding from tobacco or vaping industries, and maintain a firm stance of independence.

Agreements and disagreements with other studies or reviews

An overview of reviews of RCTs conducted in 2024 found that the majority of existing systematic reviews of trial data reached similar conclusions to those presented in this review regarding the effectiveness of nicotine-containing EC for smoking cessation [348]. Reviews by Hanewinkel and colleagues and Li and colleagues found that nicotine EC were more effective than NRT, with risk ratios (RRs) of 1.58 (95% confidence interval (CI): 1.20 to 2.08) and 1.67 (95% CI: 1.21 to 2.28), respectively [349, 350]. Levett and colleagues reported greater cessation with nicotine EC compared to non-nicotine EC (RR: 1.56, 95% CI: 1.13 to 2.15) and to non-EC interventions (RR: 1.77, 95% CI: 1.29 to 2.44) [351]. Thomas and colleagues, in a large network meta-analysis, found that high-dose nicotine EC were more effective than placebo (odds ratio (OR): 3.22, 95% credible interval (CrI): 1.63 to 6.36) [352]. Chan and colleagues, in another network meta-analysis, reported benefits of nicotine EC over non-nicotine EC (RR: 2.09, 95% CI: 1.46 to 2.99) and over NRT (RR: 1.49, 95% CI: 1.09 to 2.04) [353]. Lindson and colleagues conducted a component network meta-analysis (CNMA) and found nicotine EC significantly more effective than placebo (OR 2.37, 95% CrI: 1.73 to 3.24), with high-certainty evidence [7]. Overall, the reviews were consistent in both the direction and magnitude of effect, supporting the conclusion that nicotine EC improve quit rates at six months or longer.

Some reviews reported greater uncertainty. Quigley and colleagues found an RR of 1.17 (95% CrI: 0.65 to 1.86) for nicotine EC compared with NRT, with the credible interval including the possibility of no difference [354]. Pound (2021) reported low- or very low-certainty evidence for an RR of 1.42 (95% CI: 0.97 to 2.09) for the same comparison [355]. Patnode and colleagues conducted a narrative synthesis, reviewing five studies comparing nicotine EC to non-EC interventions and concluded that evidence was mixed and insufficient to draw firm conclusions [356]. Khoudigian and colleagues, in the earliest review included, reported a point estimate favouring nicotine EC over non-nicotine EC (RR: 2.02, 95% CI: 0.97 to 4.22) [357], though the CI included the null. Differences in search dates, number of included trials, and analytic methods, such as reliance on point prevalence rather than sustained abstinence, are likely to have contributed to variation in findings across these reviews. Huang and colleagues conducted a review including participants at high risk of lung cancer, found a benefit for smoking cessation from nicotine EC over behavioural support alone (RR: 1.51, 95% CI: 1.03 to 2.21), but raised methodological concerns, including potential double counting of participants [358].

Findings related to safety outcomes were more variable. Of the reviews that meta-analysed SAEs, two reported statistically significant increases in SAEs amongst EC users [351, 359]. Vanderkam and colleagues compared EC with NRT (RR 1.53, 95% CI: 1.02 to 2.30) [359]. However, in Levett, the increased SAEs were observed amongst users of non-nicotine EC compared with non-EC conventional smoking cessation interventions [351]. Most other reviews, including those by Li and colleagues and Ibrahim and colleagues, found no significant differences or were underpowered to detect rare events [350, 360].

Across the reviews, the certainty of evidence for SAE outcomes was generally low or very low, due to imprecision and short follow-up durations. These inconsistencies reflect variation in study quality, reporting practices and low event rates. In contrast to the relative consistency of evidence on effectiveness, evidence on safety remains limited and uncertain, highlighting the need for longer-term studies with sufficient power to assess harms.

Some reviews have examined the evidence on the role of EC flavours in quit rates. A systematic review by Liber and colleagues concluded that the evidence was inconclusive, reflecting highly

heterogeneous study definitions and methodological limitations, and called for more high-quality evidence, ideally from RCTs [361]. An overview of reviews examining the impact of EC flavours on any outcome reported that current evidence was inconclusive on the effect of flavours on quit rates [362].

AUTHORS' CONCLUSIONS

Implications for practice

Evidence suggesting that nicotine electronic cigarettes (EC) can aid in smoking cessation is consistent across several comparisons. There is high-certainty evidence that EC with nicotine increase quit rates at six months or longer compared to nicotine replacement therapy (NRT, both combined and single forms), and moderate-certainty evidence (limited by imprecision) that EC with nicotine probably increases quit rates at six months or longer compared to non-nicotine EC. There is also low-certainty evidence (limited by risk of bias) that EC with nicotine may increase quit rates compared to behavioural support alone or no support.

None of the synthesised evidence provides a clear indication that serious adverse events are increased by EC use. However, more long-term data are needed, and this conclusion relates specifically to people using regulated EC to stop smoking and not to people who have never smoked. In some studies, reduced toxicant concentrations and biomarkers of harm were observed in people who smoked and switched to vaping, consistent with reductions seen in people who stopped smoking without EC.

Implications for research

Further randomised controlled trials of nicotine EC are needed. All studies should aim to assess the safety profile of EC for as long as possible (the current review only includes data up to two years), and ideally be powered to detect differences in safety outcomes, particularly serious adverse events.

Studies with active comparators (i.e. comparing nicotine EC to frontline smoking cessation pharmacotherapies, particularly those other than nicotine replacement therapy) are likely to be of particular use to decision-makers, as are those testing EC as an adjunct to existing stop-smoking pharmacotherapies; in particular, those testing combinations of traditional nicotine replacement therapy with e-cigarettes (e.g. patch plus e-cigarettes).

Studies should offer recent devices with good nicotine delivery to participants to be most representative of what will be on the market at the time results are released. Studies should also monitor and collect data on participants switching use of other devices during trials, and use of different flavours and nicotine strengths. Protocols and statistical analysis plans should be registered in advance and openly available.

Further trials of newer devices would be of particular value, as would RCTs providing EC in a way that would be used in real-world settings (e.g. taking into account individual preferences for strengths and flavours of EC liquids and even EC devices, and also allowing for changes in preferences over time). Further studies directly comparing nicotine EC based on characteristics including nicotine content and delivery, flavour, and device type, and reporting outcomes including cessation at six months or longer, would also be particularly useful.

SUPPLEMENTARY MATERIALS

Supplementary materials are available with the online version of this article: 10.1002/14651858.CD010216.pub11.

