



ST VINCENT'S
HEALTH AUSTRALIA

I just can't talk about e-cigarettes anymore ... smoking cessation in 2023

Nexus Dual Diagnosis March 2023

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Outline

Epidemiology

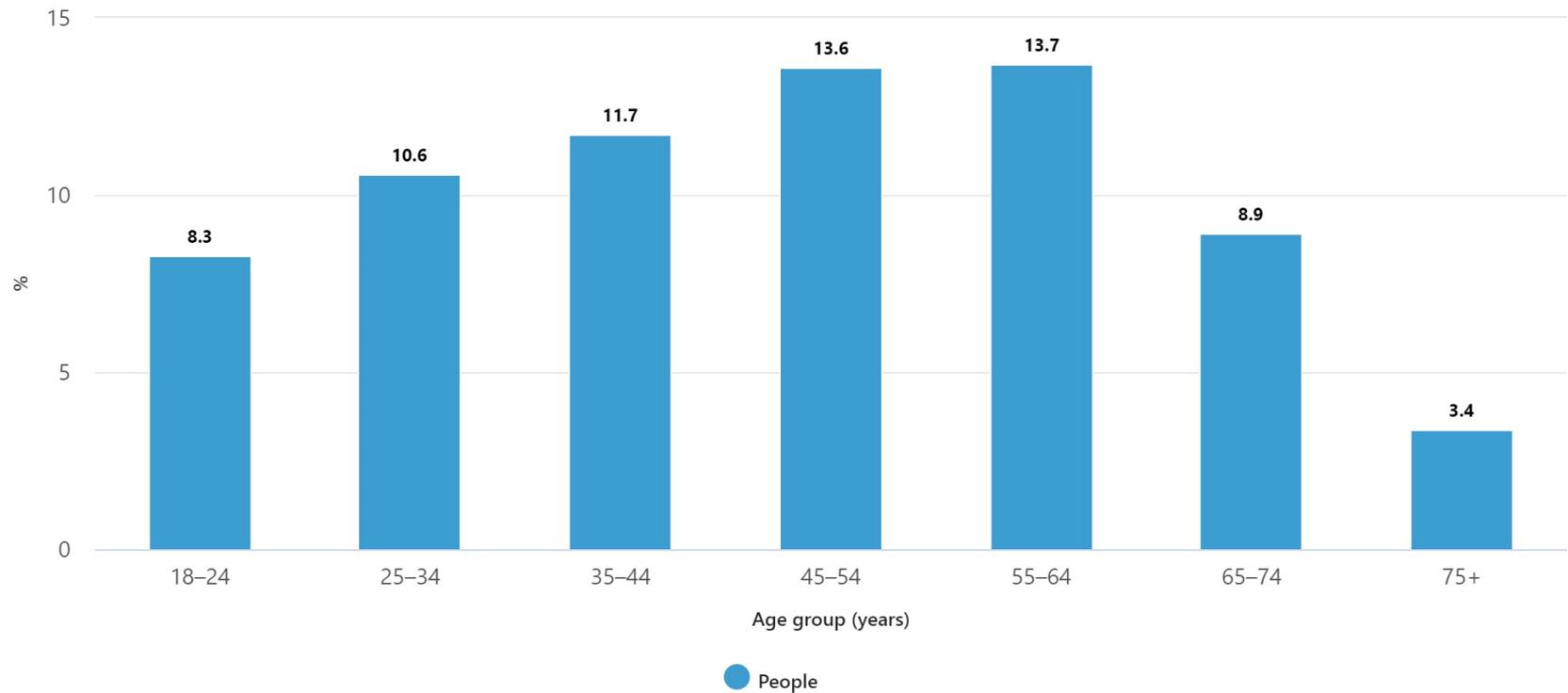
E-cigarettes – current state of play

Other equally (if not more) important things

- counselling approaches
- online/electronic
- on varenicline
- cytisine

Australia: National Health Survey

Proportion of current daily smokers by age, 2020-21



Source: Australian Bureau of Statistics, Smoking 2020-21 financial year

In 2020-21, current daily smokers aged 18 years and over had higher rates of the following long-term health conditions compared to those who had never smoked:

One in three (32.0%) had a mental health and/or behavioural diagnosis

One in four (26.2%) had back pain

One in seven (14.8%) had asthma

cigg/day approx. 10 but increased with age



E-CIGARETTES
GET THE FACTS

E-CIGARETTES CAN BE HARMFUL
They contain chemicals and toxins that can cause serious health issues.

