GoldNet Research Network

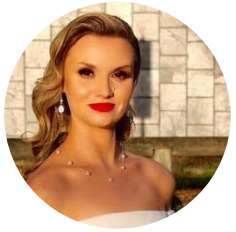
Virtual Journal Club Meeting

Nicotine Vaping for Smoking Cessation

Thank you for joining, we will commence shortly.
If you are not already a GoldNet member,
you can sign-up by scanning the QR code.

Panellists

Associate Prof. Kristin Cardon-Chahhoud
The University of Adelaide and Board Director for the Thoracic Society of Australia and New Zealand



Ms Melis Selamoglu
PhD Candidate
Department of General Practice, Monash University

Asst. Prof. Loai Albarqouni
Institute for Evidence-based Healthcare,
Faculty of Health Sciences and Medicine,
Bond University

Prof. Nick Zwar
Executive Dean,
Faculty of Health Sciences and Medicine, Bond University and Chair of GoldNet Steering committee

BOND UNIVERSITY | INSTITUTE FOR Evidence-Based Healthcare

Griffith UNIVERSITY Queensland, Australia

phn GOLD COAST An Australian Government Initiative

GPGC Healthy General Practice Healthy Gold Coast

Journal Club Agenda

- **Welcome & case study**
  - **Prof. Nick Zwar** (Chair of GoldNet Steering Committee)
- **Analysis of the research evidence**
  - **Asst. Prof. Loai Albarqouni** (article: ”Electronic cigarettes for smoking cessation”)
- **Presentation from Melis Selamoglu, Monash Uni**
- **Group discussion**
  - **Assoc. Prof Kristin Cardon-Chahhoud**
  - **Ms Melis Selamoglu**
  - **Asst. Prof. Loai Albarqouni**
  - **Prof. Nick Zwar**
- **Conclusion**

BOND UNIVERSITY | INSTITUTE FOR Evidence-Based Healthcare

Griffith UNIVERSITY Queensland, Australia

phn GOLD COAST An Australian Government Initiative

GPGC Healthy General Practice Healthy Gold Coast

GoldNet Research
The Gold Standard in Primary Care Research

GoldNet Research and our partners, acknowledges the Kombumerri people, the traditional Owners and Custodians of the land on which the University now stands. We pay respect to Elders past, present and emerging.

BOND UNIVERSITY | INSTITUTE FOR Evidence-Based Healthcare

Griffith UNIVERSITY Queensland, Australia

phn GOLD COAST An Australian Government Initiative

GPGC Healthy General Practice Healthy Gold Coast

BOND UNIVERSITY

Case Study

Case Study

- 45-year-old man, married, no children
- Presents with mental health problems, loss of enjoyment, low mood, K10 score 37
- Financial and marital difficulties
- Relapsed to smoking several months ago (10-15 cigarettes per day)
- First cigarette within half hour of waking
- Has used nicotine patch and gum in previous quit attempts and managed to quit for several months at a time before relapsing
- Also drinking every day

Past history

- Depression 2021 – saw psychiatrist and put on SSRI and also saw psychologist

GoldNet Research Network Journal Club

Nicotine Vaping for Smoking Cessation

Review > Cochrane Database Syst Rev. 2022 Nov 17;11(11):CD010216.
doi: 10.1002/14651858.CD010216.pub7.

Electronic cigarettes for smoking cessation

Jamie Hartmann-Boyce [1], Nicola Lindson [1], Ailsa R Butler [1], Hayden McRobbie [2], Chris Bullen [3], Rachna Begh [1], Annika Theodoulou [1], Caitlin Notley [4], Nancy A Rigotti [5], Tari Turner [6], Thomas R Fanshawe [1], Peter Hajek [7]

Affiliations + expand

PMID: 36384212 PMCID: PMC9668543 (available on 2023-11-17)
DOI: 10.1002/14651858.CD010216.pub7

Abstract

Background: Electronic cigarettes (ECs) are handheld electronic vaping devices which produce an aerosol by heating an e-liquid. Some people who smoke use ECs to stop or reduce smoking, although some organizations, advocacy groups and policymakers have discouraged this, citing lack of evidence of efficacy and safety. People who smoke, healthcare providers and regulators want to know if ECs can help people quit smoking, and if they are safe to use for this purpose. This is a review update conducted as part of a living systematic review.

Objectives: To examine the effectiveness, tolerability, and safety of using electronic cigarettes (ECs) to help people who smoke tobacco achieve long-term smoking abstinence.

Search methods: We searched the Cochrane Tobacco Addiction Group's Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and PsycINFO to 1 July 2022, and reference-checked and contacted study authors. SELECTION CRITERIA: We included randomized controlled trials (RCTs) and randomized cross-over trials, in which people who smoke were randomized to an EC or control condition. We also included uncontrolled intervention studies in which all participants received an EC intervention. Studies had to report abstinence from cigarettes at six months or longer or data on safety markers at one week or longer, or both.

Data collection and analysis: We followed standard Cochrane methods for screening and data extraction. Our primary outcome measures were abstinence from smoking after at least six months follow-up, adverse events (AEs), and serious adverse events (SAEs). Secondary outcomes included the proportion of people still using study product (EC or pharmacotherapy) at six or more months after randomization or starting EC use, changes in carbon monoxide (CO), blood pressure (BP), heart rate, arterial oxygen saturation, lung function, and levels of carcinogens or toxicants, or both. We used a

- What is the key question of the article?
- Are the results of the study valid? Can we trust the results of this article?
- What are the results of the study?
- Will the results help me in caring for my patient and clinical practice?

[Intervention Review]

Electronic cigarettes for smoking cessation

Jamie Hartmann-Boyce[1α], Nicola Lindson[1α], Ailsa R Butler[1], Hayden McRobbie[2], Chris Bullen[3], Rachna Begh[1], Annika Theodoulou[1], Caitlin Notley[4], Nancy A Rigotti[5], Tari Turner[6], Thomas R Fanshawe[1], Peter Hajek[7]

ABSTRACT

Background

Electronic cigarettes (ECs) are handheld electronic vaping devices which produce an aerosol by heating an e-liquid. Some people who smoke use ECs to stop or reduce smoking, although some organizations, advocacy groups and policymakers have discouraged this, citing lack of evidence of efficacy and safety. People who smoke, healthcare providers and regulators want to know if ECs can help people quit smoking, and if they are safe to use for this purpose. This is a review update conducted as part of a living systematic review.

Objectives

To examine the effectiveness, tolerability, and safety of using electronic cigarettes (ECs) to help people who smoke tobacco achieve long-term smoking abstinence.

Search methods

We searched the Cochrane Tobacco Addiction Group's Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, and PsycINFO to 1 July 2022, and reference-checked and contacted study authors.

Selection criteria

We included randomized controlled trials (RCTs) and randomized cross-over trials, in which people who smoke were randomized to an EC or control condition. We also included uncontrolled intervention studies in which all participants received an EC intervention. Studies had to report abstinence from cigarettes at six months or longer or data on safety markers at one week or longer, or both.

Data collection and analysis

We followed standard Cochrane methods for screening and data extraction. Our primary outcome measures were abstinence from smoking after at least six months follow-up, adverse events (AEs), and serious adverse events (SAEs). Secondary outcomes included the proportion of people still using study product (EC or pharmacotherapy) at six or more months after randomization or starting EC use, changes in carbon monoxide (CO), blood pressure (BP), heart rate, arterial oxygen saturation, lung function, and levels of carcinogens or toxicants, or both.

What is the key question of the article?

PICO

Population

Intervention

Control

Outcomes

OBJECTIVES

To examine the safety, tolerability and effectiveness of using electronic cigarettes (ECs) to help people who smoke tobacco achieve long-term smoking abstinence.

METHODS

Criteria for considering studies for this review

Types of studies

We include randomized controlled trials (RCTs) and randomized cross-over trials in which people who smoke are randomized to ECs or to a control condition. RCTs are the best available primary evidence, but the continued paucity of RCTs in this area requires that we also include uncontrolled intervention studies in which all participants are given an EC intervention.