Supplementary material 1 Search strategies

Supplementary material 2 Characteristics of included studies

Supplementary material 3 Characteristics of excluded studies

Supplementary material 4 Characteristics of studies awaiting classification

Supplementary material 5 Characteristics of ongoing studies

Supplementary material 6 Analyses

Supplementary material 7 Data package

Supplementary material 8 Protocol for living systematic review

Supplementary material 9 Toxins/carcinogen names and abbreviations

Supplementary material 10 Changes in methods between living review updates

Supplementary material 11 Adverse events data not contributing to meta-analyses

Supplementary material 12 Carbon monoxide (CO) data not contributing to meta-analyses

Supplementary material 13 Heart rate data not contributing to meta-analyses

Supplementary material 14 Blood pressure data not contributing to meta-analyses

Supplementary material 15 Data on known toxicants/carcinogens from studies not contributing to meta-analyses

Supplementary material 16 Data on lung function from studies not contributing to meta-analyses

Supplementary material 17 Product use at 6+ months for data not contributing to meta-analyses

ADDITIONAL INFORMATION

Acknowledgements

This update was funded through a Cancer Research UK PIC Commissioned Research Targetted Research grant (PICCTR-2024/100012). The 2025, 2024 and 2023 updates were funded through a Cancer Research UK Prevention and Population Research Committee Project grant (PRCPJT-Nov22/100012). The three previous updates (November 2022, April 2021, and October 2020) were supported through a Tobacco Advisory Group Cancer Research UK Project Grant. The 2020 update was also supported by the Cochrane Incentive Award Scheme and the University of Oxford Returning Carer's Fund, as well as through core infrastructure funding from the National Institute for Health Research (NIHR) for the Cochrane Tobacco Addiction Review Group. The views and opinions expressed are those of the authors and do not necessarily

reflect those of the Systematic Reviews Programme, NIHR, National Health Service (NHS) or the Department of Health. The addition of new outcomes relating to vaping and smoking at six months or longer was supported by the National Cancer Institute of the National Institutes of Health (NIH) and FDA Center for Tobacco Products (CTP) under Award Number 2U54CA229974. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or the Food and Drug Administration. The funders were not involved in the decision to submit for publication.

TRF receives funding from the National Institute for Health and Care Research (NIHR) HealthTech Research Centre for Community Healthcare at Oxford Health NHS Foundation Trust (NIHR205287). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

We would like to thank Assistant Professor Stephen R. Baldassarri, Drs Pasquale Caponnetto, Fabio Cibella and Professor Riccardo Polosa, Professor Matthew Carpenter, Bruce R. Lindgren and Professor Dorothy Hatsukami, Assistant Professor Tracy Smith, Assistant Professor Susan Veldheer, Lauren Hickling, Stephanie K. Bell, Associate Professor Coral Gartner, Professor Billie Bonevski, Karolien Adriaens, Dr Sharon Cox, Professor Lynne E. Dawkins, Professor Mark Eisenberg, Andrea Hebert-Losier, Kris Filion, Dr Ignatios Ikonomidis, Dr Kim Pulvers, Florian Scheibein, Dr Markos Klonizakis, Dr Scott Sherman, Dr Kylie Morphett, Dr Ivan Berlin, Marzena Orzol, Dr Katie Myers Smith, Christine Czoli, Dr Caroline Cobb, Dr Jonathan Foulds, Professor Thomas Brandon, Dr Eleanor Leavens, Dr Michael Arnold, Dr Paul Bateman, Dr Konstantinos Katogiannis, Dr Christopher Russell, Dr Francesca Pesola, Professor Christian Delles, Dr Danièle Kerr, Cassidy White, Professor Megan Piper, Dr Milly N. Kanobe, Mahathi Vojjala MPH, Dr Theodore Wagener, Dr Michael DeSarno, Dr Stephen Higgins, Dr Irene Pericot-Valverde, Dr Konstantinos Katogiannis, Dr Jaqueline Contrera Avila, Dr Dimitra Kale, Dr Susan Lee, Dr Jason Robinson, Dr Katherine Menson, and Professor Natalie Walker for providing additional data or information. We would like to thank Clareece Nevill for assistance in assessing the Society for Research on Nicotine and Tobacco (SRNT) 2025 abstracts.

Editorial and peer reviewer contributions – 2026 update

The following people conducted the editorial process for this living systematic review:

- Sign-off Editor (final editorial decision): Toby Lasserson, Cochrane;
- Managing Editor (selected peer reviewers, collated peer reviewer comments, provided editorial guidance to authors, edited the article): Joey Kwong, Cochrane Central Editorial Service;
- Copy Editor (copy editing and production): Anne Lethaby, Cochrane Central Production Service;
- Peer reviewers (provided comments and recommended an editorial decision): Lindsay Robertson, Cochrane Evidence Production and Methods Directorate (methods review); Jo Platt, Cochrane Evidence Production and Methods Directorate (search review).

Contributions of authors

Conception: JHB, PH, HM, CB.

Design and methodology: JHB, NL, PH, HM, CB, ARB, TRF, JLB.

Co-ordination of the review: NL, JHB, ARB.

Study selection, data extraction, and risk of bias assessment: NL, JHB, ARB, CM, ADW, AT, RB, TT, TRF, CN.

Syntheses and GRADE assessment: NL, JHB, JLB.

Critical appraisal, write-up, and manuscript review: NL, ARB, HM, CB, PH, RB, AT, CM, CN, NAR, TRF, ADW, JLB, TT, JHB.

Search strategy and monthly searches: JLB.

Statistical expertise: TRF.

Funding acquisition: JHB, NL, CB, HMR, NAR, CN, TRF, PH, JLB, RB, ARB.

All authors approved the final version to be published and agreed to be accountable for all aspects of the work.

Declarations of interest

RB: no relevant interests; involved in an included study (Begh 2021) - did not make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of that study.

CB: payment of travel, accommodation, subsistence and conference registration expenses from Kenvue/Johnson & Johnson Asia (a consumer pharmaceuticals company that makes NRT products for smoking cessation); employed 0.5 FTE as a Professor of Public Health by the University of Auckland; Fellow of the Royal Australasian College of Physicians; Fellow of the New Zealand College of Public Health Medicine, both of which have policy positions on e-cigarettes; Co-chair of the Smokefree Expert Advisory Group of Health Coalition Aotearoa, an NGO that advocates for public health and has a policy stance on e-cigarettes; involved in an included study (Bullen 2013) and also several other studies that may be included in the review - did/will not make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of these studies.

ARB: none known.

TRF: none known.

PH: no relevant interests; involved in two included studies (Hajek 2019 and Hajek 2022) - did not make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of these studies; provided commentaries on relevant research for Science Media Centre.

JHB: no relevant interests; Senior Editor, Cochrane Database of Systematic Reviews – not involved in the decision-making/editorial processing for this review.

NL: no relevant interests; research grants from the National Institute for Health and Care Research (NIHR), Cancer Research UK (CRUK), the Greater Manchester NHS Integrated Care Board,

Oxfordshire County Council, Reading Borough Council, the National Institutes of Health (NIH)/Food and Drug Administration (FDA), and Action on Smoking and Health (ASH); involved in two ongoing studies that may be included in this review - will not make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of these studies if they are included.

JLB: no relevant interests; involved in an included study (Pope 2024) - did not make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of that study.

HM: no relevant interests; works for Queen Mary University of London (QMUL has a contract for delivering smoking cessation services for three London Boroughs; electronic cigarettes are used to support some quit attempts); co-investigator on several studies included in this review – did not make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of these studies.

CN: no relevant interests; Editor-in-Chief, *Nicotine & Tobacco Research* (this journal publishes research relevant to this review through a process of scientific peer review); co-investigator of an included study (Pope 2024) - did not make study eligibility decisions about, extract data from, carry out the risk of bias assessment for, or perform GRADE assessments of that study.

CM: none known.

NAR: funding for research from Achieve Life Sciences (to develop cytisinicline, an investigational smoking cessation medication); research grant through home institution, Massachusetts General Hospital, to test the safety of the drug with long-term use.

AT: no relevant interests; published papers on the use of smoking cessation aids, which have been press released.