E-CIGARETTES ARE NOT PROVEN SAFE AND EFFECTIVE CESSATION AIDS
There are other proven safe and effective options to help smokers quit.

People are **MORE LIKELY TO TAKE UP TOBACCO SMOKING** if they use e-cigarettes.

www.nhmrc.gov.au/ecigs

Australian Government
National Health and Medical Research Council

NHMRC



Vaping is 95% less harmful than smoking

2014

NUTT AND COLLEAGUES

An expert group led by Professor David Nutt estimated vaping carried only 4% of the harm of cigarette smoking

2015

PUBLIC HEALTH ENGLAND

"E-cigarettes are 95% less harmful to your health than normal cigarettes" based on a comprehensive review of the scientific evidence in 2015 and again in 2018

2016

UK ROYAL COLLEGE OF PHYSICIANS

A detailed independent review concluded health risks "are unlikely to exceed 5% of those associated with smoked tobacco products, and may well be substantially lower"

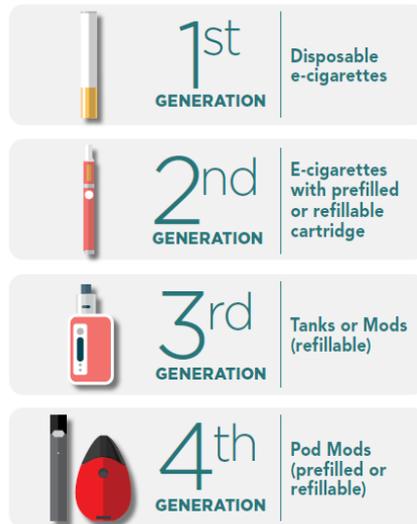
2018

NASEM

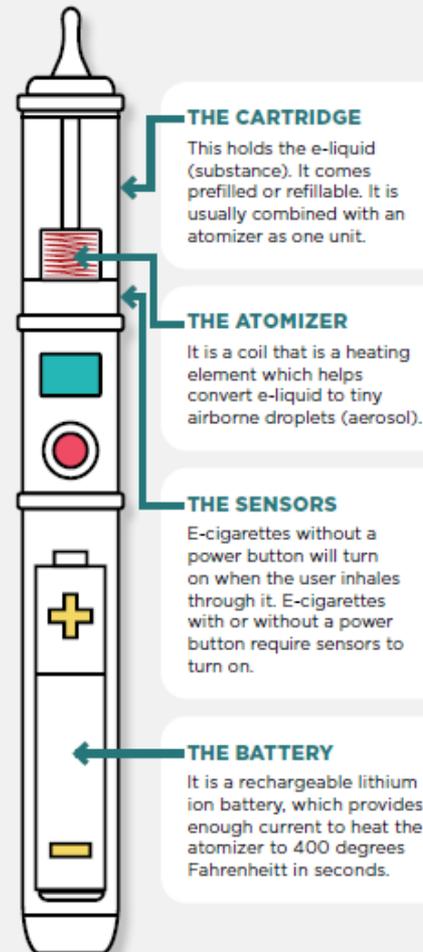
The US National Academies of Sciences, Engineering and Medicine: "while e-cigarettes are not without risks, they are likely to be far less harmful than conventional cigarettes"

US CDC E-cigarette, or Vaping, products visual dictionary

The Evolution of E-Cigarette, or Vaping, Products



THE E-CIGARETTE



Mod Box
It is a 3rd generation device that is modifiable ("Mod") allowing users to change the voltage, coils and wicks.



Sub-Ohm Tank
It is made of plastic or metal with transparent casing so liquid levels can be seen. It contains a lower resistance coil that allows the liquid to heat up faster.



Cartridge
It is made of plastic or metal with transparent casing so liquid levels can be seen. It contains an atomizer that heats up the e-liquid.



E-Liquid
E-liquid is contained in a pod, cartridge or tank. It is made up of a mixture of substances that includes nicotine, cannabis, and/or flavoring.

