

Is use of e-cigarettes an effective and safe smoking cessation method?

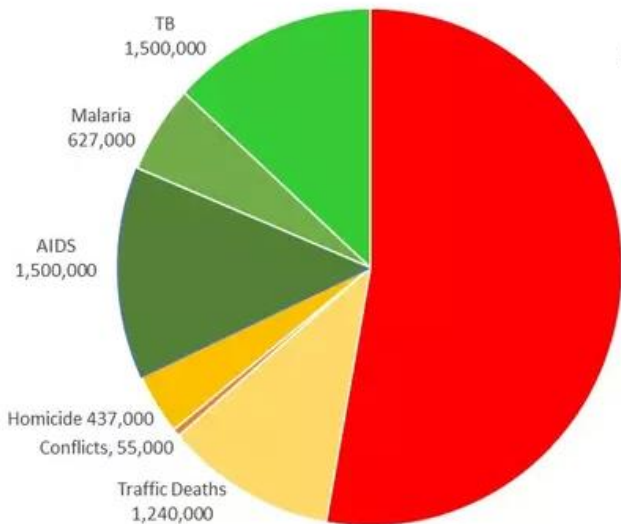
Charlotta Pisinger

Professor in tobacco and nicotine prevention
University of Southern Denmark
Center for Clinical Research and Prevention



I have nothing to declare

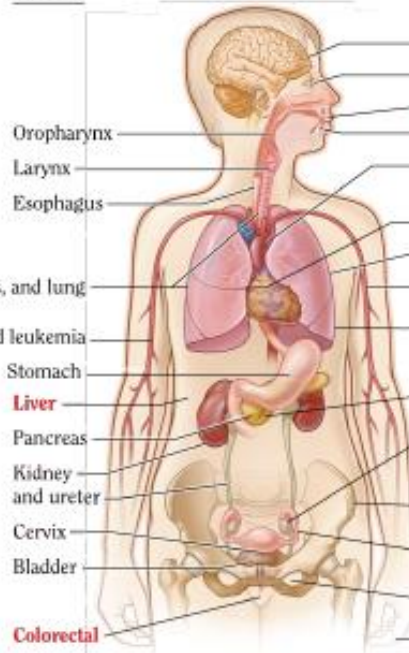
ANNUAL GLOBAL PREVENTABLE DEATHS



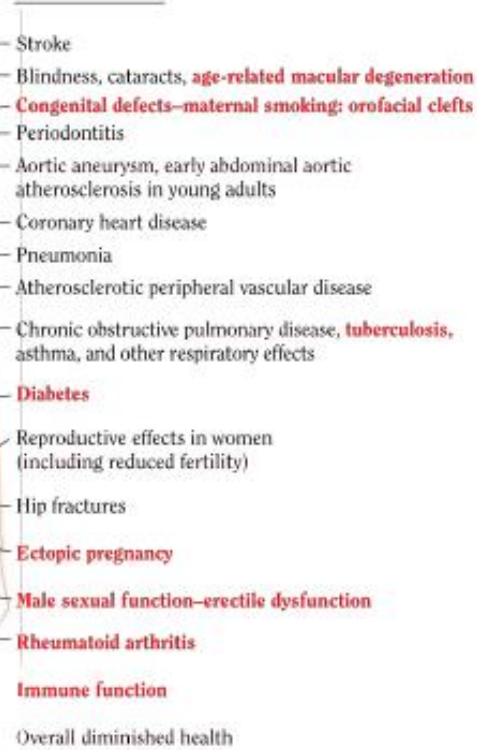
SMOKING:
6,000,000



Cancers



Chronic Diseases



How e-cigarettes changed my life

Demand for electronic cigarettes is booming, but experts are not convinced they help people to quit smoking. Whatever the case, I am still



“Quitting smoking was the easiest thing I’ve ever done, thanks to electronic cigarettes”

▲ For Stephanie Rafanelli e-cigarettes were an electric lightbulb moment in the struggle to give up tobacco. Photograph: Linda Nylind for the Guardian

It all started quite early on. My first words, uttered with a not-so-cherubic look on my face and a strange baby puffing sound, were: “Light! Light!” It was as if I had come out of the birth canal sucking not on my thumb, but a mini-Marlboro. Much excitement and hand-

How the Electronic Cigarette Changed My Life

FOR TRAIL

the Electronic Cigarette Changed My Life

...oking when I
...l. Growing up
...ighborhood in
...everyone
...had its pluses
...ong lost
...d of mine
...d got me
...ttes. At first I
...e, but before I
...haling, and
...I would get to have my next smoke.
...notice cigarettes taking over my entire life. It
...pretty soon I was making plans to sneak out to



... Growing up, you could smoke at work, in res
...pretty much wherever you wanted, and it seeme
...smoked around me, too. But now, tons of people
...was banned everywhere, it was way too expens
...could stand the smell of you around them, and yr
...to planning, scheming, and wondering when you
...your next smoke, using gum and something to h
...smell, and it was taking more and more time and
...I wanted to quit, but everything I tried didn't wo
...believe these stupid cigarettes were so impossib
...the health issues started, one after another. I w
...tails on the health issues, but I knew I had to fin
...quit, but still couldn't.

... When the digital electronic cigarette first car
...given them a try, but they weren't very good, dic
...por, didn't taste anything like a real analog cigar
...tate me. But I think the idea

READER REPORT

Vaping saved my life

Toni Brown - 11:00, Mar 30 2017



2 factors are important before recommending a therapy



Safety

THE EFFECT



Randomized controlled trials
- clinical setting/research
centers/smoking cessation clinic



Observational studies
-real world

Real world studies



Systematic reviews of longitudinal studies:

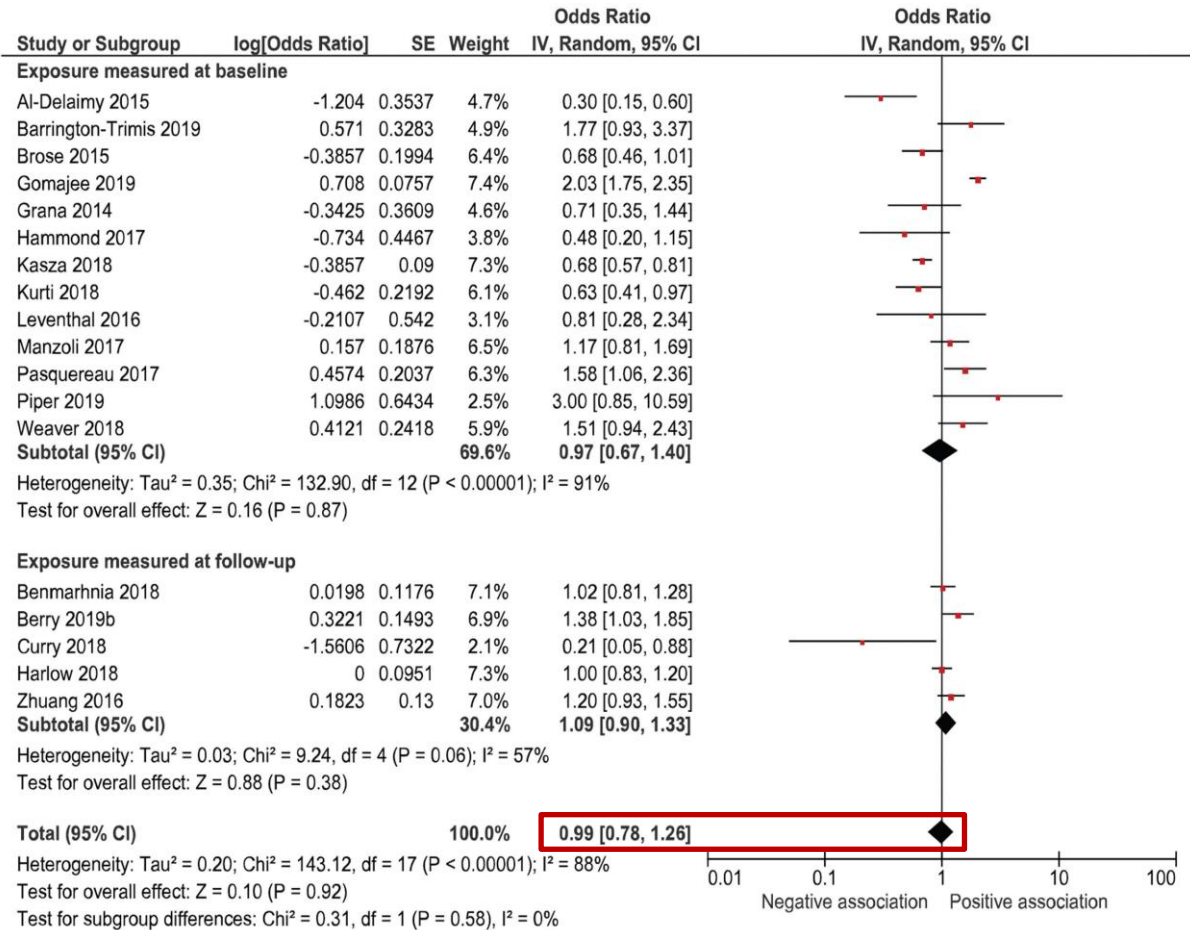
- Use of e-cigarettes in a real world setting does not help smokers to quit
 - Might be effective in daily users
 - But most use e-cigarettes as consumer/lifestyle product
 - Low evidence