TT: no relevant interests; Editorial Board Member, Cochrane Library – not involved in the decision-making/editorial processing for this review.

ADW: none known.

Sources of support

Internal sources

- 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
- University of Oxford, UK

  Support from Returning Carers' Fund
- University of Oxford, UK

  Public Policy Challenge Fund

External sources

- National Cancer Institute of the National Institutes of Health and United States Food and Drug Administration, USA

  This review was supported by the National Cancer Institute of the National Institutes of Health (NIH) and FDA Center for Tobacco Products (CTP) under Award Number 2U54CA229974. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or the Food and Drug Administration. The funders were not involved in the decision to submit for publication.
- NIHR, UK

  Infrastructure award for Cochrane Tobacco Addiction Group and Cochrane Incentive Award
- Cancer Research UK, UK

  Cancer Research UK project award funding to support living systematic review

Registration and protocol

Protocol (2012) DOI: 10.1002/14651858.CD010216 (updates to 2012 protocol available via DOI: 10.17605/OSF.IO/UPGJC)

Original Review (2014) DOI: 10.1002/14651858.CD010216.pub2

Review Update (2016) DOI: 10.1002/14651858.CD010216.pub3

Review Update (2020) DOI: 10.1002/14651858.CD010216.pub4

Review Update (2021 Apr) DOI: 10.1002/14651858.CD010216.pub5

Review Update (2021 Sep) DOI: 10.1002/14651858.CD010216.pub6

Review Update (2022) DOI: 10.1002/14651858.CD010216.pub7

Review Update (2024) DOI: 10.1002/14651858.CD010216.pub8

Review Update (2025 Jan) DOI: 10.1002/14651858.CD010216.pub9

Review Update (2025 Nov) DOI: 10.1002/14651858.CD010216.pub10

Data, code and other materials

As part of the published Cochrane review, the following is made available for users of the Cochrane Library: our search strategies, Supplementary material 1: full citations for all included studies, all ongoing studies, relevant excluded studies, and studies awaiting classification in the reference section of the review; study data, including study information, study arms and risk of bias assessments in our characteristics of studies tables, (Supplementary material 2; Supplementary material 3; Supplementary material 4; Supplementary material 5). Analysis data, including overall estimates, subgroup estimates, and individual data rows (all the rows in all the analyses) are in the main review and in Supplementary material 6. Data supporting the results of this systematic review are from published information and are available in the review. For details of the computational methods, see https://documentation.cochrane.org/revman-kb/statistical-methods-210600101.html. Analyses were conducted within Cochrane's authoring tool, RevMan, using the inbuilt computation methods. Data were extracted into Microsoft Word and are available from the authors on reasonable request. The

data are shared within the published review directly from RevMan Supplementary material 7.

Disclosure of artificial intelligence use

The authors have not explicitly used artificial intelligence to conduct this review. However, there may be artificial intelligence embedded in some of the software that we have used (e.g. Covidence). Where software has been used, this has been cited.

What's new

Date	Event	Description
26 August 2026	New search has been performed	Updated to include nine new studies: searches to 1 January 2026. Non-randomised studies have been removed, as prespecified due to the availability of substantial numbers of randomised controlled trials (n = 80).
26 August 2026	New citation required but conclusions have not changed	Main conclusions remain unchanged. Update triggered as results became available for the first study comparing nicotine EC vs. cytisine and nicotine EC + cytisine vs. cytisine, reporting abstinence at six months or longer, was published.

History

Protocol first published: Issue 11, 2012
Review first published: Issue 12, 2014

Date	Event	Description
10 November 2025	New search has been performed	Updated to include fourteen new studies; searches to 1 March 2025
10 November 2025	New citation required but conclusions have not changed	Main conclusions remain unchanged. Update triggered as the first study comparing nicotine EC vs. non-nicotine EC + varenicline reporting abstinence at six months or longer was published (results inconclusive).
29 January 2025	New search has been performed	Updated to include two new studies; searches to 1 February 2024
29 January 2025	New citation required but conclusions have not changed	Main conclusions remain unchanged. Update triggered as first study comparing flavours and reporting abstinence at six months or longer was published (results inconclusive).
8 January 2024	New search has been performed	This is a living systematic review. In this update, we incorporate data to 1st July 2023.
8 January 2024	New citation required and conclusions have changed	Certainty of evidence for cessation outcome for comparison with behavioural support/no support upgraded from very low to low
15 March 2023	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st March 2023. In addition to the studies identified from August 2022 to February 2023, we found one new reference linked to a previously identified study. We will incorporate this into the review as part of a future update. We have also fixed a typo in the plain language summary. For future monthly search results, please see 'Monthly search results' via the following link: https://www.cebm.ox.ac.uk/research/elec-

Date	Event	Description
		tronic-cigarettes-for-smoking-cessation-cochrane-living-systematic-review-1.
4 February 2023	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st February 2023. In addition to the studies identified from August 2022 to January 2023, we found one new included study, one new ongoing study and 2 linked references. We will incorporate these into the review as part of a future update. The DOI for the 1 new included study (Kanobe 2022) is: https://doi.org/10.1038/s41598-022-25054-z.
5 January 2023	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 3rd January 2023. In addition to the studies identified from August 2022 to December 2022, we found one new ongoing study. We will incorporate these into the review as part of a future update. In addition, some minor corrections were made to the Characteristics of Included Studies table for Hajek 2022 based on a published correction to the study's primary manuscript (https://doi.org/10.1038/s41591-022-02099-1).
12 December 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st December 2022. In addition to the studies identified from August 2022 to November 2022, we found one new ongoing study and 3 records linked to previously identified studies. We will incorporate these into the review as part of a future update.
25 November 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st November 2022. We found no new eligible references. As part of this amendment, we also updated the citation for additional reference [330], and corrected a slight error in wording in the Discussion section.
19 October 2022	New search has been performed	17 new included studies. Incorporates evidence up to the 1st July 2022.
19 October 2022	New citation required and conclusions have changed	Certainty changes for some of the primary outcomes.
7 October 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st October 2022. In addition to the studies identified from June 2021 to September 2022, we found one new included study, 3 new ongoing studies and 1 record linked to a previously identified study. The DOI for the 1 new included study is: Klonizakis 2022 (https://doi.org/10.1186/s12916-022-02451-9). We will incorporate these into the review as part of a future update.
27 September 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st September 2022. In addition to the studies identified from June 2021 to August 2022, we found two records linked to previously identified studies. We will incorporate these into the review as part of a future update.
17 August 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st August 2022. In addition to the studies identified from June 2021 to July 2022, we found two

