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

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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

Cochrane

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- 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

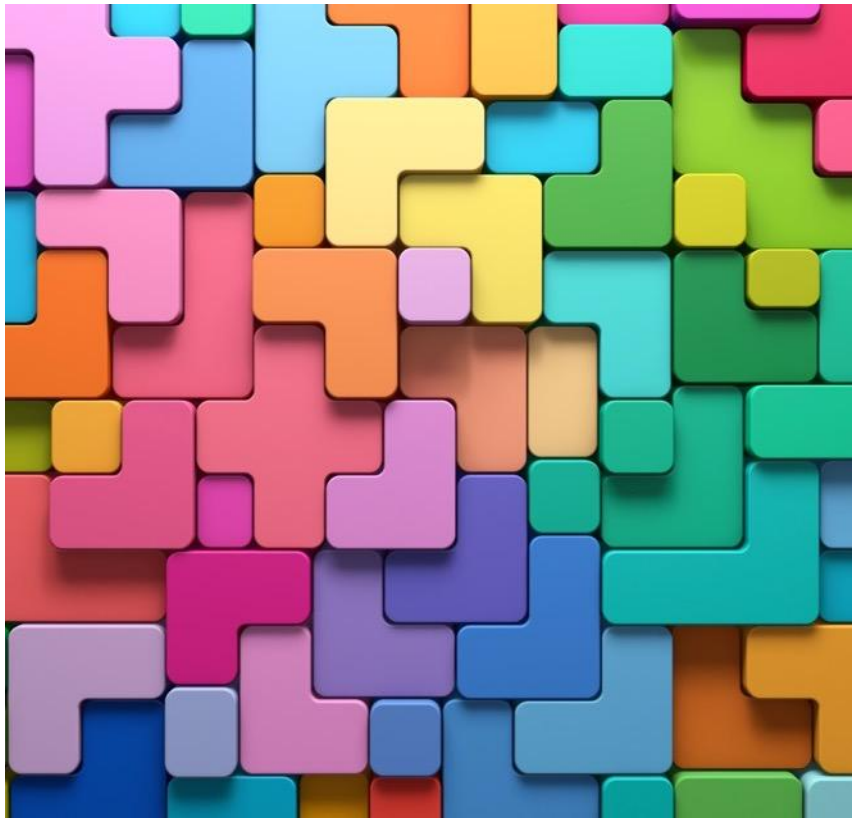
Assessing and minimizing risk of bias in randomized controlled trials of tobacco cessation interventions: Guidance from the Cochrane Tobacco Addiction Group

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 Library

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Review language : English

Title Abstract K

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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

