

Can e-cigarettes speed up the demise of smoking?

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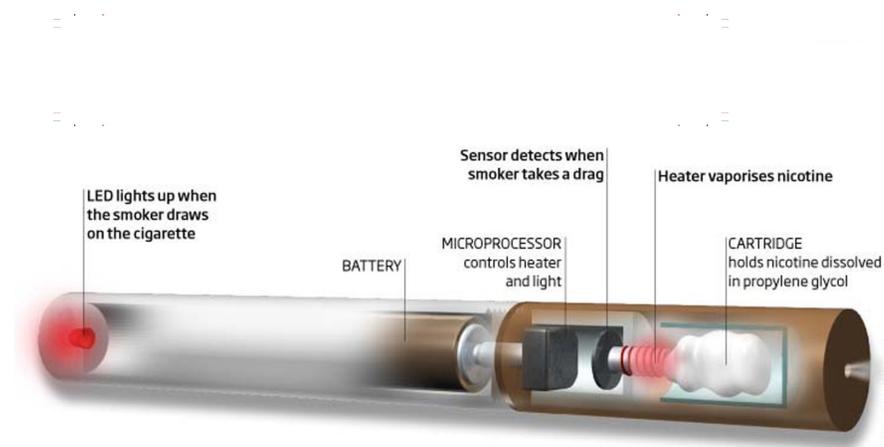
UKCTAS

UK Centre for Tobacco & Alcohol Studies

Contents

- How do risks of vaping compare to risks of smoking?
- Do e-cigarettes lure children to smoking?
- Do e-cigarettes (EC) help smokers quit?
- Will less risky nicotine delivery devices replace smoking?

Early e-cigarettes, 'cig-a-like'



Refillable EC



- Better nicotine delivery
- Choice of strengths and flavours
- Some have variable power



Pods (Juul)

- Nicotine salts make high nicotine concentrations less irritant, small batteries suffice
- US version 59 mg/ml, EU allows only 20 mg/ml



Risks of vaping versus risks of smoking

EC safety

- Some toxicants found in EC aerosol, but at levels much lower than in smoke; most smoke toxicants absent
- PG and vegetable glycerol considered safe
- Some risks may yet emerge (flavourings, impurities, metals from devices, overheated e-liquid)
- Reviews by Royal College of Physicians and Public Health England estimate these are unlikely to exceed some 5% of risks of smoking

Key harmful chemicals in cigarettes and EC

Chemical	EC vs smoke
Carbon monoxide	All gone
Particulate matter	5-10 x lower, more importantly, unlike particles from smoke or traffic, mostly liquid and containing low risk chemicals
Free radicals	<1%
Nitric oxide	All gone
Tobacco specific nitrosamines	100 - 1,000 x lower
Volatile organic compounds	Aldehydes when frying e-liquid, bad taste prevents such use; acrylamide intake 5x lower, benzene 22 x lower, the rest gone

Four sources of data on toxins from vaping

- Two generated alarms, but are of little or no relevance
 - Animals grossly overdosed with nicotine
 - Exposed cells and tissues (often to e-liquid!)
- One relevant but frequently abused
 - Chemicals in aerosol (aldehydes if fried, trace levels of chemicals presented as risks without comparisons to smoke or safety norms – it is the dose that makes the poison)
- One that provides clear and relevant information: Toxicant intake by vapers

Toxicants in vapers

- Long term vapers; long-term users of NRT; smokers (N=about 36 each group)
- Similar nicotine intake (titration)
- TSNs and VOCs: The same in NRT users and vapers – much lower than in smokers
- No non-smokers comparison (NRT and vaping levels likely the same as in non-smokers – known for NNK)

VOCs from smoking and from vaping

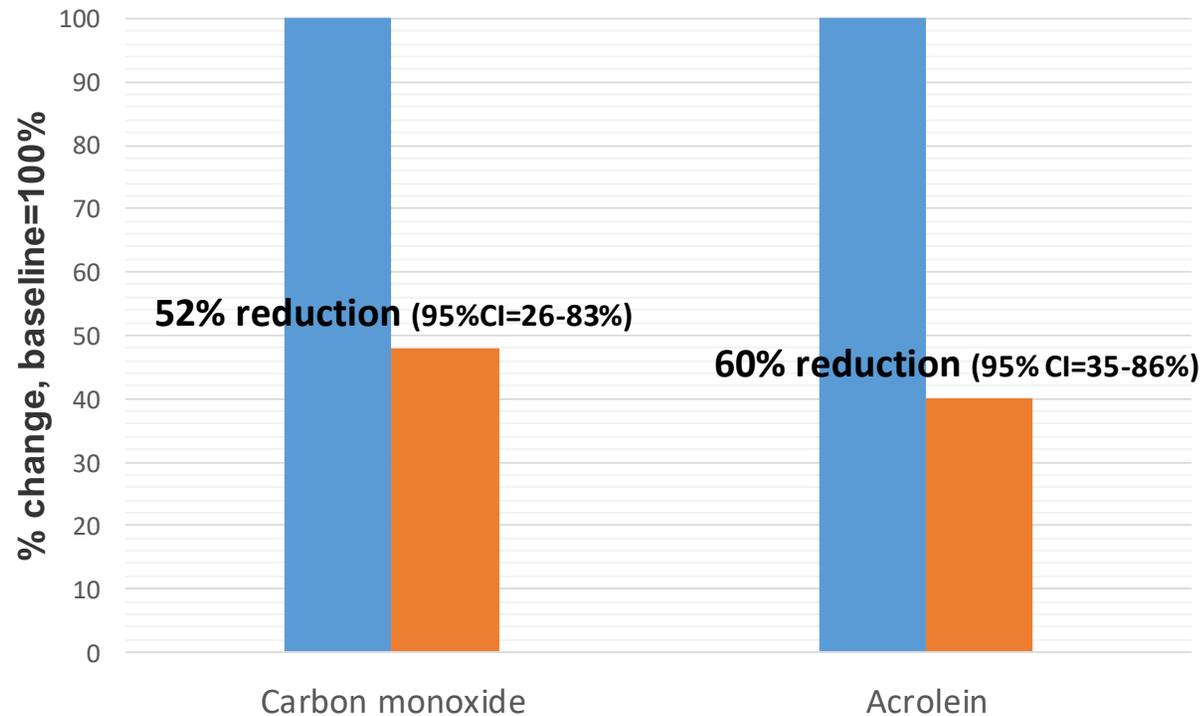
- 36 dual users; EC, cigs, or abstinent 2 days