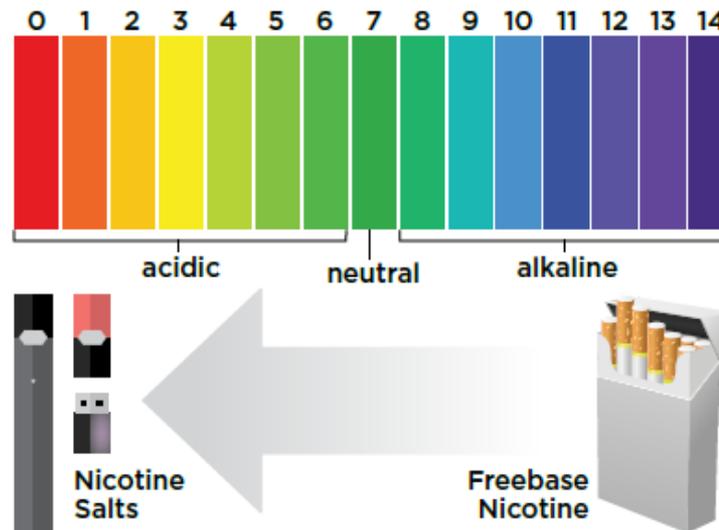
Evolving Quickly



Pod Mods

- Pod Mod is an e-cigarette, or vaping, product with a prefilled or refillable "pod" or pod cartridge with a modifiable (mod) system ("Pod-Mods")
- These are other examples of fourth generation devices. Pod Mods come in many shapes, sizes, and colors.
- Common Pod Mod brands include JUUL® and Suorin®
- There are compatible prefilled pod cartridges that contain nicotine, THC, or CBD with or without flavoring.

Evolving Quickly

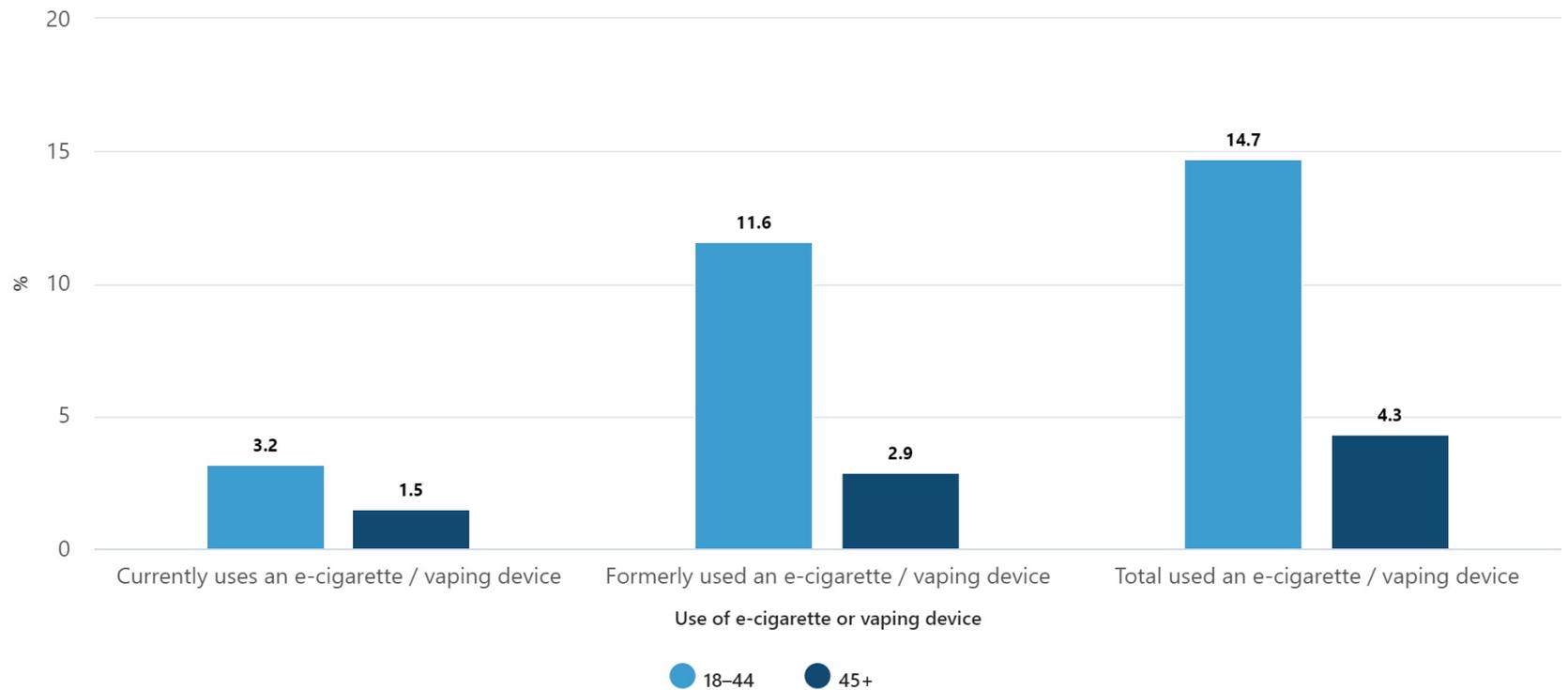


For accessibility, explanation of graphic can be found in [Appendix page 25](#).