Wang RJ et al. Am J Public Health 2021 February; 111(2): 230–246.

Hedman L et al. Tob. Prev. Cessation 2021;7(October):62

Example of a review of observational studies

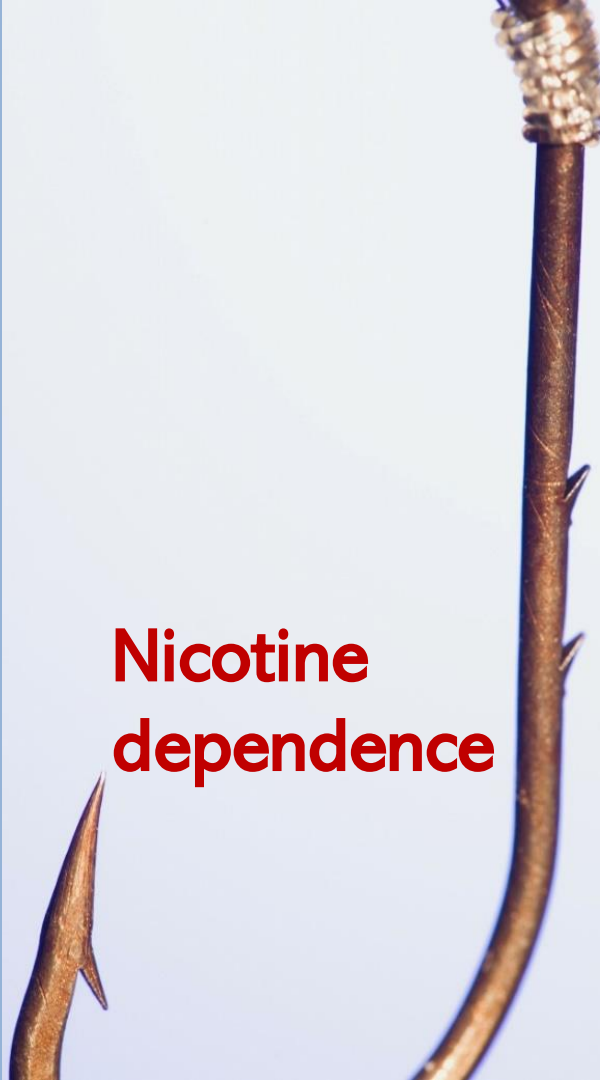
- 18 studies
- Almost 40,000 smokers
- Follow-up time: 6 months to 4 years
- Mostly: no information on participants' motivation to quit
- **E-cigarette use was not associated with abstinence**



Behavioral part
Psychological dependence

**Nicotine
dependence**

Chemical part
Physical dependence



Counselling



Psychological dependence

Best treatment



Cytisine



Varenicline



Bupropion



Physical dependence

Nicotine replacement combination therapy





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E-cigarettes are more effective than nicotine-replacement therapy in helping smokers quit

PUBLISHED
17 NOV 2022

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The latest Cochrane Review finds high certainty evidence that nicotine e-cigarettes are more effective than traditional nicotine-replacement therapy (NRT) in helping people quit smoking.

Oxford co-led study finds Britons in favour of EDI initiatives but with renewed approach

23 MAR 2024



Major new project will harness AI to transform how zero-emission buildings are designed

22 MAR 2024



New funding for development of world's first lung cancer vaccine

22 MAR 2024



AI ethics are ignoring children, say Oxford researchers

21 MAR 2024



New study highlights troubling trends in midlife mortality in the US and UK

21 MAR 2024

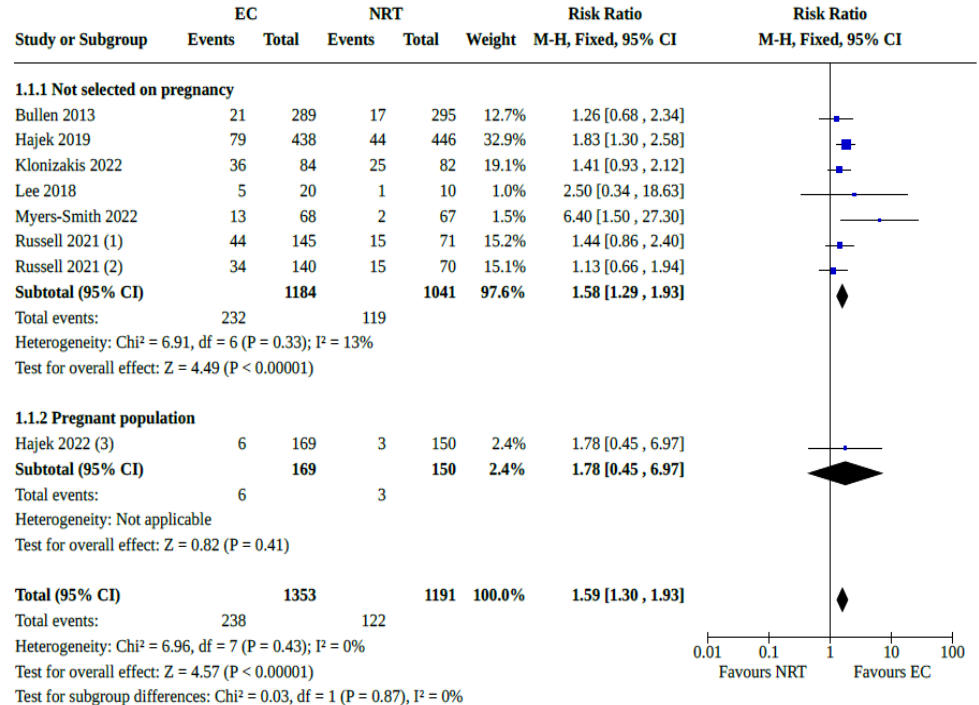


DISCOVER MORE

- [Support Oxford's research](#)
- [Partner with Oxford on research](#)

