



Electronic cigarettes for smoking cessation

Results from the most recent Cochrane update

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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







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Inclusion criteria

Randomized controlled trials	 People who smoke randomized to EC or control 	ation (6m +)	arm (1 week+)
Uncontrolled intervention studies	 Studies in people who smoke where all people in the study offered the same EC intervention 	Smoking cess	Measures of ha





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; lifethreatening; 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

*primary outcome





Searches



- 7 electronic databases searched to Jan 2020
- Researchers contacted
- Trial registries & conference abstracts for ongoing studies





Included studies

50 included studies (35 new); 12,430 participants







Included studies (cont.)







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



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





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



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





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

	EC		NRT	Г		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	
1.3.1 4 weeks								
Lee 2018 (1)	0	19	0	10		Not estimable		
Subtotal (95% CI)		19		10		Not estimable		
Total events	0		0					
Heterogeneity: Not ap	plicable							
Test for overall effect:	Not appli	cable						
4.0.0.4								
1.3.2 1 year								
Hajek 2019	27	356	19	342	100.0%	1.37 [0.77, 2.41]		
Subtotal (95% CI)		220		342	100.0%	1.37 [0.77, 2.41]		
l otal events	27		19					
Heterogeneity: Not ap	plicable							
l est for overall effect:	Z=1.07 ((P = 0.2	(8)					
Total (95% CI)		375		352	100.0%	1.37 [0.77, 2.41]	•	
Total events	27		19					
Heterogeneity: Not ap	plicable							
Test for overall effect:	Z=1.07	(P = 0.2	28)				Eavours EC Eavours NRT	
Test for subgroup diff	erences:	Not ap	plicable					
Footnotes								
(1) Data at 4 weeks post-operation; time from baseline not defined and likely to differ between participants								

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





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



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





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

	Nicotine EC		Non-nicotir	ie EC	Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% CI		
3.2.1 1 week									
Meier 2017	3	24	2	24	4.5%	1.50 [0.27, 8.19]			
Subtotal (95% CI)		24		24	4.5%	1.50 [0.27, 8.19]			
Total events	3		2						
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 0.47 (P = 0.6	4)						
3.2.2 6 months									
Bullen 2013	107	241	26	57	95.5%	0.97 [0.71, 1.34]			
Subtotal (95% CI)		241		57	95.5%	0.97 [0.71, 1.34]	•		
Total events	107		26						
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z=0.17 (P = 0.81	7)						
-									
Total (95% CI)		265		81	100.0%	1.00 [0.73, 1.36]	+		
Total events	110		28						
Heterogeneity: Chi ² =									
Test for overall effect:	Z = 0.02 (P = 0.99	9)				Eavours non-nicotine EC Eavours nicotine EC		
Test for subgroup differences: Chi ² = 0.24, df = 1 (P = 0.62), l ² = 0%									

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





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

	Nicotine	e EC	Non-nicoti	ne EC		Risk Ratio		Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixe	d, 95% Cl		
3.3.1 1 week											
Meier 2017	0	24	0	24		Not estimable					
Subtotal (95% CI)		24		24		Not estimable					
Total events	0		0								
Heterogeneity: Not ap	plicable										
lest for overall effect:	Not appli	cable									
3 3 2 A wooks										GRADE	
George 2019	Ο	37	0	37		Not estimable					
Subtotal (95% CI)		37	0	37		Not estimable				cortaint	vof
Total events	0		0							Certaint	y Ui
Heterogeneity: Not ap	plicable		-							ovidona	
Test for overall effect:	Not appli	cable								evidence	e. LOw
										(dayuna)	a d a d
3.3.3 12 weeks								_		laowngi	aueu
NCT02417467	1	128	4	127	100.0%	0.25 [0.03, 2.19]	-				la dista
Subtotal (95% CI)		128		127	100.0%	0.25 [0.03, 2.19]				two leve	els due
lotal events	1		4								、
Test for everall effect:	piicable 7 = 1.257	P = 0.2	1\							to impre	ecision)
Testion overall ellect.	Z = 1.20 (F - 0.2	0							•	· · ·
3.3.4 1 year											
Caponnetto 2013a	0	72	0	45		Not estimable					
Subtotal (95% CI)		72		45		Not estimable					
Total events	0		0								
Heterogeneity: Not ap	plicable										
Test for overall effect:	Not appli	cable									
Total (05% CI)		264		232	100.0%	0 25 [0 03 2 40]					
Total (95% CI)	4	201		233	100.0%	0.25 [0.05, 2.19]					
Hotorogonoity: Not on	nlicable		4				L				
Test for overall effect:	7 = 1.257	$P = 0.2^{\circ}$	1)				0.01	0.1 1	_	10 100	
Test for subaroup diff	erences: I	, — 0.2 Not app	licable					Favours nicotine EC	Favours no	on-nicotine EC	





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



Footnotes

(1) Although participants were given a choice of nicotine concentration including 0 mg, none of the participants chose the non-nicotine e-liquid