Pod Mods

- Pod Mods typically use nicotine salts rather than the freebase nicotine used in most other e-cigarette, or vaping, products.
- Nicotine salts, which have a lower pH than free base nicotine, allow particularly high levels of nicotine to be inhaled more easily and with less irritation to the throat than freebase nicotine.

Proportion of people who used an e-cigarette or vaping device by age, 2020-21



Source: Australian Bureau of Statistics, Smoking 2020-21 financial year

Age > 18

- Men > women (2.9% vs 1.6%)
- More common in 18-24 (4.8%) than older age groups

Of smokers

- 8.9% currently use an e-cigg and 23.8% have formerly used

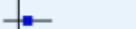
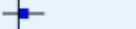
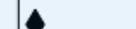
US data

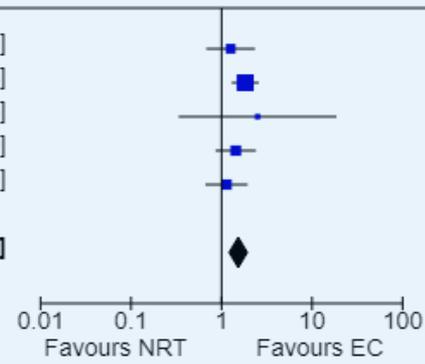
- US 3.7% current use adults, 11.3% high school students used in last 30 days
- Current ecigg users 36.9% currently smoke combustible tobacco, 39.5% ex-smokers, 23.6% never combustible tobacco smokers
- 56% of ecigg users aged 18-24 never smoked combustible tobacco

Australia Legal Status

- Vaping with or without nicotine covered by tobacco product legislation (i.e everything that pertains to tobacco pertains to non-nicotine vapes – age, therapeutic claims, marketing etc...)
- Nicotine containing are S4 products but none on ARTG so pathways for unapproved therapeutic use
- Product standard TGO 110 (child resistant closures, warning labels, max concentration 2%) – overseas supplier, script available, 3 months supply at a time. SAS authorised prescriber streamlined. (Sale of nicotine e-cigarettes and liquid nicotine illegal without a doctors prescription)
- Most e-cigarettes contain nicotine (easy access +++)
- Not allowed to vape anywhere were you can not have combustible tobacco (except in WA)
- Described as a grudging tolerance; hard to match product and supply, liability re: unapproved medicine
- Restriction to smokers vs poor enforcement

Cochrane Sep 2021 – Electronic Cigarettes for Smoking Cessation

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



Footnotes

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

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

Conclusions

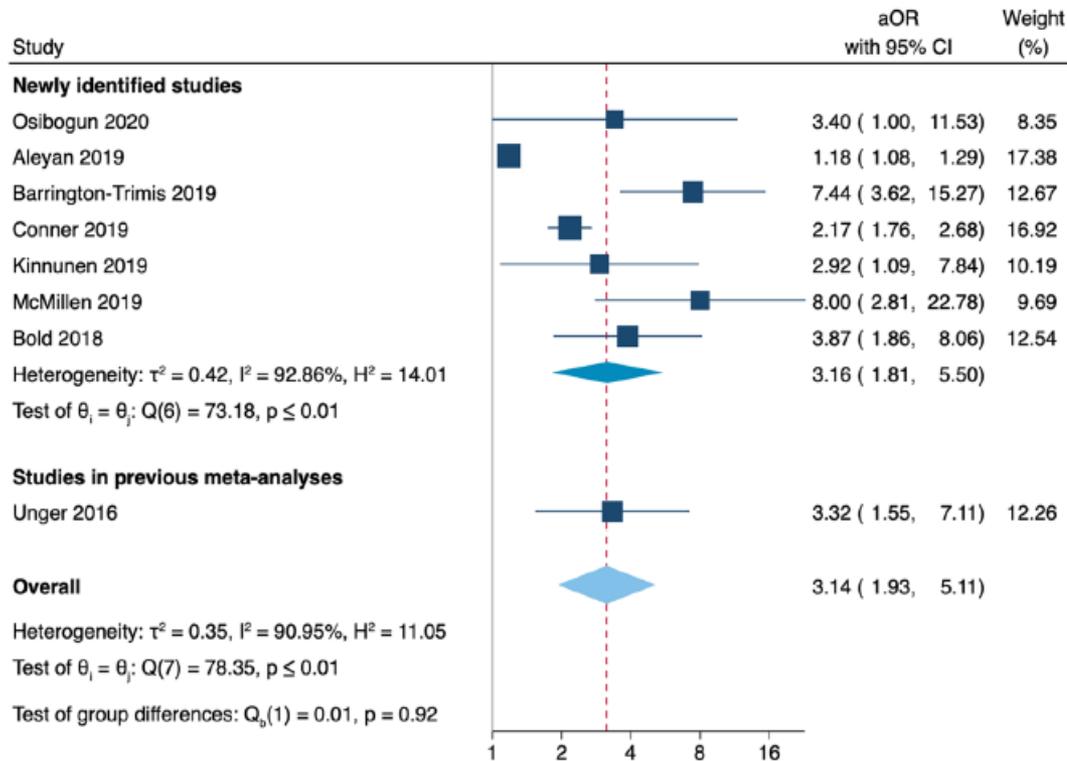
- approximately extra 3 quitters per 100 (95% CI 1 - 6) compared with NRT to six months
- similar AEs rate (low precision)
- Better results when compared to either non-nicotine eciggs or behavioural supports alone (6-7 extra quitters/100)
- Confidence intervals were wide
- No trials of nicotine salts

