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ORAL NICOTINE POUCHES AND ELECTRONIC CIGARETTES FOR SMOKING CESSATION: THE LATEST COCHRANE EVIDENCE

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Oct 2025

Acknowledgements and declarations of interest

The oral nicotine pouch 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 e-cigarette systematic review is funded primarily by Cancer Research UK, as well as through the above funding mechanism. The content is solely the responsibility of the authors and does not necessarily represent the official views of Cancer Research UK, the NIH or the Food and Drug Administration. The funders were not involved in the decision to submit for publication.

Outside of the current work, I have received research funding from the NIH-FDA, Cancer Research UK, the British Heart Foundation, the World Health Organization, the University of Oxford, and the National Institute for Health Research (UK). The views expressed here are my own and not those of my funders.

I have never received funding from tobacco, vaping, or pharmaceutical industries.

I have no conflicts of interest to declare.

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What I'll cover

Cochrane, and key Cochrane Tobacco Addiction Group methods

Oral nicotine pouches review

Latest update to our e-cigarettes for smoking cessation review

Next steps

Pause for
questions

Time for
more
questions

- Global non-profit organisation
- Produces systematic reviews to inform health decision making
- The Cochrane Library



**(Key) standard
Cochrane
Tobacco
Addiction
Group methods**



Searches, screening and data extraction



Protocols published in advance



Studies identified through: study registers, databases, screening of SRNT abstracts, and researcher contacts



Screening and data extraction conducted in duplicate

Risk of bias assessment

- Conducted using standard Cochrane Tobacco Addiction Group methods (ROB v1)
- Assessed the following domains as at high, low, or unclear risk of bias: random sequence generation, allocation concealment, performance bias, detection bias, attrition bias, other risk of bias
- Studies were judged to be at high risk of bias overall if high in one or more domains, low if low across all domains, and the remainder unclear

Addiction / Volume 118, Issue 9 / pp. 1811-1816

METHODS AND
TECHNIQUES

 **Open Access**



Assessing and minimizing risk of bias in randomized controlled trials of tobacco cessation interventions: Guidance from the Cochrane Tobacco Addiction Group

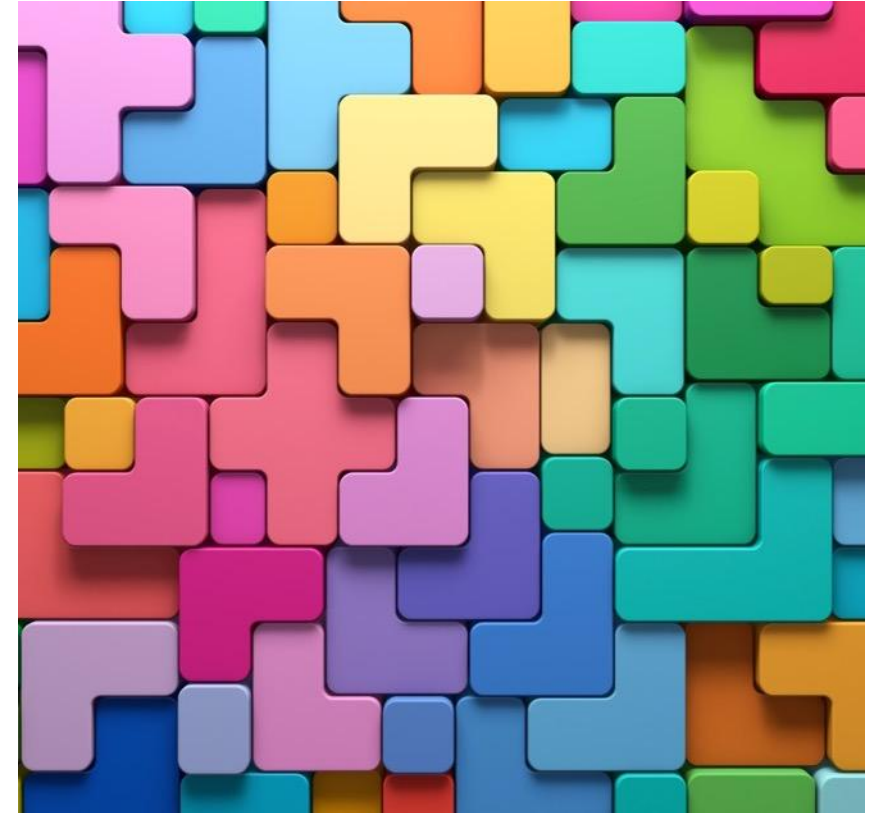
Jamie Hartmann-Boyce , Nicola Lindson

First published: 02 May 2023

<https://doi.org/10.1111/add.16220>

Statistical synthesis

- We pool dichotomous outcome data using a Mantel-Haenszel random effects model, with results reported as risk ratios (RRs) and 95% confidence intervals (CIs)
- Continuous data are pooled using generic inverse variance models, with results reported as mean differences (MDs) with 95% CIs
- For abstinence, we use the strictest definition at longest follow-up, counting those lost to follow-up as non-abstinent (intention to treat)
- For all other outcomes, we use complete case data
- Sensitivity analyses test sensitivity of findings to removal of studies with industry funding and/or at high risk of bias



GRADE Working Group grades of evidence



High certainty: we are very confident that the true effect lies close to that of the estimate of 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.

For randomized controlled trials, GRADE is based on five domains: risk of bias; imprecision; indirectness; inconsistency; and publication bias.


Cochrane reviews ▾

Searching for trials ▾

Clinical Answers ▾

About ▾

Help ▾


Cochrane Database of Systematic reviews | [Review - Intervention](#) Open access

Oral nicotine pouches for cessation or reduction of use of other tobacco or nicotine products

✉ [Jamie Hartmann-Boyce](#) , Harry Tattan-Birch, Jamie Brown, Lion Shahab, Maciej L Goniewicz, Claire L Ma, Angela Difeng Wu, Nargiz Travis, Holly Jarman, Jonathan Livingstone-Banks^a, Nicola Lindson^a

Version published: 24 October 2025 [Version history](#)<https://doi.org/10.1002/14651858.CD016220.pub2> 

Searches to 13 Jan 2025



Full
review
published
today!

Objectives

Primary

To evaluate:

- benefits and harms of oral nicotine pouches (ONPs) when used to help people stop tobacco smoking
- ~~the impact of ONPs on prevalence of tobacco smoking~~

Secondary

To evaluate:

- ~~benefits and harms of ONPs when used to stop using other non-combustible tobacco/commercial nicotine product use (e.g., heat not burn; e cigarettes)~~
- ~~the impact of ONPs on prevalence of other non-combustible tobacco/commercial nicotine products use~~

Eligibility criteria

For objectives related to benefits & harms of ONPs only*

Study design	Randomized controlled trials
Participants	People using tobacco or other (non-pharma) nicotine products
Intervention	Provision of ONPs to reduce or quit tobacco/other (non-pharma) nicotine product use
Comparators	<ul style="list-style-type: none">• Another commercial tobacco/nicotine product• Another ONP intervention• Smoking cessation pharmacotherapy• Non-nicotine pouches (placebo)• No or minimal intervention
Outcomes	<ul style="list-style-type: none">• Tobacco/nicotine abstinence at 4+ weeks• Biomarkers/adverse events at 1+ weeks

* Eligibility criteria for studies related to prevalence objectives can be found in the published protocol/review

Included studies

Four (small) RCTs (total n=282)