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

Types of participants Population

People defined as currently smoking cigarettes at enrolment into the studies. Participants could be motivated or unmotivated to quit.

Types of interventions Interventions

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

Types of comparators ① Nicotine ECs vs. non-nicotine ECs ② ECs vs alternative smoking cessation aid ③ ECs + cessation aids vs cessation aid alone

We compare ① nicotine ECs with non-nicotine ECs, ② ECs versus alternative smoking cessation aids, including NRT or no intervention, and ③ ECs added to standard smoking cessation treatment (behavioural or pharmacological or both) with standard treatment alone.

Types of outcome measures

Primary 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 adverse events or serious adverse events at one week or longer (as defined by study authors)

BOND UNIVERSITY | INSTITUTE FOR Evidence-Based Healthcare

PICO

Population

Intervention

Control

Outcomes

FAITH

Are the results of the study valid?
Can we trust the results of this article?

Find

Did the search **FIND** all relevant studies?

Appraised

Have the included studies been critically **APPRAISED**?

Included

Did the review **INCLUDE** the right type of studies?

Totaled

Have the results been **TOTALLED** up with appropriate summary tables and plots?

Heterogeneity?

Has **HETEROGENITY** between studies been assessed and explained?

FAITH

F Did the search FIND all the relevant studies?

F Did the search FIND all the relevant studies?

What is best?	Where do I find the information?
Searches for studies should be as extensive as possible in order to identify as much relevant evidence as possible. A comprehensive search for relevant studies includes a search of major bibliographic databases (e.g. Medline, Cochrane, EMBASE, etc). The database searches should include both MeSH terms and text words and should not be limited to English language studies only. Reference lists of included studies and other relevant systematic reviews should be checked, and for systematic reviews of interventions trial registries (e.g. ClinicalTrials.gov) should be searched. Additional methods such as contacting relevant individuals and organisations, searching for unpublished reports and theses and forward citation searching may also be conducted.	**The** Methods section should describe the search strategy used. Sometimes details about the searches will be found in a supplementary file. The **Results** section will outline the number of titles and abstracts found by the searches, the number of titles and abstract screened, the number of studies obtained in full text and the number of studies excluded from the review (with reason for exclusion). This information may be presented in a figure or flow chart.

Search methods for identification of studies

Electronic searches

Searches are conducted monthly. This update includes results from searches conducted up to 1st July 2022:

- Cochrane Tobacco Addiction Group Specialized Register (CRS-Web)
- Cochrane Central Register of Controlled Trials (CENTRAL 2022; Issue 6) via CRS-Web
- MEDLINE (OVID SP; 1st January 2004 to 1st July 2022)
- Embase (OVID SP; 1st January 2004 to 1st July 2022)
- PsycINFO (OVID SP; 1st January 2004 to 1st July 2022)
- ClinicalTrials.gov (via CENTRAL 2022; Issue 6)
- WHO International Clinical Trials Registry Platform (ICTRP: www.who.int/ictrp/en/, via CENTRAL 2022; Issue 6)

At the time of the search, the Register included the results of searches of MEDLINE (via OVID) to update 20220614; Embase (via OVID) to week 202224; PsycINFO (via OVID) to update 20220613. 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. All current search strategies are listed in Appendix 3. The previously-used search strategy is shown in Appendix 4. The search date parameters of the original searches were limited to 2004 to the present, due to the fact that ECs were not available before 2004.

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 abstracts from the Society for Research on Nicotine and Tobacco (SRNT) Annual Meetings.

FAITH

F Did the search FIND all the relevant studies?

F Did the search FIND all the relevant studies?

What is best?	Where do I find the information?
Searches for studies should be as extensive as possible in order to identify as much relevant evidence as possible. A comprehensive search for relevant studies includes a search of major bibliographic databases (e.g. Medline, Cochrane, EMBASE, etc). The database searches should include both MeSH terms and text words and should not be limited to English language studies only. Reference lists of included studies and other relevant systematic reviews should be checked, and for systematic reviews of interventions trial registries (e.g. ClinicalTrials.gov) should be searched. Additional methods such as contacting relevant individuals and organisations, searching for unpublished reports and theses and forward citation searching may also be conducted.	**The** Methods section should describe the search strategy used. Sometimes details about the searches will be found in a supplementary file. The **Results** section will outline the number of titles and abstracts found by the searches, the number of titles and abstract screened, the number of studies obtained in full text and the number of studies excluded from the review (with reason for exclusion). This information may be presented in a figure or flow chart.

Ovid databases (MEDLINE, Embase, PsycINFO)

1. exp case control studies/ or exp cohort studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw.

2. (e-cig$ or ecig$ or electr$ cigar$ or electronic nicotine).mp. or (vape or vapes or vaporizer or vapourizer or vaporiser or vapouriser or vaper or vapers or vaping).ti,ab. or exp Electronic Nicotine Delivery Systems/

3. (randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.ab. or trial.ti.

4. exp animals/ not human/

5. 3 not 4

6. 2 and 5

7. 1 and 2

8. 6 or 7

9. smoking cessation.mp. or exp Smoking Cessation/

10. tobacco cessation.mp. or "Tobacco-Use-Cessation"/

11. (nicotine dependence or tobacco dependence).mp.

12. exp Smoking/th

13. "Tobacco-Use-Disorder"/

14. Smoking reduction/ or Smoking reduction.mp.

15. exp Pipe smoking/ or exp Tobacco smoking/ or exp Tobacco Products/

16. ((quit$ or stop$ or ceas$ or giv$ or abstain* or abstinen*) adj5 (smoking or smoke* or tobacco)).ti,ab.

17. exp Tobacco/ or exp Nicotine/

18. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17

19. 8 and 18

FAITH

A Have the included studies been critically APPRAISED?

A Have the included studies been critically APPRAISED?	
What is best?	**Where do I find the information?**
It is critical that the strengths and limitations of the studies included in the review are assessed. The review should describe how risk of bias in the included studies was assessed using predetermined criteria appropriate to the type of clinical question. For studies of interventions these criteria include randomisation, blinding and completeness of follow-up.	The **Methods** section should describe the assessment of risk of bias and the criteria used.

Assessment of risk of bias in included studies

Two review authors (for this update from: ARB, AT, CN, PB) independently assessed the risks of bias for each included study, using the Cochrane risk of bias tool v1 (Higgins 2011). This approach uses a domain-based evaluation that addresses seven different areas: random sequence generation; allocation concealment; blinding of participants and providers; blinding of outcome assessment; incomplete outcome data; selective outcome reporting; and other potential sources of bias. We assigned a grade (low, high, or unclear) for risk of bias for each domain. We resolved disagreements by discussion or by consulting a third review author.

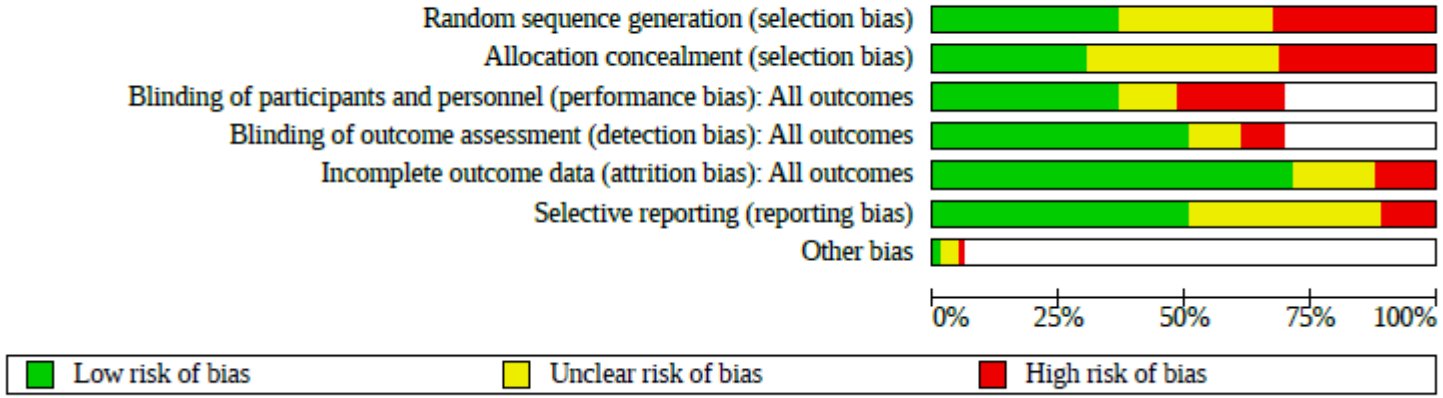
Specific considerations about judgements for individual domains in this review are outlined below:

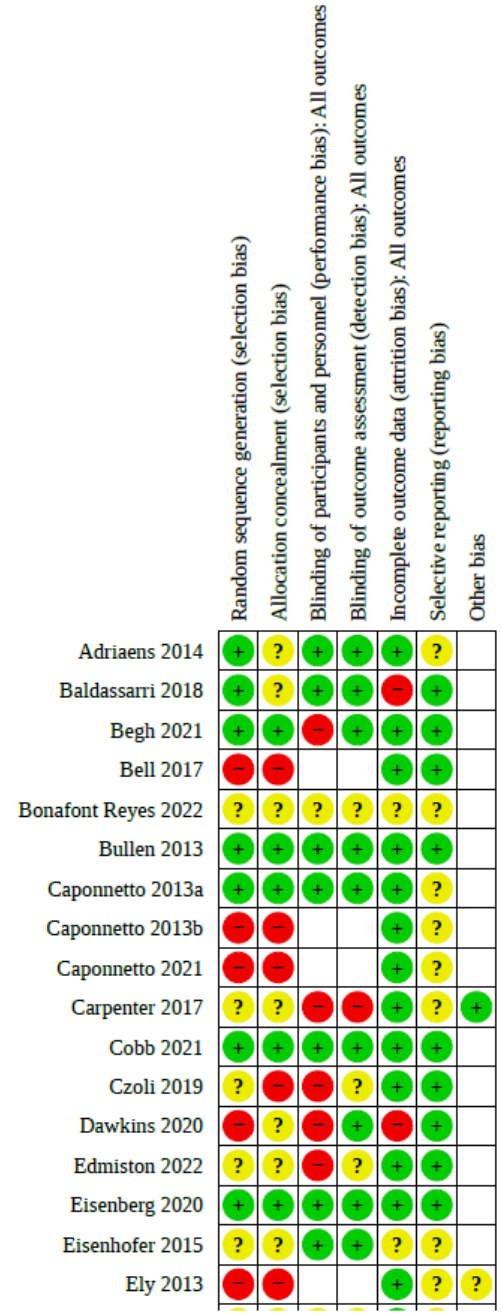
- Random sequence generation/allocation concealment: We rated all non-randomized studies at high risk in these domains;
- Blinding of participants and personnel: We did not evaluate this domain for non-randomized studies, as we considered it not to be applicable. For randomized studies which did not 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 standard methods of the Cochrane Tobacco Addiction Review Group, 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 standard methods of the Cochrane Tobacco Addiction Group, we rated studies 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.

UTE FOR
nce-Based Healthcare

Figure 8.

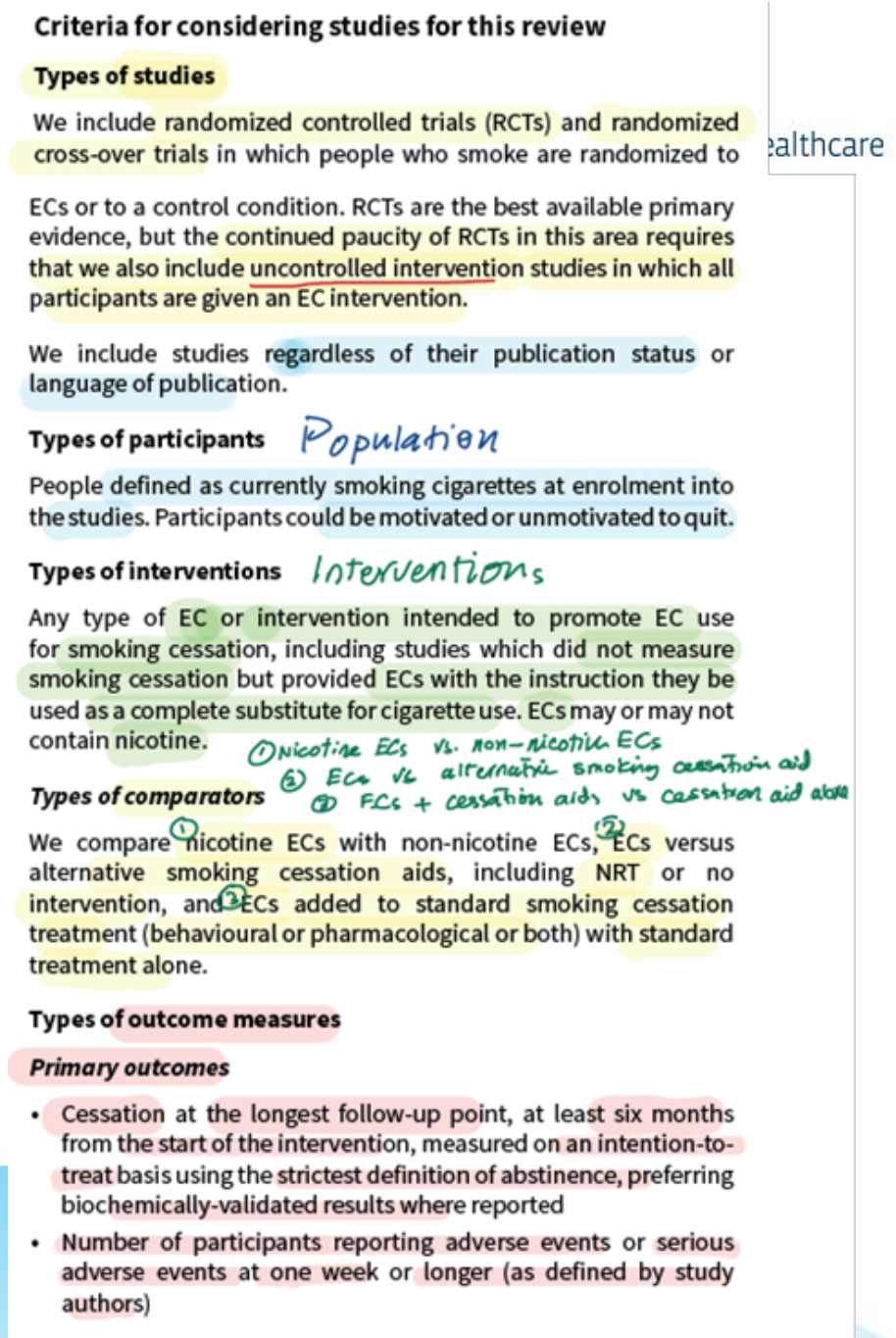

Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias): All outcomes
Blinding of outcome assessment (detection bias): All outcomes
Incomplete outcome data (attrition bias): All outcomes
Selective reporting (reporting bias)
Other bias
0%
25%
50%
75%
100%
Low risk of bias
Unclear risk of bias
High risk of bias


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
Adriaens 2014
Baldassarri 2018
Begh 2021
Bell 2017
Bonafont Reyes 2022
Bullen 2013
Caponnetto 2013a
Caponnetto 2013b
Caponnetto 2021
Carpenter 2017
Cobb 2021
Czoli 2019
Dawkins 2020
Edmiston 2022
Eisenberg 2020
Eisenhofer 2015
Ely 2013

FAITH

I Did the review INCLUDE the right type of studies?

I Did the review INCLUDE the right type of studies and assess their risk of bias?	
What is best?	**Where do I find the information?**
Some study designs are more appropriate than others for answering certain questions. Systematic reviews of interventions should primarily focus on randomised trials and randomised trials should be included if they are feasible for the intervention being studied.	The **Methods and Results** sections should describe the type of studies included, how the risk of bias in the included studies was assessed and the result of that assessment.