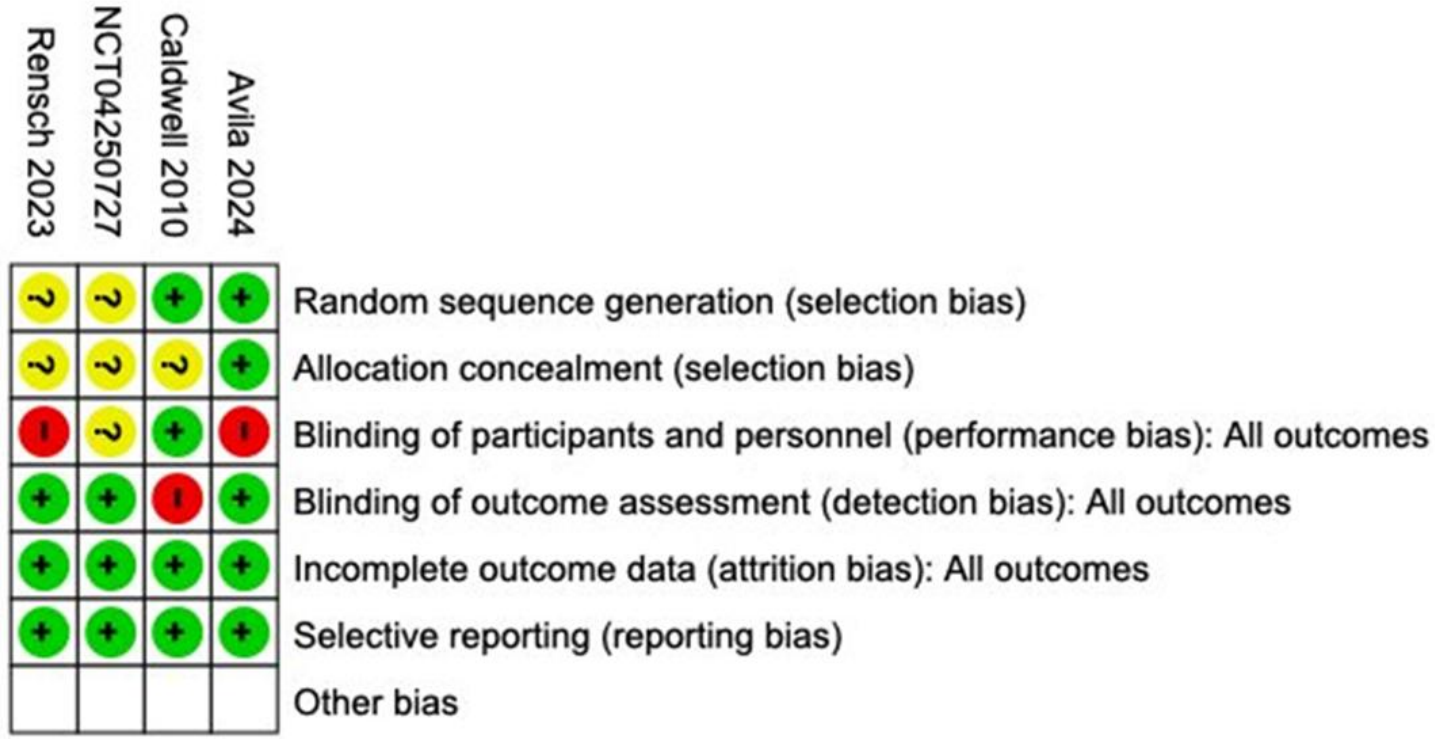
	For objectives related to benefits & harms of ONPs only*
Study design	Randomized controlled trials
Participants	People using tobacco or other (non-pharma) nicotine products
Intervention	Provision of ONPs to reduce or quit tobacco/other (non-pharma) nicotine product use
Comparators	• Another commercial tobacco/nicotine product • Another ONP intervention • Smoking cessation pharmacotherapy • Non-nicotine pouches (placebo) • No or minimal intervention
Outcomes	• 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