- All participants smoked cigarettes at baseline
- Size ranged from 30 - 146 participants
- One study (Rensch 2023) was tobacco industry funded
- 3 studies specifically included people not motivated to quit smoking
- Compared ONP to e-cigs (1 study), snus (1 study), NRT (1 study), minimal control (2 studies), tobacco abstinence (1 study), other ONP (varying dose; 2 studies)
- 3 studies high risk of bias; one unclear risk of bias

Rensch 2023	NCT04250727	Caldwell 2010	Avila 2024	
?	?	+	+	Random sequence generation (selection bias)
?	?	?	+	Allocation concealment (selection bias)
-	?	+	-	Blinding of participants and personnel (performance bias): All outcomes
+	+	-	+	Blinding of outcome assessment (detection bias): All outcomes
+	+	+	+	Incomplete outcome data (attrition bias): All outcomes
+	+	+	+	Selective reporting (reporting bias)
				Other bias

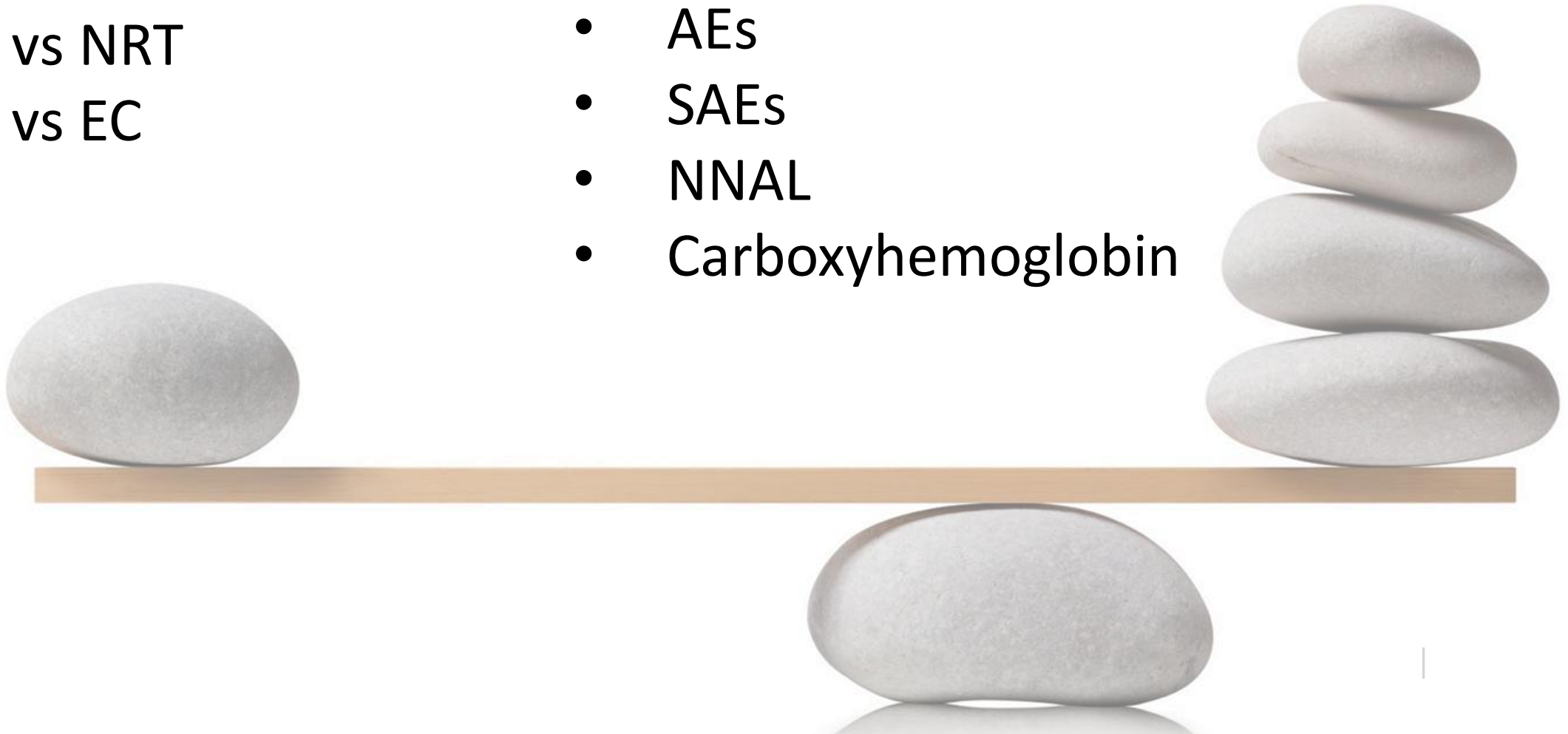
Results (from pre-specified comparisons/outcomes)

Comparisons

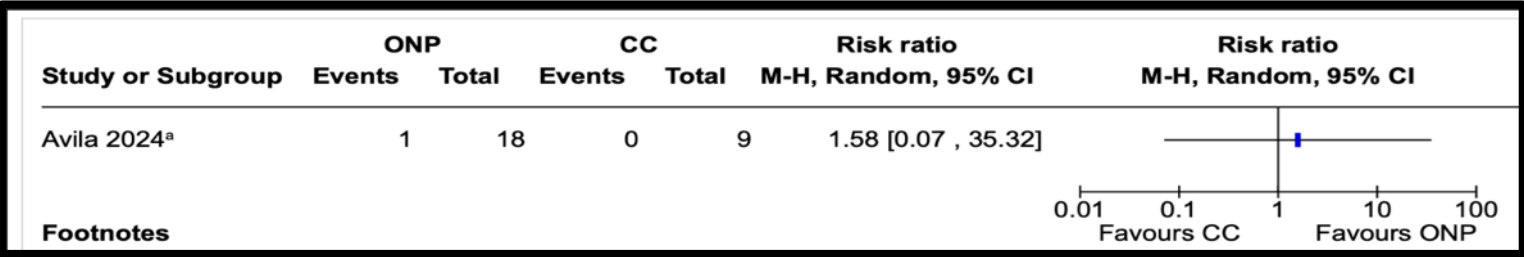
- ONP vs minimal control
- ONP vs NRT
- ONP vs EC

Outcomes

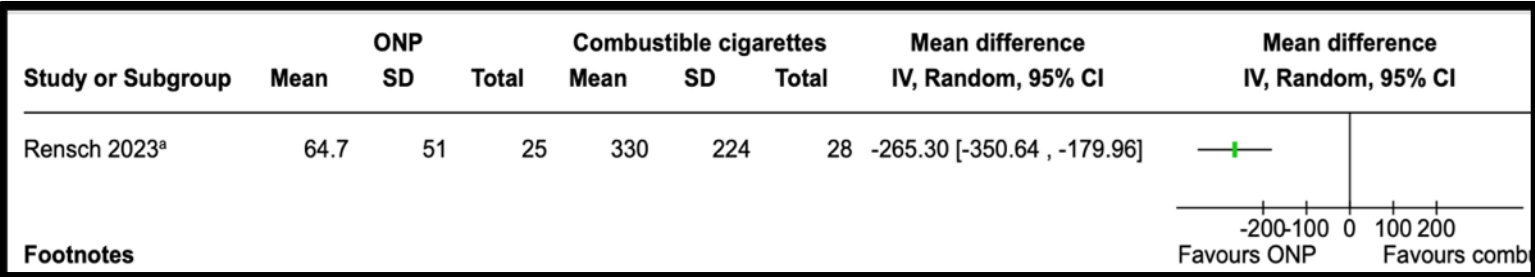
- Smoking abstinence
- AEs
- SAEs
- NNAL
- Carboxyhemoglobin