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

	Nicotin	e EC	Usual	care		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	
4.2.1 12 weeks								
Walele 2018 Subtotal (95% CI)	271	306 306	80	102 102	91.3% 91.3%	1.13 [1.01, 1.26] 1.13 [1.01, 1.26]	, GRADE ce	rtainty of
Total events	271		80				ovidonco	VEDV
Heterogeneity: Not ap	plicable						evidence.	VENT
Test for overall effect:	Z = 2.18 (P = 0.03	3)					ungradad
4.0.0.46 waaka								Inglaueu
4.2.2 10 weeks				4.0	0.00	4 4 9 19 6 7 9 9 7	due to ric	c of bioc
Carpenter 2017 (1) Subtotal (95% CI)	20	34 34	8	16	8.3%	1.18 [0.67, 2.07]		
Total events	20	54	8	10	0.070	1.10 [0.01, 2.01]	and impre	cision)
Heterogeneity: Not an	nlicable							cision
Test for overall effect:	Z = 0.56 (P = 0.53	7)					
	,		,					
4.2.3 6 months								
Holliday 2019 (2)	5	29	0	29	0.4%	11.00 [0.64, 190.26]		
Subtotal (95% CI)		29		29	0.4%	11.00 [0.64, 190.26]		
Total events	5		0					
Heterogeneity: Not ap	plicable							
Test for overall effect:	Z = 1.65 (P = 0.11))					
Total (95% CI)		369		147	100.0%	1.17 [1.04, 1.31]	•	
Total events	296		88					
Heterogeneity: Chi ² =	2.79, df=	2 (P = 0).25); l² =	28%				
Test for overall effect:	Z= 2.71 (P = 0.00	J7)				Favours nicotine EC Favours usual care	
Test for subgroup diff	erences:	Chi ^z = 2	.46, df=:	2 (P = 0	.29), I ≊ = 1	18.8%		
Footnotes					_			
(1) 24mg EC arm included here; 16mg data reported elsewhere								
(2) Participants onered choice of nicoune of no-nicotine EC; all chose nicotine-containing EC								





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

	Nicotine EC	Usi	ual care		Risk Ratio	Risk Ratio	
Study or Subgroup	Events To	al Ever	nts Tota	l Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl	
4.3.1 4 weeks							
George 2019 Subtotal (95% CI)	0	87 8 7	0 40 40))	Not estimable Not estimable		
Total events	0		0				
Heterogeneity: Not ap	plicable						
Test for overall effect:	Not applicable						
4.3.2 12 weeks						_	
NCT02417467	1 1:	28	2 121	73.3%	0.47 [0.04, 5.15]		
Walele 2018	5 3)6	0 102	26.7%	3.69 [0.21, 66.17]		
Subtotal (95% CI)	4	54	- 22.	5 100.0%	1.33 [0.25, 6.96]		
Total events	6 4 00 - 46 - 4 (D	0.070	2				
Heterogeneity: Uni*=	1.20, at = 1 (P 7 = 0.24 /P = 1	= 0.27); LZOV	1*= 17%				
restion overall ellect.	Z = 0.34 (F = 1	1.73)					
4.3.3 16 weeks						G	ADF certainty of
Carpenter 2017 (1)	0	34	0 16	ì	Not estimable		
Subtotal (95% CI)		34	16	5	Not estimable		
Total events	0		0			ev	Idence: VERY LOW
Heterogeneity: Not ap	plicable						
Test for overall effect:	Not applicable	•					owngraded due to risk
121Cmonths							
4.3.4 6 monuns						of	bias and improvision)
Holliday 2019 (2) Subtotal (95% CI)	U	29	0 29	9	Not estimable		bias and imprecision)
Total events	0		0	, 	notestimubic		
Heterogeneity: Not an	nlicable		0				
Test for overall effect:	Not applicable						
Total (95% CI)	5	34	308	3 100.0%	1.33 [0.25, 6.96]		
Total events	6		2				
Heterogeneity: Chi ² =	1.20, df = 1 (P	= 0.27);	l² = 17%				
Test for overall effect:	Z = 0.34 (P = 1						
Test for subgroup diffe	erences: Not a	pplicabl	le				
HOOTHOTES	ma (0 auanta i	16		sus			
(1) Data from 24mg a	rm (u events li d choice of cir						
(2) Participants offere	a choice of hid	oune or	no-mcour	ie EC, all C	nose nicoune-conta	ining EC	





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.
- Provide EC in a way that would be used in real-world settings.

Further reviews, using best available methods, need to be conducted to evaluate the possible relationships between EC use and availability and youth uptake of EC and conventional cigarettes.





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



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Tobacco Addiction



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

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Cochrane December 2020 briefing docur

This briefing document brings you the most up to date information (cigarettes (ECs) to help people who smoke achieve long-term smo most recent Cochrane review of EC for quitting smoking. Cochrane available evidence on a particular topic. Our findings help people to

Key findings

- Our review showed more people probably stop smoking for at least six months using nicotine e-cigarettes than using nicotine replacement therapy, or nicotine-free e-cigarettes.
- Nicotine e-cigarettes may work better than no support for guitting 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, courd and





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Can electronic cigarettes (EC) help people stop smok to use for this purpose?

Findings from the most recent Cochrane review December 2020

This briefing document brings you the most up to date information on the effe electronic cigarettes (ECs) to help people who smoke achieve long-term smo

Key findings

 Findings across the main comparisons consistently favoured by the main comparisons consistent by the main comparisons consequarisons consequarisons consequarisons consequarisons consequ 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.







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-cigarettesfor-smoking-cessation-cochrane-living-systematic-review-1