Clinical setting: comparing with nicotine replacement therapy (Cochrane review)

- 8 trials included
- 60% higher odds to quit with e-cigarettes than with NRT
 - significant
- Evidence graded as HIGH



Clinical setting: comparing with nicotine replacement therapy (other recent reviews)

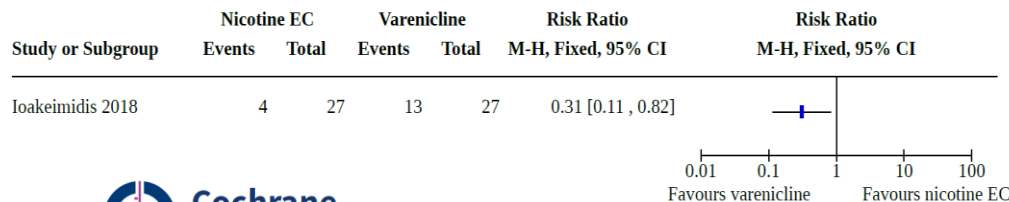


	Country	Min. 6 months follow-up	Studies with COI excluded	Unpublished studies included	Number of studies	Risk ratio (RR) (95% CI)	Level of evidence
Lindson N (Cochrane)	UK	Yes	No	Yes	8	1.59 (1.29 -1.93)	High
Chan GCK	Australia	No	No	No	4	1.49 (1.09-2.04)	Not assessed
Pound CM	Canada	No	No	No	5	1.42 (0.97-2.09)	Low
Li J	China	Yes	No	No	5	1.67 (1.21-2.28)	Low
Grabovac I	Austria	No	No	No	3	1.69 (1.25–2.27)	Low
Quigley J	Ireland	Yes	No	No	8	1.17 (0.66-1.86)	Low
Vanderkam	France	Yes	No	No	3	1.49 (1.14–1.95)	Not assessed
Banks E	Australia	Yes	Yes	No	3	1.25 (0.74-2.11)	Low

Reviews published since 2021

Clinical setting: comparing with varenicline or cytisine or bupropion

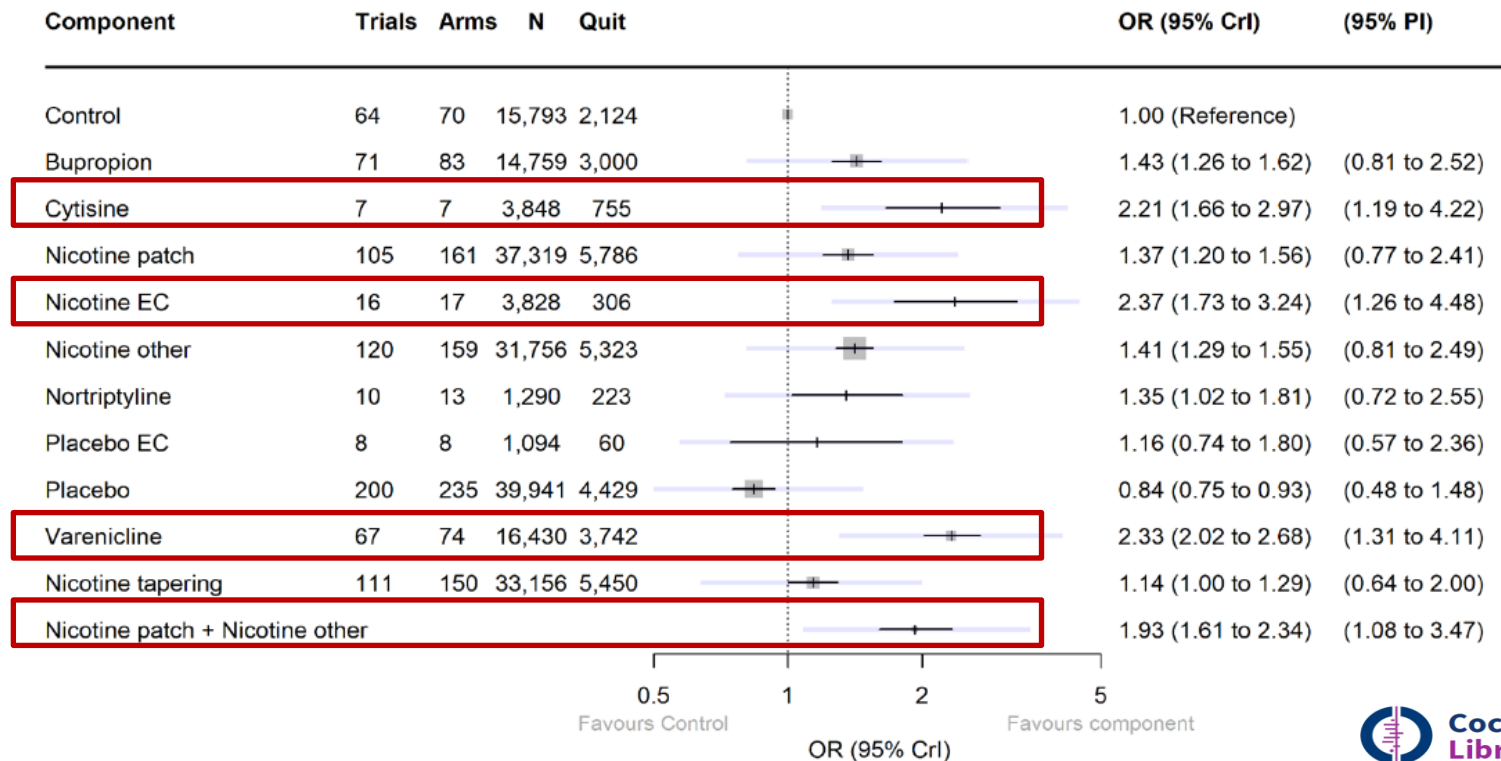
- 1 small varenicline study
- Varenicline significantly better
- Evidence graded as: very low



- E-cigarettes + varenicline vs. varenicline
- The trial was stopped early due to COVID-19 restrictions and a varenicline recall

Tattan-Birch et al. Nicotine and Tobacco Research, 2023, 25, 395–403

Cochrane review: comparing with placebo/no treatment



Cochrane review: The same effect of e-cigarettes and pharmacotherapy

Varenicline



E-cigarette



Cytisine



Nicotine replacement combination therapy

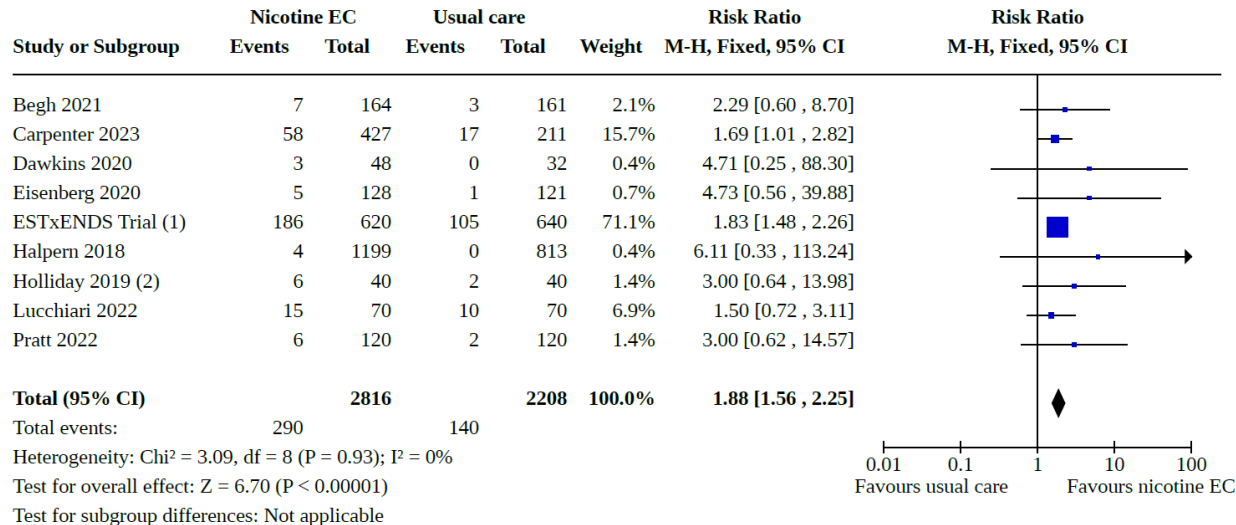


Bupropion



Clinical setting: comparing with counselling or no support

- 7 studies included
- Almost 2 times higher probability to quit with e-cigarettes
 - significant
- Evidence graded as LOW