However

- people are unlikely to stop using electronic cigarettes (c/w NRT)
- In smokers randomised to ENDS; dual use was more likely than quitting
- high, effective delivery of nicotine makes them 'addictive' themselves



Vaping to Combustible Tobacco



Random-effects REML model

Figure 3 Forest plot and random-effects meta-analysis for the adjusted odds of current (past 30-day) smoking at follow-up among non-current smokers and current e-cigarette users at baseline compared with non-current e-cigarette users at baseline. aOR, adjusted OR; REML, Restricted Maximum Likelihood

Health implications

- Lower levels of known toxins than combustible cigarettes
- Some unique/devastating but likely fleeting risks (EVALI) – regulation, constituents etc...
- Approx. 200 episodes of burns in US (unlikely to be more than tobacco?)
- Acutely – no AE on cardiac function, but some effect on endothelial progenitor cells, markers of oxidative stress increase (greater increase in tobacco smokers)

Pregnancy and vaping

Developing foetus

- **Nicotine itself is a known teratogen**
- **No trials vaping in pregnancy**

Harm reduction? - Longer cohort studies are not reassuring

The Health Effects of Real-World Dual Use of Electronic and Conventional Cigarettes versus the Health Effects of Exclusive Smoking of Conventional Cigarettes: A Systematic Review Pisinger and Rasmussen in International Journal of Environmental Research and Public Health Oct 2022

Dual Use vs exclusive cigarette smoking

- # of cigarettes/day may not have been different
- Health outcomes tended to worse (13 studies/10 prospective)
- Longest follow up 6 years
- Dual use at least as harmful

Tobacco vs Electronic cigarettes: absence of harm reduction after six years follow up. Flacco et al ... European Review for Medical and Pharmacological Sciences 2020 – 6 year prospective follow up

- 228 ecigg, 469 tobacco, 215 dual use (adult users)
- 9.9% (n=90) smoking related disease, 1.2% mortality, no difference between groups

Discussion

Monitoring and Evaluation

- good data
- willingness to change approach/regulation if situation changes

Skewing products to older age groups (diminish influence of bad actors)

Monitoring for harm – acknowledging if there is little

Monitoring for benefit – acknowledging if there is little

Development of practical prescribing-dispensing if appropriate

We also need to consider the next steps in tobacco control

What else?

Changing rapidly in line with market and regulatory forces rather than research...

Individual clinician involvement will depend on risk appetite, approach to individual patient, what it means to have exhausted other options etc...

Has this debate diverted attention from other methods of reducing tobacco related harm ... on a treatment level and on a regulatory level

-eg. NZ no sales tobacco to anyone born after Jan 1 2009 (due for implementation 2027)



Easy things we don't do very much

Old and new technology

Quit dates and financial incentives

Mental Health considerations

CO monitoring

Telephone counselling for smoking cessation (Review)

Matkin W, Ordóñez-Mena JM, Hartmann-Boyce J

Interventions for callers to quitlines - effect of additional proactive calls for smoking cessation
Patient or population: callers to quitlines

Intervention: additional proactive calls

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Additional proactive calls				
Smoking cessation Self-reported abstinence (majority) Follow-up: 6+ months	Study population		RR 1.38 (1.19 to 1.61)	32,484 (14 studies)	⊕⊕⊕⊙ moderate ^{b,c}	-
	72 per 1000	100 per 1000 (85 to 116)				