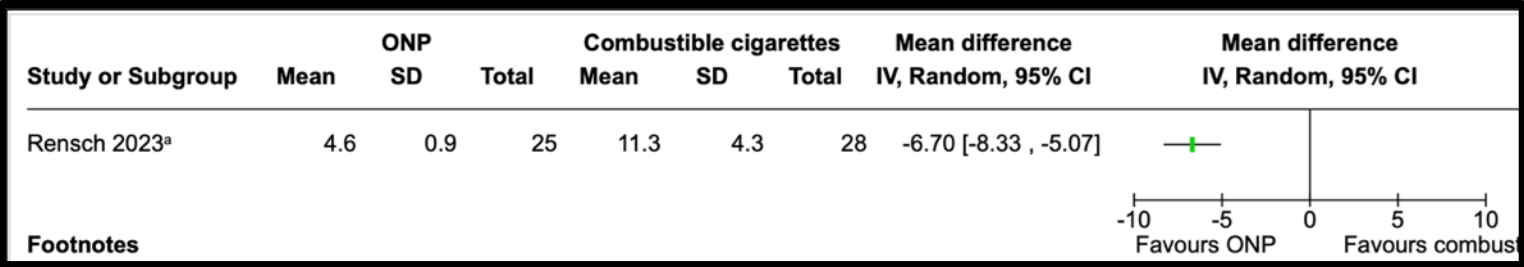
ONP versus minimal control (2 studies)



Smoking Cessation: Very low certainty evidence. No conclusions can be drawn



NNAL: Very low certainty evidence of lower NNAL in those randomized to ONP



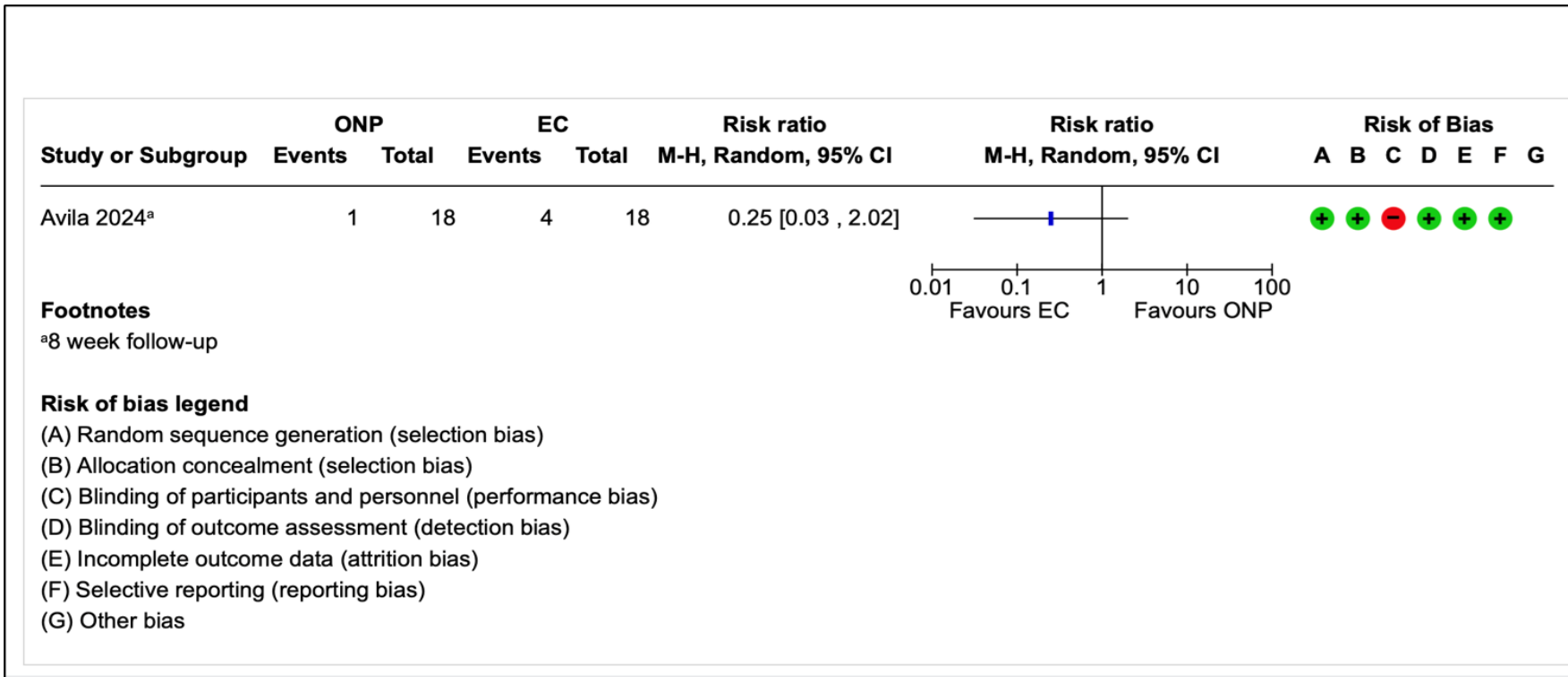
Carboxyhemoglobin: Very low certainty evidence of lower levels in those randomized to ONP

No other key outcomes reported

ONP versus NRT (1 study)

- Of our key outcomes this study (Caldwell 2020) only reported non-serious adverse events
- ONP use was associated with fewer reports of 'bad taste' or 'gastrointestinal side effects' than NRT. One participant reported discontinuing ONP use due to gastrointestinal symptoms, compared to two participants who discontinued gum use for the same reason.

ONP versus nicotine e-cigarettes (1 study)



Smoking cessation:

Low certainty evidence of higher quit rates in those randomized to nicotine e-cigarettes

No other key outcomes reported

Serious adverse events (SAEs)

- 3 of the 4 included studies measured SAEs
- All three studies reported that none occurred
- This equates to very low certainty evidence



Ongoing studies

Study ID (funder/sponsor)	Sample size	Expected comparator(s)	Expected (relevant) outcome(s)	Anticipated completion
Cheng 2024 (Altria)	400	ONPs varying on flavour	3 and 6 weeks: <u>smoking abstinence/reduction</u> , CO,	June 2025
Hammeed 2024 (NS)	600	E-cigarettes; minimal control	1 year: <u>smoking abstinence/reduction</u> , adverse events,	April 2025
ISRCTN13243849 (Swedish Match)	46	ONPs varying on texture (moist vs dry) and strength	Timeline unclear: biomarkers of exposure, “safety”	Dec 2025
NCT06043362 (Penn State)	375	ONPs varying on strength and flavour	16 weeks: <u>smoking abstinence/reduction</u> , NNAL, CO	August 2028
NCT06088862 (Global Action to End Smoking)	325	E-cigarettes; NRT	10 weeks: <u>smoking abstinence</u> , CO	Dec 2024
NCT06315881 (Ohio State)	160	ONPs varying on strength; minimal control	12 weeks: smokeless tobacco or <u>smoking abstinence</u>	August 2028
NCT06372899 (NCI)	200	E-cigarettes	6 months: <u>smoking abstinence</u> , NNAL, CO, biomarkers of exposure	March 2028
NCT06506162 (NCI)	320 (EC)	ONPs varying on flavour and strength; NRT	1 week: product use	Feb 2028
NCT06568900 (Swedish Match)	450	ONPs varying on flavour; minimal control	12 weeks: NNAL	Aug 2024
NCT06678789 (NIDA)	50	ONPs varying on strength	8 weeks: <u>smoking abstinence/reduction</u> , product use	July 2026

We estimate we are aware of 50-70% of ongoing studies prior to publication, so this is not an exhaustive list!