Date	Event	Description
		new included studies, 1 new ongoing study and 3 records linked to previously identified studies. The DOIs for the 2 new included studies are: Coffey 2020 (DOI: 10.1177/1757913920912436) and Price 2022 (DOI: https://doi.org/10.1186/s12889-022-13711-x). We will incorporate these into the review as part of a future update.
8 July 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st July 2022. In addition to the studies identified from June 2021 to June 2022, we found four new included studies, 1 new ongoing study and 8 records linked to previously identified studies. The DOIs for 3 of the new included studies are: Edmiston 2022 (DOI: 10.1093/ntr/ntac029); Tattan-Birch 2022 (DOI: 10.1093/ntr/ntac149) and Morphett 2022a (DOI: 10.1093/ntr/ntab266). The fourth new included study was presented at SRNT 2022 (abstract reference: SYM17-4). We will incorporate these into the review as part of a future update.
15 June 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st June 2022. In addition to the studies identified from June 2021 to May 2022, we found three new included studies (all previously listed as ongoing studies) and 2 records linked to a previously identified study. The DOIs for the new included studies are: Hajek 2022 (https://doi.org/10.1038/s41591-022-01808-0); Bonafont Reyes 2022 (https://doi.org/10.1111/jgs.17755) and Vickerman 2022 (https://doi.org/10.1093/ntr/ntac129). We will incorporate these into the review as part of a future update.
6 May 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st May 2022. In addition to the studies identified from June 2021 to April 2022, we found two new included studies (previously listed as ongoing studies), 3 new ongoing studies and 2 records linked to previously identified studies. The DOIs for the new included studies are: Skelton 2022 (doi: 10.1016/j.addbeh.2022.107328); Pratt 2022 (doi: 10.1093/ntr/ntac082). We will incorporate these into the review as part of a future update.
6 April 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st April 2022. In addition to the studies identified from June 2021 to March 2022, we found 4 new ongoing studies. We will incorporate these into the review as part of a future update.
7 March 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st March 2022. In addition to the studies identified from June 2021 to February 2022, we found 1 record linked to a study already identified as ongoing. We will incorporate these into the review as part of a future update.
11 February 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st February 2022. In addition to the studies identified from June 2021 to January 2022, we found 2 ongoing studies and 2 records linked to studies already included in the review. We will incorporate these into the review as part of a future update.

Date	Event	Description
12 January 2022	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st January 2022. In addition to the studies identified from June to December 2021, we found 4 ongoing studies and 1 record linked to a study already included in the review. We will incorporate these into the review as part of a future update.[Enter text here]
16 December 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date: 1st December 2021. In addition to the studies identified from June to November 2021, we found six new included studies, 15 ongoing studies and 18 records linked to studies already included in the review. The DOI or trial IDs for the new included studies are: NCT02433015; NCT03111537; NCT03185546; NCT03358953; Caponnetto 2021 (DOI: 10.1093/ntr/ntab005); Lum 2021 (DOI: 10.1016/j.addbeh.2021.107097). We will incorporate these into the review as part of a future update.
3 November 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date 1st November 2021. In addition to the studies identified from June to October 2021, we found one new included study. The DOI for the new included study (Okuyemi 2021) is 10.1093/ntr/ntab212. We will incorporate these into the review as part of a future update.
20 October 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date 1st October 2021. In addition to the studies identified from June to September 2021, we found one new included study two reports linked to studies already in the review, and one new ongoing. The DOI for the new included study (Morris 2021) is https://doi.org/10.1007/s11739-021-02813-w. We will incorporate these into the review as part of a future update.
16 September 2021	Amended	Change made to correct data; SAE data from Cobb 2021 moved from comparison with NRT to comparison with no-nicotine EC. No changes to conclusions.
6 September 2021	New search has been performed	Updated with five new included studies. Incorporates evidence up to 1 May 2021.
6 September 2021	New search has been performed	This is a Living Systematic Review. We run and screen searches monthly. Last search update 1st September 2021. We found no new studies for inclusion this month; however results from searches carried out from June to August 2021 will be incorporated into a future update of the review.
6 September 2021	New citation required and conclusions have changed	New secondary outcome added (continued product use), first study of pod device contributing data to cessation meta-analysis added, two new comparisons added (nicotine salt EC versus freebase nicotine EC; advice on how to quit smoking using EC versus no EC advice). Conclusions for primary outcomes remain largely unchanged.
5 August 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date 2nd August 2021. In addition to the studies identified from March to July 2021, we found two new ongoing studies and one report linked to a study already in the

Date	Event	Description
		review. We will incorporate these into the review as part of a future update.
7 July 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date 1st July 2021. In addition to the studies identified from March to June 2021, we found two new included studies and two reports linked to studies already in the review. DOIs for the two new included studies are as follows: Myers-Smith 2021: https://doi.org/10.1111/add.15628 & Kimber 2021: 10.1016/j.addbeh.2021.106909. We will incorporate these into the review as part of a future update.
9 June 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date 1st June 2021. In addition to the studies identified from March to May 2021, we found one report linked to a study already in the review, one ongoing study, and one potentially new study that we are looking into further. We will incorporate these into the review as part of a future update. As part of this new update we will also include a new outcome - proportion of people still using e-cigarettes or other pharmacotherapy at longest follow-up.
12 May 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date 4th May 2021. In addition to the studies identified from March and April 2021, we found four new ongoing studies. We will incorporate these into the review as part of a future update.
15 April 2021	New search has been performed	Updated with six new included studies and new data from one previously included study. Most recent search 1 Feb 2021.
15 April 2021	New citation required and conclusions have changed	6 new included studies added (Czoli 2019; Ikonomidis 2020a [363]; Ozga-Hess 2019; Pulvers 2020; Yingst 2020), certainty in finding of no difference in adverse events between nicotine EC and non-nicotine EC updated to moderate (from low). First study of pod EC device included.
1 April 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date 1st April 2021. In addition to the studies identified from March 2021 we found two new ongoing studies and one paper linked to a study already included in the review. We will incorporate these into the review as part of a future update.
17 March 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date 1st March 2021. Studies identified in March are not included in this version of the review, but will be incorporated into a subsequent version. We found four new included studies, five new ongoing studies and five papers linked to studies already included in the review. The four new included studies were all conference abstracts; three of which were identified from the SRNT 2021 abstract book (SYM2A, SYM2B, PH-353; www.srnt.org/page/2021_Meeting). The fourth is available here: dx.doi.org/10.1016/j.drugalcdep.2015.07.1091.
4 February 2021	Amended	This is a Living Systematic Review. We run and screen searches monthly. Last search date 1st February 2021. In addition to the studies identified from our December 2020 and January 2021

Date	Event	Description
		searches we found one paper linked to a study already included in the review (Lucchiari 2022), and have preliminary results from a study listed as ongoing (Begh 2021). We will incorporate this paper and data into the review as part of a future update.
20 January 2021	Amended	This is a Living Systematic Review. Searches are run and screened monthly. Last search date 4th January 2021. In addition to the studies identified from our December 2020 searches we found four new completed studies, one new ongoing study and one paper linked to a study already included in the review. These studies and papers will be incorporated into the review at the next update. DOIs for the four new included studies are as follows: Ozga-Hess et al. 2019: 10.1016/j.addbeh.2019.106105; Pulvers et al. 2020: 10.1001/jamanetworkopen.2020.26324; Yingst et al. 2020: 10.1080/09540121.2019.1687835
15 December 2020	Amended	This is a Living Systematic Review. Searches are run and screened monthly. Last search date 1st December 2020. Searches found 3 new completed studies, 11 new ongoing studies and 9 papers linked to studies already included in the review. These studies and papers will be incorporated into the review at the next update. DOIs for the three new included studies are as follows: Czoli et al:10.1093/ntr/nty174; Bonevski et al: 10.1093/ntr/ntaa143; Eisenberg et al: 10.1001/jama.2020.18889.
20 July 2020	New search has been performed	New searches run January 2020. 35 new studies added. Living systematic review protocol incorporated
20 July 2020	New citation required and conclusions have changed	Strength of evidence increased for existing comparisons; new comparisons added
14 December 2016	Amended	Clarification on outcome data from Adriaens - no changes to conclusions
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.