Proactive telephone counselling for smokers not calling quitlines
Patient or population: smokers not calling quitlines

Intervention: proactive telephone counselling

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Proactive telephone counselling				
Smoking cessation Self-reported abstinence (majority) Follow-up: 6+ months	Study population		RR 1.25 (1.15 to 1.35)	41,233 (65 studies)	⊕⊕⊕⊙ moderate ^{a,b}	
	110 per 1000 ^a	137 per 1000 (127 to 149)				

My quitbuddy



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Quit Now: My QuitBuddy

Automated text messaging - quitcoach

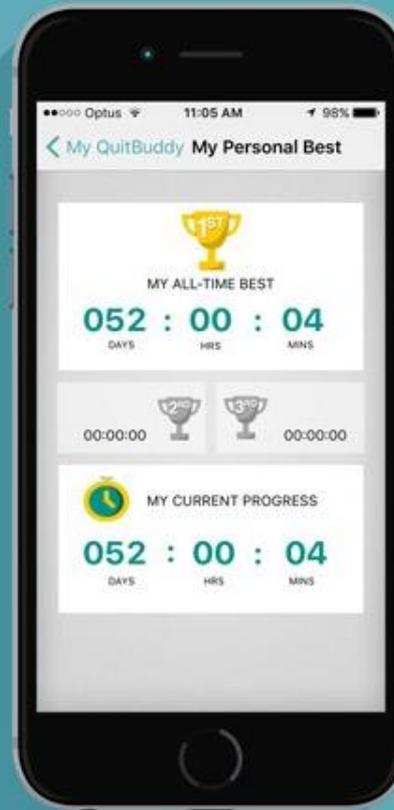
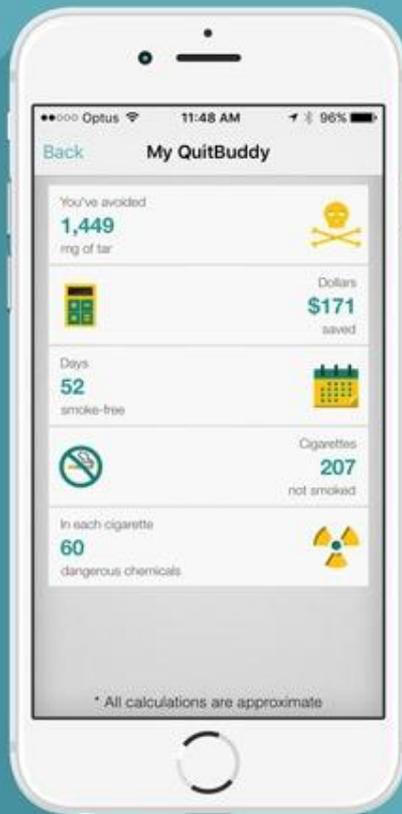
4 functional domains

1. Rational eg. Savings, health costs
2. Emotional eg. Positive influence on family
3. Social eg. Community forums and links
4. Gamification

Small RCT (n=64)

- acceptable, increased motivation to quit,
4 quitters in intervention arm vs 2 in control

myquitbuddy



Quit date vs cutting down

Clear effectiveness data for quit dates

Original Investigation

Understanding the Association Between Spontaneous Quit Attempts and Improved Smoking Cessation Success Rates: A Population Survey in England With 6-Month Follow-up

Nicotine & Tobacco Research, 2020, Vol. 22, No. 9

Table 4. Adjusted Models Between Quit Success and Spontaneous Quit attempts and Potential Confounder