Conclusions

- There is limited evidence on using ONPs for smoking cessation or reduction
- There is no evidence on using ONPs for cessation/reduction of other tobacco/nicotine products
- There is no data on whether ONP use affects prevalence of use of tobacco/other nicotine products
- Low certainty evidence suggests that people randomized to ONPs may be slightly less likely to quit smoking than those randomised to nicotine e-cigarettes, but data is from one small study & very imprecise
- Evidence from all other comparisons & outcomes was either entirely absent, or very low certainty, meaning we are not able to draw conclusions
- The 3 studies that reported SAEs found that none occurred
- Future trials should prioritise comparing ONP to other active interventions, e.g., NRT; e-cigarettes
- They should aim to measure abstinence and SAEs for as long as possible (i.e., 6 months +)



Pause for questions



PLEASE NOTE:

This update is still going through editorial processes.

Please do not share the contents of the second half of this presentation more widely!

Electronic cigarettes for smoking cessation

Nicola Lindson, Ailsa R Butler, Hayden McRobbie, Chris Bullen, Peter Hajek, Angela Difeng Wu, Rachna Begh, Annika Theodoulou, Caitlin Notley, Nancy A Rigotti, Tari Turner, Jonathan Livingstone-Banks, Tom Morris,

✉ [Jamie Hartmann-Boyce](#) [Authors' declarations of interest](#)

Version published: 29 January 2025 [Version history](#)

<https://doi.org/10.1002/14651858.CD010216.pub9> [↗](#)



Searches to 1 March 2025

Objective:

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.

Living systematic review (LSR)

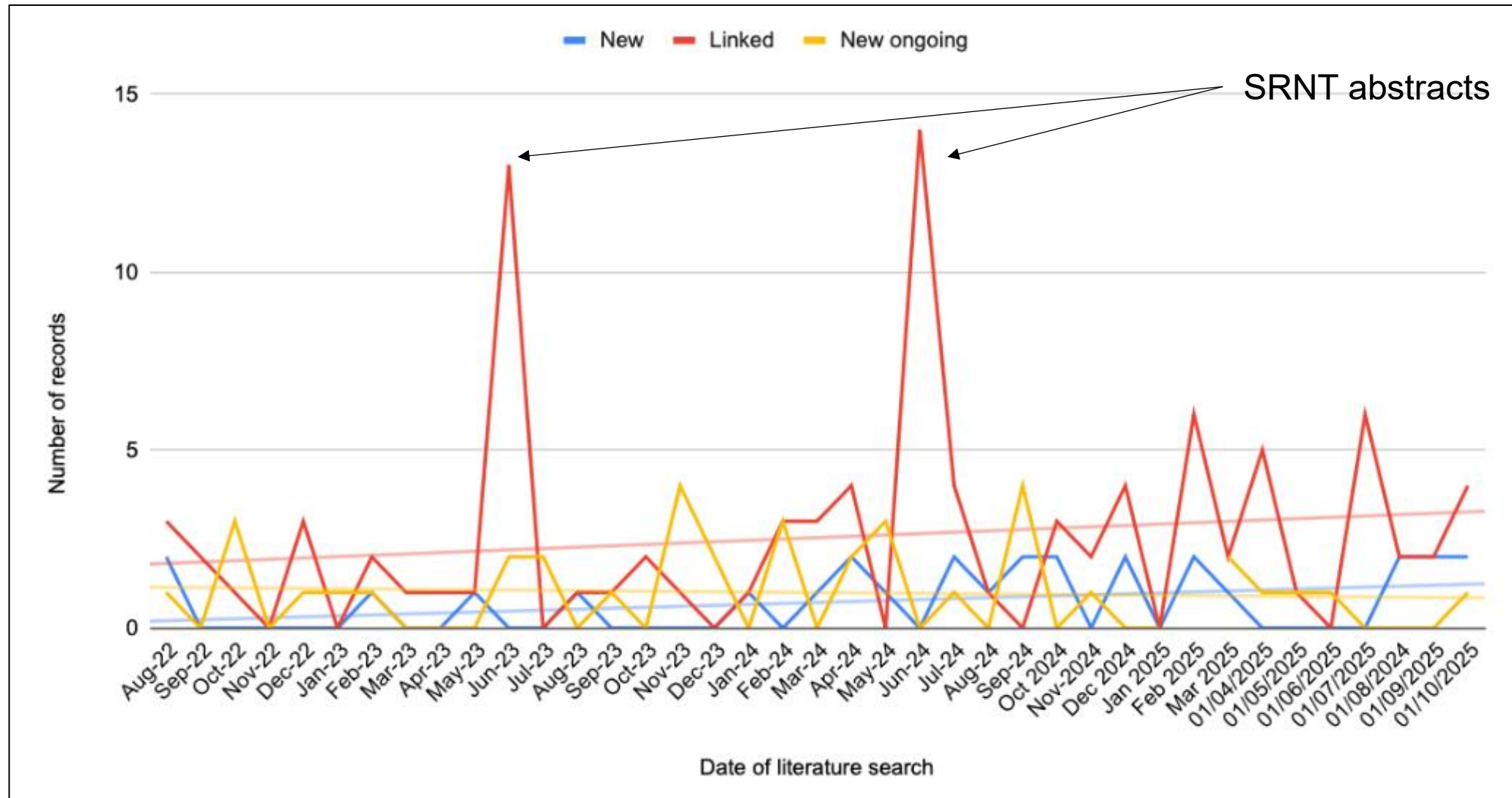


- Search for new evidence monthly
- Publish links to new evidence monthly
- Update full review when new data emerges that changes, strengthens, or weakens existing conclusions, or relates to new comparisons or outcomes

Are all other reviews 'dead'?



Number of new records picked up in monthly searches



Eligibility criteria

	Comparison between EC and ONP reviews
Study design	Randomized controlled trials and uncontrolled intervention studies
Participants	People who smoke using tobacco or other (non-pharma) nicotine products
Intervention	Provision of electronic cigarettes or information about electronic cigarettes ONPs to reduce or quit smoking tobacco/other (non-pharma) nicotine product use
Comparators	<ul style="list-style-type: none">• Another commercial tobacco/nicotine product• Another nicotine e-cigarette ONP intervention• Smoking cessation pharmacotherapy• Non-nicotine e-cigarettes pouches (placebo)• No or minimal intervention
Outcomes	<ul style="list-style-type: none">• Tobacco/nicotine abstinence at 6+ months 4+ weeks (key outcome)• Biomarkers/adverse events at 1+ weeks (key: SAEs, AEs)

Results (from pre-specified comparisons/outcomes)

Comparators

- Nicotine EC vs NRT
- Nicotine EC vs non-nicotine EC (placebo EC)
- Nicotine EC vs behavioral support only/no support