Switching is not quitting



**WHY QUIT?
SWITCH TO BLU**

Be in the smart choice for smokers wanting a change. Take back your freedom to smoke when and where you want without ash or smell. BLU is everything you worry about smoking and nothing else. Nicotely. Plus a filter, so make the switch today.

Visit blucigs.com

PREMIUM ELECTRONIC CIGARETTES

18+ only. CAPSULE PROVISION IS: Warning: No products containing or derived from tobacco or any of its constituents should be used in the workplace.

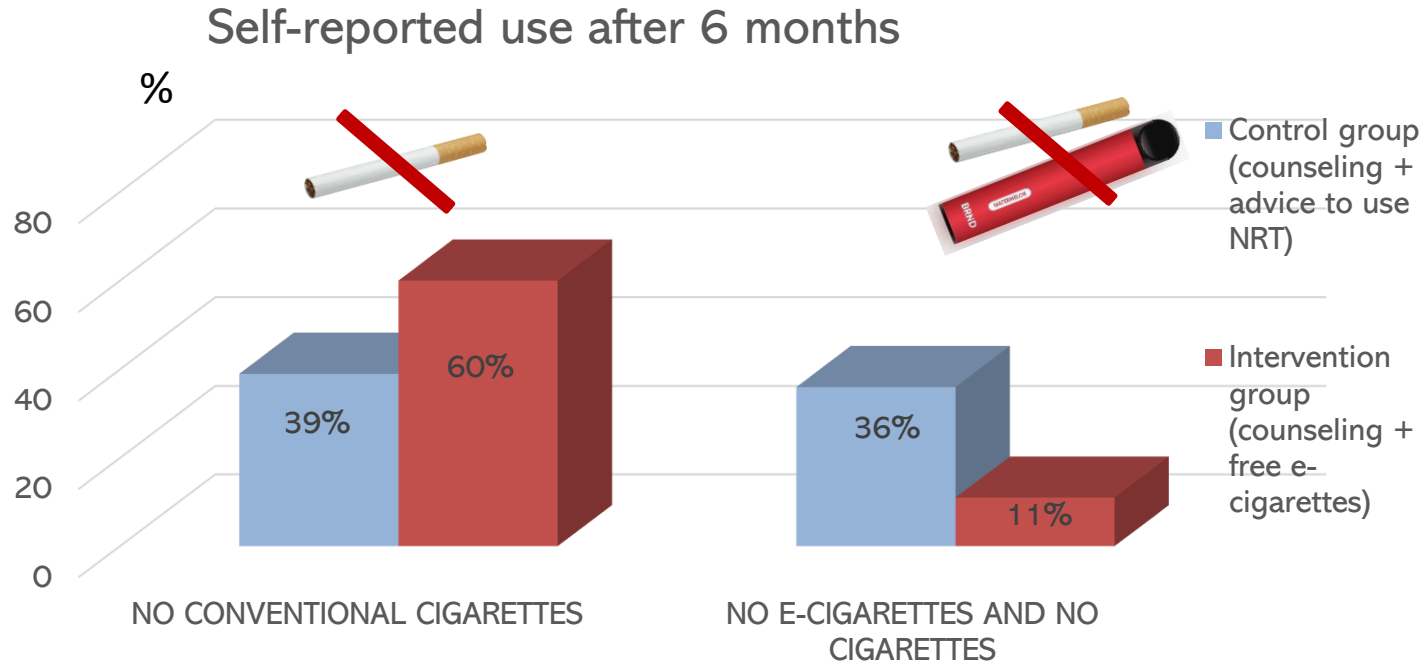
70% of participants continued using e-cigarettes after 6-12 months

- not rid of addiction
- not the health benefits of quitting
- best-case: reduction in health damage

Butler AR et al. Prev Med 2022;165

New e-cigarette smoking cessation study

Auer 2024



... important things to consider

- Selected persons participate in clinical trials
 - More motivated to quit
 - Healthier
 - Younger



- Users were also offered counseling

... important things to consider

- Generally: low quit rates with e-cigarettes
 - Typically only 10-20% quit



THE SAFETY

Safety considerations: recommended duration of use

Short-term use

Varenicline



Cytisine



Bupropion



Nicotine replacement combination therapy



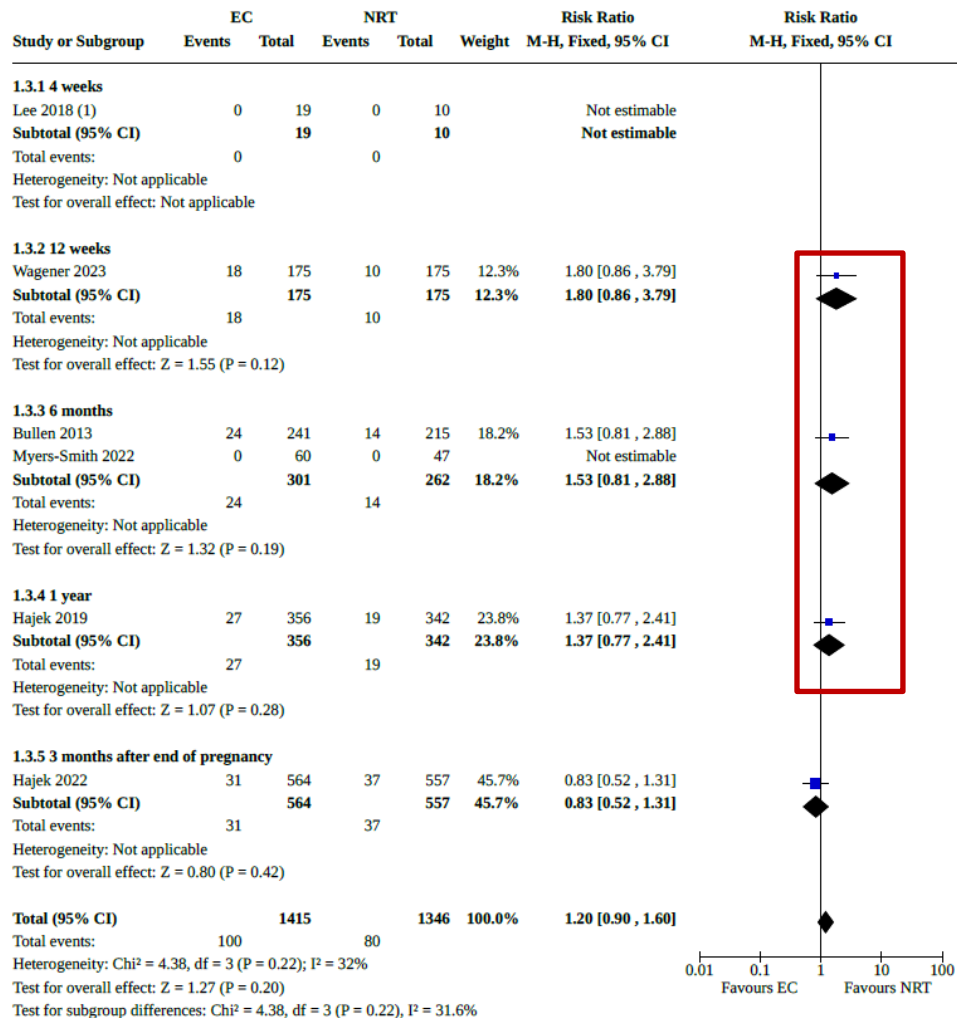
Long-term use

E-cigarette



Serious adverse events in smoking cessation trials

- 1 year follow-up or shorter
- No significant difference between NRT and e-cigarettes in trials
- But a tendency of a higher risk in e-cigarette users, except in a pregnancy study