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ADDITIONAL TABLES

Table 1. Overview of included RCTs

Study ID	Number randomised	Study arms	Length follow-up (months)	Motivated to quit smoking	Specific population characteristics (e.g. pregnant or HIV +ve)	Overall RoB judgement	Tobacco or EC industy-funded	Country	NRT single/combination/unclear (NA not applicable)
Adriaens 2014 [364]	48	1) Nicotine EC1 2) Nicotine EC2 3) Control	6			Unclear	No	Belgium	NA
Auer 2024 [365, 366, 367, 368, 369, 370, 371, 372, 373, 374, 375, 376, 377, 378, 379, 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 392, 393, 394]	1246	1) Nicotine EC 2) Control	24			High	No	Switzerland	NA
Avila 2024	45	1) Nicotine EC 2) Nicotine pouch 3) Control (smoking as usual)	2	No	Lower economic status	High	No	USA	NA (nicotine pouch)
Baldassarri 2018	40	1) Nicotine EC + NRT (patch) + counselling 2) Non-nicotine EC + NRT (patch) + counselling)	6	Yes ('willing to quit smoking')	Recruitment: outpatient pulmonary and primary care clinics, Tobacco Treatment Service, referrals from medical providers	High	No	USA	NRT single form (patch)

Table 1. Overview of included RCTs *(Continued)*

Begh 2021	325	1) Nicotine EC 2) Control (standard care)	8	No	Diagnosed with 1 or more of the following chronic conditions: ischaemic heart disease, peripheral vascular disease, hypertension, diabetes mellitus (Type 1 and Type 2), stroke, asthma, COPD, chronic kidney disease, depression, schizophrenia, bipolar disorder or other psychoses	High	No	UK	NA
Bonafont Reyes 2022	48	1) Nicotine EC 2) NRT	3	Yes	Moderate COPD	Unclear	NR	USA	NRT unclear
Bonevski 2025	363	1) Nicotine EC 2) NRT (combination)	9	Yes	Participants discharged from residential withdrawal services	High	No	Australia	NRT combination
Bonevski 2021	100	1) Nicotine EC 2) NRT	3	Median (SD) = 7.3 (2.4) on 1 to 10 scale with 10 "highly motivated"	Participants discharged from a smoke-free alcohol or other drugs residential withdrawal service	High	No	Australia	NRT combination
Bullen 2013	657	1) Nicotine EC 2) Nicotine patch (NRT) 3) Non-nicotine EC	6	Yes		Low	No	New Zealand	NRT single form (patch)

Table 1. Overview of included RCTs *(Continued)*

		plus all participants referred to quitline							
Caponnetto 2013*	300	1) Nicotine EC 7.2 mg for 12 weeks 2) Nicotine EC 7.2 mg for 6 weeks, then 5.4 mg for 6 weeks 3) Non-nicotine EC	12	No (Not currently or intending to quit smoking in the next 30 days)	In good health	Unclear	Yes	Italy	NA
Caponnetto 2023*	220	1) Nicotine EC 2) Heated tobacco products (HTP)	6	No		High	Yes	Italy	NA
Carpenter 2017 [395, 396, 397]	68	1 Nicotine EC 2) CC	4	Medium interest in quitting smoking.		High	No	USA	NA
Carpenter 2023 [398, 399, 400, 401, 402, 403, 404, 405, 406]	638	1) Nicotine EC 2) No intervention	6	Limited interest in quitting smoking.		High	No	USA	NA
Cioe 2025	35	1) Nicotine EC 2) No intervention	3	No	HIV-positive CC smokers, who are not ready or willing to quit smoking	High	No	USA	NA
Cobb 2021	520	1) Nicotine EC (36 mg) 2) Nicotine EC (8 mg) 3) Non-nicotine EC 4) Cigarette substitute	8.5	No (but interested in reducing)		Low	No	USA	NA
Courtney 2025	1048	1) Nicotine EC 2) NRT single form (gum OR lozenge)	3	Yes	Receiving a government pension/allowance (proxy for social disadvantage)	Low	No	Australia	NRT single form (participants select one form of NRT from gum or lozenge)

Table 1. Overview of included RCTs *(Continued)*

Cox 2022	477	1) Nicotine EC 2) No intervention (usual care) Cluster-RCT	6		Currently accessing homeless centre services	High	No	UK	NA
Cravo 2016*	408	Phase 1 (RCT): 1) Nicotine EC 2) CC. 3 months (N = 419) Phase 2 (single arm): 1) Nicotine EC Followed for 24 months. (N = 209) Phase 2 not eligible	3	No		High	Yes	UK	NA
Czoli 2019	48	1) EC to CC to no product 2) CC to EC to no product (within participant cross-over)	0.75	No	Dual users of EC and CC	High	No	Canada	NA
Edmiston 2022*	450	1) Nicotine EC (tobacco flavour) 2) Nicotine EC (menthol flavour) 3) No intervention	3	Willing to replace CC with EC		High	Yes	USA	NA
Eisenberg 2020	376	1) Nicotine EC + counselling 2) Non-nicotine EC + counselling 3) Counselling	12	Yes		Low	No	Canada	NA
Eisenhofer 2015	11	1) Nicotine EC 2) NRT (patch 16 mg	0.75		Veterans	Unclear	No	USA	NRT single (patch)
Elling 2023	331	1) Tailored EC information 2) Control (no tailored EC information	6	Yes (within 5 years)		High	No	Netherlands	NA
Felicione 2019	25	1) Nicotine EC 2) Non-nicotine EC	1	Quit ladder score average: 5.6 (range 1 to 10)	Opioid-dependency	Unclear	NR	USA	NA
George 2019	145	1) Nicotine EC 2) Non-nicotine EC 3) CC	1	Yes (in nicotine EC and non-nicotine EC groups)		High	No	UK	NA

Table 1. Overview of included RCTs *(Continued)*

Hajek 2019	886	1) Nicotine EC 2) NRT	12	Yes		Low	No	UK	NRT combination
Hajek 2022	1140	1) Nicotine EC 2) NRT	6+	Yes	Pregnant women	Low	No	UK	NRT. Single (patches different strengths provided in study) Participants encouraged to access combination form NRT
Halpern 2018 [407, 408, 409]	6006	1) Usual care, quit smoking programme (Vitality) 2) as (1) plus Nicotine EC 3) as (2) plus access to free NRT, bupropion or varenicline 4) as (3) plus incentives for quitting 5) as (4) plus money at start and lose money if do not test negative across 6 months	12	Yes 28% No 9% Quit later 62%	Employees and spouses at 54 companies that used Vitality wellness programmes	High	No	USA	NRT unclear
Hatsukami 2020	264	1) Nicotine EC complete substitution for CC 2) Nicotine EC partial substitution for CC 3). NRT complete substitution for CC 4) CC	2	No		Unclear	No	USA	NRT single (gum or lozenge)
Higgins 2024	326	1) Nicotine EC (tobacco flavour) + VLNC 2) Nicotine EC (preferred flavour) + VLNC 3) VLNV 4) CC	4	No	Vulnerable populations: people with affective disorders; opioid use; women of reproductive age with maximum educational attainment of gradu-	Unclear	No	USA	NA