Outcomes

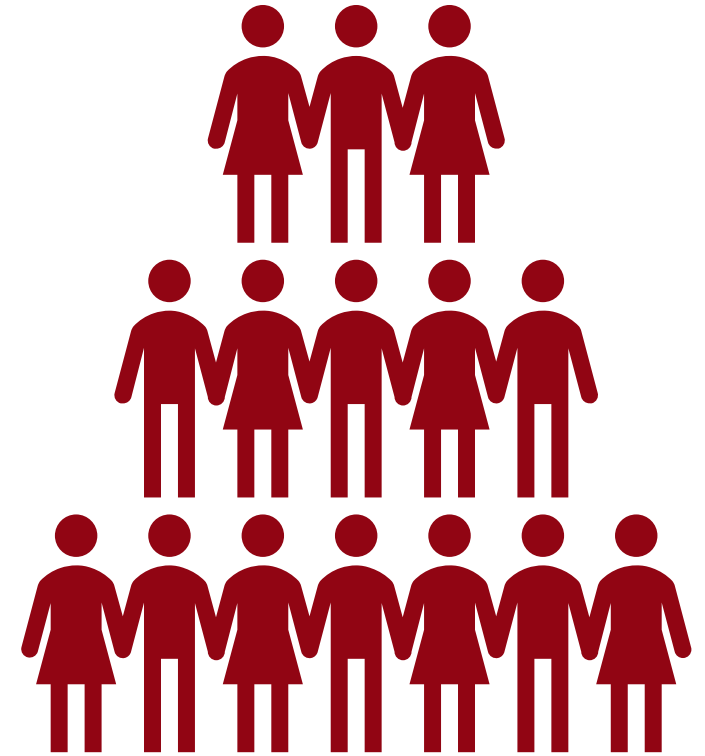
- Smoking abstinence
- SAEs



Included studies

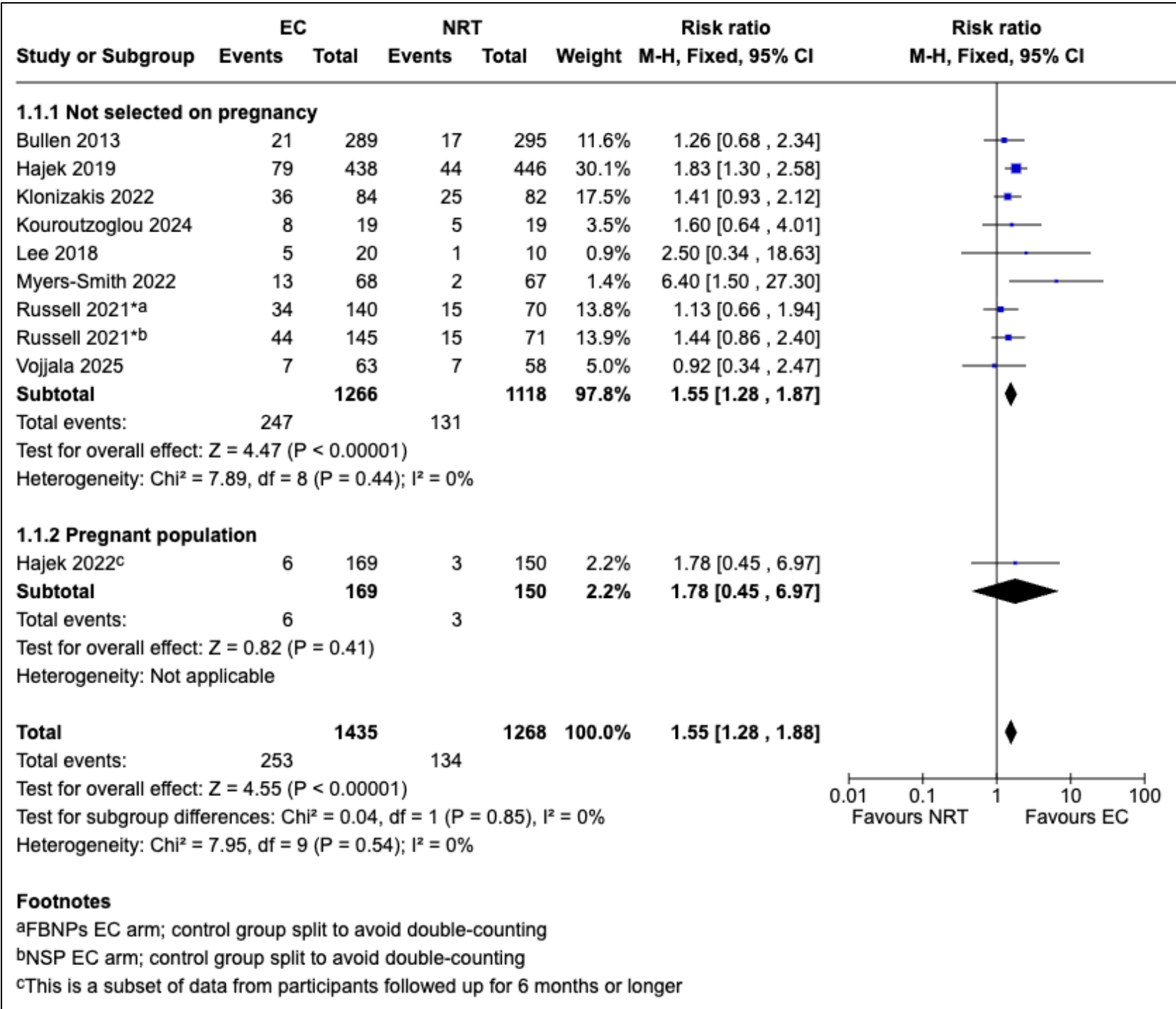
104 trials (total n=30,366); 61 RCTs (14 new to this update)

- All participants smoked cigarettes at baseline
- 48 studies conducted in USA, 21 in UK, 9 in Italy, 6 in Greece, 5 in Australia (all other countries 2 or fewer studies)
- 30 studies exclusively recruited people not motivated to quit smoking
- 16 reported funding from tobacco/vaping industries (no analyses were sensitive to their exclusion)
- 11 at low risk of bias, 70 at high risk (including all non-randomized studies), remainder at unclear risk



