

# E-cigarettes for smoking cessation

## The latest Cochrane evidence

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October 2021



## Acknowledgements and funding

The work presented today has been supported by Cancer Research UK and the National Institute for Health Research (NIHR).

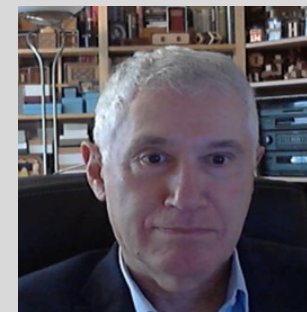
Within the past 3 years, I have received funding from Cancer Research UK, the NIHR, the British Heart Foundation, Cochrane, and the University of Oxford.

The views and opinions expressed therein are those of myself (and for the paper results, my co-authors) and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, National Health Service (NHS) or the Department of Health.

**I have never received industry funding and have no conflicts of interest to declare.**



# Our author team



# About Cochrane

## WHAT?

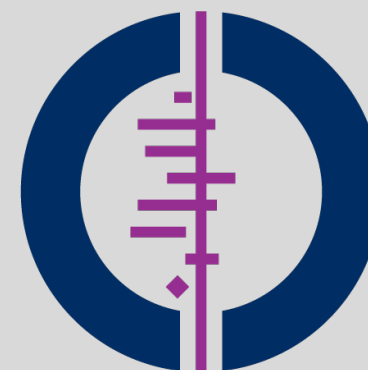
- Gathers and combines the best evidence from research to determine the benefits and risks of treatments/interventions

## HOW?

- By systematically reviewing the available evidence, with strong emphasis on quality assessment
- Cochrane methods considered gold-standard

## WHY?

- To help healthcare providers, patients, carers, researchers, funders, policy makers, guideline developers improve their knowledge and make decisions



**Cochrane**



# 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



Also as part of the living systematic review project...

Review update published Sept 2021  
Latest searches 1 May 2021  
Five new included studies

nicotine e-cigarettes than using nicotine replacement therapy, or 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

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December 2020

This briefing document brings you the most up to date information on the effects of electronic cigarettes (ECs) to help people who smoke achieve long-term smoking cessation.

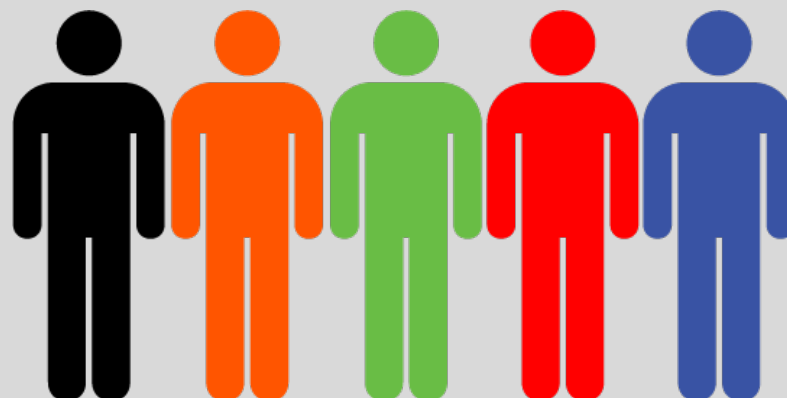
#### Key findings

- Findings across the main comparisons consistently favoured ECs for smoking cessation at 6 months or longer. Quit rates were higher with nicotine EC compared to: non-nicotine EC; to nicotine replacement therapy (NRT) and to behavioural support only or no support.

**e-cigarettes**

## Inclusion criteria: participants

- People defined as current smokers at enrolment into study, motivated or unmotivated to quit



## Inclusion criteria

Randomized  
controlled trials

- Smokers randomized to EC or control

Uncontrolled  
intervention  
studies

- All people in the study offered EC

Not included after 2016 due to nature  
of design and risk of confounding

Smoking cessation (6m +)

Measures of harm  
(1 week+)

Sept update:  
61 studies  
(34 RCTs)  
16,759  
participants



# Primary comparisons

- Nicotine e-cigarette versus NRT
- Nicotine e-cigarette versus behavioural support only/no-support
- Nicotine e-cigarette versus non-nicotine e-cigarette

# Outcomes

## Cessation\*

- 6 months+
- Intention to treat
- Strictest definition of abstinence
- Biochemically verified where available
- (as per standard Cochrane methods)

## Adverse events (AE)\*

- One week or longer of EC use
- Defined as any undesirable experience associated with the use of a medical product in a patient

## Serious adverse events (SAE)\*

- One week or longer of EC use
- Any AE where the patient outcome is death; life-threatening; hospitalization; disability; birth defect; or requires intervention to prevent any of the above

## Changes in relevant biomarkers

- One week or longer of EC use
- Known carcinogens and toxicants
- Exhaled carbon monoxide
- Airway and lung function
- Blood oxygen levels


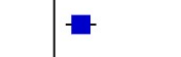




## *new outcome*

### Product use

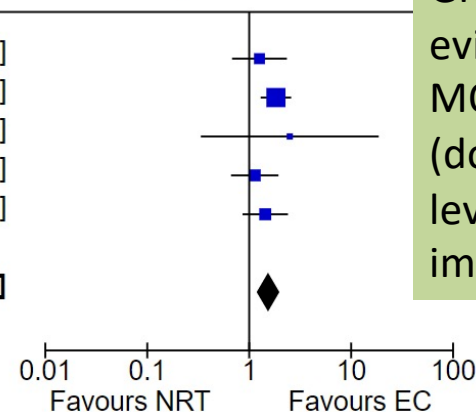
- 6 months or longer
- Proportion of participants still using assigned study product (EC or medication) at longest follow-up
- Added as part of LSR process at request from multiple policymakers