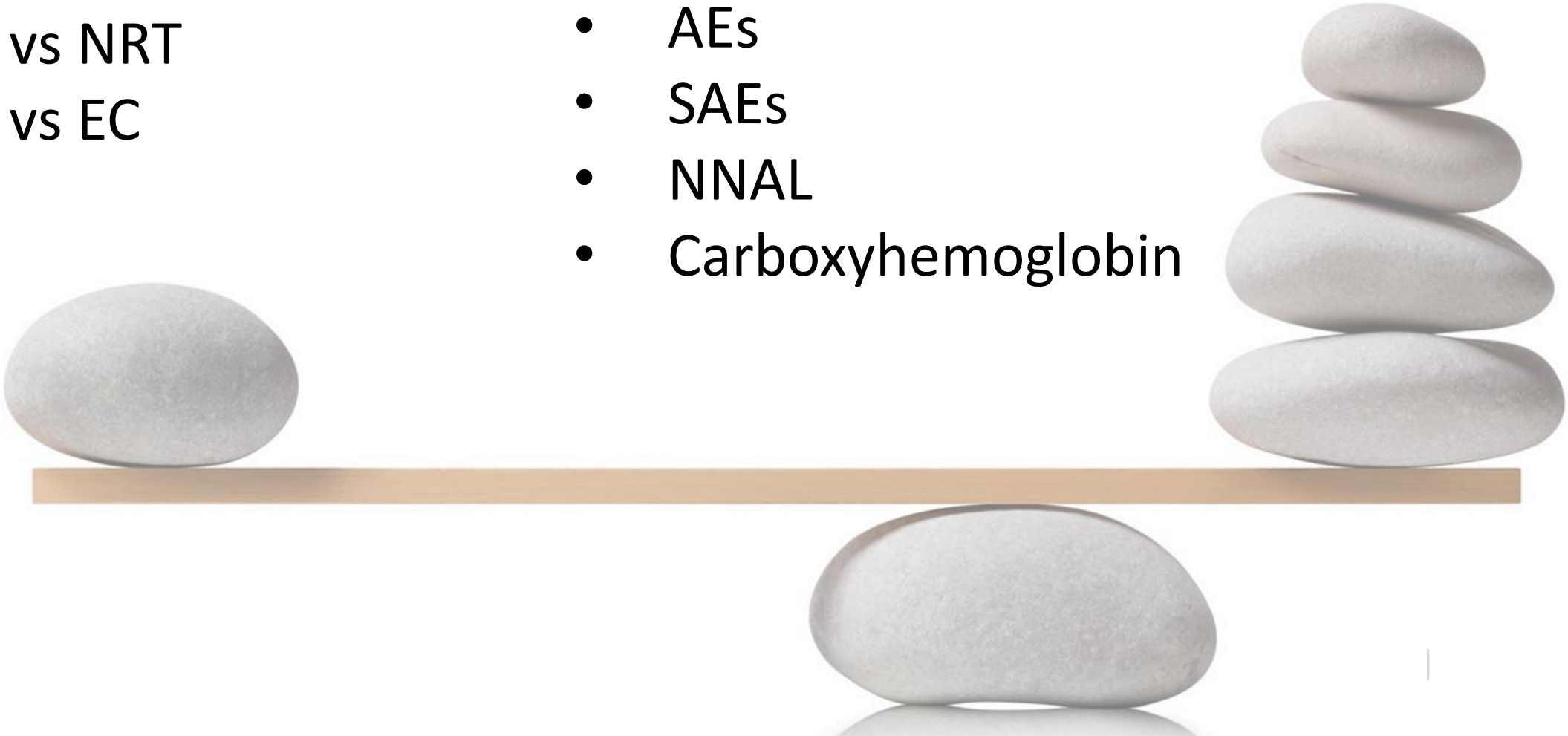
Results (from pre-specified comparisons/outcomes)

Comparisons

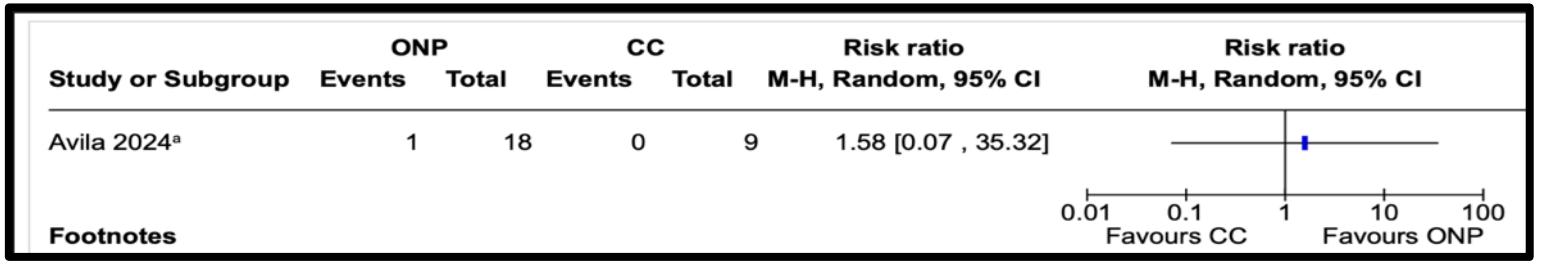
- ONP vs minimal control
- ONP vs NRT
- ONP vs EC

Outcomes

- Smoking abstinence
- AEs
- SAEs
- NNAL
- Carboxyhemoglobin



ONP versus minimal control (2 studies)



Study or Subgroup	ONP Events	ONP Total	CC Events	CC Total	Risk ratio M-H, Random, 95% CI
Avila 2024[a]	1	18	0	9	1.58 [0.07 , 35.32]