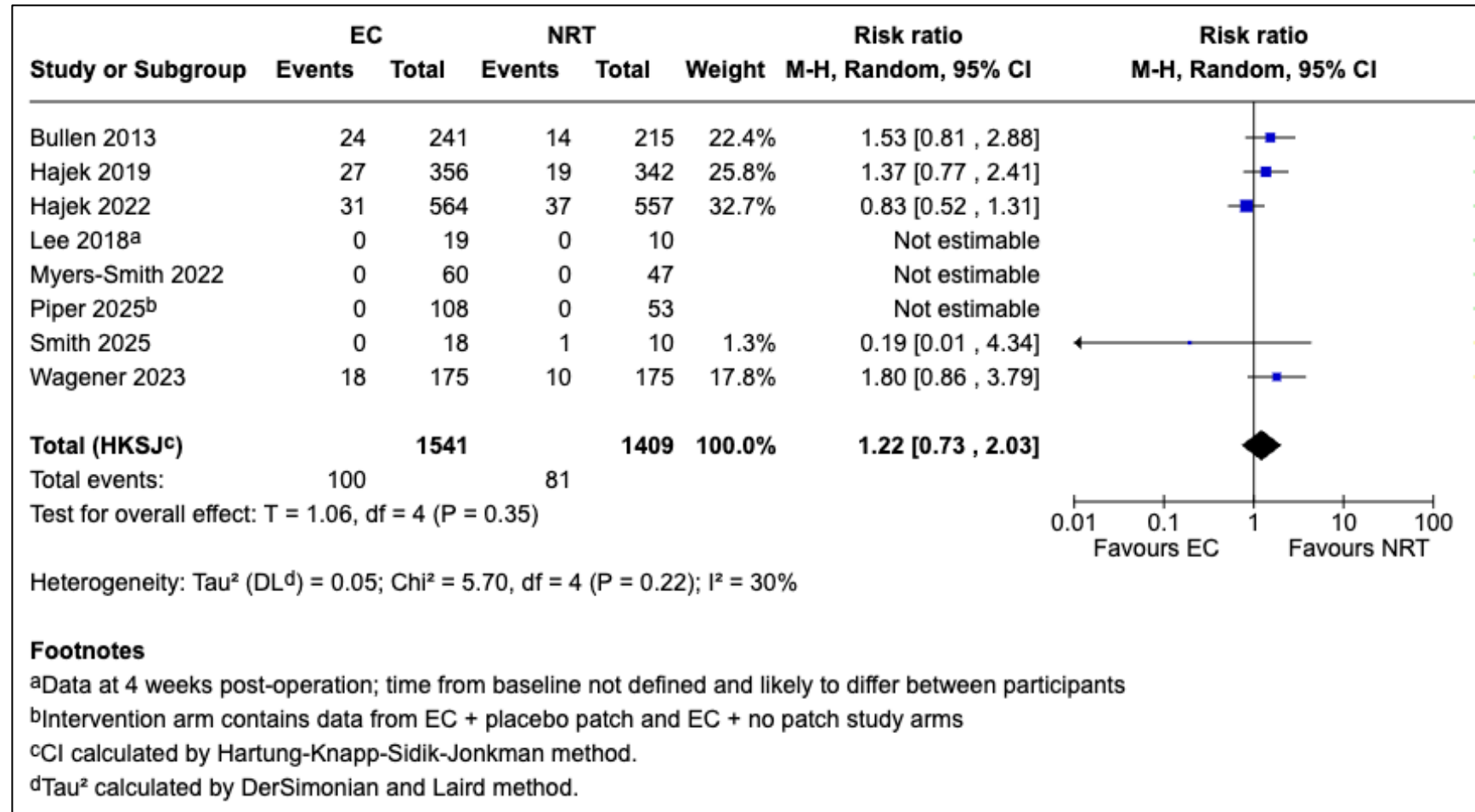
Nicotine EC versus NRT, Smoking cessation at 6+ months

GRADE
certainty of
evidence:
HIGH



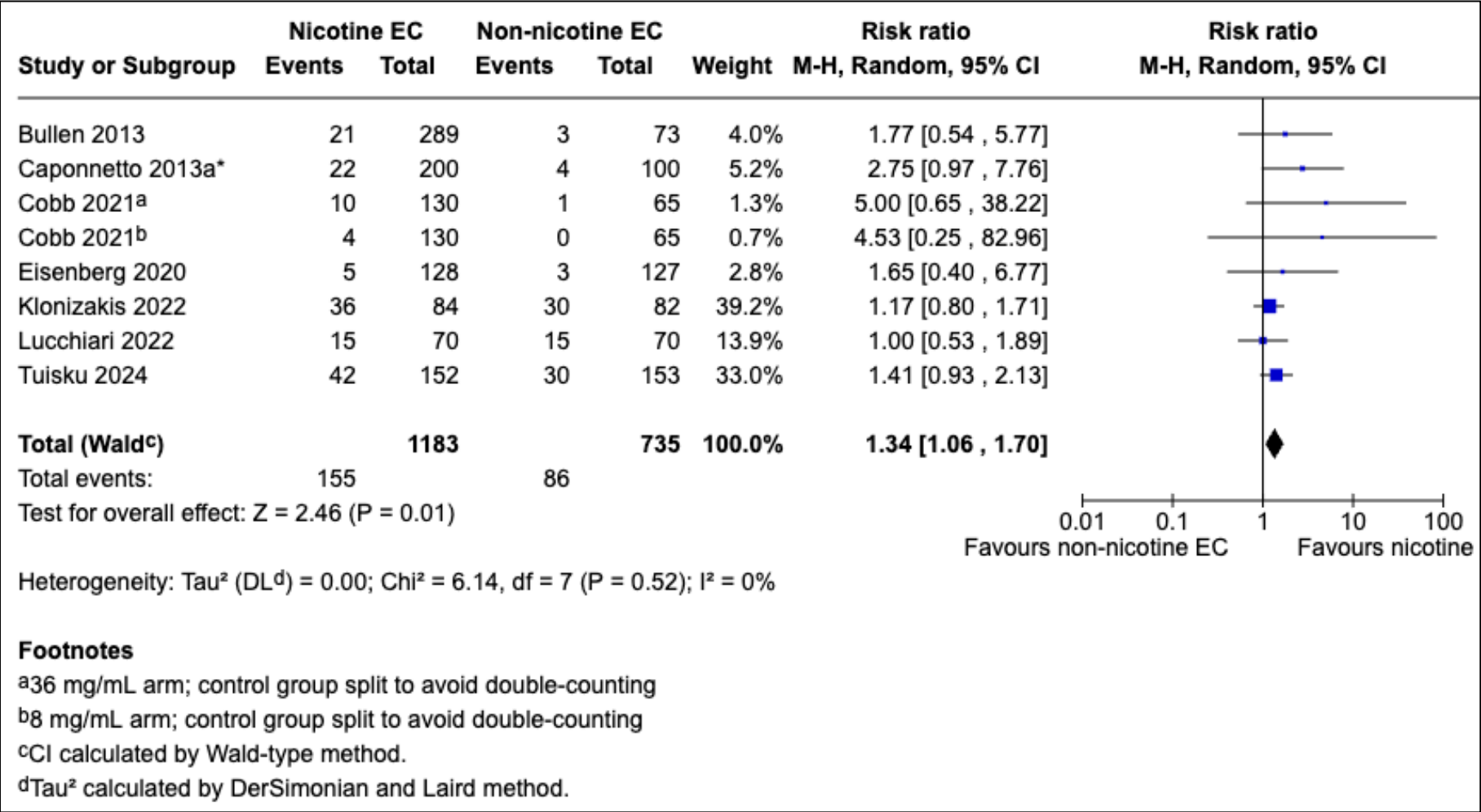
Nicotine EC versus NRT, Serious adverse events at 1+ weeks

