E-Cigarettes: A 21st Century Cessation Device? A Review of the Literature

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THE UNIVERSITY OF AUCKLAND NEW ZEALAND

Disclosures

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Heart Foundation Douglas Senior Fellowship in Heart Health (Prevention)

- Pharmaceutical industry
  - Consultancy, honoraria, benefits in kind, travel support and research grants
- Tobacco industry
  - Purchased very low nicotine content cigarettes for research purposes
- e-cigarette industry
  - Co-investigator on an e-cigarette trial (funded by Health Research Council of New Zealand)

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Objective

- To summarize the scientific evidence for the use of e-cigarettes for smoking cessation
  - Hypothesis generating
  - Hypothesis proving
  - Information ‘waiting in the wings’

What do e-cig users say about quitting?

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- Vapers ‘on-line’ blogs

- On-line user surveys
  - Etter J-F. *BMC Public Health* 2010 (n=81)
  - Etter & Bullen. *Addiction* 2011 (N=3587)
    - 96% helped them quit, 92% helped them reduce cpd
  - Siegel et al. *Am J Prevent Med* 2011 (n=222)
    - First time purchasers in 2010
    - 6 month self-reported PPA = 31% (57% of these people were still using e-cigs at 6 months)
    - 70% quit rate in those than used >20 times per day, 67% reduced cpd.
  - Dawkins et al. *Addiction* 2013, n=1347, 33 countries
    - 76% wanted a complete alternative to smoking
    - 89% had used them to help stop smoking
    - 68% said they were as satisfying as normal cigarettes

What do e-cig users say about quitting?

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Surveys

- **USA panel 2009-10** (n~10,000): found no difference in desire to quit tobacco between e-cig users (n=120) and non-users (n=662) [Regan et al. *Tob Control,* 2013]
- **ITC Four country survey 2010/11** (n=5,939) 85% using them to help quit, 75% to reduce cpd [Adkison et al. *Am Prevent Med* 2013]
- **USA: Quitline callers** (n=2,758) 31% reported 'ever used' or 'tried' , 51% used to quit, 30 day PPA lower (22%, 17%, 31% p<0.001) [Vickerman et al. *Nic Tob Control 2013]*

Case series

- Italy: Caponnetto et al. *J Med Case Reports* 2011
- Italy: Caponnetto et al. *Inter J Clin* Med 2011

Prospective follow-up studies

- Italy: n=40 smokers unwilling to quit, 24 weeks. CA (not even a puff in last 30 days) in 9 (22.5%). [Polosa et al. *BMC Public Heath* 2011]
- Italy: n=100 [Polosa et al. # NCT01194583]

How might e-cigs help with quitting?

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Deliver nicotine at low dose (like NRT)

Help address the behavioural aspects of smoking

- Placebo e-cigs:
  - Cross-over trial (n=40), unmotivated to quit: Reduced desire to smoke, withdrawal and cpd (Bullen et al *Tob Control* 2010)
- Placebo inhalers
  - Trial (n=120), motivated to quit: Higher cessation at 26 week if the handling of cigarettes important to them (Caponnetto et al *ERJ* 2011)
- Very low nicotine content cigarettes
  - Trial (n=1410) motivated to quit: < 1.5mg nicotine content and ≤ 0.05mg nicotine per cigarette. Higher 6 month CA and PP quit rates, time to relapse, and cpd (Walker et al *Addiction* 2012)

Reducing CPD and quitting

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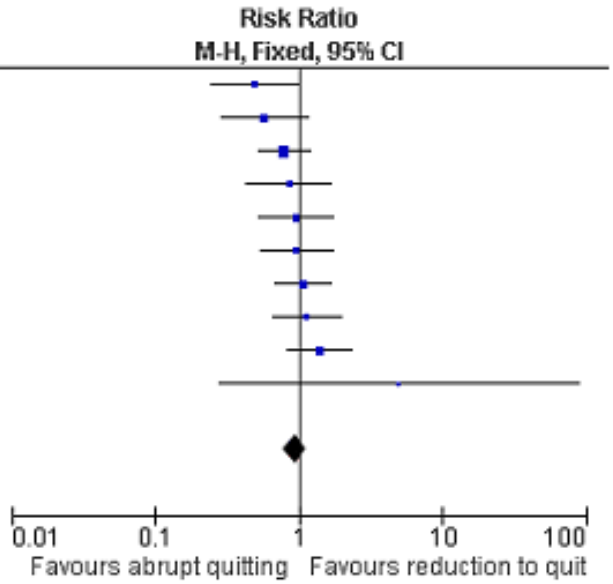
Figure 2. Reduction to quit versus abrupt quitting. Outcome: abstinence