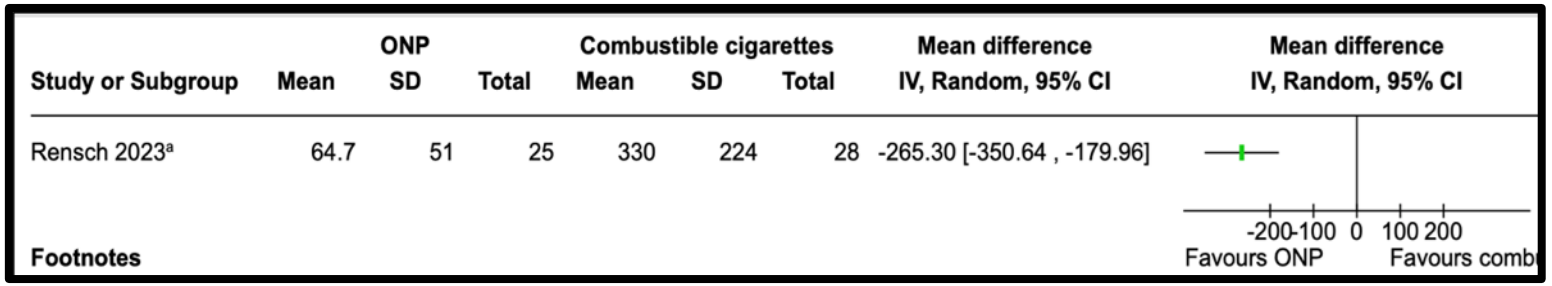
Risk ratio M-H, Random, 95% CI

0.01 0.1 1 10 100

Favours CC Favours ONP

Footnotes

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



Study or Subgroup	ONP Mean	ONP SD	ONP Total	Combustible cigarettes Mean	Combustible cigarettes SD	Combustible cigarettes Total	Mean difference IV, Random, 95% CI
Rensch 2023[a]	64.7	51	25	330	224	28	-265.30 [-350.64 , -179.96]

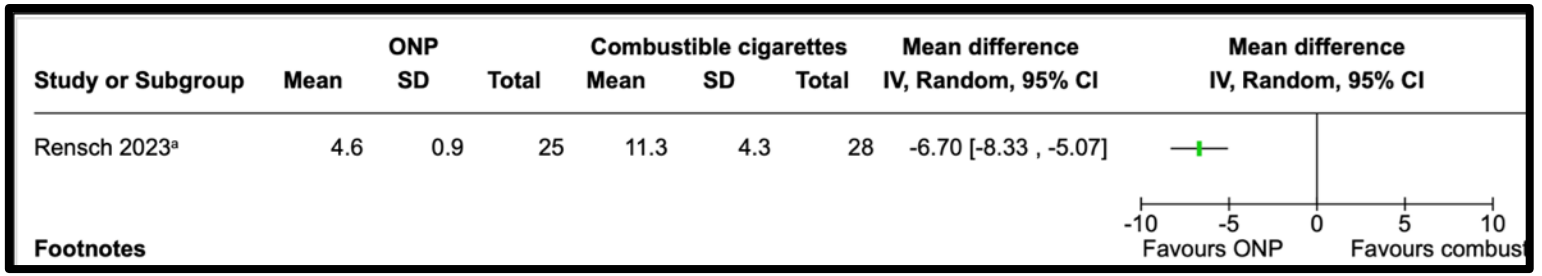
Mean difference IV, Random, 95% CI

-200 -100 0 100 200

Favours ONP Favours comb

Footnotes

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



Study or Subgroup	ONP Mean	ONP SD	ONP Total	Combustible cigarettes Mean	Combustible cigarettes SD	Combustible cigarettes Total	Mean difference IV, Random, 95% CI
Rensch 2023[a]	4.6	0.9	25	11.3	4.3	28	-6.70 [-8.33 , -5.07]