	Exposure abstinent	Change with EC	Change with smoking	Fold- difference	Exposure from EC
Acrolein	280	-21	+685		NONE
Acrylamide	93	+20	+97	5-fold	Some?
Acrylonitrile	33	-11	+108		NONE
1.3-Butadiene 1+2	0.7	-0.19	+2.73		NONE
1.3-Butadiene 3	0.15	+0.02	+0.06		NS vs abst
Benzene	0.43	+0.06	+1.35	22-fold	Some
Crotonaldehyde	146	+22	+343		NS vs abst
Ethylene oxide	1.84	-0.37	+2.44		NONE
Methylating agent	18	-0.7	-2.5		NONE
Propylene oxide	42	+12	+41		NS vs abst

- Acrylamide has 14h half-life, could be carry-over from smoking because 'abstinent' condition was always last

St Helen et al. 2019 Cancer Prev Res

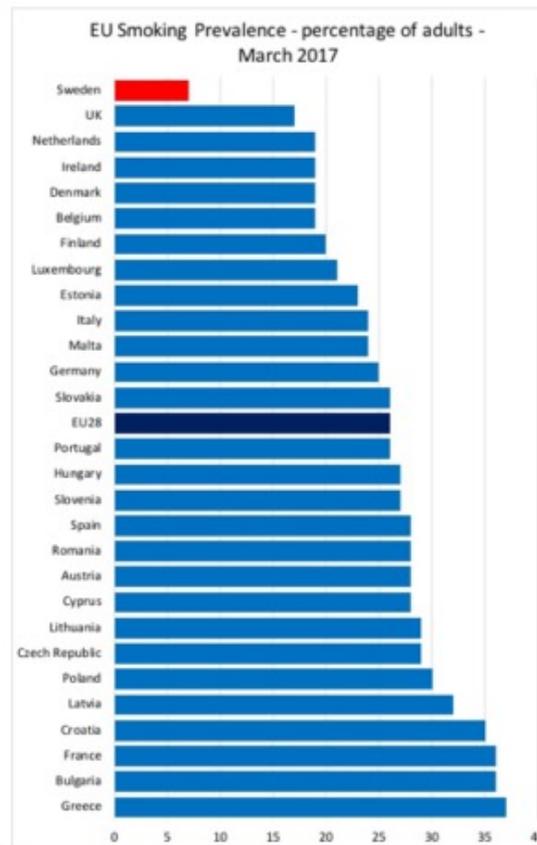
Smokers using EC for 4 weeks and smoking (dual users)



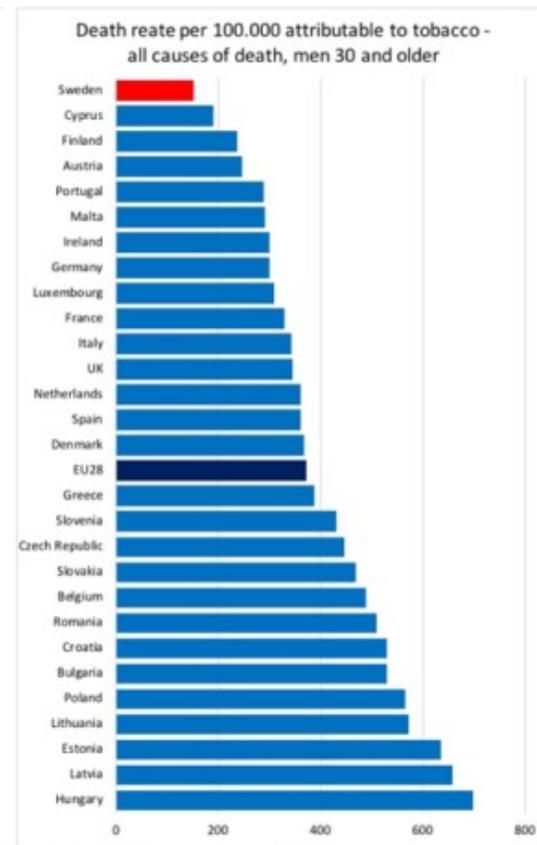
What about long term effects

- Elimination of most toxins and large reductions in the few remaining means that the risk must be massively reduced (e.g. Stephens 2018 TC, cancer risk cca 1% of smoking)
- Documented in snus (where tobacco chemicals persist, just combustion removed). Sweden shows population level reductions of cancer, myocardial infarction and tobacco-attributable mortality

Effects of less risky products on smoking (and on health)



Source: Eurobarometer, 2017²⁵



Source: WHO & Ramström L. ²⁶

Passive vaping?

- Unlike smoking, exhaled vapour does not expose bystanders to carbonyls or phenolics (Long 2014 Int J ERPH) or volatile compounds (Marco 2015 J Chromatogr A)
- Particulates: smoker's home=576; vaper's =10; smoke/vape free homes=10+9 (Fernandes 2015 Curr Env Health Rep)
- Negligible nicotine on surfaces (Bush and Goniewitz 2015 Int J Drug Policy), a baby would need to lick 30m² of floor to ingest 1mg of nicotine

Some health scares putting smokers off switching

- Nicotine has a well-known transient effect on aortic stiffness and blood pressure. Little relevance for health, same when watching a thriller or a football match, or exercising
- Drinking coffee produces the same response, but larger and of much longer duration
- Studies reporting this effects for nicotine in EC are interpreted as showing that vaping is dangerous

Popcorn lung

- Still used, though long de-bunked
- Bronchiolitis obliterans in popcorn workers exposed to high levels of diacetyl
- Cigarette smoke contains at least 100 times levels found in EC with diacetyl flavourings
- There is no link between smoking and bronchiolitis obliterans, but if there was,
- Switching to vaping would reduce it dramatically

Vaping and myocardial infarction

- Vapers were twice as likely to report having had a heart attack than non-vapers *
- Interpreted as vaping causing MI
- BUT most vapers had MI before they started to vape !
- When MIs predating EC use were removed, the link disappeared
- The paper was retracted, but the claim is still made by WHO and others

* Bhatta and Glanz 2019, J Amer Heart Assoc

EVALI misinformation

- Vitamin E acetate mixed in cannabis oil caused deaths in 2019, outbreak stopped when the illicit product off market
- Never found in nicotine EC. Some patients denied using marijuana (illegal in some states, parents present at hospital admission), but all with confirmed diagnosis had the chemical in their bodies
- Yet, the condition was labelled 'EC, or vaping, product use-associated lung injury', disinformation blamed nicotine vaping; scared vapers returning to smoking

Does vaping lure young non-smokers to cigarettes?