Criteria for considering studies for this review

Types of studies

We include randomized controlled trials (RCTs) and randomized cross-over trials in which people who smoke are randomized to ECs or to a control condition. RCTs are the best available primary evidence, but the continued paucity of RCTs in this area requires that we also include uncontrolled intervention studies in which all participants are given an EC intervention.

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

Types of participants Population

People defined as currently smoking cigarettes at enrolment into the studies. Participants could be motivated or unmotivated to quit.

Types of interventions Interventions

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

① Nicotine ECs vs. non-nicotine ECs
② ECs vs alternative smoking cessation aid
③ ECs + cessation aids vs cessation aid alone

Types of comparators

We compare nicotine ECs with non-nicotine ECs, ECs versus alternative smoking cessation aids, including NRT or no intervention, and ECs added to standard smoking cessation treatment (behavioural or pharmacological or both) with standard treatment alone.

Types of outcome measures

Primary 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 adverse events or serious adverse events at one week or longer (as defined by study authors)

FAITH

TH

Have the results been TOTALLED up with appropriate summary tables and plots?
Has HETEROGENEITY between the studies been assessed and explained?

T Have the results of the included studies been TOTALLED up with appropriate summary tables and plots?

What is best?	Where do I find the information?
The results of included studies should be presented in a summary table. If the studies are considered similar enough (in terms of their PICOs, methods and results) there may be a meta-analysis with the results of studies presented in a forest plot.	The **Results** section should include the summary table and plots and an explanation of the results.

H Has HETEROGENEITY between the studies been assessed and explained?

Ideally the results of the included studies should be similar or 'homogeneous'. The extent of heterogeneity (variation in the results of studies) can be measured with the I^2 test. The review should explore potential reasons for heterogeneity due to differences in study PICOS and methods.	The **Results** section should describe the extent of heterogeneity for each outcome and discuss possible reasons. The forest plot should show the results of the I^2 test.

BOND | INSTITUTE FOR Evidence-Based Healthcare

Assessment of heterogeneity

We assessed the clinical and methodological diversity between studies to guide our decision whether data should be pooled. We were also guided by the degree of statistical heterogeneity, assessed by calculating the I^2 statistic (Higgins 2003), and considering a value greater than 50% as evidence of substantial heterogeneity. We did not present pooled results where I^2 values exceeded 75%.

Assessment of reporting biases

Reporting bias can be assessed using funnel plots, where 10 or more RCTs contribute to an outcome. However, there was only one analysis with sufficient studies to support this approach.

Data synthesis

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

For continuous outcomes, we pooled mean differences (or standardized mean differences for studies using different measures for the same construct), using the inverse variance approach (also with a 95% CI).

Subgroup analysis and investigation of heterogeneity

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

- Intensity of behavioural support used;
- Type of EC (cartridge; refillable; pod);
- Instructions for EC use (e.g. study provision, length of provision, whether participants had a role in product choice);
- Type of participants (e.g. experience of EC use).

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
Setting: New Zealand, UK, USA
Intervention: Nicotine EC
Comparison: NRT

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of partici-pants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with NRT	Risk with Nicotine EC				
Smoking cessation at 6 months to 1 year Assessed with biochemical validation	Study population 6 per 100	10 per 100 (8 to 12)	RR 1.63 (1.30 to 2.04)	2378 (6 RCTs)	⨁⨁⨁⨁ HIGH	-
Adverse events at 4 weeks to 6-9 months Assessed by self-report	Study population 27 per 100	27 per 100 (24 to 32)	RR 1.02 (0.88 to 1.19)	1702 (4 RCTs)	⨁⨁⨁◯ MODERATE[a]	-
Serious adverse events at 4 weeks to 1 year Assessed via self-report and medical records	Study population 6 per 100	7 per 100 (5 to 9)	RR 1.12 (0.82 to 1.52)	2411 (5 RCTs)	⨁⨁◯◯ LOW[b]	2 studies reported no events; effect estimate based on the three studies in which events were reported

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). For cessation, the assumed risk in the control group is based on assumed quit rates for NRT assuming receipt of limited behavioural stop-smoking support (as per Hartmann-Boyce 2018a). The assumed risk for adverse events and serious adverse events is a weighted mean average of quit rates across control groups in contributing studies.

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Adriaens 2014

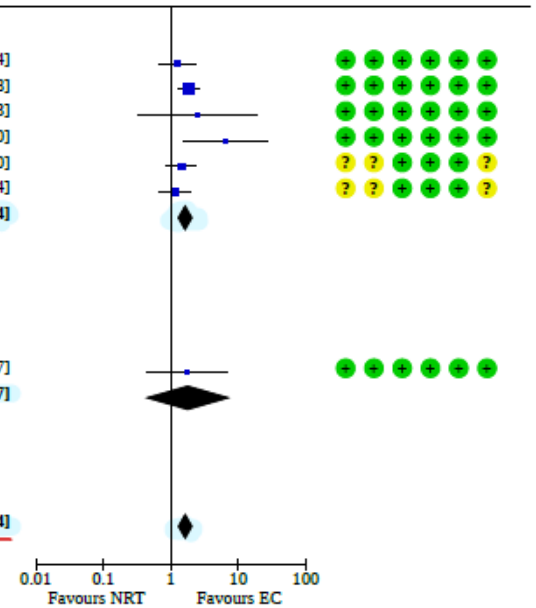
Study characteristics	
Methods	Design: 3-armed RCT; with all participants then assigned to nicotine EC (treated as cohort in this review) Recruitment: Advertisement on university website, flyers on university campuses, emails to personnel and advertisement in local newspaper Setting: Community and laboratory, Belgium Study start date/end date: Not stated
Participants	Total N: 48 provided data Randomized to: EC1 16; EC2 17; control 17 Inclusion criteria: smoke ≥ 3 yrs; ≥ 10 cpd; not intending to quit in the near future but willing to try a less unhealthy alternative. Exclusion criteria: diabetes; severe allergies; asthma or other respiratory diseases; psychiatric problems; dependence on chemicals other than nicotine; pregnancy; breastfeeding; hypertension; CV disease; currently using any kind of smoking cessation therapy; prior use of EC. 56% women, mean age 44, mean cpd 19, mean FTCD 5.79, all unwilling to quit with no baseline EC use
Interventions	**EC: Refillable** **Intervention:** 2 intervention groups (EC1 and EC2) provided with EC and instructed to use EC or smoke ad libitum (EC1 group provided with Joyetech eGO-C, EC2 group provided with Kanger T2-CC) and provided guidance on EC use. For both types, provided 30 mL bottles of tobacco-flavoured e-liquid (Dekang "Turkish Blend"), containing 18 mg/mL of nicotine. 4 bottles at baseline replenished at 4 weeks, keep any remaining after 8 weeks **Control:** 6 bottles for 2 months at week 8 (half offered EC1, half offered EC2); no guidance on use
Outcomes	3 lab sessions over 2 months (weeks 1, 4 and 8), plus online questionnaires, further follow-up at 3 and 6 m after last lab session. Cessation: measured but definition not provided, validated with eCO 5 ppm or less Adverse events and biomarkers: eCO, salivary cotinine measured during lab sessions. Also collected craving and withdrawal symptoms via lab sessions, "benefits and complaints", mood, EC usage
Study funding	"No external funding for this study was obtained. Electronic cigarettes and e-liquids were purchased at E-cig4U (`t Rond 10, 4285 DE Woudrichem, The Netherlands; http://www.e-cig4u.nl/) with balances of previous research funds obtained by Frank Baeyens."
Author declarations	The authors declare no conflict of interest.
Notes	Randomization was for short-term outcomes only. Additional data provided from authors

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomization was performed by using a randomization tool available on the website www.randomizer.org
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Unblinded but as this review only includes data on objective measurements and not cessation judged unlikely to affect outcomes