Mean difference IV, Random, 95% CI

-10 -5 0 5 10

Favours ONP Favours combust

Footnotes

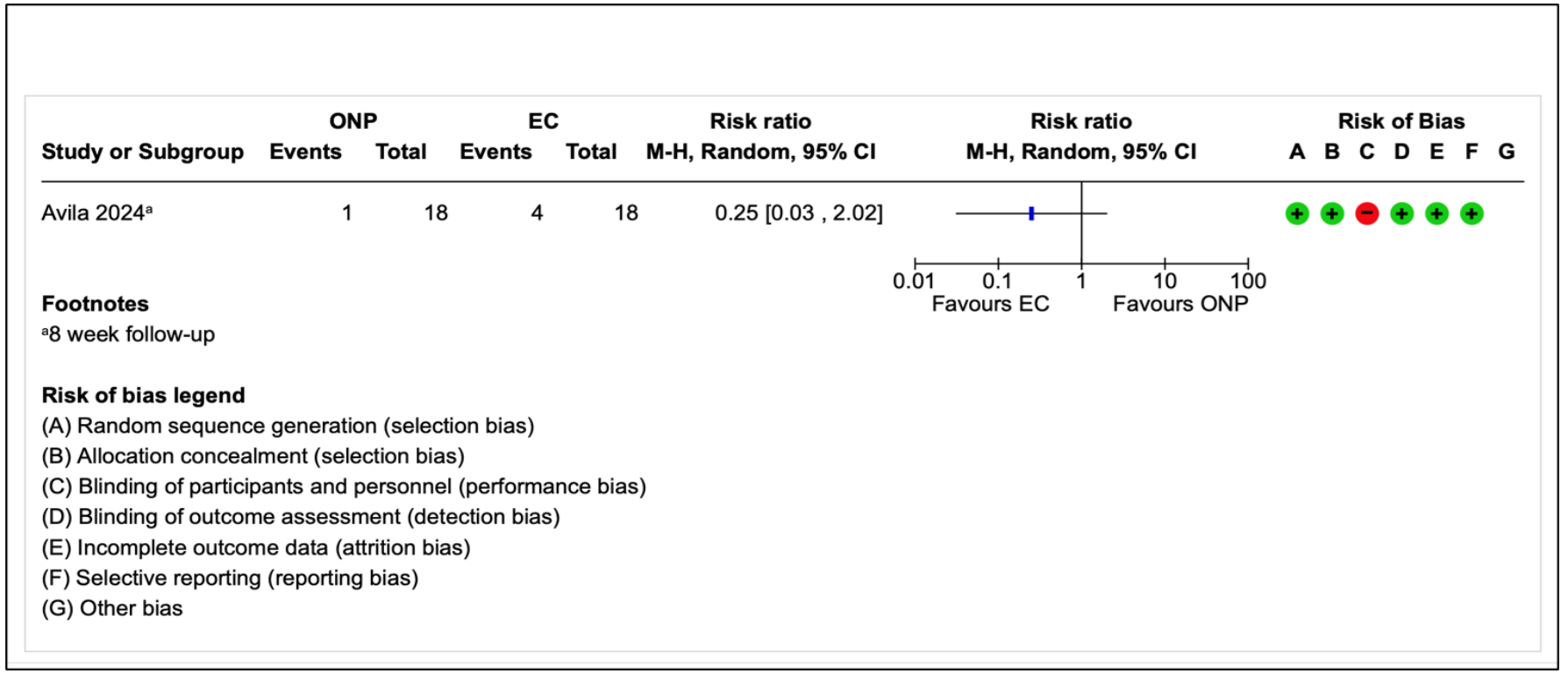
Carboxyhemoglobin: Very low certainty evidence of lower levels in those randomized to ONP

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)



Study or Subgroup	ONP Events	ONP Total	EC Events	EC Total	Risk ratio M-H, Random, 95% CI	Risk of Bias A B C D E F G
Avila 2024[a]	1	18	4	18	0.25 [0.03 , 2.02]	+ + − + + +

Footnotes

[a]8 week follow-up

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

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: smoking abstinence/reduction, CO,	June 2025
Hammeed 2024 (NS)	600	**E-cigarettes; minimal control**	**1 year**: smoking abstinence/reduction, 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: smoking abstinence/reduction, NNAL, CO	August 2028
NCT06088862 (Global Action to End Smoking)	325	**E-cigarettes; NRT**	10 weeks: smoking abstinence, CO	Dec 2024
NCT06315881 (Ohio State)	160	ONPs varying on **strength**; **minimal control**	12 weeks: smokeless tobacco or smoking abstinence	August 2028
NCT06372899 (NCI)	200	**E-cigarettes**	**6 months**: smoking abstinence, 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: smoking abstinence/reduction, 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 +)