Non-smokers experiment with EC but rarely progress to regular use

- Non-smoking adolescents vaping on 15 or more days in the past month (daily vaping is even rarer)
- Canada: 0.6%; USA: 1.5% (Hammond et al. 2019, BMJ) or 0.5% (NYTS –bigger sample)
- In USA, most of these (60%) use EC to vape marijuana, not nicotine !
- UK: 2019 YouGov youth survey: among never smokers, 0.1% vaped weekly and none vaped daily !

The US 'Epidemic of youth nicotine addiction' does not exist

- The alarm was caused by NYTS surveys
- 28% of high school students used EC in past 30 days
- BUT, mostly those with history of tobacco use
- 'Frequent use' in 2% of tobacco naïve students
- Of these, 9% reported craving and 3% use within 30 minutes of waking (65% and 49% among smokers)
- <0.2% of tobacco naïve youth show any sign of nicotine dependence

Jarvis et al. 2020 Queios

Where does the 'luring' claim come from?

Correlation versus causation

- 'There is substantial evidence that e-cigarette use increases risk of smoking among youth and young adults'*
- Based on findings that those trying vaping also try smoking
- Could be that one lead to the other; but could also be that people who try stuff, try stuff (common liability)
- Epidemiology can provide a clear answer – is smoking in young people going up?

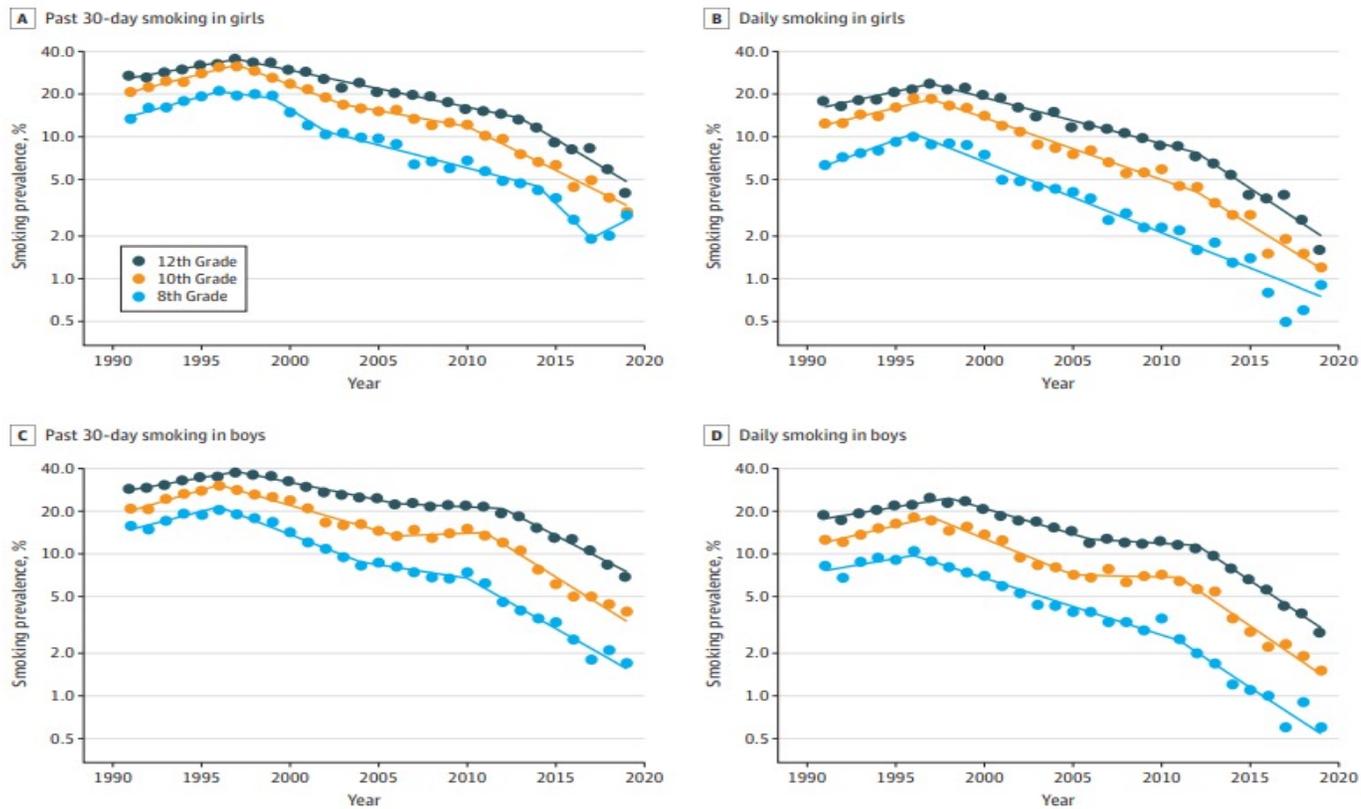
* Eaton et al. Public health consequences of e-cigarettes. 2018, NASEM

EC do not lure adolescents to smoking

- Smoking among young adults (18-24 years)
- **2014: 16.7%** **2018: 7.8%**
- Unprecedented 50% decline in five years over which EC experimentation increased

Smoking in US youth almost eradicated

Figure 1. Past 30-Day and Daily Cigarette Smoking Prevalence Among Adolescents by Sex and Grade From 1991 to 2019