\*primary outcome

# Nicotine e-cigarette versus NRT: Quitting at 6+ months

Study or Subgroup	EC		NRT		Weight	Risk ratio	Risk ratio
	Events	Total	Events	Total		M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Bullen 2013	21	289	17	295	16.5%	1.26 [0.68 , 2.34]	
Hajek 2019	79	438	44	446	42.8%	1.83 [1.30 , 2.58]	
Lee 2018	5	20	1	10	1.3%	2.50 [0.34 , 18.63]	
Russell 2021 (1)	34	140	15	70	19.6%	1.13 [0.66 , 1.94]	
Russell 2021 (2)	44	145	15	71	19.8%	1.44 [0.86 , 2.40]	
<b>Total (95% CI)</b>		<b>1032</b>		<b>892</b>	<b>100.0%</b>	<b>1.53 [1.21 , 1.93]</b>	
Total events:	183		92				
Heterogeneity: Chi <sup>2</sup> = 2.90, df = 4 (P = 0.58); I <sup>2</sup> = 0%							
Test for overall effect: Z = 3.60 (P = 0.0003)							
Test for subgroup differences: Not applicable							

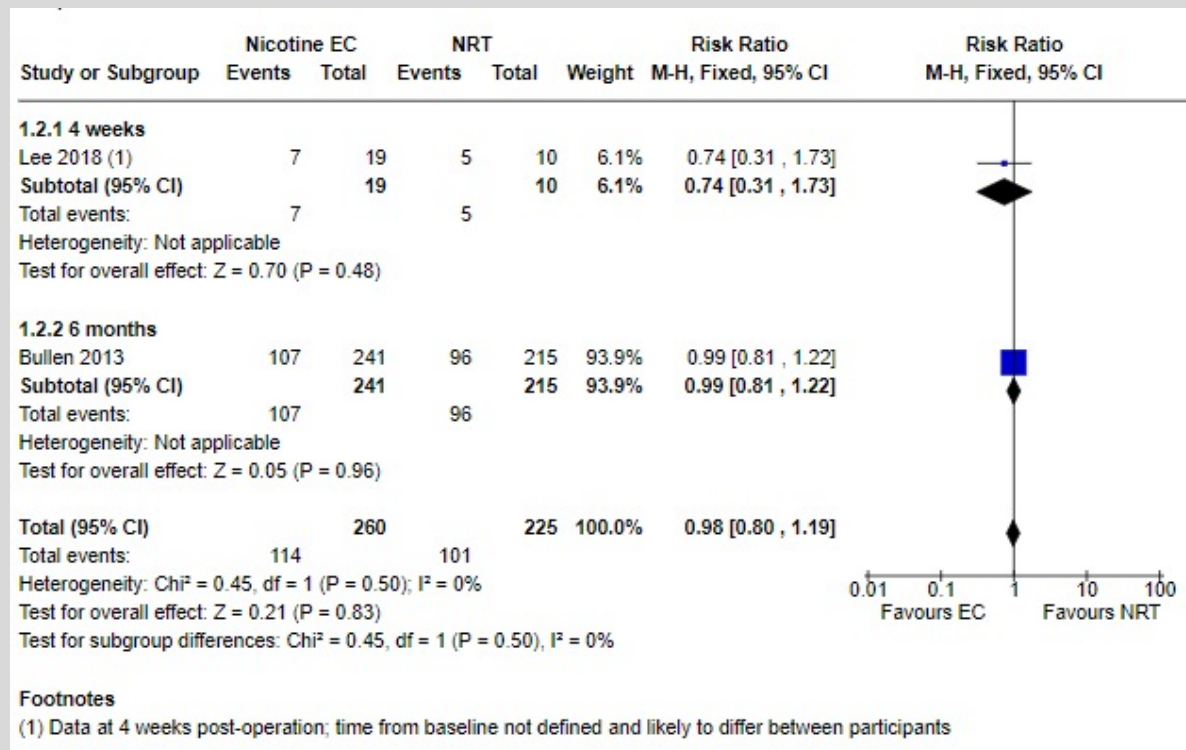
GRADE certainty of evidence:  
**MODERATE**  
(downgraded one level due to imprecision)



## Footnotes

- (1) FBNPs EC arm; control group split to avoid double-counting
- (2) NSP EC arm; control group split to avoid double-counting