Safety considerations: adverse events

Few

Nicotine replacement
combination therapy



Cytisine



Some

Varenicline



Bupropion



Some on short term

E-cigarette



but what about
long-term effects?



Public Health
England

E-cigarettes

Current evidence

Are E-cigs safe?

E-cigarettes are significantly less harmful (95%) to health than smoking tobacco

Twitter

WORLD VAPE DAY
— 30 MAY 2020 —

Vaping is NOT smoking.
It's at least 95% less harmful.

Tobacco Harm Reduction is a human ri
#WorldVapeDay #SayYesToTHR

Facebook

95%
LESS HARMFUL

Hale Vaping - Research by Public Health En
that vaping is a staggering 95% less harmf

Facebook

VAPING
95% less harmful than
SMOKING

Lebanon Vape Zone

E-cigarettes are 95% less harmful than... - Lebanon Vape Zone | Facebook

Twitter

VAPING IS
95% LESS HARMFUL
THAN SMOKING

*Public Health England

v4pril
2022
Vaping Awareness Month

T-Juice on Twitter: "Did you know... Vaping is 95% less harmful than smoking! *publichealthengland..."

Besog

Background research paper for the PHE report



GLOBAL NETWORK
FOR TOBACCO FREE
HEALTHCARE SERVICES

Research Report

European
Addiction
Research

Eur Addict Res 2014;20:218–225
DOI: [10.1159/000360220](https://doi.org/10.1159/000360220)

Received: December 23, 2013
Accepted: January 30, 2014
Published online: April 3, 2014

A limitation of this study is the lack of hard evidence for the harms of most products on most of the criteria.

David J. Nutt^a Lawrence D. Phillips^b David Balfour^f H. Valerie Curran^c
Martin Dockrell^d Jonathan Foulds^h Karl Fagerstromⁱ Kgosi Letlape^k
Anders Milton^j Riccardo Polosa^l John Ramsey^e David Sweanor^g

^aImperial College London, UK; ^bDepartment of Management, London School of Economics and Political Science, and Facilitations Ltd., UK; ^cUniversity College London, UK; ^dAction on Smoking and Health London, UK; ^eTICTAC Communications Ltd. at St. George's, University of London, London, UK; ^fUniversity of Dundee, Dundee, UK; ^gFaculty of Law, University of Ottawa, Ottawa, Canada; ^hPennsylvania State University, College of Medicine, Hershey Pa., USA; ⁱFagerström Consulting, Vaxholm, Sweden; ^jWorld Medical Association, Milton Consulting, Stockholm, Sweden; ^kWorld Medical Association, Johannesburg, South Africa; ^lCentre for the Prevention and Cure of Tobacco Use, University of Catania, Catania, Italy

Some of the authors have a conflict of interest with the tobacco industry



Public Health
England

E-cigarettes

Current evidence

Are E-cigs safe?

Update in 2022

“...we believe that the ‘at least 95% less harmful estimate’ remains broadly accurate **at least over short- and medium-term periods**” (<one year)

Short term eksperimental studies

- Some short-term studies show potential health benefits of switching
- Example:
- 186 participants
- **6 weeks** randomized controlled trial
 - Intervention: e-cigarette with flavors, 5% nicotine + brief education
 - Control: continue smoking
- Results:
 - E-cigarette group: significantly greater reductions in NNAL(carcinogen), carbon monoxide and respiratory symptoms





30-60 years



No studies with sufficiently long-term follow-up



- Most comprehensive reviews:
- NASEM report. US 2018
- Australian report. 2022
- +189 studies
- Health outcomes
- Human studies only
- *“The impact of e-cigarettes on important clinical health outcomes (...) is not known, as reliable evidence is lacking.”*

Banks E. et al. Electronic cigarettes and health outcomes: systematic review of global evidence. Report for the Australian Department of Health. 2022

Health outcome	Meta-analyses	Randomised controlled trial	Cohort study	Non-randomised intervention study	Case-control study	Surveillance report	Cross-sectional survey	Case series	Case report
Dependence and abuse liability		13 7/6	1 0/1	17 9/8			20 11/9		
Cardiovascular health outcomes	1 0/1	11 3/8	1 0/1	6 5/1			8 1/7		1 0/1
Cancer			1 1/0				2 1/1		3 2/1
Respiratory health outcomes*		9 5/4	5 2/3	5 1/4		18 0/18	21 4/17	11 0/11	26 0/26
Oral health			2 1/1	2 2/0			19 1/18		1 0/1
Developmental and reproductive effects			2 0/2				1 0/1		
Burns and injuries						7 1/6		24 14/10	16 5/11
Poisoning						25 13/12		4 2/2	23 14/9
Mental health effects			1 0/1				8 0/8		
Environmental hazards with health implications**				17 9/8		2 0/2		5 0/5	
Neurological outcomes						3 0/3		2 0/2	7 1/6
Sleep outcomes							4 0/4		
Less serious adverse events		11 3/8	3 1/2	2 2/0		1 0/1	3 0/3		
Optical health				1 0/1			1 0/1		
Wound healing									2 0/2
Olfactory outcomes							1 0/1		
Endocrine outcomes							2 0/2		
Allergic diseases							2 0/2	1 0/1	3 2/1
Haematological outcomes									2 0/2

Numbers in green relate to evidence most relevant to the assessment of causation

Conclusive evidence on short-term effects

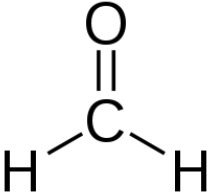
Negative immediate and short-term health effects

- **addiction**
- throat irritation, nausea
- poisoning, injuries, burns
- seizures
- increased heart rate and blood pressure
- increased arterial stiffness
- **EVALI**
 - (acute lung injury (cannabis oil/vitamin E related in 8 of 10 cases))

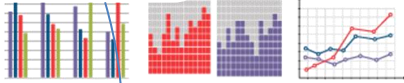
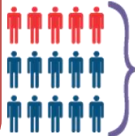


Banks E. et al. Electronic cigarettes and health outcomes: systematic review of global evidence. Report for the Australian Department of Health. 2022