Table 1. Overview of included RCTs *(Continued)*

					ating from high school				
Holliday 2019 [410, 411, 412]	80	1) Nicotine EC + standard stop smoking advice 2) Standard stop smoking advice only	6	NR	People diagnosed with periodontitis (setting dental clinic)	High	No	UK	NA
Ikonomidis 2020a	40	1) Nicotine EC 2) CC	4	Yes (attending smoking cessation clinic)		Unclear	No	Greece	NA
Ikonomidis 2020b [413]	40	1) Nicotine EC 2) CC	1	Yes (attending smoking cessation clinic)		High	No	Greece	NA
Ikonomidis 2024	100	1) Nicotine EC 2) Heat not burn cigarette 3) Control	1	Yes		Unclear	No	Greece	NA
Ioakeimidis 2018	54	1) Nicotine EC + low intensity counselling 2) Varenicline + low level counselling	6	Yes	Participants hospitalised with acute coronary syndrome	High	NR	Greece	NA
Kale 2025 [414, 415]	43	1) Nicotine EC 2) Usual care	1	Yes (willing to quit)	All participants had a diagnosed mental health condition and were receiving treatment in primary or secondary care.	High	No	UK	NA
Kanobe 2022*	125	1) Nicotine EC (Vuse solo 4.8%, 57.4 mg/mL 2) Nicotine EC (Vuse ciro 1.5%) 3) Nicotine EC (Vuse vibe 3%, 36 mg/mL	0.25	No		High	Yes	USA	NA

Table 1. Overview of included RCTs *(Continued)*

		4) Abstinence							
Katz 2025	21	Two 2-week phases CC phase EC phase Cross-over	0.5	NR	COPD diagnosis	High	No	USA	NA
Kerr 2020	55	1) Nicotine EC + behavioural support 2) NRT + behavioural support	3	Yes (willing to quit)		Low	No	UK	NRT single (patches supplied; participants also able to use other forms of NRT)
Kimber 2021	50	1) Nicotine EC cig-a-like 18 mg/mL 2) Nicotine EC tank 18 mg/mL 3) Nicotine EC tank 6 mg/mL	0.5	Yes (willing to quit)		High	No	UK	NA
Klonizakis 2022	248	1) Nicotine EC 2) Non-nicotine EC 3) Referral to NHS stop smoking clinic (NRT + behavioural support)	6	Yes		Unclear	No	UK	NRT not stated/unclear
Kouroutzoglou 2024	57	1) Nicotine EC 2) NRT 3) NRT + buproprion	6	NR	People with obesity	Unclear	No	Greece	NRT single form (patch)
Kumral 2016	98	1) Nicotine EC 2) Cognitive behaviour therapy	3	Yes (willing to quit)		High	NR	Turkey	NA
Lee 2018	30	1) Nicotine EC 2) NRT	6	NR	Veterans awaiting surgery	Low	No	USA	NRT single form (patch)
Lee 2019	150	1) Nicotine EC 2) NRT. Both arms received 50-minute smoking cessation education session.	6	Yes	All male (motor company)	Low	No	Korea	NRT single form (gum)
Lucchiari 2022	210	1) Nicotine EC 2) Non-nicotine EC	12	Yes	Participants in the early lung cancer detection pro-	High	No	Italy	NA

Table 1. Overview of included RCTs *(Continued)*

					gramme (Cosmos II)				
Martinez 2021	2896	1) Smoking cessation self-help booklet targeted to dual users 2) Generic smoking cessation self-help booklet 3) Assessment only	24	Not required to be motivated to quit	Dual users of EC and CC	Low	No	USA	NA
Meier 2017	24	1) Nicotine EC 2) Non-nicotine EC Cross-over	0.5	No		Unclear	No	USA	NA
Morphett 2022a	1712	1) Usual care standard cessation advice + NRT (short-term) 2) Quit or substitute advice + NRT (advice to use NRT longer-term) 3) Quit or substitute advice + NRT and / or EC	12	58% want to quit a lot		High	No	Australia	NRT combination
Morphett 2022b	355	1) Quitline + NRT + EC 2) Quitline + NRT. At 6 months, arm 2 participants still smoking switched to EC (nicotine vaporiser) intervention. Partial cross-over	24	Yes (referred to quitline)	Diagnosed with/treatment for HIV or hepatitis C (HCV) or receiving opioid substitution therapy (OST) or receiving treatment for priority health conditions	Unclear	No	Australia	NRT combination
Myers-Smith 2022	135	1) Nicotine EC 2) NRT. Both groups: minimal behavioural support	6		People who find quitting difficult	Low	No	UK	NRT combination
NCT03274956	60	1) Nicotine EC (SREC) usual flavour (tobacco/menthol) 2) Nicotine EC (SREC) choice of flavours (tobacco, menthol, blueberry, watermelon)	4			Unclear	No	USA	NA
NCT03625986	104	1) Nicotine EC 2) Non-nicotine EC	1.4			Unclear	NR	USA	NA

Table 1. Overview of included RCTs *(Continued)*

NCT05278065	17	1) Nicotine EC 2) No intervention	4	No	People with asthma	High	No	USA	NA
NCT02918630 [416]	7	1) Nicotine EC + NRT 2) NRT	1	No	Diagnosis of schizophrenia	Unclear	No	USA	NRT single (patch)
NCT03113136	372	1) Nicotine EC (low wattage) 2) Nicotine EC (high wattage) 3) CC	12	No		High	No	USA	NA
Okuyemi 2022	234	1) Nicotine EC 2) Non-nicotine EC	3	No	African-American	Unclear	No	USA	NA
Oncken 2015 [417, 418, 419]	27	Cross-over study Nicotine EC tobacco flavour Nicotine EC tobacco and menthol flavour	0.5	No		Unclear	No	USA	NA
Ozga-Hess 2019	60	1) Nicotine EC 2) CC	2	Yes		High	No	USA	NA
Piper 2025	209	1) EC + active patch (NRT) week 1, placebo patch week 2 2) EC + placebo patch week 1, active patch week 2 3) VLNC + active patch week 1, placebo patch week 2 4) VLNC + placebo patch week 1, active patch week 2 5) Placebo patch week 1, active patch week 2 6) Active patch week 1, placebo patch week 2	1	No		High	No	USA	NRT single form (patch)
Pope 2024	972	1) Nicotine EC 2) Brief smoking cessation advice 3) Referral to stop smoking services	6	NR	People attending the Emergency Department	High	No	UK	NA
Pratt 2022	240	1) Nicotine EC 2) Assessment only	6	No	Diagnosis of schizophrenia, schizoaffec-	High	No	USA	NA