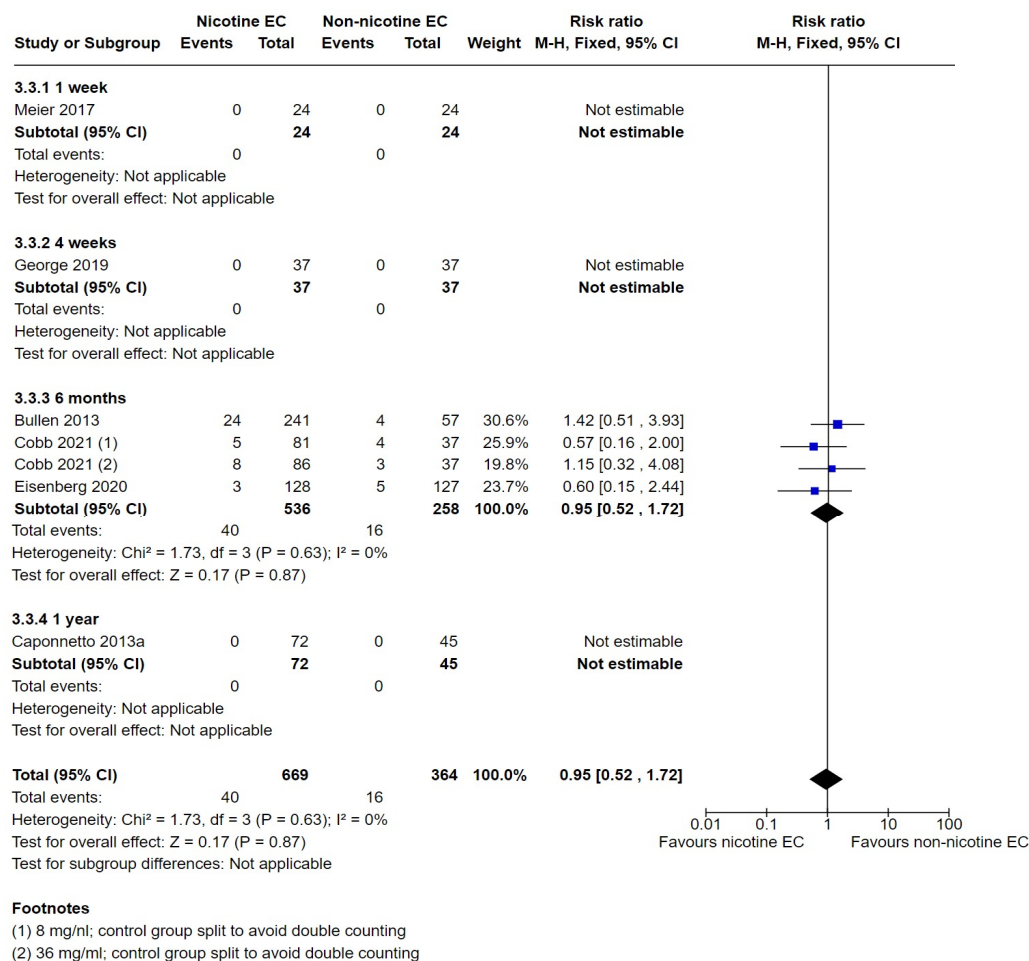
# Nicotine e- cigarette versus NRT: Adverse events at 1+weeks



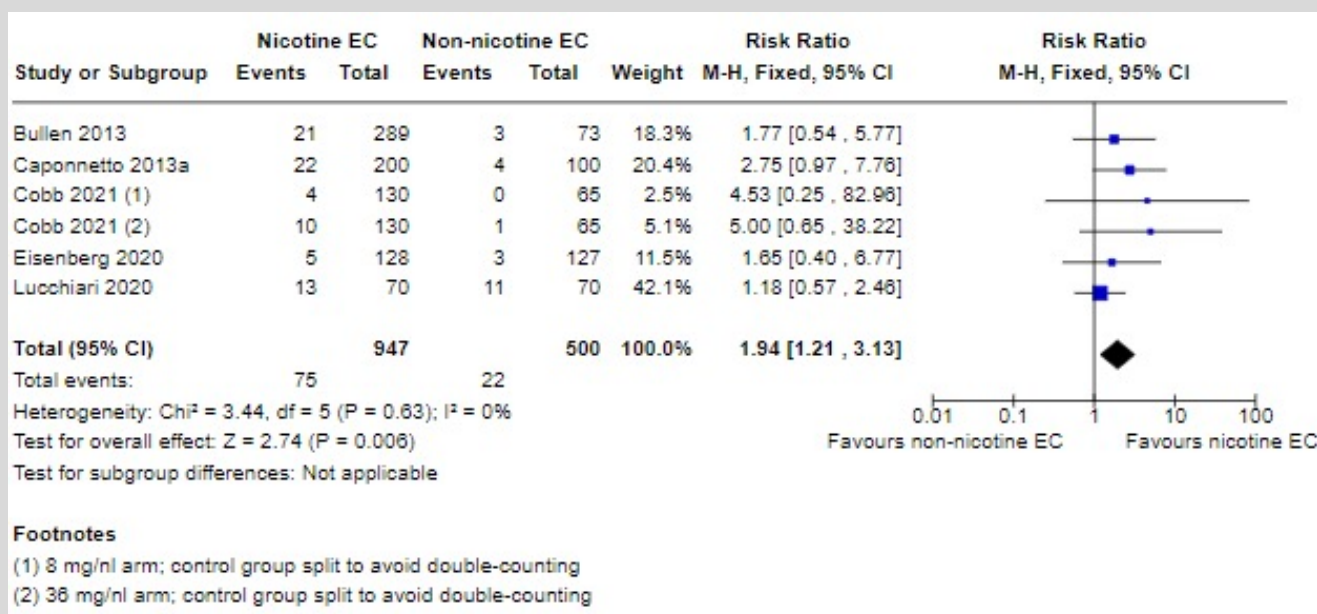
GRADE certainty of evidence: MODERATE (downgraded one level due to imprecision)

# Nicotine e-cigarette versus NRT: Serious adverse events at 1+weeks

GRADE certainty of evidence:  
LOW (downgraded two levels  
due to imprecision)