Analysis 1.1. Comparison 1: Nicotine EC versus NRT, Outcome 1: Smoking cessation

Study or Subgroup	EC Events	EC Total	NRT Events	NRT Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Not selected on pregnancy						
Bullen 2013	21	289	17	295	15.7%	1.26 [0.68 , 2.34]
Hajek 2019	79	438	44	446	40.7%	1.83 [1.30 , 2.58]
Lee 2018	5	20	1	10	1.2%	2.50 [0.34 , 18.63]
Myers-Smith 2022	13	68	2	67	1.9%	6.40 [1.50 , 27.30]
Russell 2021 (1)	44	145	15	71	18.8%	1.44 [0.86 , 2.40]
Russell 2021 (2)	34	140	15	70	18.7%	1.13 [0.66 , 1.94]
Subtotal (95% CI)		**1100**		**959**	**97.0%**	**1.62 [1.29 , 2.04]**
Total events:	196		94			
Heterogeneity: Chi² = 6.67, df = 5 (P = 0.25); I² = 25%						
Test for overall effect: Z = 4.19 (P < 0.0001)						
1.1.2 Pregnant population						
Hajek 2022 (3)	6	169	3	150	3.0%	1.78 [0.45 , 6.97]
Subtotal (95% CI)		**169**		**150**	**3.0%**	**1.78 [0.45 , 6.97]**
Total events:	6		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.82 (P = 0.41)						
Total (95% CI)		**1269**		**1109**	**100.0%**	**1.63 [1.30 , 2.04]**
Total events:	202		97			
Heterogeneity: Chi² = 6.70, df = 6 (P = 0.35); I² = 10%						
Test for overall effect: Z = 4.27 (P < 0.0001)						
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.90), I² = 0%						



Footnotes

(1) NSP EC arm; control group split to avoid double-counting
(2) FBNPs EC arm; control group split to avoid double-counting
(3) 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

BOND UNIVERSITY | INSTITUTE FOR Evidence-Based Healthcare

Can we trust this review?

ie.

BOND UNIVERSITY | INSTITUTE FOR Evidence-Based Healthcare

Results

Included studies

In total, we include 78 studies, with 17 new included studies and 61 eligible included studies included in previous versions of the review. Key features of the included studies are summarized below. Further details on each included study can be found in the Characteristics of included studies tables.

Participants

The 78 included studies represented 22,052 participants. Thirty-four studies were conducted in the USA, 16 were conducted in the UK, eight in Italy, five in Australia, four in Greece, two each in New Zealand and Canada, and one each in Belgium, Ireland, Poland, the Republic of Korea, South Africa, Switzerland, and Turkey. All studies were conducted in adults who smoke. Twenty-two studies exclusively recruited participants who were not motivated to quit smoking, and 39 studies exclusively recruited participants motivated to quit; motivation was not specified for the other studies. Twenty-nine studies were recruited from specific population groups; these included nine studies which recruited participants based on physical health condition (heart attack, cancer, HIV, periodontitis, awaiting surgery, smoking-related chronic disease), five studies which recruited participants with serious mental illness, four studies which recruited participants in treatment or having recently completed treatment for alcohol or other drug use, and three studies in dual users of EC and conventional cigarettes. Two studies recruited people accessing homeless centres or using supported temporary accommodation. One study each recruited: people aged 55 or older, young adults, people who self-identified as African-American, pregnant women, and black and Latino participants.

Outcomes

Of the 78 included studies:

- 32 reported data on abstinence at six months or longer
- 55 reported data on adverse events
- 38 reported data on serious adverse events
- 46 reported data on carbon monoxide
- 11 reported data on heart rate
- 13 reported data on blood pressure
- 4 reported data on blood oxygen saturation
- 14 reported data on at least one known toxin/carcinogen
- 7 reported data on at least one measure of lung function
- 14 reported data on study product use at six months or longer

One study (Skelton 2022) measured safety outcomes but did not report them in the text available at time of writing (they may be forthcoming), hence this study currently does not contribute any data to this review.

Study types and funding

Forty studies were RCTs, 22 of which contributed to cessation analyses. Seven studies used randomized cross-over designs, and the remainder were uncontrolled cohort studies. Of the 65 studies which reported funding information, 47 had no EC industry funding or support.

Excluded studies

We list 91 studies excluded at full-text stage, along with reasons for exclusion, in the Characteristics of excluded studies table. The most common reason for exclusion was that studies were short-term, following up participants for periods of less than one week.

Effects of interventions

See: **Summary of findings 1** Nicotine EC compared to NRT for smoking cessation; **Summary of findings 2** Nicotine EC compared to non-nicotine EC for smoking cessation; **Summary of findings 3** Nicotine EC compared to behavioural support only/no support for smoking cessation

Data on our outcomes of interest are summarized below. Due to the volume of data available, some relevant information is hosted on a companion repository; these data are open-access and can be found at https://doi.org/10.5287/bodleian:JbB1VNgDq. They are referred to below as supplemental tables. Forest plots are available through 'analysis' links; for some outcomes, benefit is plotted on the right, for others 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.

Direct comparisons between nicotine EC and other pharmacotherapies

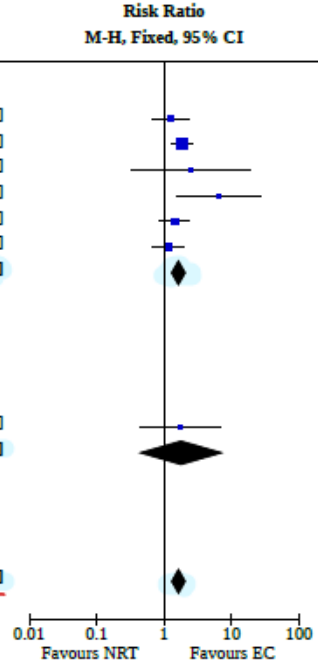
Comparisons reported here include cartridge and refillable nicotine ECs versus NRT, and cartridge nicotine ECs versus varenicline. Only randomized controlled trials contributed data.

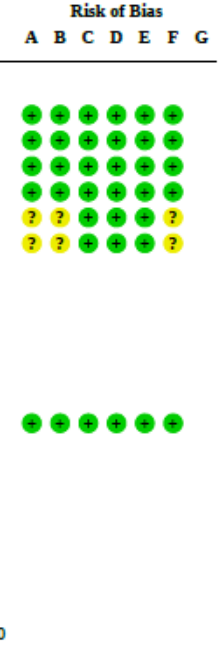
Cessation

Pooled data from six studies (2 cartridges, 3 refillable, 1 pod), five of which were rated at low risk of bias and the sixth as unclear, showed higher quit rates in people randomized to nicotine EC than to NRT (risk ratio (RR) 1.63, 95% confidence interval (CI) 1.30 to 2.04; I^2 = 10%; 2378 participants; Analysis 1.1). 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 = 0.90, I^2 for subgroup differences = 0%). Follow-up time was based on end of pregnancy, and our primary analysis included only those participants with follow-up of at least six months. Results were not sensitive to including all participants followed-up at end of pregnancy (RR 1.49, 95% CI 1.21 to 1.84, I^2 = 0%; analysis not shown).