Studies investigating composition of fluid/vapor



Epidemiological studies



Human eksperimental studies

Animal studies



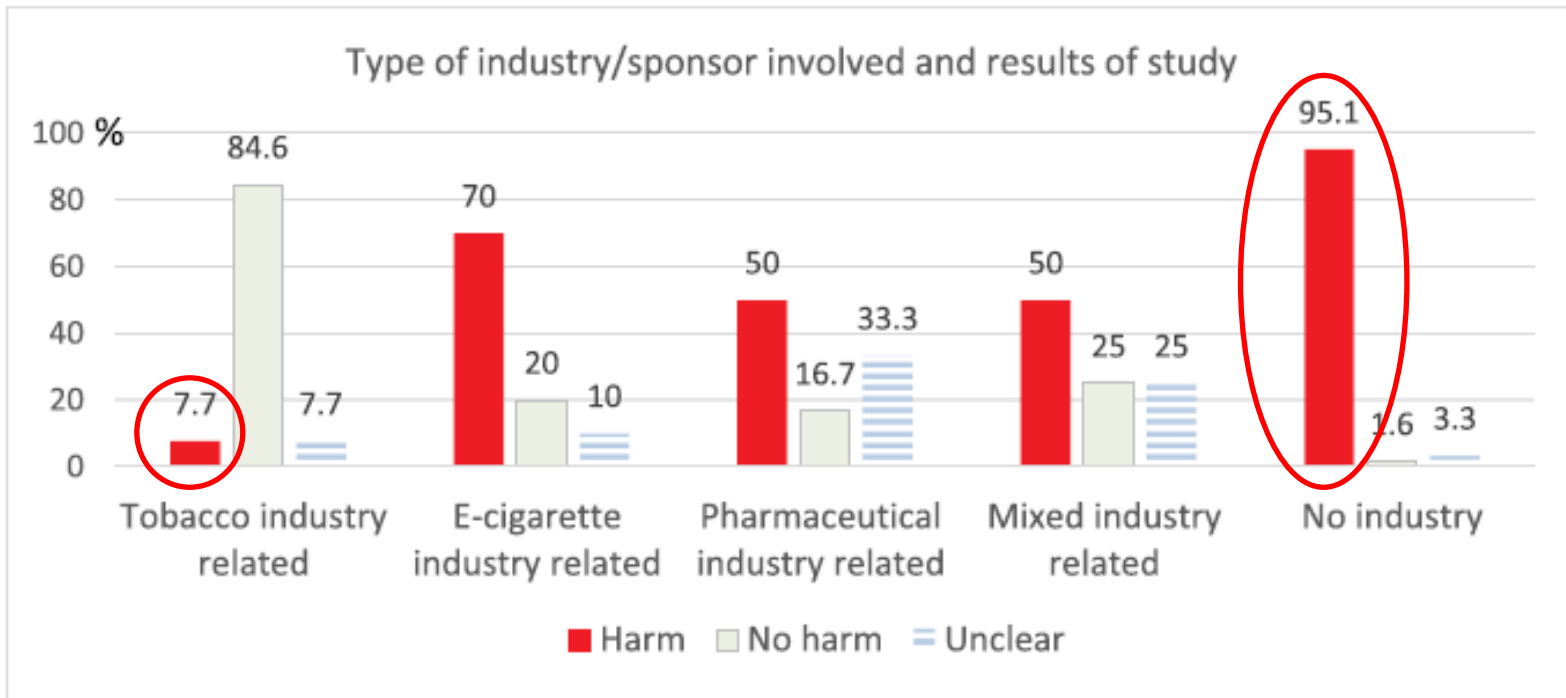
In vitro studies



Case reports

The screenshot shows the homepage of the Case Reports website. At the top, there is a logo with a cross and the text 'case reports THE CASE REPORTS JOURNAL'. Below the logo, there are navigation links for 'Home', 'About Case Reports', and 'CASE Checklist'. The main content area features a 'Welcome to the Website for Case Reports' message. To the right, there is a section titled 'About CASE' which explains that CASE (Case Reports) is a journal for reporting on case reports. It mentions that CASE is a peer-reviewed journal and that authors are encouraged to use the CASE Statement when submitting their work. There are also links for 'About CASE Statement', 'CASE Checklist', and 'CASE Statement'.

Tobacco industry related papers almost never find potentially harmful effects of vaping

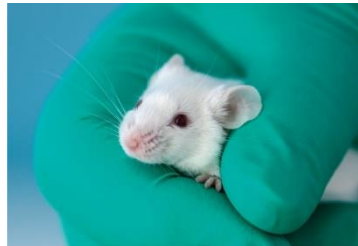


Pisinger C. et al. A conflict of interest is strongly associated with tobacco industry-favourable results, indicating no harm of e-cigarettes. Prev Med. 2019 Feb;119:124-131.

Toxicity and biological effects

- **Animal studies**

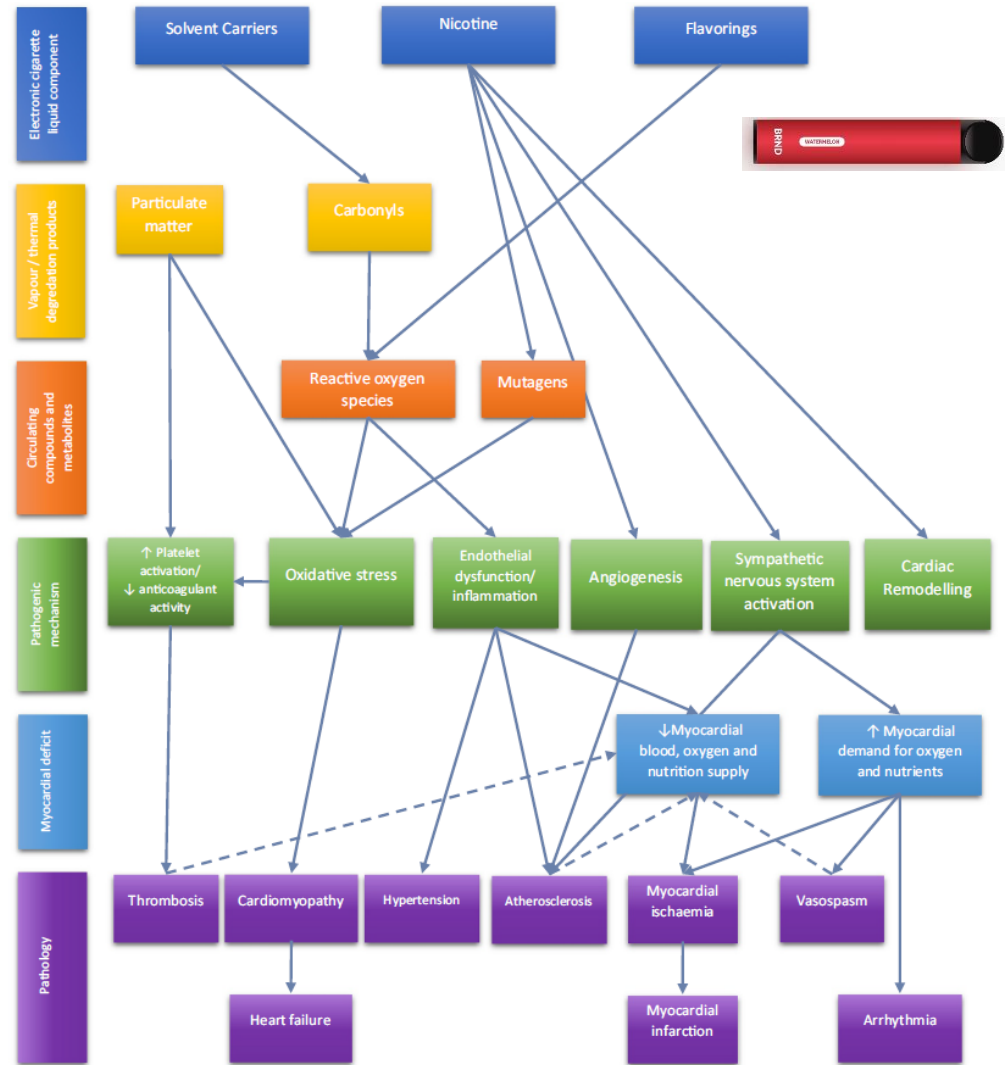
- higher mortality when exposed to infections
- DNA damage
- lung cancer
- impaired kidney development
- cardiac arrhythmia
- arterial dysfunction
- cerebrovascular dysfunction
- lung dysfunction
- airway inflammation
- asthma
- ...