## Nicotine e-cigarette versus non-nicotine e-cigarette: Quitting at 6+ months

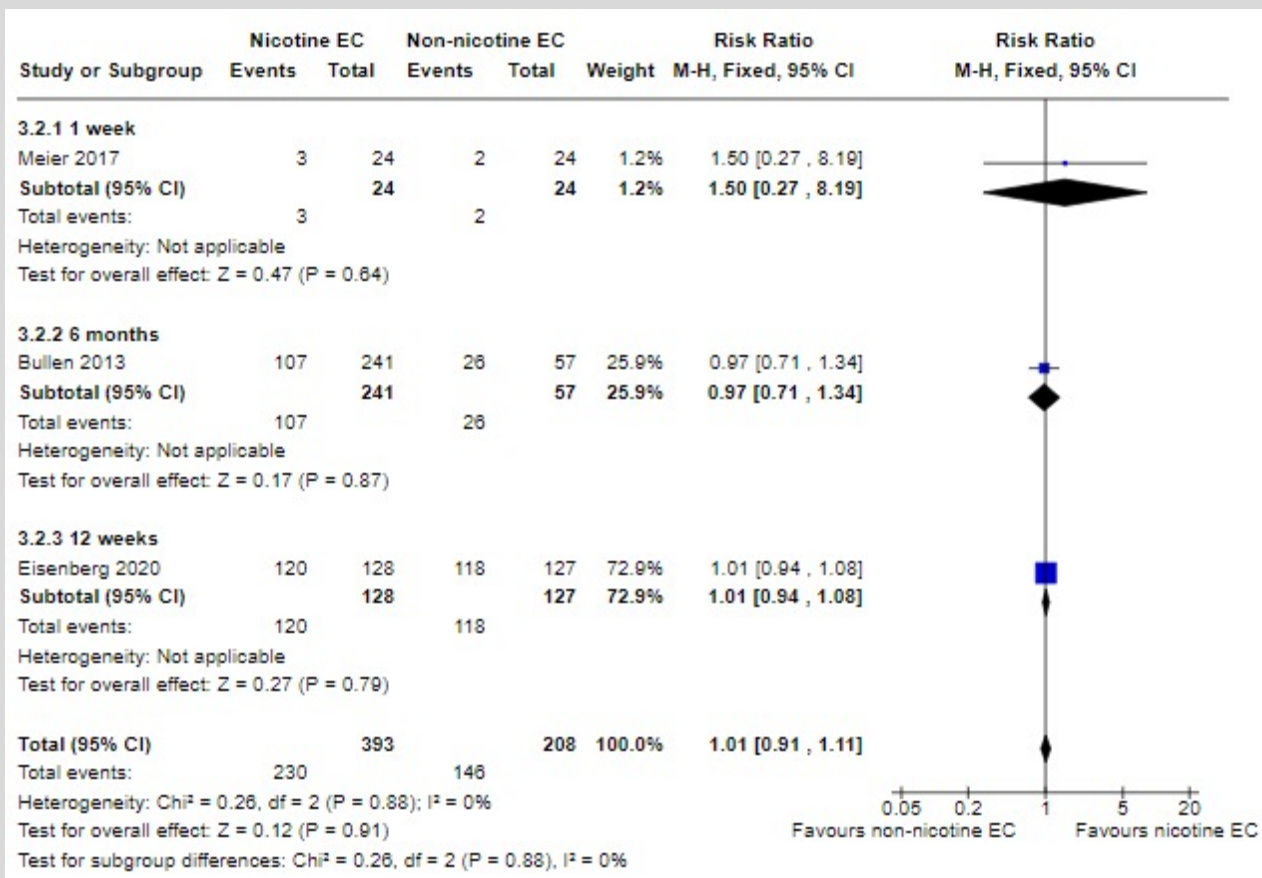


GRADE certainty of evidence: MODERATE (downgraded one level due to imprecision)



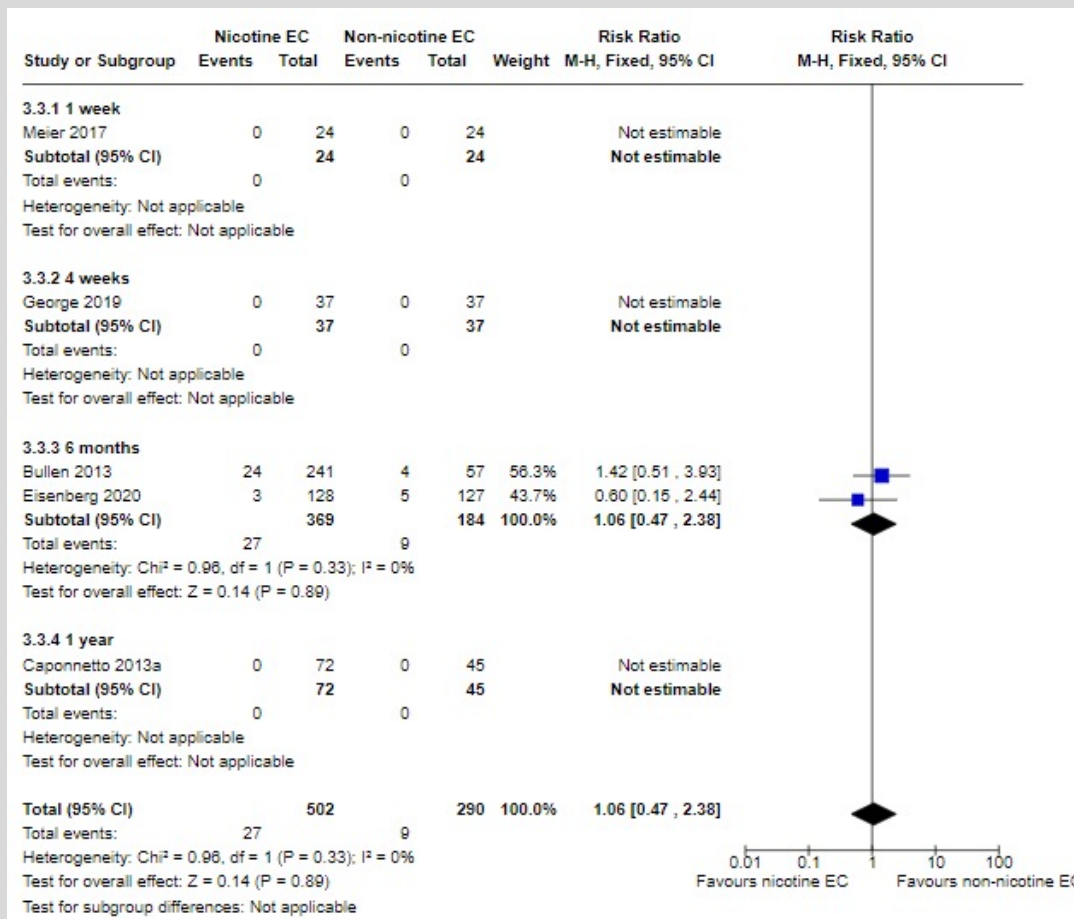
## Nicotine e-cigarette versus non-nicotine e-cigarette: Adverse events at 1+ weeks