Meza et al. 2020 JAMA Network Open

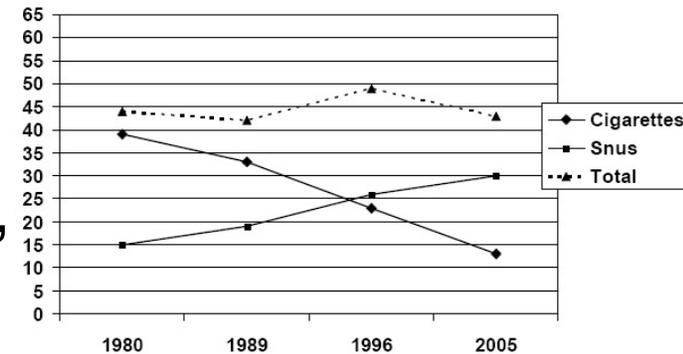
EC may be a gateway away from smoking

- N=24,111 French 17-18 years olds who tried cigs or EC in the past
- Daily smoking among those who tried EC first and cigs first
- Starting with EC reduces the risk of smoking - RR=0.58 (0.54-0.62)

Legleye et al. 2020 Addiction

When smoking gone, nicotine remains - should we worry?

- This may be the main moralist concern behind the anti-vaping sentiment – not smoking, but nicotine use
- Use may increase, though the % of people attracted to nicotine seems limited, see the stability of nicotine use in Sweden
- Even if nicotine use increases, the problem is death and disease from smoking, not the use of a mild stimulant
- Concerns about nicotine may look as odd in future as past concerns about caffeine look odd now



Coffee fears

- Harmful to the brain, leads to exhaustion, paralysis and impotence; Causes stomach ulcers and heart disease
- Proposals to include compulsory health warnings and making it available on medical prescription only
- Director of FDA forerunner USBC Wiley called for ban on Coca-Cola because of caffeine in it “Use led to wild parties and sexual indiscretions by coeds and induced boys to masturbatory wakefulness.”

Juma: Innovation and its enemies. Oxford Univ Press 2016

Weinberg and Bealer: The world of caffeine. Routledge 2001

An early RCT

- King Gustav III of Sweden (1746-1792): a convicted murderer to drink coffee daily to show it is poisonous. Another drank tea daily, as a control.
- Two doctors oversaw the experiment. Both died and Gustav was murdered before either prisoner succumbed.
- The tea drinker died before the coffee drinker, aged 83.

Weinberg and Bealer: The world of caffeine. Routledge 2001

Do EC help smokers quit?

Effects on abstinence and reduction at 1 year

	EC (N=438)	NRT (N=446)	RR (95% CI)
% abstinent for 52 weeks*	18.1%	9.9%	1.83 (1.30 to 2.58)
<i>Results similar for a range of sensitivity analyses and secondary outcomes</i>			
CO validated reduction in non-abstainers	12.8%	7.4%	1.75 (1.12 to 2.72)

*biochemically validated

Hajek et al. 2019 NEJM

High on-going EC use in abstainers

- 9% in NRT arm still on NRT, 56% in EC arm on nicotine EC and another 24% on nicotine free EC
- Good if it prevents relapse (as long-term NRT use does), helps with discomfort and weight gain, maintains smoking rewards
- Bad if it poses health risks later on, but still good if the alternative is smoking

Elicited respiratory symptoms: Vaping may have a positive effect

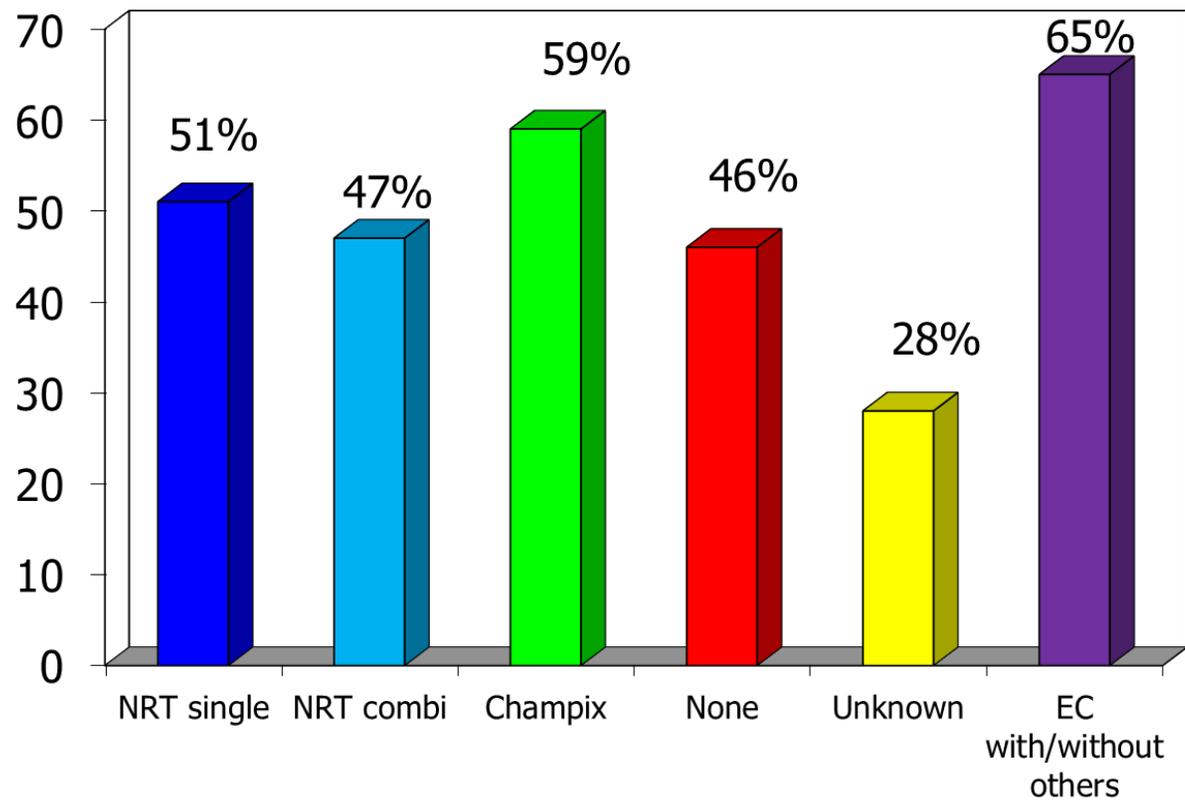
	EC (N=315)		NRT (N=279)		RR (95% CI)
	Baseline	52 weeks	Baseline	52 weeks	
Shortness of breath	38%	21%	33%	23%	NS
Wheezing	32%	24%	31%	21%	NS
Cough	55%	31%	52%	40%	0.8 (0.6 to 0.9)
Phlegm	44%	25%	43%	37%	0.7 (0.6 to 0.9)