	Adjusted		
	OR (95% CI)	<i>p</i>	BF _(HN)
Model 1			
Spontaneous quit attempt (not spontaneous ^a)	1.18 (0.96 to 1.46)	.113	0.94 ^e
Quit attempt made without cutting down first (with cutting down first ^a)	3.15 (2.54 to 3.91)	<.001	>10 000 ^d
Model 2			
Spontaneous quit attempt (not spontaneous ^a)	1.28 (1.04 to 1.57)	.017	3.86 ^d
Strength of urges			
None ^a (<i>n</i> = 154)			
Slight (<i>n</i> = 272)	1.32 (0.87 to 2.02)	.199	1.18 ^e
Moderate (<i>n</i> = 944)	0.75 (0.52 to 1.09)	.127	1.46 ^e
Strong (<i>n</i> = 468)	0.55 (0.37 to 0.84)	.005	24.33 ^d
Very strong (<i>n</i> = 135)	0.62 (0.36 to 1.05)	.079	2.73 ^e
Extremely strong (<i>n</i> = 45)	0.66 (0.29 to 1.41)	.302	1.24 ^e
Model 3			
Spontaneous quit attempt (not spontaneous ^a)	1.25 (1.02 to 1.54)	.029	2.16 ^e
Daily cigarette consumption	0.80 (0.71 to 0.89)	<.001	136.82 ^d
Model 4			
Spontaneous quit attempt (not spontaneous ^a)	1.36 (1.11 to 1.67)	.003	31.70 ^d
Social grade			
AB ^a (<i>n</i> = 260)			
C1 (<i>n</i> = 465)	1.10 (0.79 to 1.54)	.561	0.40 ^e
C2 (<i>n</i> = 438)	0.81 (0.57 to 1.14)	.216	0.83 ^e
D (<i>n</i> = 349)	0.71 (0.49 to 1.02)	.064	2.25 ^e
E (<i>n</i> = 506)	0.48 (0.33 to 0.68)	<.001	1114.57 ^d

Contingency management (financial incentives)

Incentives for smoking cessation (Review)

Notley C, Gentry S, Livingstone-Banks J, Bauld L, Perera R, Hartmann-Boyce J

Summary of findings for the main comparison. Incentives vs no incentives for smoking cessation in mixed populations

Smoking cessation: Incentives compared to no incentives in mixed populations

Patient or population: Adult smokers

Setting: Mixed

Intervention: Incentives for smoking cessation

Comparison: No incentives

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	Risk with Incentives: mixed populations				
Smoking cessation in mixed populations - Longest follow-up Follow-up: 6 months to 24 months)	71 per 1000	106 per 1000 (91 to 123)	RR 1.49 (1.28 to 1.73)	21,627 (adjusted n = 20,097) (30 studies, 33 comparisons)	⊕⊕⊕⊕ HIGH ^a	For 1 included study extractable data were available but did not contribute anything to the analysis as no events (episodes of smoking cessation) occurred in either arm; we excluded a further two studies from the formal analysis, since no extractable data were available on programme participants at follow-up. More recent studies were higher quality and routinely included longer-term follow up beyond 6 months assessment

Smoking cessation for improving mental health (Review)

Taylor GMJ, Lindson N, Farley A, Leinberger-Jabari A, Sawyer K, te Water Naudé R, Theodorou A, King N, Burke C, Aveyard P

Associations between quitting smoking and change in mental health symptoms

Patient or population: various, including general population, pregnant people, psychiatric populations (ADHD, anxiety disorder, depression, psychosis, PTSD, various SMI) and populations with chronic health conditions (AIDS, AS, brain injury, cancer, CHD, COPD, HIV)

Setting: Australia, Belgium, Canada, China, Japan, Netherlands, Portugal, South Korea, Spain, Turkey, UK, US

Intervention: Quitting tobacco smoking

Comparison: Continuing to smoke tobacco

Outcomes	Probable outcome with intervention	Nº of participants (studies)	Certainty of the evidence (GRADE)
<p>Change in anxiety assessed with various anxiety symptom scales follow-up: range 6 weeks to 2 years</p> <p>Higher score indicates higher-intensity anxiety symptoms</p>	<p>The mean change in anxiety score was 0.28 SDs lower (95% CI: -0.43 to -0.13) in people who quit smoking compared to people who continued smoking</p>	<p>3141 (15 observational studies)</p>	<p>⊕⊕⊕⊕ LOW^{a,b,c}</p>
<p>Change in depression assessed with various depression symptom scales follow-up: range 6 weeks to 6 years</p> <p>Higher score indicates higher-intensity depression symptoms</p>	<p>The mean change in depression score was 0.3 SDs lower (95% CI: -0.39 to -0.21) in people who quit smoking compared to people who continued smoking</p>	<p>7156 (34 observational studies)</p>	<p>⊕⊕⊕⊕ VERY LOW^{d,e,f}</p>
<p>Mixed anxiety and depression assessed with various mixed anxiety and depression symptom scales follow-up: range 3 months to 6 years</p>	<p>The mean change in mixed anxiety and depression score was 0.31 SDs lower (95% CI: -0.40 to -0.22) in people who quit smoking compared to people who continued smoking</p>	<p>2829 (8 observational studies)</p>	<p>⊕⊕⊕⊕ MODERATE^g</p>