GRADE certainty of evidence: LOW  
(downgraded two levels due to imprecision)



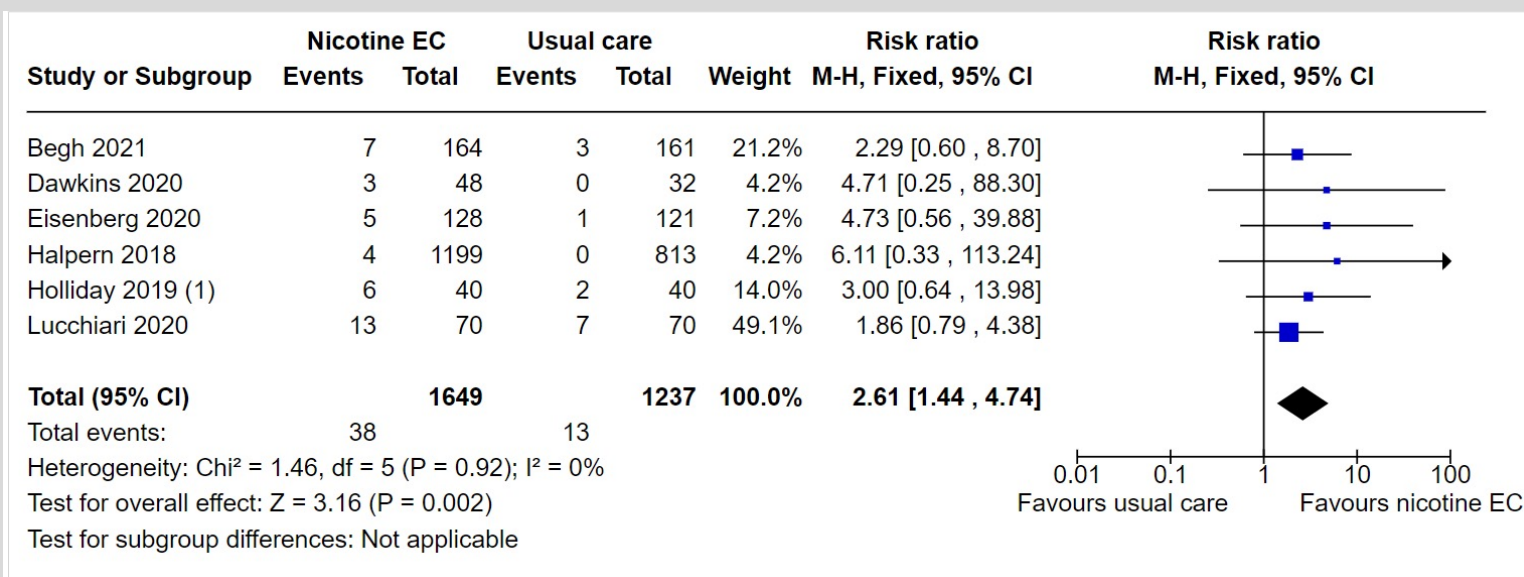
# Nicotine e-cigarette versus non-nicotine e-cigarette: Serious adverse events at 1+weeks

GRADE  
certainty of  
evidence: **LOW**  
(downgraded  
two levels due  
to imprecision)