Analysis 1.1. Comparison 1: Nicotine EC versus NRT, Outcome 1: Smoking cessation

Study or Subgroup	EC Events	EC Total	NRT Events	NRT Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Not selected on pregnancy						
Bullen 2013	21	289	17	295	15.7%	1.26 [0.68 , 2.34]
Hajek 2019	79	438	44	446	40.7%	1.83 [1.30 , 2.58]
Lee 2018	5	20	1	10	1.2%	2.50 [0.34 , 18.63]
Myers-Smith 2022	13	68	2	67	1.9%	6.40 [1.50 , 27.30]
Russell 2021 (1)	44	145	15	71	18.8%	1.44 [0.86 , 2.40]
Russell 2021 (2)	34	140	15	70	18.7%	1.13 [0.66 , 1.94]
Subtotal (95% CI)		**1100**		**959**	**97.0%**	**1.62 [1.29 , 2.04]**
Total events:	196		94			
Heterogeneity: Chi² = 6.67, df = 5 (P = 0.25); I² = 25%						
Test for overall effect: Z = 4.19 (P < 0.0001)						
1.1.2 Pregnant population						
Hajek 2022 (3)	6	169	3	150	3.0%	1.78 [0.45 , 6.97]
Subtotal (95% CI)		**169**		**150**	**3.0%**	**1.78 [0.45 , 6.97]**
Total events:	6		3			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.82 (P = 0.41)						
Total (95% CI)		**1269**		**1109**	**100.0%**	**1.63 [1.30 , 2.04]**
Total events:	202		97			
Heterogeneity: Chi² = 6.70, df = 6 (P = 0.35); I² = 10%						
Test for overall effect: Z = 4.27 (P < 0.0001)						
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.90), I² = 0%						





Footnotes

(1) NSP EC arm; control group split to avoid double-counting
(2) FBNPs EC arm; control group split to avoid double-counting
(3) 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

BOND UNIVERSITY | INSTITUTE FOR Evidence-Based Healthcare

BOND UNIVERSITY | INSTITUTE FOR Evidence-Based Healthcare

Decision Aid

Our Decision Aids are designed to help you discuss treatment options with your physician, and choose the option that works best for you. These tools were developed with the help of patients and clinicians sharing real-life decisions together. All information displayed is gathered from current best research and appraised by experts in the field. This document is a printable take-home version of the decision aid. It summarizes the benefits and harms as well as practical issues that could matter to you when considering each available option. Take the time to go again through this information, and perhaps discuss it with your close ones. Don't forget to note your questions and discuss them with your physician during your next appointment.

This tool is addressing the following choice

Nicotine E-cigarettes **vs** Nicotine replacement therapy

for Adults who currently smoke

This decision can impact on the following issues (as detailed below)

- Smoking cessation
- Adverse events
- Serious adverse events
- Practical issues

Explore in the next pages how the decision impacts on the issues that matter to you