Study or Subgroup	Reduction to quit Events	Reduction to quit Total	Abrupt quitting Events	Abrupt quitting Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Flaxman 1978	9	32	9	16	5.9%	0.50 [0.25, 1.01]
Hughes 2009	12	297	21	299	10.3%	0.58 [0.29, 1.15]
Jerome 1999	43	415	39	296	22.5%	0.79 [0.52, 1.18]
Gunther 1992	12	55	14	55	6.9%	0.86 [0.44, 1.68]
Riley 2005	21	227	19	196	10.1%	0.95 [0.53, 1.72]
Curry 1988	16	65	19	74	8.8%	0.96 [0.54, 1.70]
Etter 2009	32	154	31	160	15.0%	1.07 [0.69, 1.67]
Cinciripini 1995	20	65	17	63	8.5%	1.14 [0.66, 1.97]
Cummings 1988	35	662	23	615	11.8%	1.41 [0.85, 2.36]
Roales-Nieto 1992	2	7	0	7	0.2%	5.00 [0.28, 88.53]
Total (95% CI)		**1979**		**1781**	**100.0%**	**0.94 [0.79, 1.13]**
Total events	202		192			

Heterogeneity: Chi² = 10.41, df = 9 (P = 0.32); I² = 14%

Test for overall effect: Z = 0.65 (P = 0.51)



"Reducing cigarettes smoked before quit day and quitting abruptly, with no prior reduction, produced comparable quit rates"

Lindson et al. Reduction versus abrupt cessation in smokers who want to quit. *Cochrane Systematic Review* 2010

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Published trials

	Caponnetto (2013) (PlosOne)	Bullen (2013) (Lancet)
Population	Unmotivated to quit	Motivated to quit
Inclusion criteria	≥10cpd for at least 5 years, 18-70 years	≥10cpd for last year, ≥18 years
Brand	Categoria	Elusion
Sample size	300	657
Intervention	7.2 mg E-cig 7.2-5.4 mg E-cig 0 mg E-cig No behavioural support	16mg E-cig 21mg NRT patch 0mg E-cig Minimal behavioural support
Intervention period	12 weeks	13 weeks (includes one week pre-quit)
Follow-up	12 months	6 months
Power	75%	80%
Primary outcome	Verified continuous abstinence at 6 months	Verified continuous abstinence at 6 month

Published trials

- **Both trials excluded :**
  - Pregnant or breastfeeding women
  - Current users of smoking cessation therapies, or currently enrolled in a smoking cessation programme or another cessation study
  - Those with cardiovascular disease
  - Those with a serious medical condition
  - Those with symptomatic respiratory disease / poorly controlled asthma or other airways disease (e.g. emphysema, COPD)
  - Those using regular psychotropic medication / poorly controlled psychiatric disorder
  - Those with current or past alcohol abuse / a current chemical dependency other than nicotine
  - Using smokeless tobacco [Italian study only]

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Italian trial

OPEN ACCESS Freely available online

PLOS ONE

EffiCiency and Safety of an eLectronic cigAreTte (ECLAT) as Tobacco Cigarettes Substitute: A Prospective 12-Month Randomized Control Design Study

Pasquale Caponnetto[1,2], Davide Campagna[1,2], Fabio Cibella[3], Jaymin B. Morjaria[4], Massimo Caruso[2], Cristina Russo[1,2], Riccardo Polosa[1,2]*

1 Centro per la Prevenzione e Cura del Tabagismo, Azienda Ospedaliero-Universitaria "Policlinico-V. Emanuele", Università di Catania, Catania, Italy, **2** Institute of Internal Medicine, S. Marta Hospital, Azienda Ospedaliero-Universitaria "Policlinico-V. Emanuele", Università di Catania, Catania, Italy, **3** National Research Council of Italy, Institute of Biomedicine and Molecular Immunology, Palermo, Italy, **4** Division of Cardiovascular and Respiratory Studies, Hull York Medical School, University of Hull, Castle Hill Hospital, Cottingham, United Kingdom