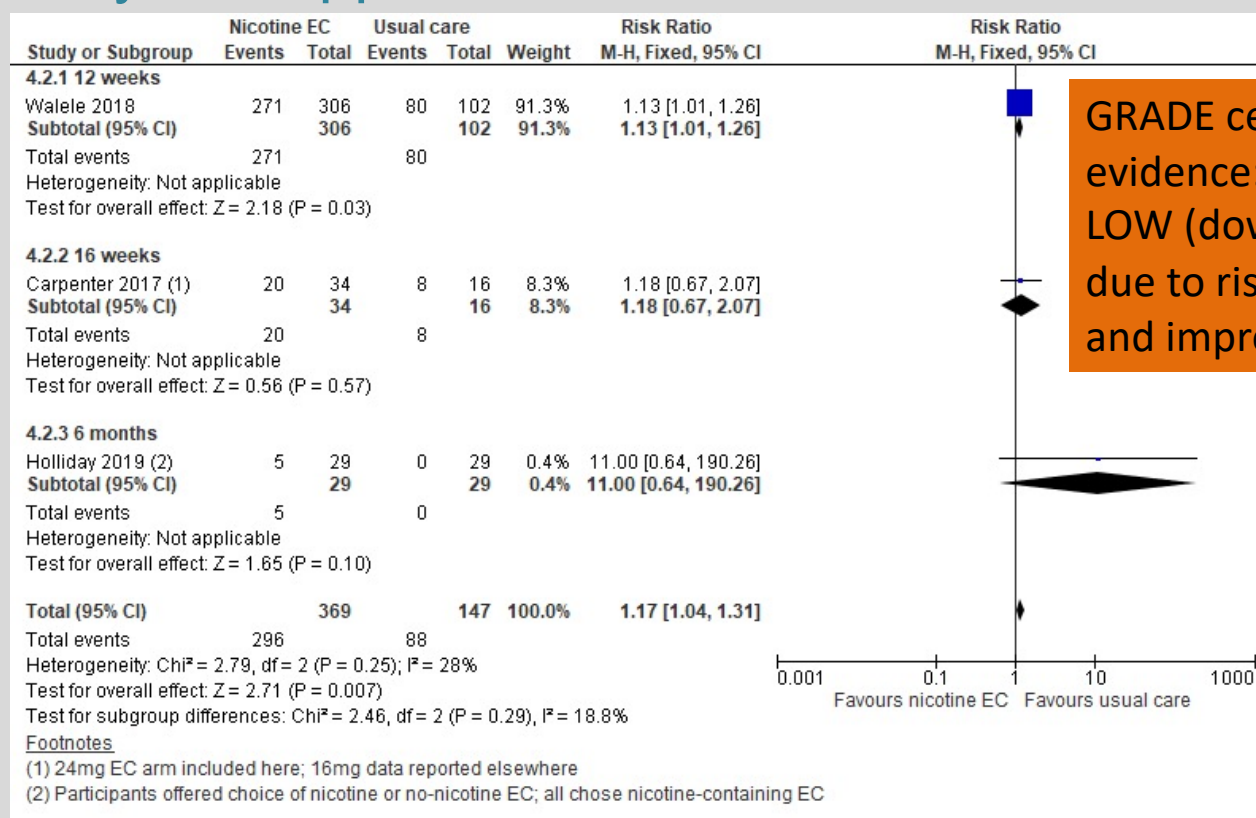


## Nicotine e-cigarette versus behavioural support only/no support: Quitting at 6+ months

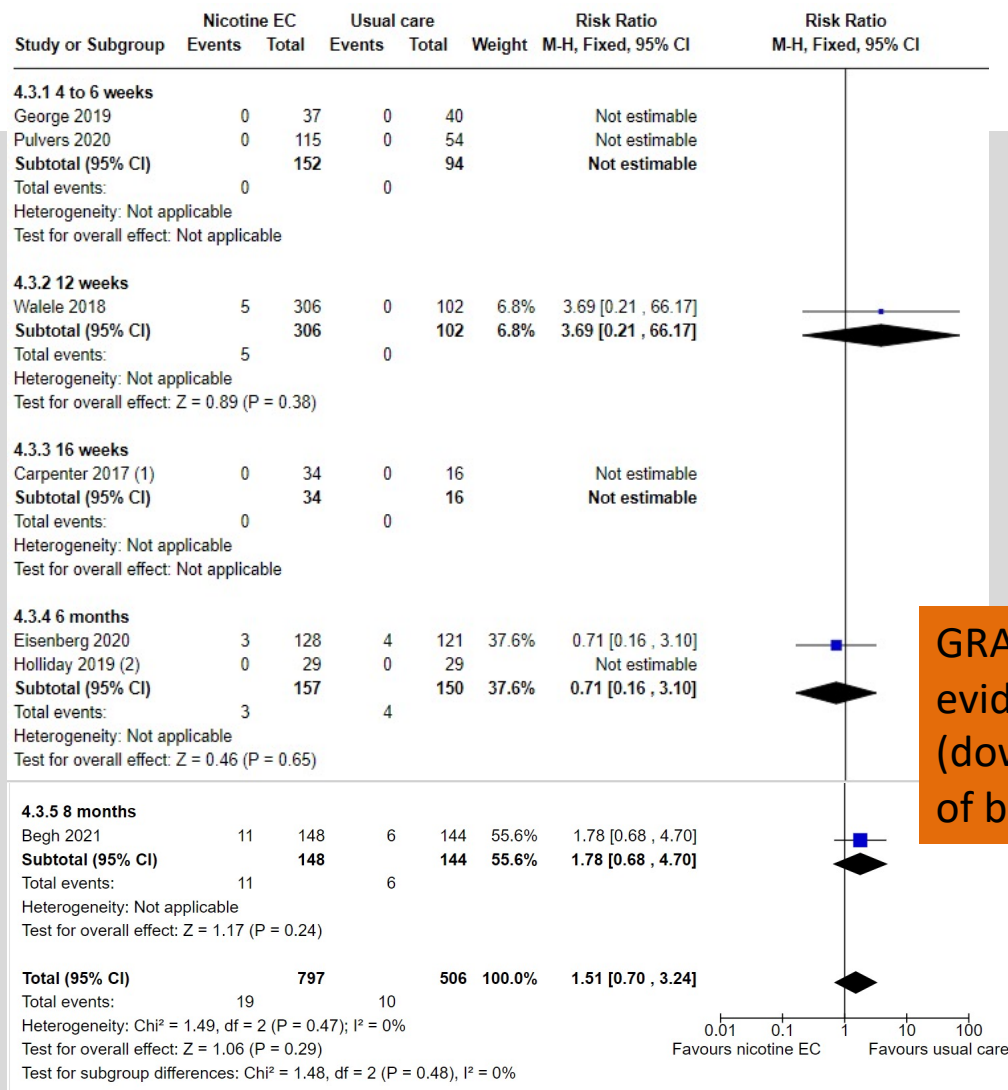


**GRADE certainty of evidence: VERY LOW (downgraded two levels due to risk of bias; one level due to imprecision)**

## Nicotine e-cigarette versus behavioural support only/no support: Adverse events at 1+weeks



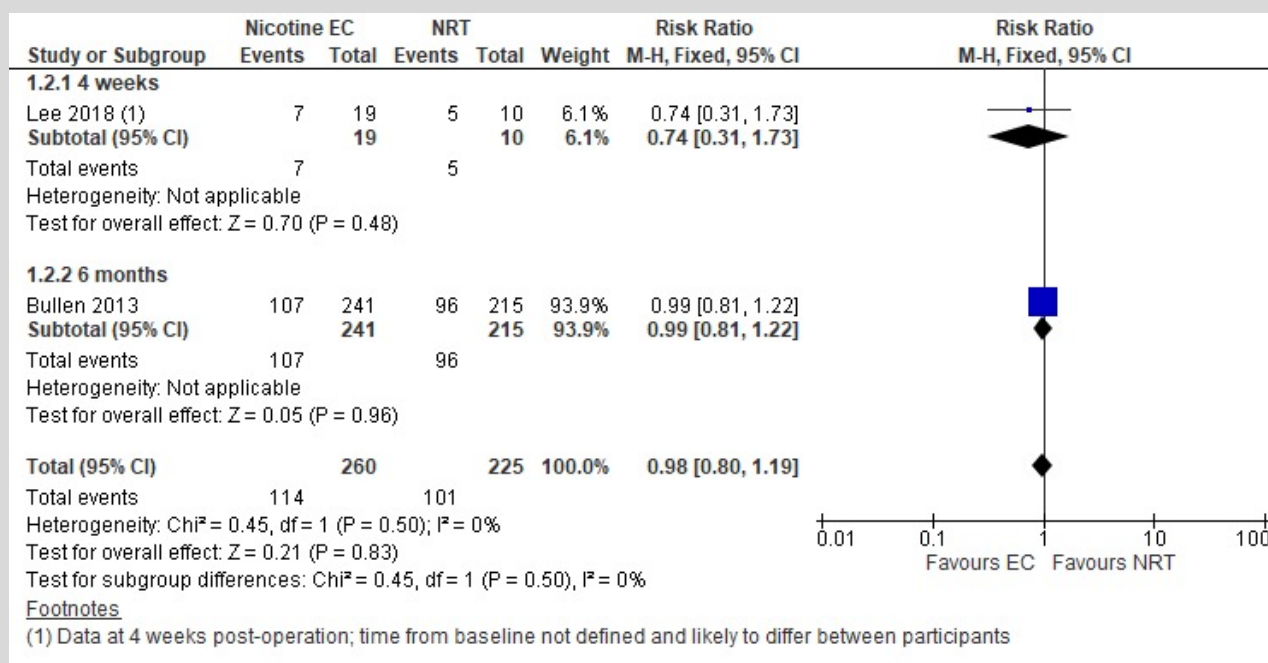