- Content of fluid/vapor: many toxic and carcinogenic compounds
- Cell studies: inflammation, cytotoxicity/cell death, oxidative stress...

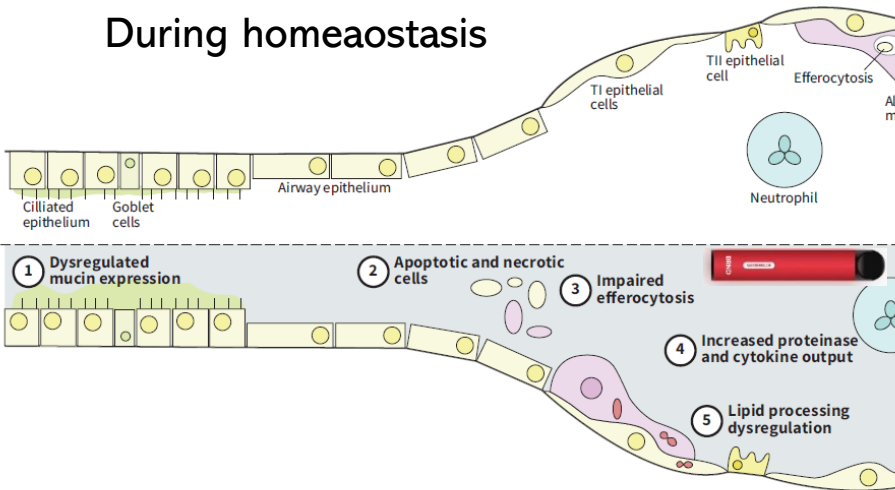


Cardiovascular system: biological effects and pathways

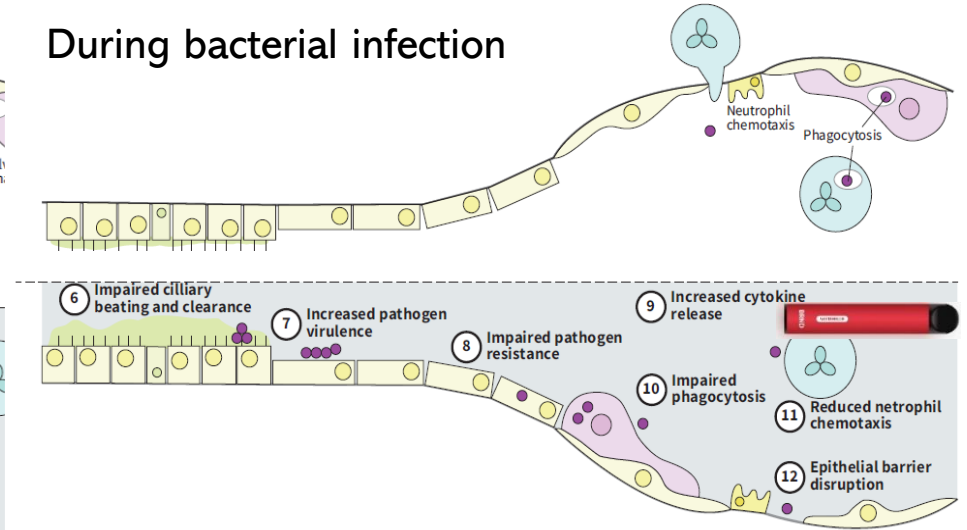


Pulmonary system: biological effects

During homeaostasis



During bacterial infection



①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	⑪	⑫
Dysregulated mucin expression alters consistency and velocity	Exposures cause build-up of apoptotic and necrotic epithelial and immune cells in the airways	Impaired efferocytosis by macrophages perpetuates apoptotic cell build-up	Immune cells and epithelial cells release increased inflammatory mediators, including proteases, reactive oxygen species and cytokines	Lipid dysregulation causes endogenous lipid inclusions and impaired lipid catabolism in macrophages and impaired lipid export in epithelial cells	Impaired ciliary beating prevents mucus clearing and permits pathogen establishment in the airways	Increased virulence allows immune evasion and pathogen persistence	Impaired infection resistance in epithelial cells and macrophages	Exaggerated cytokine release	Impaired pathogen phagocytosis by macrophages and neutrophils increases pathogen load	Reduced neutrophil chemotaxis prevents appropriate pathogen containment	Epithelial barrier disruption increases vulnerability to infection

First meta-analysis on health effects of e-cigarettes

- **Meta-analysis** of 107 very large population-based surveys
- 30 longitudinal studies
 - same findings as the cross-sectional studies
 - most adjusted for smoking



Risk of disease in e-cigarettes users compared with cigarette users



- Cardiovascular disease, stroke, metabolic disease: no difference in odds of disease
- Lung disease: lower risk in e-cig users
 - asthma: 16% lower odds in e-cig users
 - COPD: 47% lower odds in e-cig users
- Oral disease: lower risk in e-cig users
 - 13% lower odds in e-cig users



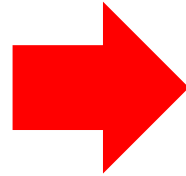
Public Health
England

E-cigarettes Current evidence

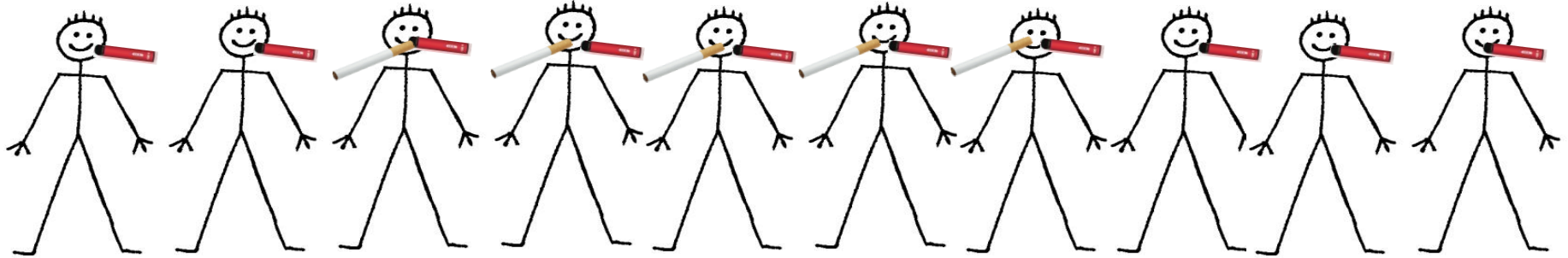
Are E-cigs safe?

E-cigarettes are significantly less harmful (95%) to health than smoking tobacco

Switching



Many/most e-cigarette users in the general population also smoke = "dual users"



E-cigarettes, population-based surveys:

39% in the USA, adults, Mayer M, *JAMA Netw Open* 2020 ;3:e2020694-E2020694

45% in UK. <https://smokinginengland.info/graphs/e-cigarettes-latest-trends>. 2022

56% in USA, men. Okunna N. *American journal on addictions*, 2021, Vol.30(2), p.138-146

57% in Europe, adults. *IJERPH*. 2020 Mar 17;17(6):1971

67% in Sweden. Hedman L. *JAMA Netw Open* 2018, 1(3):e180789.