Abstract

Background: Electronic cigarettes (e-cigarettes) are becoming increasingly popular with smokers worldwide. Users report buying them to help quit smoking, to reduce cigarette consumption, to relieve tobacco withdrawal symptoms, and to continue having a 'smoking' experience, but with reduced health risks. Research on e-cigarettes is urgently needed in order to ensure that the decisions of regulators, healthcare providers and consumers are based on science. *Methods* ECLAT is a prospective 12-month randomized, controlled trial that evaluates smoking reduction/abstinence in 300 smokers not intending to quit experimenting two different nicotine strengths of a popular e-cigarette model ('Categoria'; Arbi Group Srl, Italy) compared to its non-nicotine choice. GroupA (n = 100) received 7.2 mg nicotine cartridges for 12 weeks; GroupB (n = 100), a 6-week 7.2 mg nicotine cartridges followed by a further 6-week 5.4 mg nicotine cartridges; GroupC (n = 100) received no-nicotine cartridges for 12 weeks. The study consisted of nine visits during which cig/day use and exhaled carbon monoxide (eCO) levels were measured. Smoking reduction and abstinence rates were calculated. Adverse events and product preferences were also reviewed.

Results: Declines in cig/day use and eCO levels were observed at each study visits in all three study groups ($p<0.001$ vs baseline), with no consistent differences among study groups. Smoking reduction was documented in 22.3% and 10.3% at week-12 and week-52 respectively. Complete abstinence from tobacco smoking was documented in 10.7% and 8.7% at week-12 and week-52 respectively. A substantial decrease in adverse events from baseline was observed and withdrawal symptoms were infrequently reported during the study. Participants' perception and acceptance of the product under investigation was satisfactory.

Conclusion: In smokers not intending to quit, the use of e-cigarettes, with or without nicotine, decreased cigarette consumption and elicited enduring tobacco abstinence without causing significant side effects.

Trial Registration: ClinicalTrials.gov NCT01164072

Caponnetto et al *PlosOne*, 2013, June

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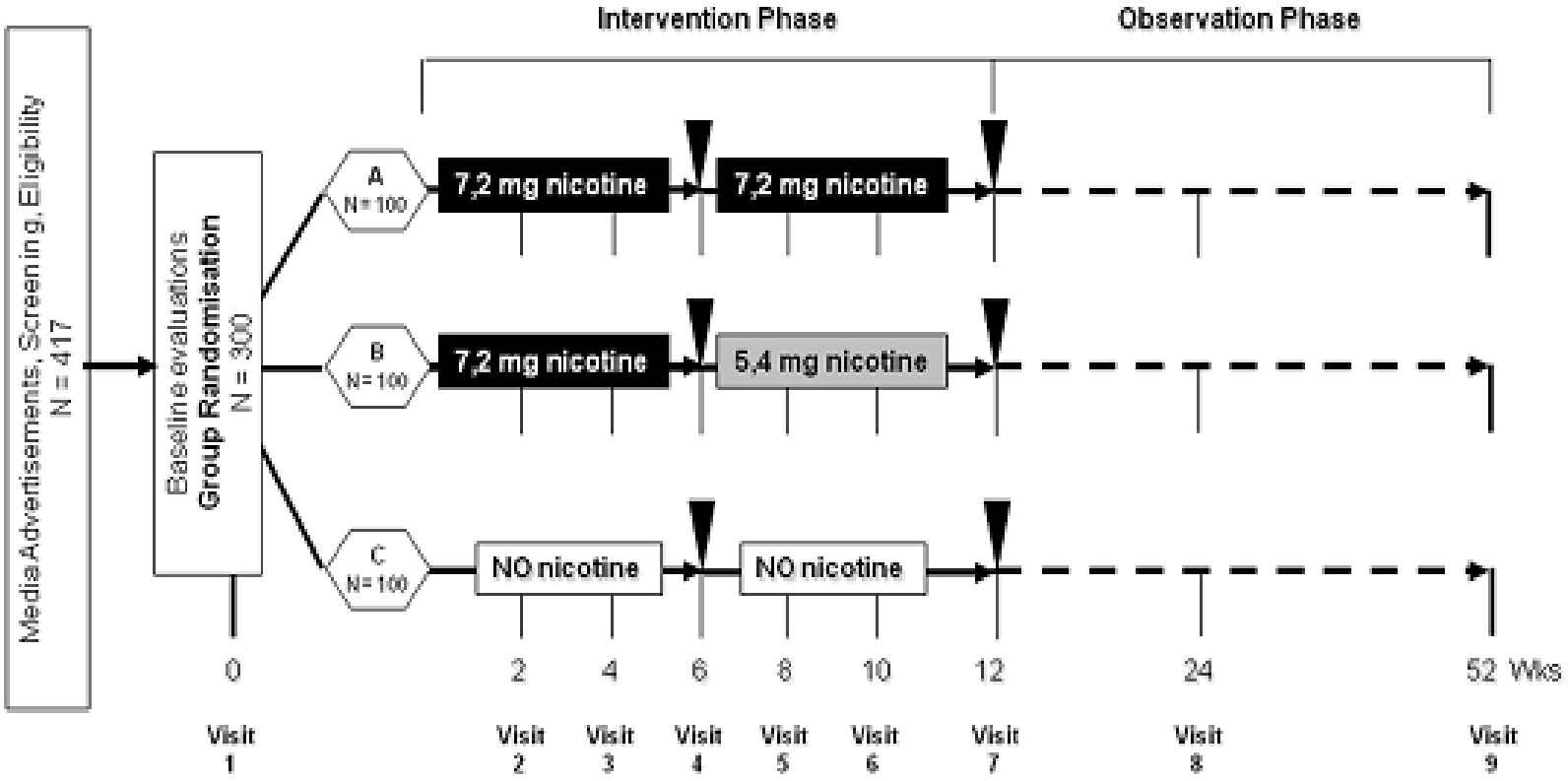
Study design