Smoking cessation

38 more

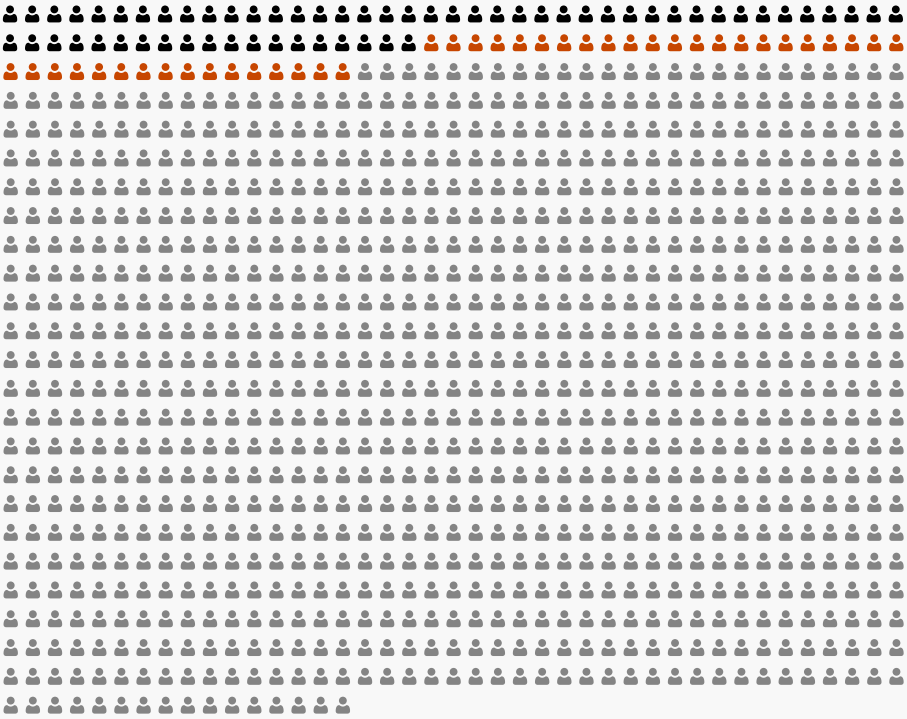
at 6 months to 1 year

Nicotine replacement therapy	Nicotine E-cigarettes
60 per 1000	98 per 1000

Certainty

HIGH

Among a 1000 patients like you, with Nicotine E-cigarettes



902 with no event

Adverse events

5 more

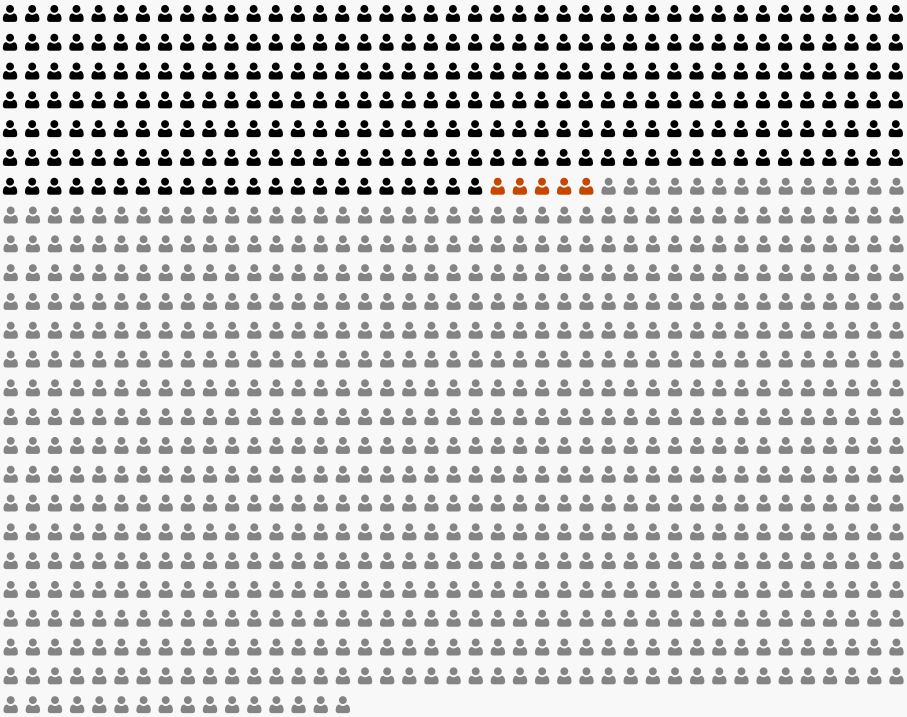
at 4 weeks to 6-9 months

Nicotine replacement therapy	Nicotine E-cigarettes
268 per 1000	273 per 1000

Certainty

MODERATE

Among a 1000 patients like you, with Nicotine E-cigarettes



727 with no event

Serious adverse events

7 more

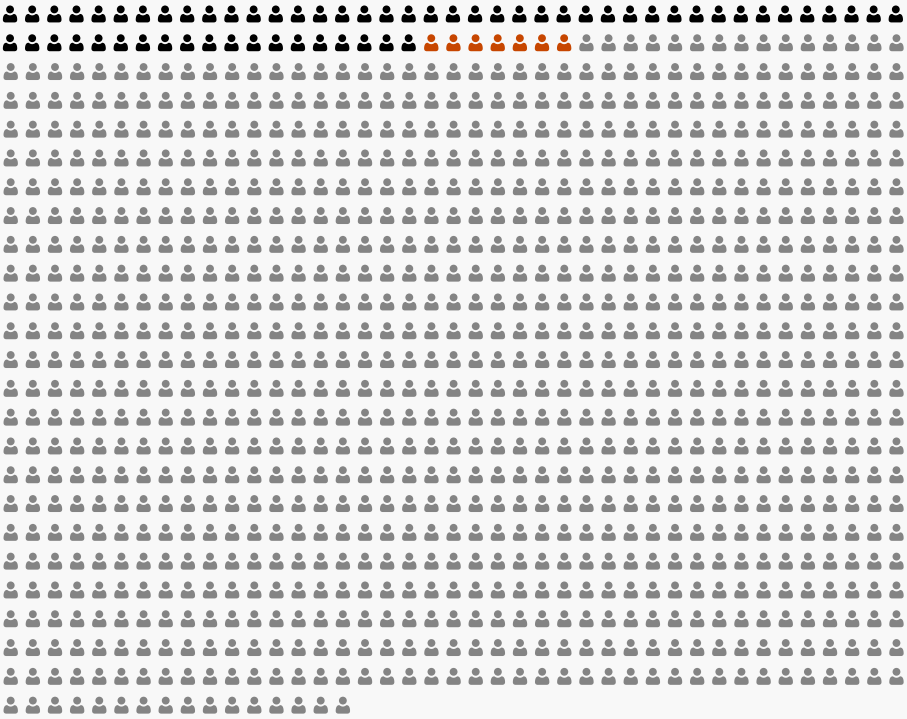
at 4 weeks to 1 year

Nicotine replacement therapy	Nicotine E-cigarettes
60 per 1000	67 per 1000

Certainty

LOW

Among a 1000 patients like you, with Nicotine E-cigarettes



933 with no event

Decision Aid

Our Decision Aids are designed to help you discuss treatment options with your physician, and choose the option that works best for you. These tools were developed with the help of patients and clinicians sharing real-life decisions together. All information displayed is gathered from current best research and appraised by experts in the field. This document is a printable take-home version of the decision aid. It summarizes the benefits and harms as well as practical issues that could matter to you when considering each available option. Take the time to go again through this information, and perhaps discuss it with your close ones. Don't forget to note your questions and discuss them with your physician during your next appointment.

This tool is addressing the following choice

Nicotine EC **vs** behavioural support only/no support

for Electronic cigarettes for smoking cessation

This decision can impact on the following issues (as detailed below)

- Smoking cessation
- Adverse events
- Serious adverse events
- Practical issues

Explore in the next pages how the decision impacts on the issues that matter to you