Nicotine e-  
cigarette  
versus  
behavioural  
support only/no  
support:  
Serious  
adverse events  
at 1+wks



GRADE certainty of evidence: VERY LOW (downgraded due to risk of bias and imprecision)

# Nicotine e-cigarette versus NRT: Adverse events at 1+weeks

No  
change

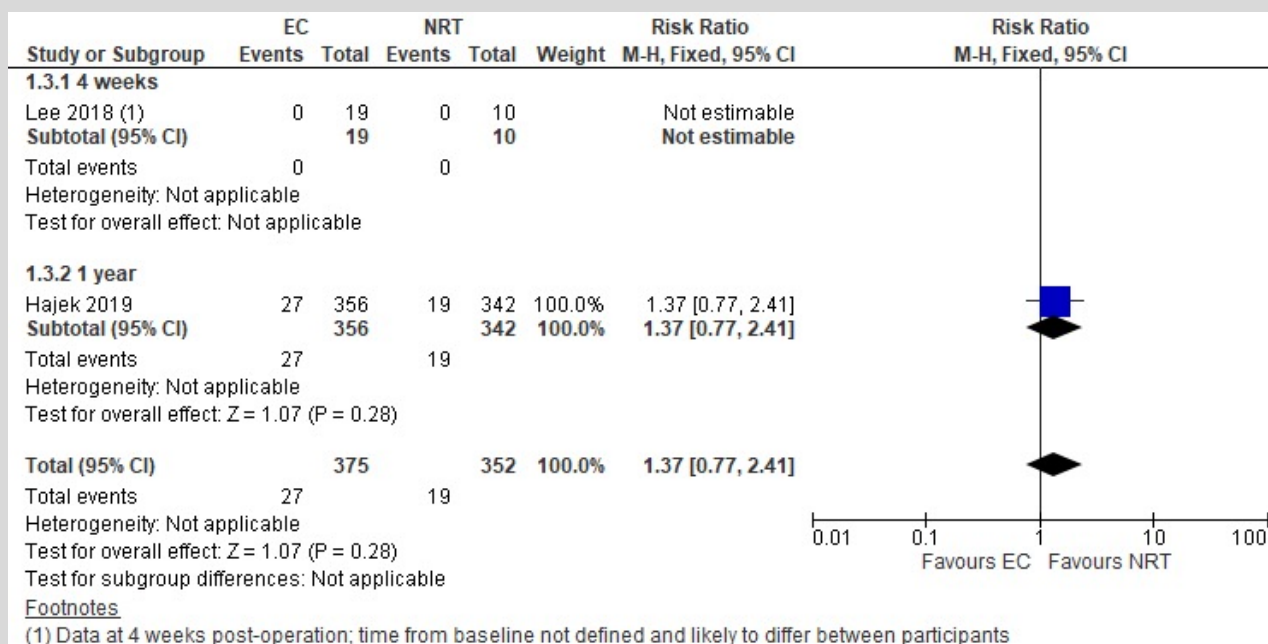


GRADE certainty of evidence: LOW (downgraded two levels due to imprecision)