Pharmacological interventions for smoking cessation among people with schizophrenia spectrum disorders: a systematic review, meta-analysis, and network meta-analysis

Dan J Siskind, Brian T Wu, Tommy TWong, Joseph Firth, Steve Kisely

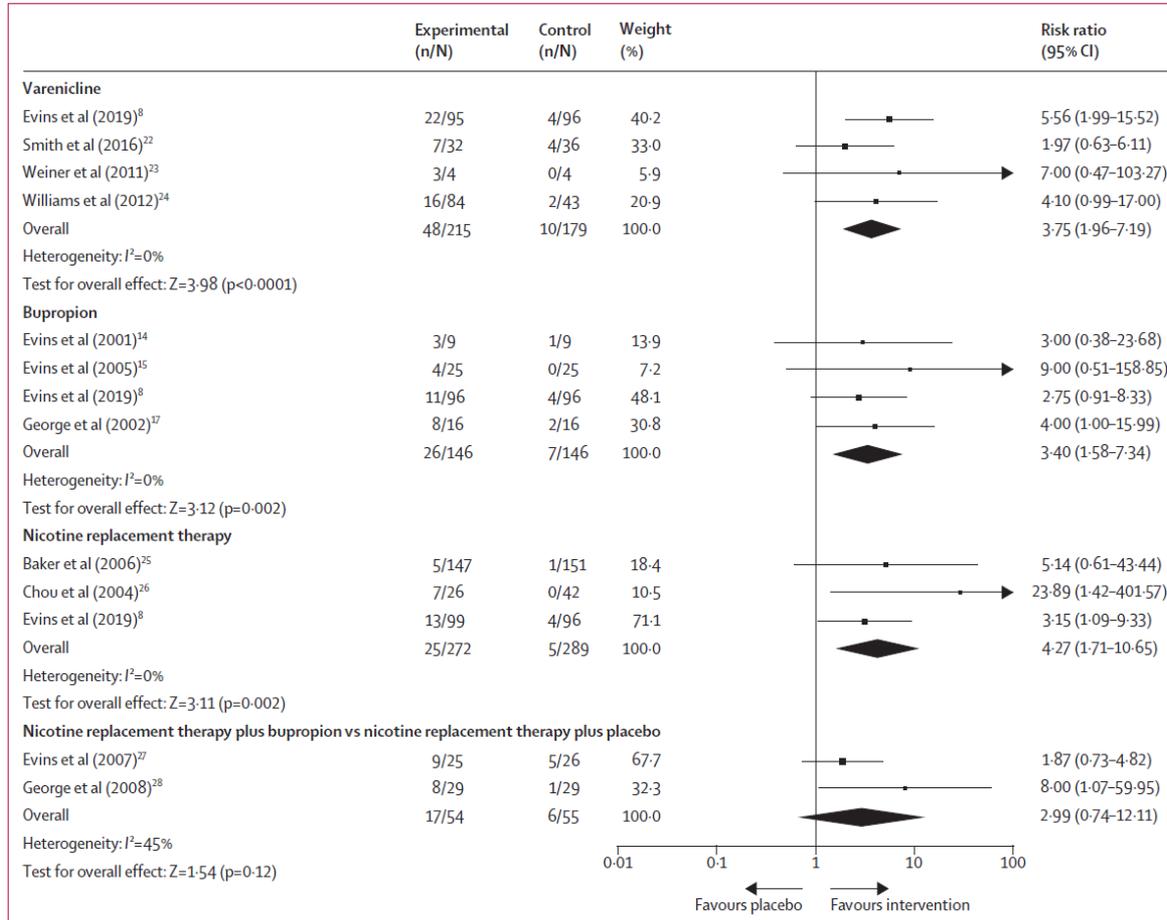


Figure 2: Forest plots of pairwise meta-analyses of smoking abstinence with varenicline (A), bupropion (B), nicotine replacement therapy (C) and nicotine replacement therapy plus bupropion versus nicotine replacement therapy plus placebo (D) in people with schizophrenia spectrum disorders

CO monitoring

level of $< 4\text{ppm}$ separates tobacco smokers from non smokers

mixed studies for biofeedback for improving tobacco cessation



Cytisine

Plant based alkaloid

Short acting alpha4beta2 partial agonist

Licensed in some Eastern and Central European countries for many decades

- one month treatment 4-6 tablets daily for 1-2 weeks then wean

Multiple randomised control trials show efficacy

- Recent trial missed non-inferiority margin against varenicline but a single quit

Available for import as Tabex/Desmo



Questions