GRADE
certainty of
evidence:
LOW



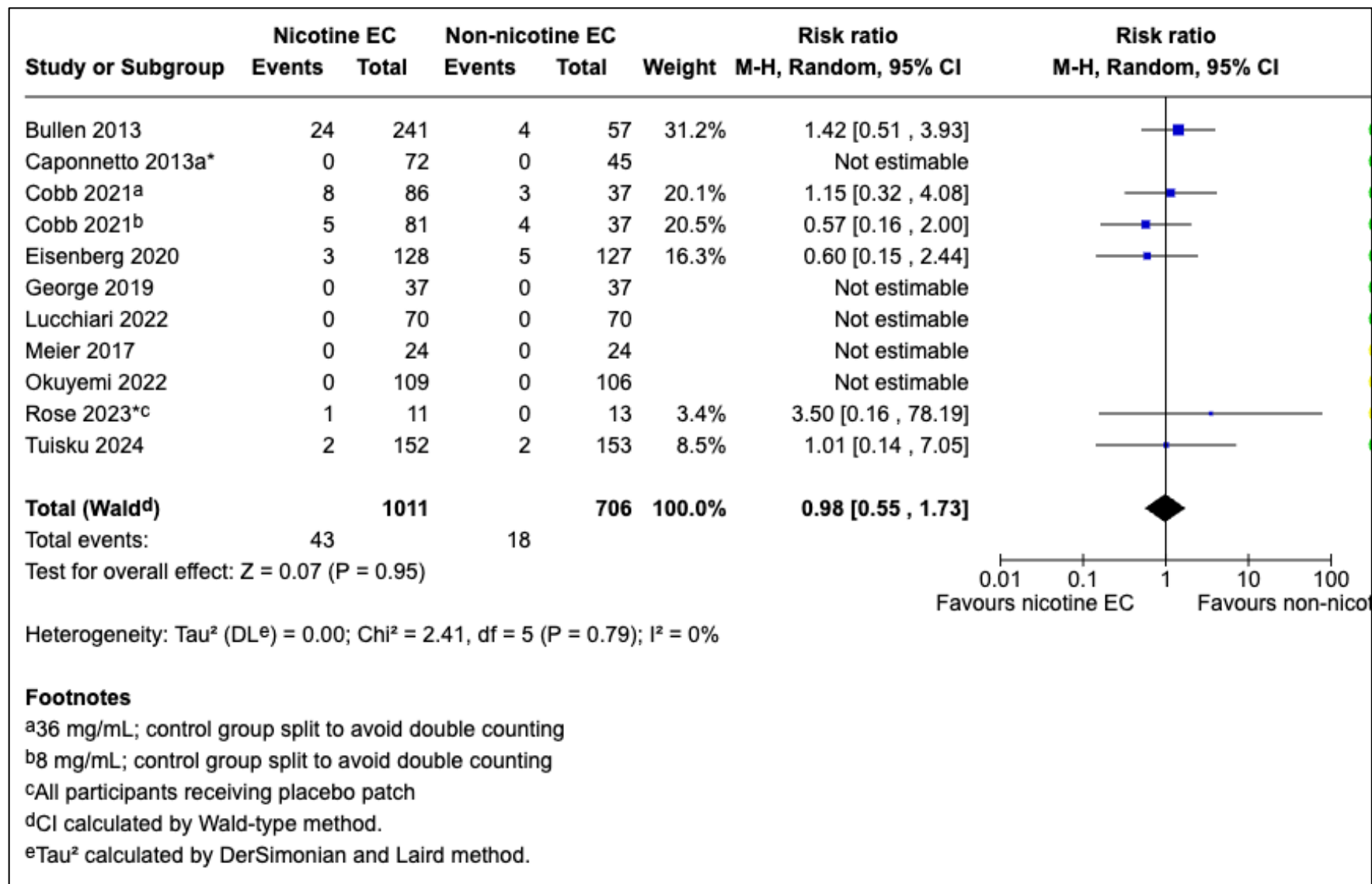
Nicotine EC
versus non-
nicotine
(placebo) EC,
Smoking
cessation at 6+
months

GRADE
certainty of
evidence:
MODERATE



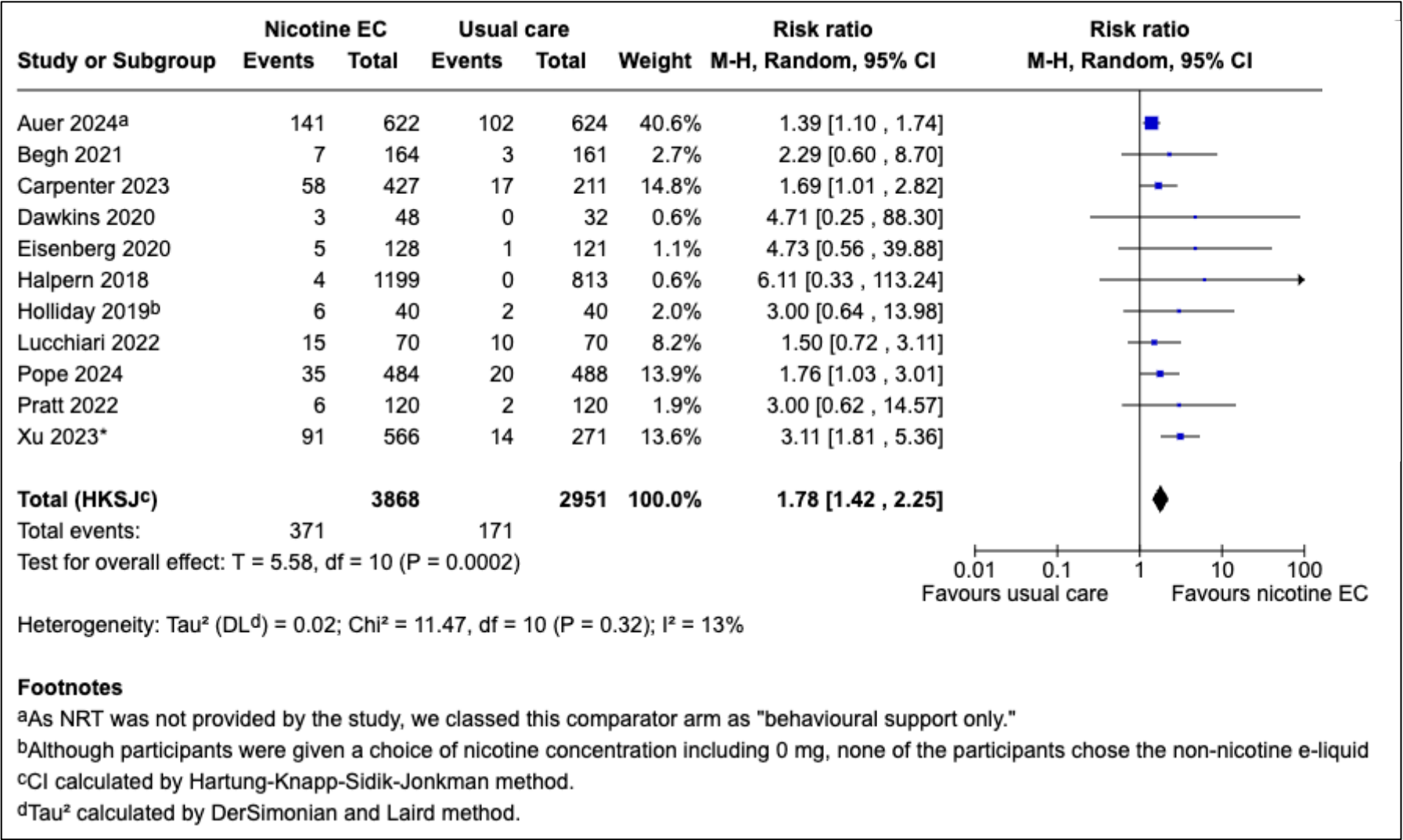
Nicotine EC versus non- nicotine (placebo) EC, SAEs at 1+ weeks