Cochrane review 2020

- Draws on 10 randomised comparisons
- ECs with nicotine increase quit rates compared to ECs without nicotine and compared to NRT (moderate-certainty evidence)
- More studies needed of the degree of effect, particularly for modern ECs
- No evidence of harm from nicotine EC used for up to 2 years

Hartmann-Boyce et al. 2020

English stop-smoking service 4-week quit rates 2019-2020 (N=221,678)

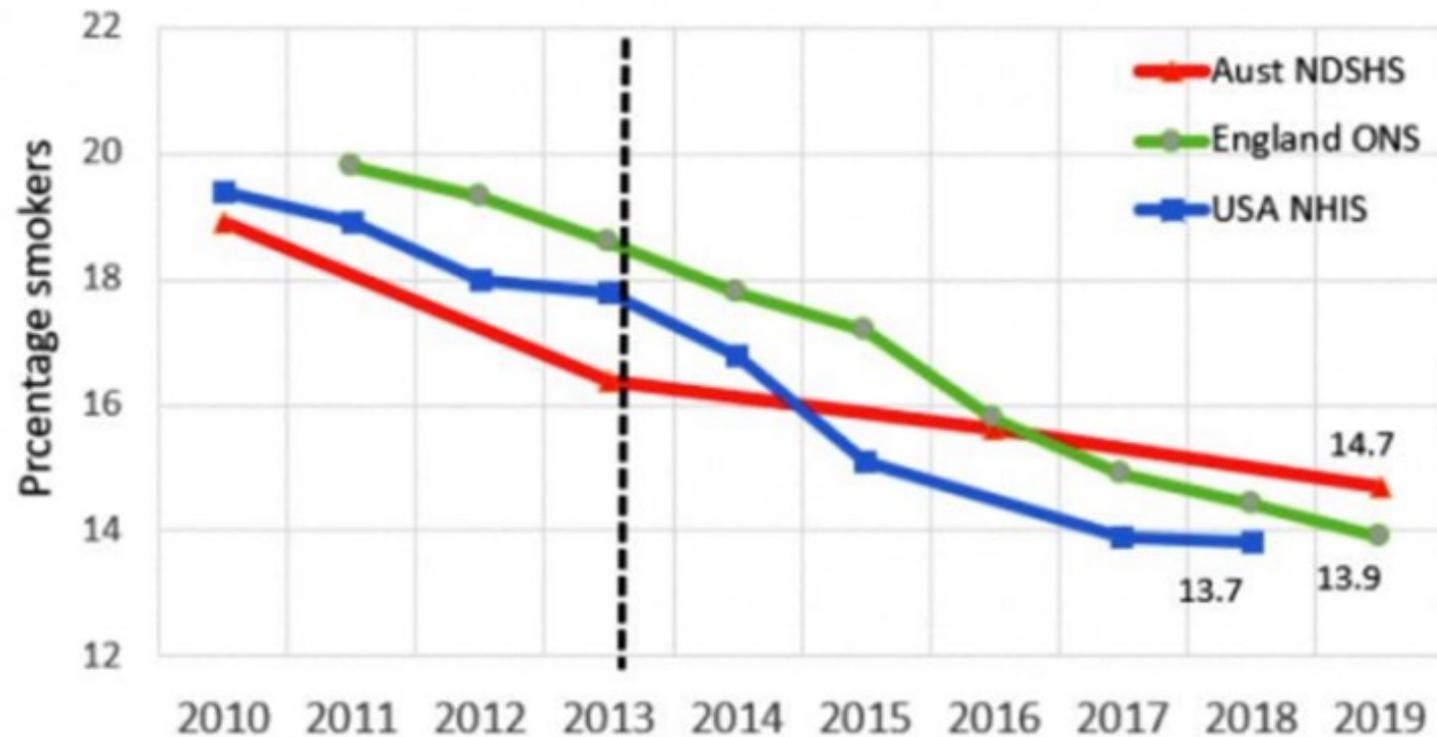


Effect of EC use on population level smoking cessation

- US population survey (CPS-TUS)
- 2014-2015 (N=161,054); compared with previous 4 surveys
- Tried to quit? Quit for at least 3M?
- EC users quit rate: 8.2%; non-users: 2.5%-4.8%
- Population quit rate significantly increased