12 month lost to follow- up: 35%, 37%, 45% respectively

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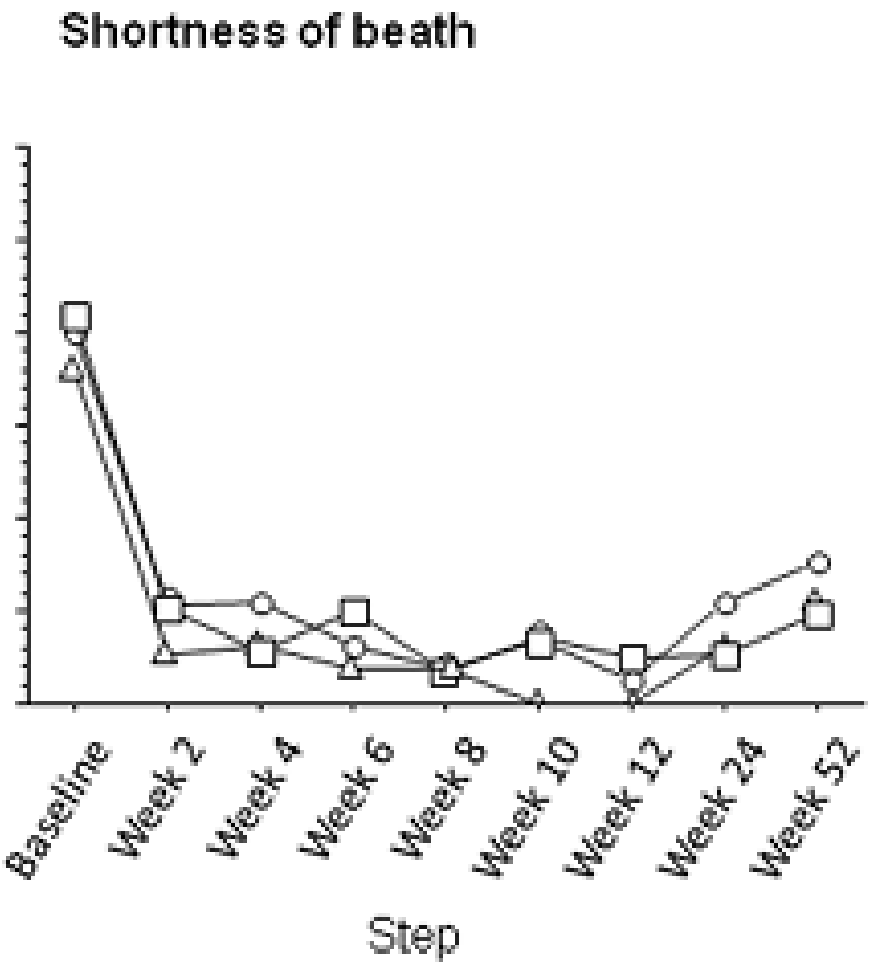
Validated abstinence (not even a puff)