85% in South Korea. Kim CY. *Sci Rep* 2020, 10(1):5612.

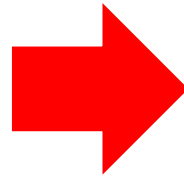
Prof Robert West, BBC "Inside Health" Feb 2016
<http://www.bbc.co.uk/programmes/b070dq8h>



Cutting down "not much"

- 10m40s: "We know that most people who use ecigarettes are continuing to smoke and when you ask them they tell you that they are mostly doing that to cut down the amount they smoke. But we also know they are smoking, it's not really that much different from what they would have done since they started using ecigarettes."

The reality



Risk of disease in dual users compared with exclusive cigarette users

- Dual use associated with 20-40% higher odds of disease compared with exclusive smoking



Table 1. Pooled Adjusted* Odds Ratios of Each Disease Outcome (95% Confidence Intervals) from the Meta-analyses.

Comparisons	Cardiovascular	Stroke	Metabolic Dysfunction	Asthma	COPD	Oral Disease
Comparison to cigarette use						
E-cigarettes vs. cigarettes	0.81 (0.58–1.14)	0.73 (0.47–1.13)	0.99 (0.91–1.09)	0.84 (0.75–0.95)	0.53 (0.38–0.74)	0.87 (0.76–1.00)
Dual use vs. cigarettes	1.23 (0.99–1.54)	1.26 (1.06–1.50)	1.22 (1.15–1.31)	1.20 (1.12–1.28)	1.41 (1.12–1.64)	1.27 (1.15–1.39)
Comparison to no use						
E-cigarette vs. nonuse	1.24 (1.05–1.46)	1.32 (0.99–1.76)	1.25 (1.18–1.33)	1.24 (1.19–1.30)	1.46 (1.31–1.61)	1.47 (1.19–1.82)
Dual use vs. nonuse	2.23 (1.59–3.14)	2.39 (2.02–2.83)	1.49 (1.17–1.91)	1.56 (1.22–2.00)	3.29 (1.97–5.51)	1.78 (1.49–2.12)
Cigarette vs. nonuse	1.64 (1.24–2.16)	2.08 (1.91–2.27)	1.27 (1.17–1.37)	1.56 (1.34–1.80)	2.99 (2.29–3.92)	1.69 (1.40–2.03)

How do we help the (old) heavy smokers who do not want to quit?



Hospital setting

- Cochrane review states that e-cigarettes are more effective than NRT
- Some experiments show health benefits when smokers switch
- *An **alternative** for the heavy smoker who will not quit?*

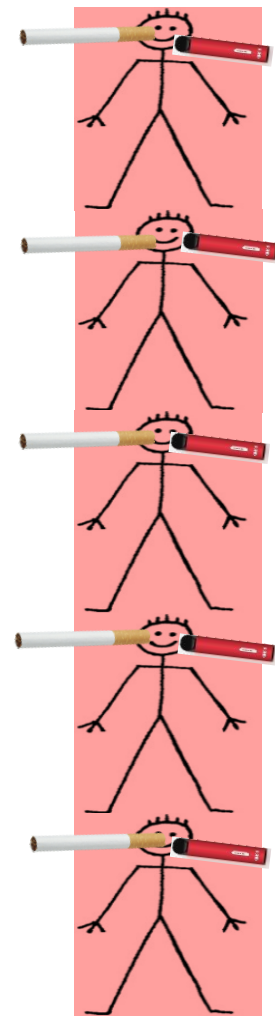
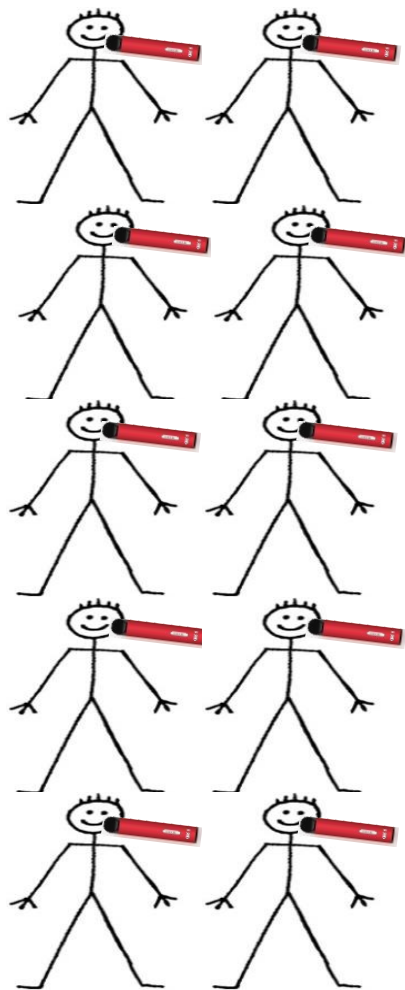
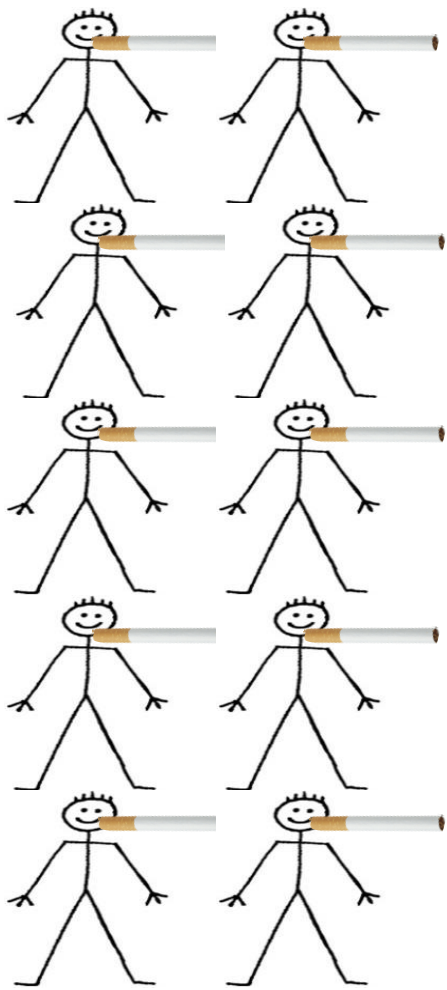


I have tried
EVERYTHING to
quit

I have tried to quit
> 100 times

I have tried nicotine
gum and will power

I have tried hypnosis
and acupuncture



We know what works

Evidence based

High long-term quit rates can be achieved

- Repeated (5-6 (up to 8)) smoking cessation counseling sessions
- +
- Varenicline, cytisine or combined nicotine replacement therapy



or



or



Effective AND safe

	Effective	Safe
Counseling	Yes	Yes
Varenicline, cytisine, combination nicotine replacement	Yes	Yes
E-cigarettes	Yes (probably)	No (+ high risk of dual use)

Recommendations for smoking cessation

- Do not recommend e-cigarettes



**Hippocratic Oath:
First, do no harm**

Thank you
for your
attention

charlotta.pisinger@regionh.dk

DEAR SMOKING BAN,



blu ELECTRONIC CIGARETTE



Take back your freedom to smoke anywhere with blu electronic cigarettes. blu produces no smoke and no ash, only vapor, making it the smarter alternative to regular cigarettes. It's the most satisfying way to tell the smoking bans to kiss off. Okay, maybe the second-most satisfying way.

New blu Smart Pack

blucigs.com

18+ only. CALIFORNIA PROPOSITION 65 Warning: This product contains nicotine, a chemical known to the state of California to cause birth defects or other reproductive harm.