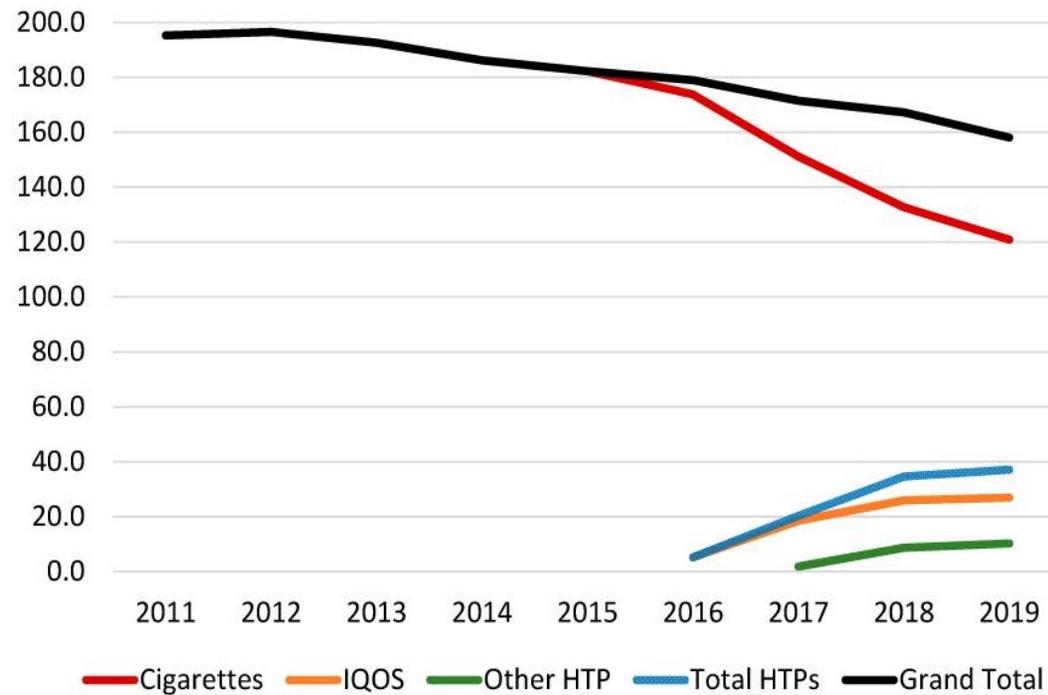
Smoking in countries that allow and ban EC

England, US, Australia $\geq 18y$
smoking rates 2010-2019



Data. England: Office of National Statistics | US: NHIS | Australia: NDSHS

Effect of IQOS on cigarette sales in Japan



Cummings et al. 2020 Int J Environ Res Public health

Current balance of evidence

- RCTs show that when provided pro-actively, EC are effective in helping smokers quit and that they are more effective than traditional NRTs
 - Efficacy not compared with varenicline yet, but even if efficacy similar, EC reach is much larger
- Population data show that EC help smokers in quitting outside clinical settings as well and that less risky nicotine delivery products are replacing cigarettes

Will less risky nicotine delivery products
replace smoking?

To make cigarettes obsolete, alternatives need to

- Deliver **nicotine** in the way smokers want
- Provide '**added value**' to compensate for the likely enjoyment deficit and the effort of the switch, e.g.
 - Additional attractants such as flavours
 - Lower cost
 - Acknowledgment of lower risk, reduced stigma
 - Regulatory advantages over smoking

Is the attractiveness of alternatives improving?

- Market forces are succeeding in driving some product improvements (nicotine delivery, ease of use)
- Hostile regulations, bans, and misleading publicity are slowing down product developments, and sabotaging the 'added value' elements

Product developments
that are helping smokers

Nicotine delivery and sensory characteristics

- Several groups have generated useful knowledge. Will review our studies that employ an ad-lib use paradigm rather than scheduled puffing
 - A cohort with data from own cigs and own EC
 - Ad-lib use for 5 min after overnight abstinence
 - All with tobacco flavour
 - PK + changes in urge to smoke + product ratings