	Reduction rates (%)			Quit rates (%)			
Groups	A	B	C	A	B	C	p value*
Week-2	29.0	38.0	36.0	20.0	12.0	5.0	0.02
Week-4	29.0	33.0	29.0	14.0	14.0	6.0	0.25
Week-6	24.0	26.0	25.0	11.0	15.0	2.0	0.03
Week-8	23.0	21.0	20.0	9.0	12.0	4.0	0.31
Week-10	26.0	15.0	19.0	7.0	15.0	3.0	0.01
Week-12	26.0	20.0	21.0	11.0	17.0	4.0	0.04
Week-24	17.0	19.0	15.0	12.0	10.0	5.0	0.39
Week-52	10.0	9.0	12.0	13.0	9.0	4.0	0.24

ITT analysis

Safety data

- Collected long term (12 months)
-
- Dry cough, mouth irritation, shortness of breathe, throat irritation and headache
- No difference in frequency of side effects between groups
- A significant reduction in frequency of side effects over time
- No serious side effects reported
- No significant changes in body weight, resting heart rate or blood pressure over time or between groups



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New Zealand trial

Electronic cigarettes for smoking cessation: a randomised controlled trial

Christopher Bullen, Colin Howe, Murray Laugesen, Hayden McRobbie, Varsha Parag, Jonathan Williman, Natalie Walker

Summary

Background Electronic cigarettes (e-cigarettes) can deliver nicotine and mitigate tobacco withdrawal and are used by many smokers to assist quit attempts. We investigated whether e-cigarettes are more effective than nicotine patches at helping smokers to quit.

Methods We did this pragmatic randomised-controlled superiority trial in Auckland, New Zealand, between Sept 6, 2011, and July 5, 2013. Adult (≥18 years) smokers wanting to quit were randomised (with computerised block randomisation, block size nine, stratified by ethnicity [Māori; Pacific; or non-Māori, non-Pacific], sex [men or women], and level of nicotine dependence [>5 or ≤5 Fagerström test for nicotine dependence]) in a 4:4:1 ratio to 16 mg nicotine e-cigarettes, nicotine patches (21 mg patch, one daily), or placebo e-cigarettes (no nicotine), from 1 week before until 12 weeks after quit day, with low intensity behavioural support via voluntary telephone counselling. The primary outcome was biochemically verified continuous abstinence at 6 months (exhaled breath carbon monoxide measurement <10 ppm). Primary analysis was by intention to treat. This trial is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12610000866000.

Findings 657 people were randomised (289 to nicotine e-cigarettes, 295 to patches, and 73 to placebo e-cigarettes) and were included in the intention-to-treat analysis. At 6 months, verified abstinence was 7·3% (21 of 289) with nicotine e-cigarettes, 5·8% (17 of 295) with patches, and 4·1% (three of 73) with placebo e-cigarettes (risk difference for nicotine e-cigarette *vs* patches 1·51 [95% CI −2·49 to 5·51]; for nicotine e-cigarettes *vs* placebo e-cigarettes 3·16 [95% CI −2·29 to 8·61]). Achievement of abstinence was substantially lower than we anticipated for the power calculation, thus we had insufficient statistical power to conclude superiority of nicotine e-cigarettes to patches or to placebo e-cigarettes. We identified no significant differences in adverse events, with 137 events in the nicotine e-cigarettes group, 119 events in the patches group, and 36 events in the placebo e-cigarettes group. We noted no evidence of an association between adverse events and study product.