GRADE
certainty of
evidence:
LOW



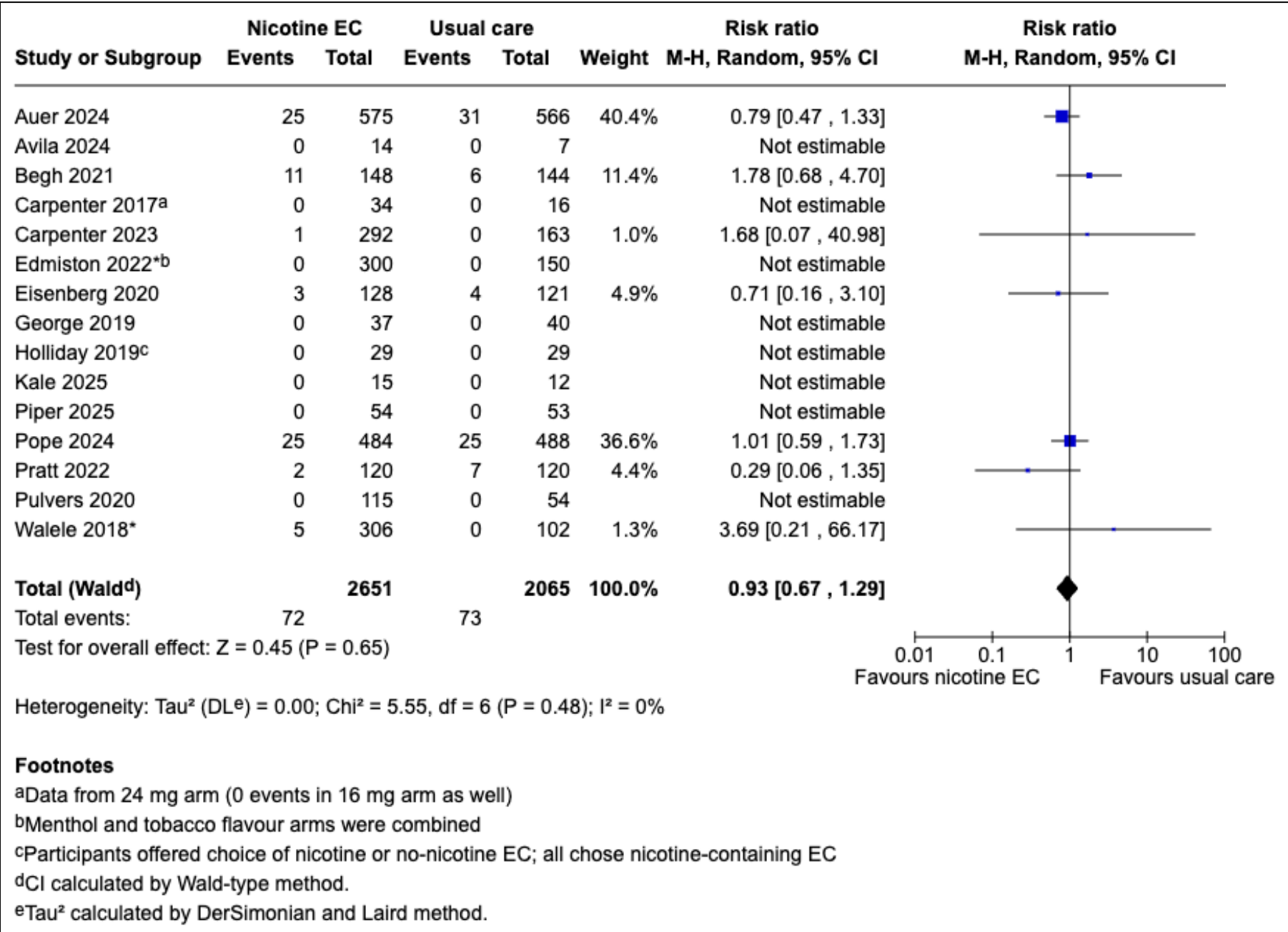
Nicotine EC versus behavioral support only/no support, Smoking cessation at 6+ months

GRADE
certainty of
evidence:
LOW



Nicotine EC versus behavioral support only/no support, SAEs at 1+ weeks

GRADE
certainty of
evidence:
VERY LOW



Conclusions

- There is high-certainty evidence that nicotine EC increase quit rates compared to NRT, and moderate-certainty evidence they increase quit rates compared to EC without nicotine. Evidence comparing nicotine EC with behavioral support or no support also suggests benefit, but is less certain due to lack of blinding.
- Overall incidence of SAEs was low across all study arms. We did not detect evidence of serious harm, but longer, larger trials are needed to fully evaluate safety. Included studies tested regulated nicotine-containing EC; other products may have different harm profiles.
- We need more RCTs that:
 - Aim to assess safety for as long as possible (and ideally be powered to detect differences in SAEs)
 - Use active comparators, particularly those other than NRT, or other EC characteristics (e.g. flavor, nicotine strength)
 - Test EC as an adjunct to other treatments
 - Test newer EC devices

ONPs versus vaping for smoking cessation – very different evidence bases!

	ONP	EC
RCTs	4	61
Participants	282	30,366
Strength of evidence for cessation	No studies following up for 6+ months	Compared to NRT: high certainty, more effective Compared to placebo: moderate certainty, more effective Compared to minimal control: low certainty, more effective
Strength of evidence, serious adverse events	Low/very low (no clear difference)	Low/very low (no clear difference)


Thank you! For further information...



See our living review project website for briefing documents, infographics, and a link to our monthly podcast

See full reviews for:

- More detail on everything that's been presented
- Secondary outcomes
- Other comparisons
- Data from uncontrolled studies
- Comparison with other reviews



Can electronic cigarettes (EC) help people stop smoking and are they safe to use for this purpose?

Findings from the January 2025 Cochrane review

This briefing document brings you the most up-to-date information on the effect and safety of using electronic cigarettes (ECs) to help people who smoke to stop smoking. This evidence comes from our latest Cochrane Review. Cochrane is a non-profit organisation that reviews all of the available evidence on a particular topic. Our findings help people to make healthcare decisions.

Key findings

- Our review showed more people stop smoking for at least six months using nicotine e-cigarettes than using nicotine replacement therapy.
- More people probably stopped smoking for at least six months using nicotine e-cigarettes than using nicotine-free e-cigarettes.
- Nicotine e-cigarettes may work better than no support for quitting smoking, or than behavioural support alone.
- Nicotine e-cigarettes may not be associated with serious unwanted effects.
- The unwanted effects reported most often with nicotine e-cigarettes were throat or mouth irritation, headache, cough and feeling sick. These effects reduced over time as people continued using nicotine e-cigarettes.

We need more, reliable evidence to be confident about the effects of e-cigarettes, particularly the effects of newer types of e-cigarettes that have better nicotine delivery.

Why this is this topic important?

Stopping smoking reduces the risk of getting lung cancer and other diseases. Many people find it difficult to quit. We want to find out if e-cigarettes can help and if people using them experience any unwanted effects.

In our latest full review (searches up to 1st February 2024) we found 90 studies in 20,044 adults who smoked.

What we are doing?

Each month we are searching for studies that look at the use of e-cigarettes to help people stop smoking. As we search monthly this is called a living systematic review. We look for randomized controlled trials, in which the treatments people received were decided at random. This type of study usually gives the most reliable evidence about the effects of a treatment. We also search for studies in which everyone received an e-cigarette treatment.

What we are looking at?

The studies we looked at compared electronic cigarettes to nicotine replacement therapy (for example, patches or gum), to stop smoking medication (varenicline), to non-nicotine e-cigarettes, and to behavioural support or no support.



Or just email me, at jhartmannboy@umass.edu