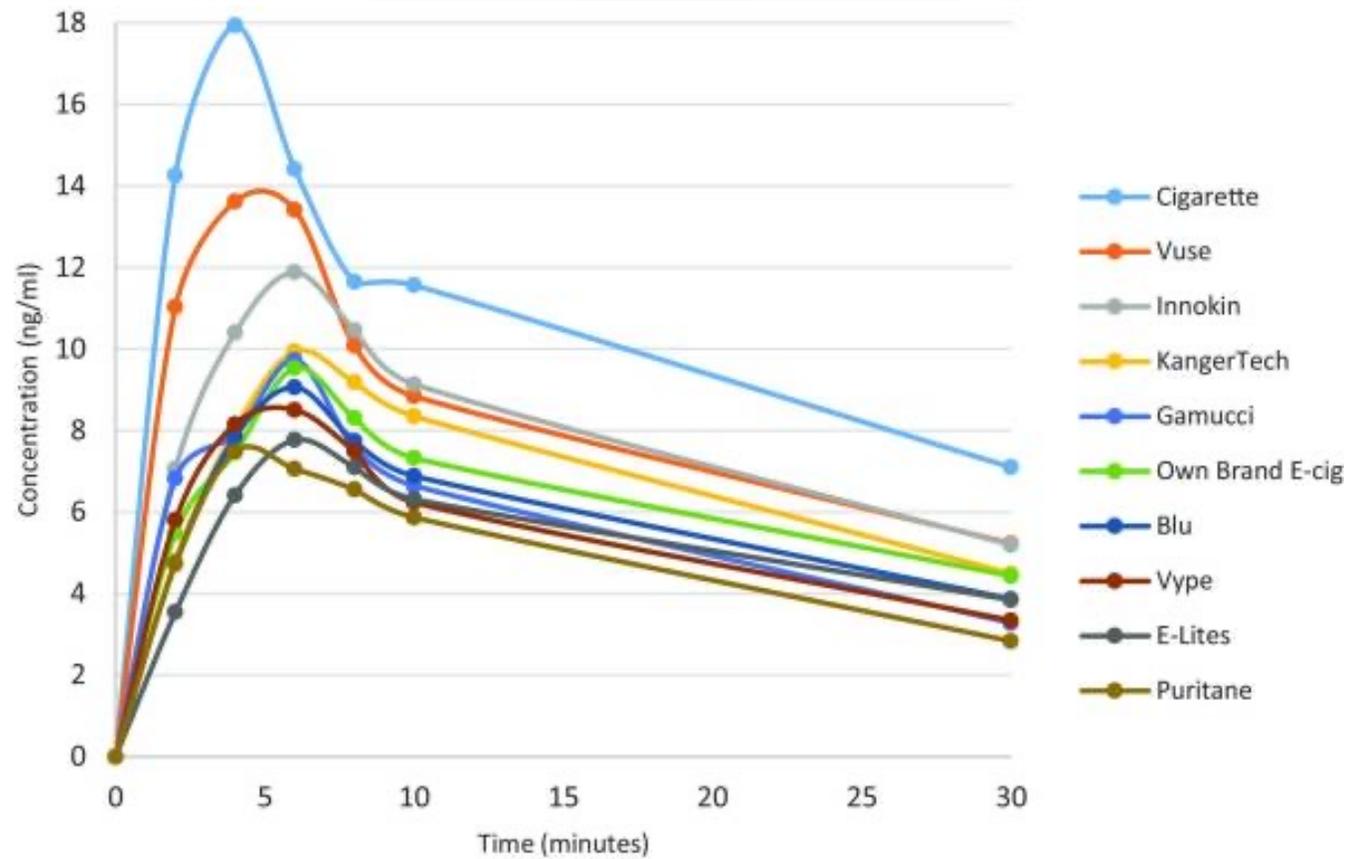
Cig-a-likes vs refillables

- 8 EC brands, 6 first generation (5 tobacco industry brands), 2 refillables
- 16 to 24 mg/ml nicotine, apart from Vuse with 48 mg/ml
- Refillables have better user ratings and craving relief; better nicotine delivery than non-Vuse EC