Table 1. Overview of included RCTs *(Continued)*

					tive disorder, or bipolar disorder				
Pulvers 2020	186	1) Nicotine EC 2) CC	6	NR. Willing to switch to EC for 6 weeks		High	No	USA	NA
Robinson 2025	169	1) Nicotine EC 2) Non-nicotine EC Cross-over	2.3	No		Unclear	No	USA	NA
Rose 2023*	94	1) Nicotine EC + nicotine patch 2) Non-Nicotine EC + nicotine patch 2x2 factorial design	2	NR		Unclear	Yes	USA	NRT single form (patch)
Russell 2021*	426	1) Nicotine salt EC 2) Nicotine freebase EC 3) NRT	6	NR		Unclear	Yes	UK	NRT unclear
Skelton 2022	66	1) Nicotine EC abrupt CC cessation 2) Nicotine EC gradual CC cessation	3	Yes	Clients of alcohol or drug centre	High	No	Australia	NA
Smith 2020 [420]	30	1) Nicotine EC PG/VG ratio 70/30 2) Nicotine EC PG/VG ratio 50/50 3) Nicotine EC PG/VG ratio 0/100	0.25	NR		Unclear	No	USA	NA
Smith 2025	30	1) Nicotine EC 2) NRT	1	Yes	People who have failed to quit with pharmacotherapy	Unclear	No	USA	NRT combination (patch and lozenge)
Strasser 2016 [421]	24	1) Nicotine EC (5 brands (4 analysed)) Factorial design	0.3	No		High	No	USA	NA
Tattan-Birch 2023	92	1) EC + varenicline 2) Varenicline only	3	Yes		High	No	UK	NA
Tseng 2016	99	1) Nicotine EC 2) Non-nicotine EC	0.75	Willing to reduce CC		Unclear	No	USA	NA
Tuisku 2024	458	1) Nicotine EC + placebo varenicline tablets	12	Yes		Low	No	Finland	NA

Table 1. Overview of included RCTs *(Continued)*

		2) Varenicline + non-nicotine EC 3) Non-nicotine EC + placebo tablets. All arms offered 8 motivational interview sessions							
Vickerman 2022	110	1) Enhanced EC coaching quitline, NRT available + EC advice only 2) Quitline treatment-as-usual, NRT available	3	Yes	Dual users of EC and CC	Unclear	No	USA	NRT unclear (patch, gum, and/or lozenge)
Vojjala 2025	121	1) Nicotine EC + counselling 2) NRT + counselling	6	Yes	Patients with COPD/chronic disease	High	No	USA	NRT combination (patch + lozenges or gum)
Wagener 2023	350	1) Nicotine EC + counselling 2) Quitline treatment-as-usual + NRT + counselling	3	Participated in tobacco helpline	Quitline recent treatment failure	Unclear	No	USA	NRT combination (patch and lozenge)
Walker 2023	209	Phase 1 (RCT): 1) Nicotine EC 2) CC. 3 months Phase 2 (single arm): 1) Nicotine EC Follows up at 24 months	24	No		High	NR	UK	NA
Walker 2020	1124	1) Nicotine EC + nicotine patch 2) Non-Nicotine EC + nicotine patch 3) Nicotine patch	12	Yes		High	No	New Zealand	NRT single form (patch)
Xu 2023*	837	1) Nicotine EC tobacco flavour 2) Nicotine EC flavour choice 3) Quit advice	12	No		High	Yes	USA	NA
Yingst 2020	17	1) Nicotine EC cig-a-like 2) Nicotine EC refillable Cross-over	0.75	No	Documented history of positive HIV status	Unclear	No	USA	NA

Abbreviations:
CC: combustible cigarettes
COPD: chronic obstructive pulmonary disease
EC: electronic cigarettes

HCV: hepatitis C
HIV: human immunodeficiency virus
HTP: heated tobacco products
NA: not applicable
NHS: National Health Service
NR: not reported
NRT: nicotine replacement therapy
OST: opioid substitution therapy
PG: propylene glycol
RoB: risk of bias
SD: standard deviation
SREC: standardised research e-cigarette
VG: vegetable glycerine
VLNC: very low nicotine content

Table 2. Sensitivity analysis for all relevant analyses

Comparison	Analysis number	Sensitivity analysis removing studies at high risk of bias	Sensitivity analysis removing industry-funded studies
Nicotine EC versus NRT	Analysis 1.1	1.1 Overall: RR 1.74 (1.30, 2.34), I^2 = 55% 1.1.1. Not selected on pregnancy: RR 1.74 (1.26, 2.42), I^2 = 60% 1.1.2 Pregnant population: N/A 1	1.1 Overall: RR 1.72 (1.23, 2.39), I^2 = 56% 1.1.1. Not selected on pregnancy: RR 1.71 (1.18, 2.48), I^2 = 61% 1.1.2 Pregnant population: N/A 1
	Analysis 1.2	1.2 Overall: RR 1.74 (1.30, 2.34), I^2 = 55% 1.2.1. Combination NRT: RR 1.95 (1.01, 3.73), I^2 = 74% 1.2.2. Single-form NRT: N/A 1 1.2.3 Unclear: N/A 1	1.2 Overall: RR 1.72 (1.23, 2.39), I^2 = 56% 1.2.1. Combination NRT: RR 1.90 (0.87, 4.15), I^2 = 74% 1.2.2. Single-form NRT: N/A 1 1.2.3. Unclear: N/A 1
	Analysis 1.3	RR 0.90 (0.71, 1.14), I^2 = 66%	N/A 1
	Analysis 1.4	RD 0.01 (-0.01, 0.03), I^2 = 0%	N/A 1
	Analysis 1.5 to Analysis 1.18	N/A 1	N/A 1
	Analysis 1.19	N/A 1	N/A 3
	Analysis 1.20	RR 6.63 (3.30, 13.31), I^2 = 0%	N/A 1
	Analysis 1.21	RR 0.48 (0.19, 1.23), I^2 = 47%	N/A 1
	Analysis 1.22 to Analysis 1.23	N/A 1	N/A 1
Nicotine EC versus varenicline	Analysis 2.1 to Analysis 2.2	N/A 2	N/A 3
Nicotine EC versus non-nicotine EC + varenicline	Analysis 3.1 to Analysis 3.2	N/A 1	N/A 1
Nicotine EC versus cytisine	Analysis 4.1 to Analysis 4.2	N/A 1	N/A 1
Nicotine EC versus NRT + bupropion	Analysis 5.1	N/A 1	N/A 1
Nicotine EC versus heated tobacco	Analysis 6.1 to Analysis 6.2	N/A 2	N/A 2
	Analysis 6.3	MD -0.20 (-3.23, 2.83), I^2 not estimable	MD -0.20 (-3.23, 2.83), I^2 not estimable
	Analysis 6.4	N/A 2	N/A 2