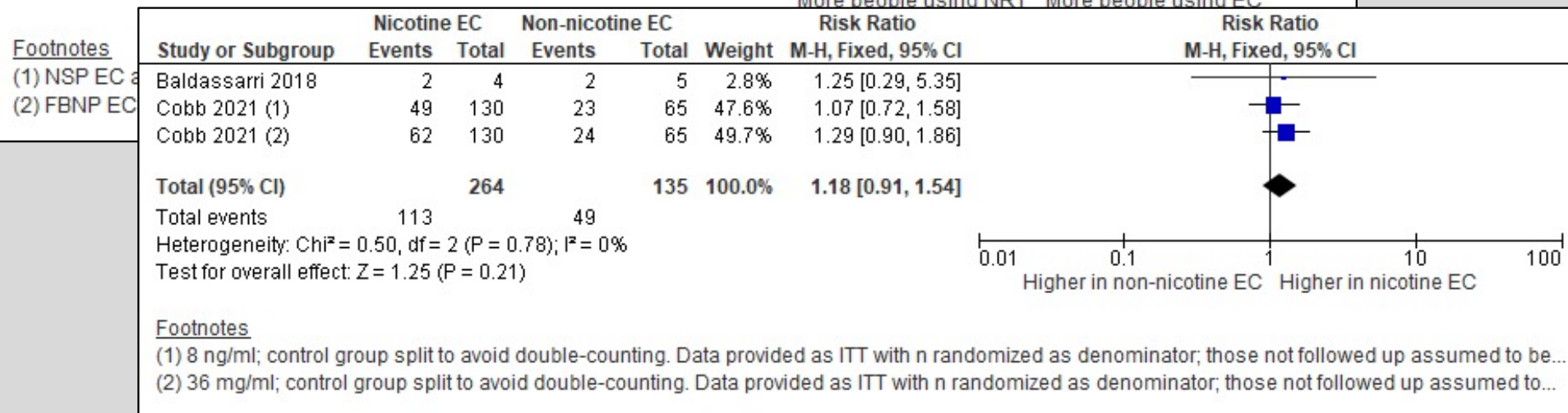
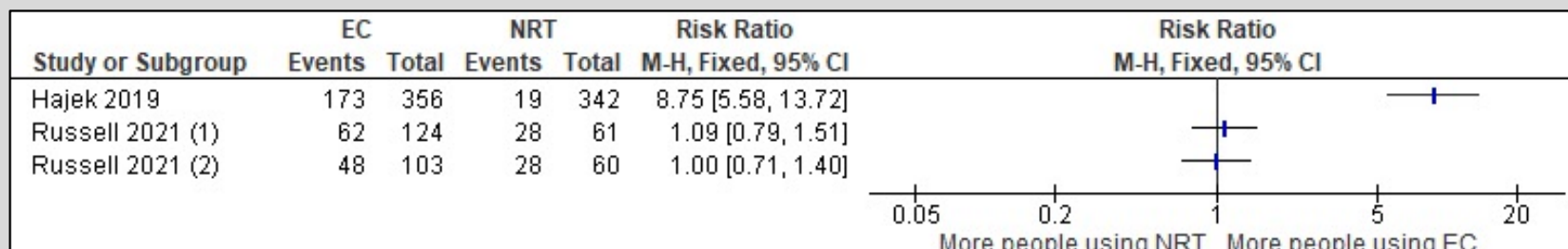
# Nicotine e- cigarette versus NRT: Serious adverse events at 1+weeks

No  
change

GRADE certainty of evidence:  
LOW (downgraded two levels  
due to imprecision)



# New outcome: product use at 6+ months





## New comparisons

- Nicotine salt versus free-base nicotine (one study, no difference in smoking cessation or product use, wide CIs)
- Advice to quit using EC versus standard advice in dual users (2 studies, only one reported cessation, no difference, but wide CIs and in the shorter term favoured intervention)

## Implications for practice

- Evidence suggesting nicotine EC can aid in smoking cessation is consistent across several comparisons. There was moderate certainty evidence, limited by imprecision, that EC with nicotine increased quit rates at six months or longer compared to non-nicotine EC and compared to NRT. There was very low certainty evidence that EC with nicotine increased quit rates compared to behavioural support only or no support.
- The effect of nicotine EC when added to NRT was unclear.
- None of the included studies (short- to mid-term, up to two years) detected serious adverse events considered possibly related to EC use.
- The most commonly reported adverse effects were throat/mouth irritation, headache, cough, and nausea, which tended to dissipate over time. In some studies, reductions in biomarkers were observed in people who smoked who switched to vaping consistent with reductions seen in smoking cessation.



## Implications for research

Further trials should:

- Measure cessation at six months or longer.
- Use active comparators
- Assess safety profile for as long as possible
- Be powered to detect differences in safety outcomes
- Present safety in both absolute and relative risk terms (in comparison to the risks of continuing to smoke tobacco).
- Offer recent devices to participants, to be most representative of what will be on the market at the time results are released. Data on pod type EC are particularly lacking. Protocols and statistical analysis plans should be registered in advance and openly available. (First trial of pod device reporting on cessation included in this version!)
- Provide EC in a way that would be used in real-world settings.

## See full review for

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

Updates to and information on the living systematic review:  
<https://www.cebm.ox.ac.uk/research/electronic-cigarettes-for-smoking-cessation-cochrane-living-systematic-review-1>