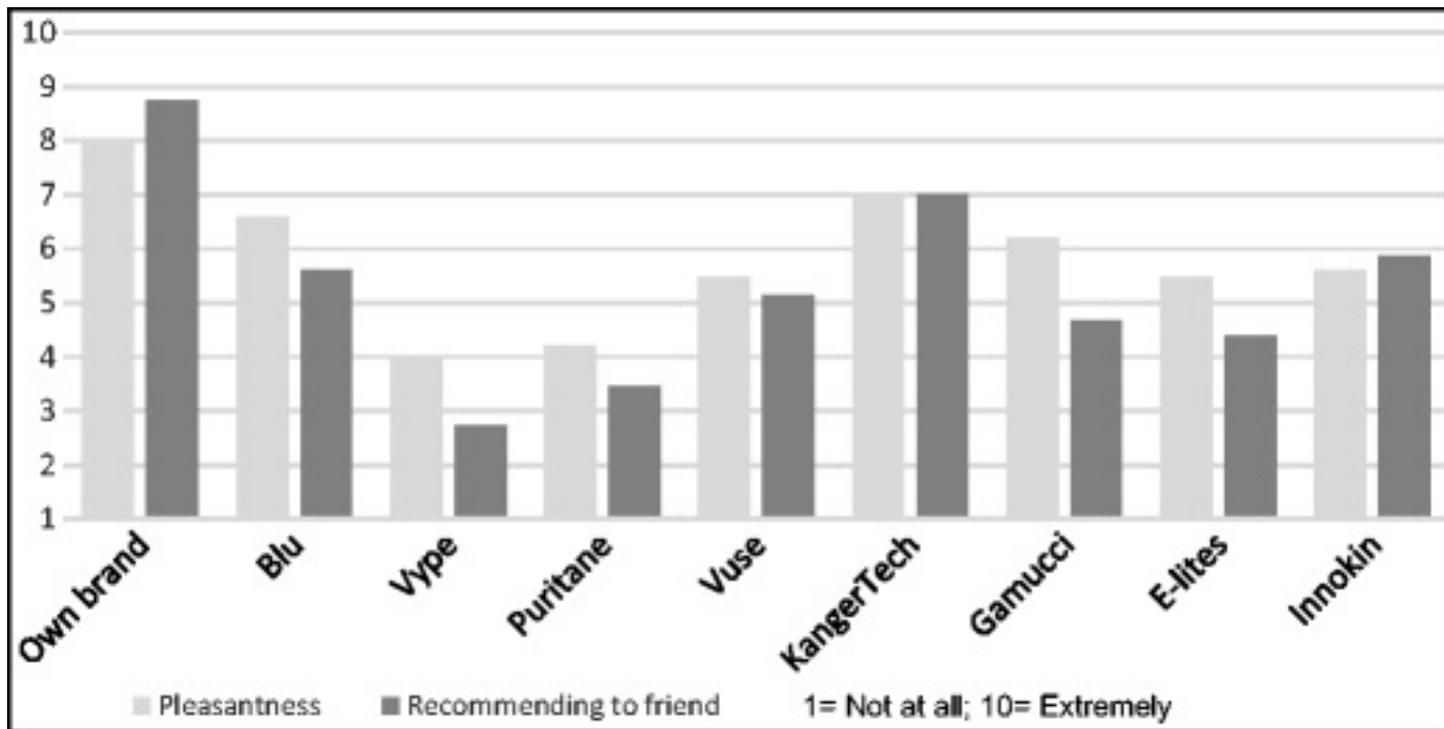
Hajek et al. Psychopharmacology 2017

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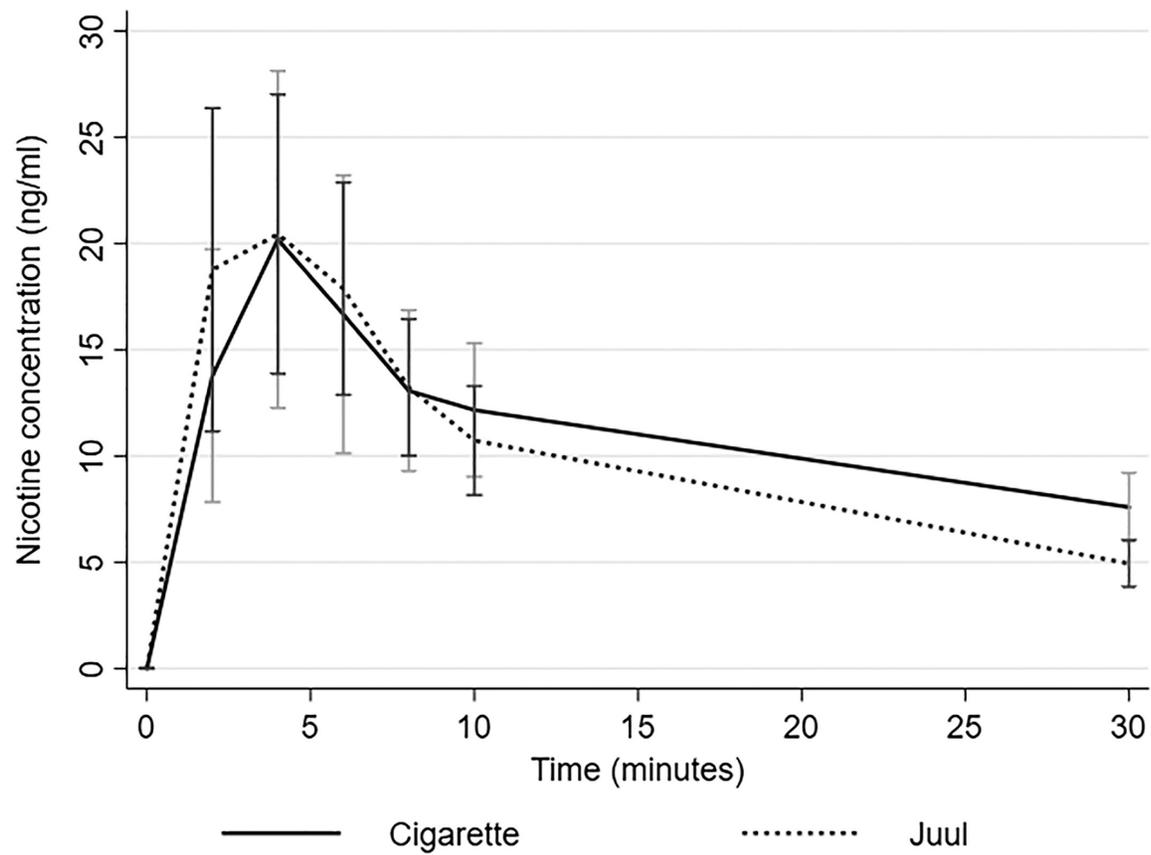
Cig-a-likes vs refillables



Product ratings



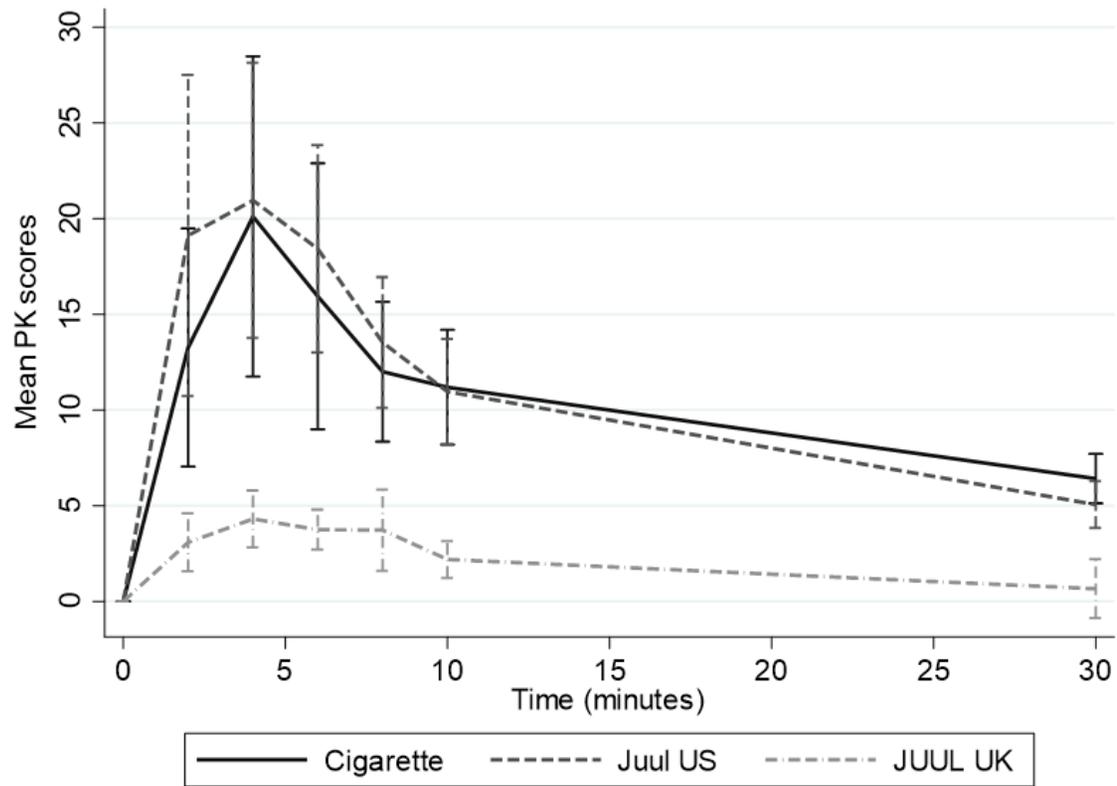
Juul US vs cigs



Juul US

- Cigs relieved urges to smoke better, but not faster, the same subjective nicotine delivery, taste and pleasantness
- Juul provides much higher and faster nicotine delivery than other ECs (despite fewer puffs), faster urge relief, better ratings
- Nicotine salt formulation avoids local irritation, a substantial leap in catching up with cigarettes

Effects of bad regulation: Juul EU



Phillips-Waller et al. 2020

So are we nearly there yet?

- Alternatives are getting better at giving smokers what they want from cigarettes, but slowed down by hostile regulations
- ‘Added value’ elements undermined by current policies
- US bans on flavours are likely to cause harm
- Misleading campaigns (EVALI) and anti-vaping regulations keep smokers smoking
- Not getting nearer at the moment

Message to regulators lobbied to ban EC or make them unattractive

- Smoking kills many more people than COVID-19
- Letting smokers switch to non-combustion nicotine products can dramatically reduce cancer, heart disease and lung disease caused by smoking
- Do not bar this exit route from unnecessary suffering and death because of misinformed puritanical concerns

Answers

- How do risks of vaping compare to risks of smoking?
Current estimate: Unlikely to exceed 5% of risks of smoking
- Do e-cigarettes (EC) help smokers quit? Yes
- Do e-cigarettes lure children to smoking? No, if anything, they deflect potential smokers away from cigarettes
- Will less risky nicotine delivery devices replace smoking?
Yes, but misinformation and anti-vaping policies are slowing down the process