Table 2. Sensitivity analysis for all relevant analyses *(Continued)*

Nicotine EC versus oral nicotine pouches	Analysis 7.1 to Analysis 7.2	N/A 2	N/A 1
Nicotine EC versus non-nicotine EC	Analysis 8.1	RR 1.40 (1.09, 1.81), I^2 = 0%	RR 1.28 (1.01, 1.64), I^2 = 0%
	Analysis 8.2	N/A 1	RR 1.01 (0.95, 1.08), I^2 = 0%
	Analysis 8.3	RD 0.00 (-0.01, 0.01), I^2 = 0%	RD -0.00 (-0.01, 0.01), I^2 = 0%
	Analysis 8.4	N/A 1	N/A 3
	Analysis 8.5	N/A 1	MD -0.60 (-3.52, 2.32), I^2 not estimable
	Analysis 8.6	N/A 1	MD 2.67 (-0.47, 5.82), I^2 not estimable
	Analysis 8.7	N/A 1	N/A 1
	Analysis 8.13	N/A 1	N/A 2
	Analysis 8.8	N/A 1	MD 0.16 (-0.86, 1.17), I^2 = 0%
	Analysis 8.9	N/A 1	MD 0.29 (-1.73, 2.31), I^2 not estimable
	Analysis 8.10 to Analysis 8.18	N/A 1	N/A 1
	Analysis 8.19 with Robinson	N/A 1	RR 1.01 (0.95, 1.08), I^2 =0
	Analysis 8.20 with Robinson	RR 0.00 (-0.01, 0.01), I^2 = 0%	RR -0.00 (-0.01, 0.01), I^2 = 0%
Nicotine EC versus behavioural support only/no support	Analysis 9.1	RR 8.51 (0.46, 156.44), I^2 not estimable	RR 1.53 (1.30, 1.79), I^2 = 0%
	Analysis 9.2	RR 1.29 (1.15, 1.45), I^2 not estimable	RR 1.26 (0.96, 1.66), I^2 = 60%
	Analysis 9.3	RD -0.01 (-0.05, 0.03), I^2 not estimable	RD 0.00 (-0.00, 0.01), I^2 not estimable
	Analysis 9.4	N/A 3	N/A 1
	Analysis 9.5	N/A 1	N/A 1
	Analysis 9.6	MD 0.24 (-10.05, 10.52), I^2 = 0%	N/A 1
	Analysis 9.7	N/A 1	N/A 1
	Analysis 9.8	N/A 3	N/A 3
	Analysis 9.9	SMD -0.30 (-0.74, 0.13), I^2 not estimable	SMD -0.30 (-0.74, 0.13), I^2 not estimable

Table 2. Sensitivity analysis for all relevant analyses *(Continued)*

	Analysis 9.10 to Analysis 9.14	N/A 1	N/A 1
	Analysis 9.15	N/A 2	N/A 2
	Analysis 9.16	SMD 0.16 (-0.70, 1.02), I^2 not estimable	SMD -0.01 (-0.40, 0.39), I^2 = 0%
	Analysis 9.17	SMD 0.20 (-1.08, 1.48), I^2 not estimable	SMD 0.20 (-1.08, 1.48), I^2 not estimable
	Analysis 9.18	SMD 0.09 (-0.77, 0.95), I^2 not estimable	N/A 1
	Analysis 9.19	N/A 2	MD -0.14 (-0.36, 0.07), I^2 = 0%
	Analysis 9.20	N/A 2	N/A 1
	Analysis 9.21	N/A 2	N/A 2
	Analysis 9.22 to Analysis 9.26	N/A 2	N/A 1
Higher versus lower nicotine content	Analysis 10.1	N/A 1	N/A 1
	Analysis 10.2	N/A 2	N/A 2
	Analysis 10.3	N/A 1	RD 0.03 (0.05, 0.11), I^2 not estimable
	Analysis 10.4	MD -0.90 (-1.70, -0.10), I^2 = 0%	MD -1.15 (-2.05, -0.24), I^2 = 0%
	Analysis 10.5	N/A 1	MD 1.92 (-0.89, 4.73), I^2 not estimable
	Analysis 10.6	N/A 1	MD 1.13 (-2.76, 5.02), I^2 not estimable
	Analysis 10.7	N/A 1	N/A 1
	Analysis 10.8	N/A 1	MD 0.15 (-0.04, 0.34), I^2 not estimable
	Analysis 10.9	N/A 1	MD -0.12 (-0.36, 0.12), I^2 not estimable
	Analysis 10.10	N/A 1	MD 0.89 (-1.56, 3.34), I^2 not estimable
	Analysis 10.11 to Analysis 10.17	N/A 1	N/A 1
Choice of flavours vs. tobacco flavour only	Analysis 11.1	N/A 2	N/A 2
	Analysis 11.2 to Analysis 11.5	N/A 1	N/A 1
	Analysis 11.6	N/A 2	N/A 2

Table 2. Sensitivity analysis for all relevant analyses *(Continued)*

Choice of flavour vs. usual cigarette flavour (tobacco/menthol)	Analysis 12.1 to Analysis 12.5	N/A 2	N/A 1
Tobacco vs. menthol flavour	Analysis 13.1 to Analysis 13.4	N/A 2	N/A 2
Refillable versus cartridge	Analysis 14.1	N/A 2	N/A 1
Nicotine salt EC versus free-based nicotine EC	Analysis 15.1 to Analysis 15.2	N/A 1	N/A 2
Higher versus lower wattage	Analysis 16.1 to Analysis 16.3	N/A 2	N/A 1
Non-nicotine EC versus NRT	Analysis 17.1 to Analysis 17.4	N/A 1	N/A 1
Non-nicotine EC versus behavioural support only/no support	Analysis 18.1	RR 2.86 (0.30, 27.10), I^2 not estimable	N/A 1
	Analysis 18.2	N/A 1	N/A 1
	Analysis 18.3	RD 0.01 (-0.04, 0.05), I^2 not estimable	N/A 1
Non-nicotine EC + NRT versus NRT	Analysis 19.1 to Analysis 19.3	N/A 2	N/A 1
Advice to use e-cigarettes compared to no advice to use e-cigarettes	Analysis 20.1	RR 1.04 (0.89, 1.22), I^2 not estimable	N/A 1
	Analysis 20.2 to Analysis 20.5	N/A 1	N/A 1
	Analysis 20.6	N/A 3	N/A 1
	Analysis 20.7	N/A 1	N/A 1
Nicotine EC + NRT versus non-nicotine EC + NRT	Analysis 21.1	N/A 2	N/A 1
	Analysis 21.2	RR 1.25 (0.78, 1.99), I^2 not estimable	RR 1.09 (0.90, 1.31), I^2 not estimable
	Analysis 21.3	RD -0.04 (-0.16, 0.09), I^2 not estimable	RD -0.02 (-0.04, 0.01), I^2 not estimable
	Analysis 21.4	MD -9.10 (-15.83, -2.37), I^2 not estimable	MD -1.40 (-4.26, 1.46), I^2 not estimable
	Analysis 21.5 to Analysis 21.12	N/A 2	N/A 1
Nicotine EC + NRT versus NRT	Analysis 22.1	RR 3.85 (1.91, 7.74), I^2 not estimable	N/A 1

Table 2. Sensitivity analysis for all relevant analyses *(Continued)*

	Analysis 22.2	N/A 2	N/A 3
	Analysis 22.3 to Analysis 22.5	N/A 2	N/A 1
Nicotine EC + varenicline vs. varenicline	Analysis 23.1 to Analysis 23.2	N/A 2	N/A 1
Nicotine EC + cytisine versus cytisine	Analysis 24.1 to Analysis 24.3	N/A 1	N/A 1
Nicotine EC + VLNC versus VLNC	Analysis 25.1 to Analysis 25.7	N/A 1	N/A 1

N/A 1 = no studies at high risk of bias/no industry-funded studies
N/A 2 = all studies at high risk of bias/industry-funded
N/A 3 = results not pooled
Abbreviations
EC: electronic cigarette(s)
I^2: measure of heterogeneity. We considered a value greater than 50% as evidence of substantial heterogeneity.
MD: mean difference
NRT: nicotine replacement therapy
RD: risk difference
RR: risk ratio
SMD: standardised mean difference
VLNC: very low nicotine content