Smoking cessation

2 more

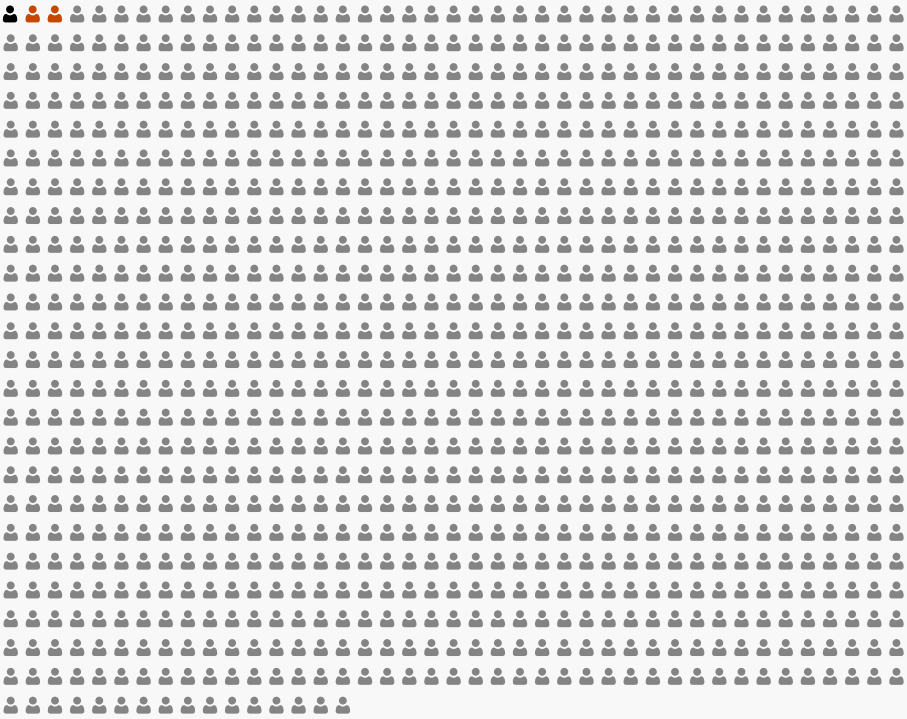
6 to 12 months

behavioural support only/no support	Nicotine EC
1 per 1000	3 per 1000

Certainty

VERY LOW

Among a 1000 patients like you, with Nicotine EC



997 with no event

Adverse events

15 more

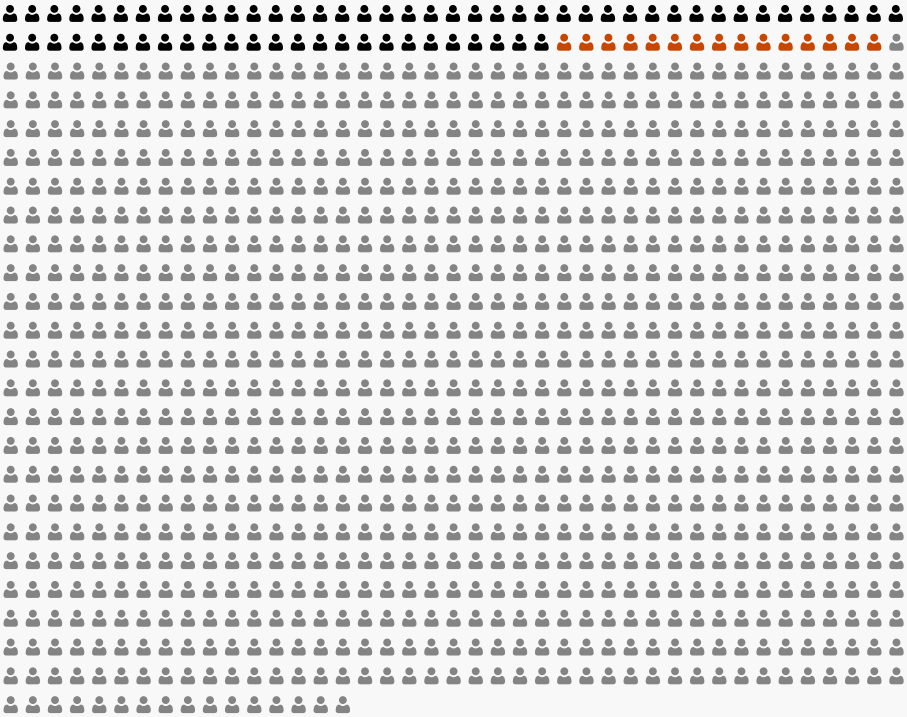
12 weeks to 6 months

behavioural support only/no support	Nicotine EC
66 per 1000	81 per 1000

Certainty

LOW

Among a 1000 patients like you, with Nicotine EC



919 with no event

Serious adverse events

0 fewer

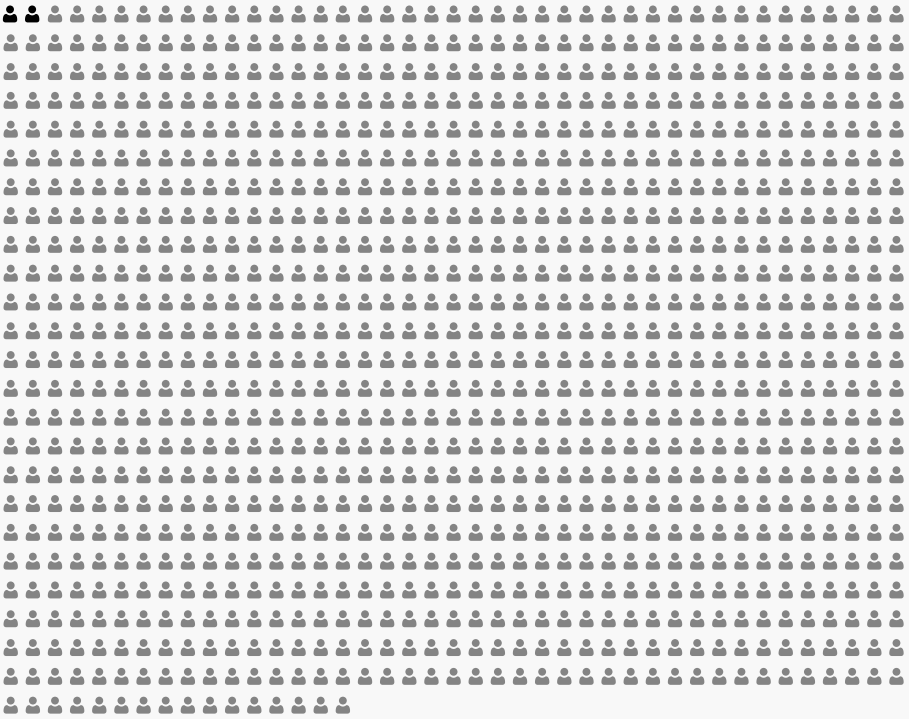
4 weeks to 8 months

behavioural support only/no support	Nicotine EC
2 per 1000	2 per 1000

Certainty

VERY LOW

Among a 1000 patients like you, with Nicotine EC



998 with no event

Decision Aid

Our Decision Aids are designed to help you discuss treatment options with your physician, and choose the option that works best for you. These tools were developed with the help of patients and clinicians sharing real-life decisions together. All information displayed is gathered from current best research and appraised by experts in the field. This document is a printable take-home version of the decision aid. It summarizes the benefits and harms as well as practical issues that could matter to you when considering each available option. Take the time to go again through this information, and perhaps discuss it with your close ones. Don't forget to note your questions and discuss them with your physician during your next appointment.

This tool is addressing the following choice

Nicotine EC **vs** non-nicotine EC

for Electronic cigarettes for smoking cessation

This decision can impact on the following issues (as detailed below)

- Smoking cessation
- Adverse events
- Serious adverse events
- Practical issues

Explore in the next pages how the decision impacts on the issues that matter to you

Smoking cessation

7 more

6-12 months

non-nicotine EC	Nicotine EC
7 per 1000	14 per 1000

Certainty

MODERATE

Among a 1000 patients like you, with Nicotine EC

986 with no event

Adverse events

0 fewer

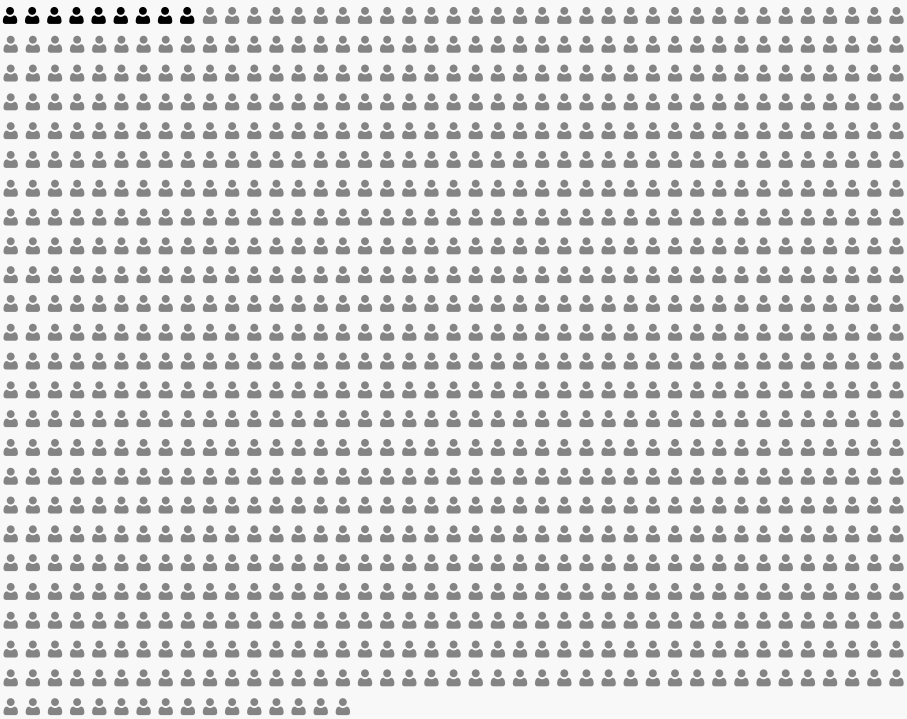
1 week to 6 months

non-nicotine EC	Nicotine EC
9 per 1000	9 per 1000

Certainty

MODERATE

Among a 1000 patients like you, with Nicotine EC



991 with no event

Serious adverse events

0 fewer

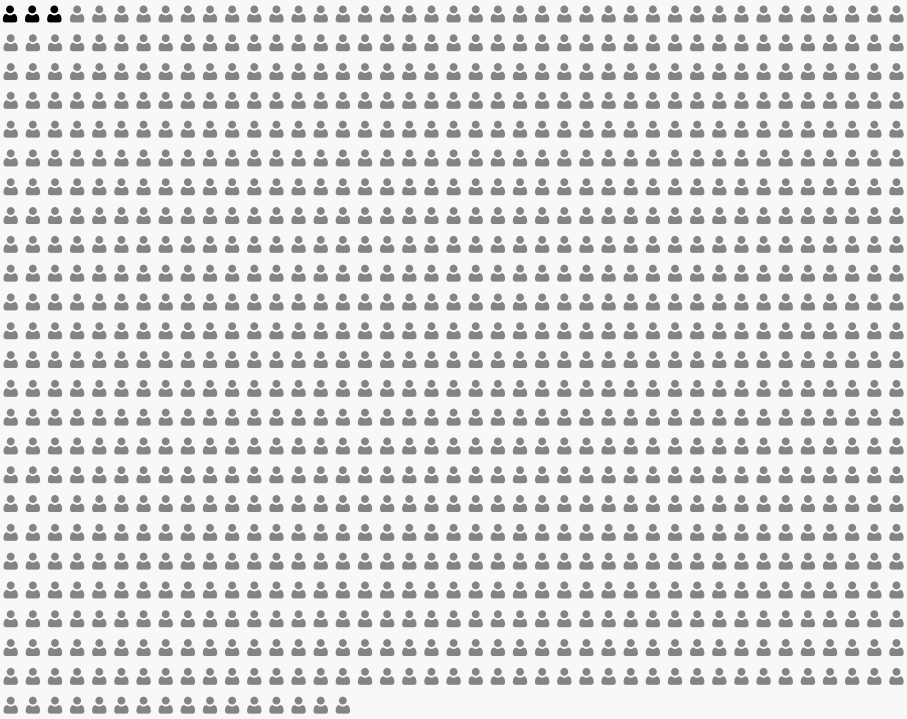
1 week to 1 year

non-nicotine EC	Nicotine EC
3 per 1000	3 per 1000

Certainty

LOW

Among a 1000 patients like you, with Nicotine EC



997 with no event

GoldNet Research Network

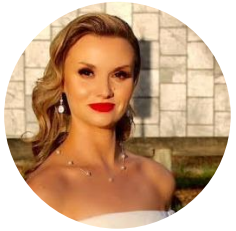
Virtual Journal Club Meeting, 29th June 2023

Nicotine Vaping for Smoking Cessation

Thank you for watching the journal club recording.
GoldNet would like to thank our guest panellists for their time to provide insights into this relevant topic.
If you are not already a GoldNet member, you can sign-up by scanning the QR code.
For future events, please submit topics you would like to see discuss to goldnet@bond.edu.au.
Please check out our website www.goldnetresearch.com.au for future events and research projects we support!

Panellists

Associate Prof. Kristin Cardon-Chahhoud
The University of Adelaide and Board Director for the Thoracic Society of Australia and New Zealand



Ms Melis Selamoglu
PhD Candidate
Department of General Practice, Monash University

Asst. Prof. Loai Albarqouni
Institute for Evidence-based Healthcare,
Faculty of Health Sciences and Medicine,
Bond University

Prof. Nick Zwar
Executive Dean,
Faculty of Health Sciences and Medicine, Bond University and Chair of GoldNet Steering committee

BOND UNIVERSITY | INSTITUTE FOR Evidence-Based Healthcare

Griffith UNIVERSITY Queensland, Australia

phn GOLD COAST An Australian Government Initiative

GPGC Healthy General Practice Healthy Gold Coast