Interpretation E-cigarettes, with or without nicotine, were modestly effective at helping smokers to quit, with similar achievement of abstinence as with nicotine patches, and few adverse events. Uncertainty exists about the place of e-cigarettes in tobacco control, and more research is urgently needed to clearly establish their overall benefits and harms at both individual and population levels.

Funding Health Research Council of New Zealand.

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Bullen et al *Lancet* 2013, 7th September

Context

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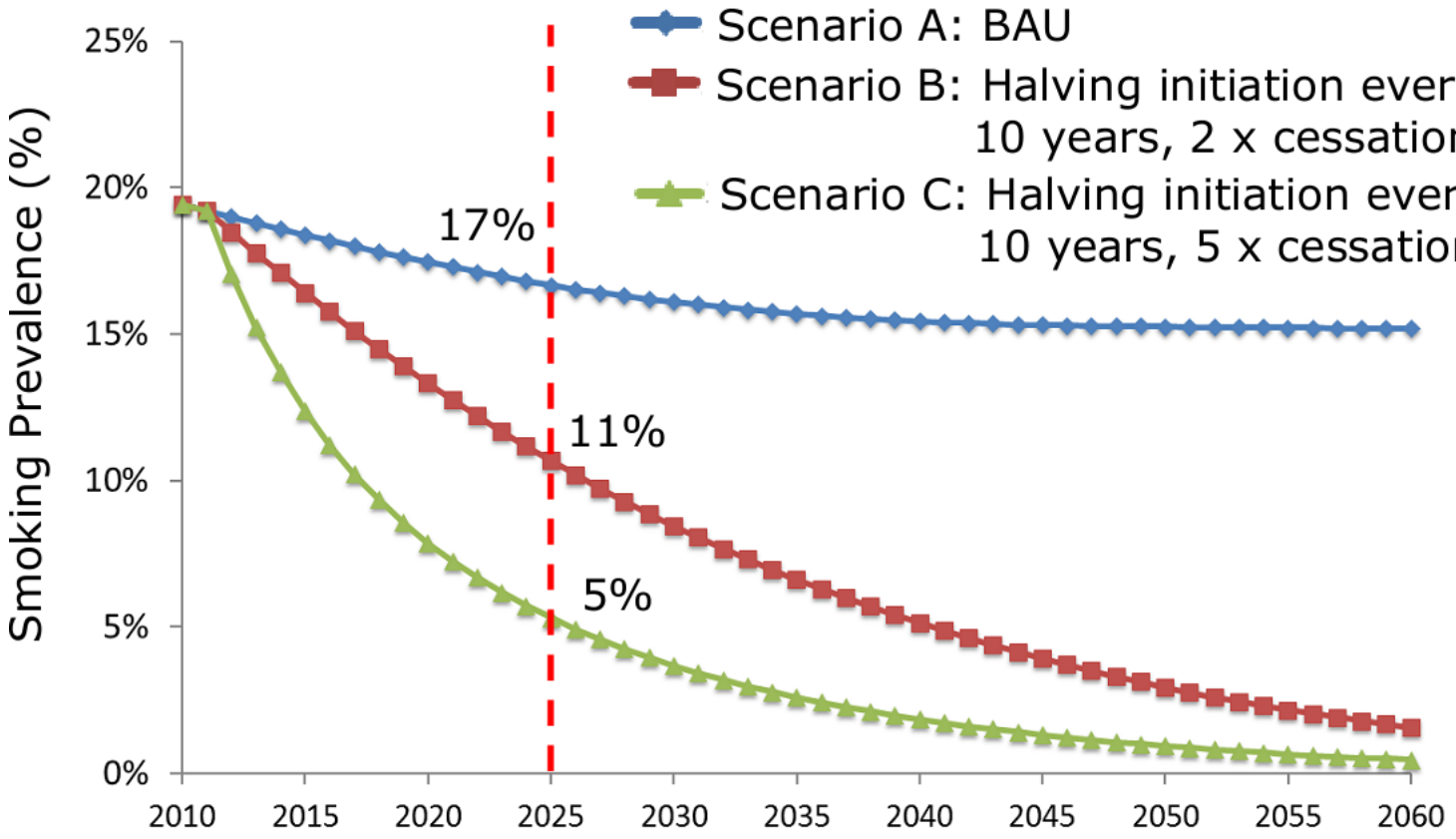
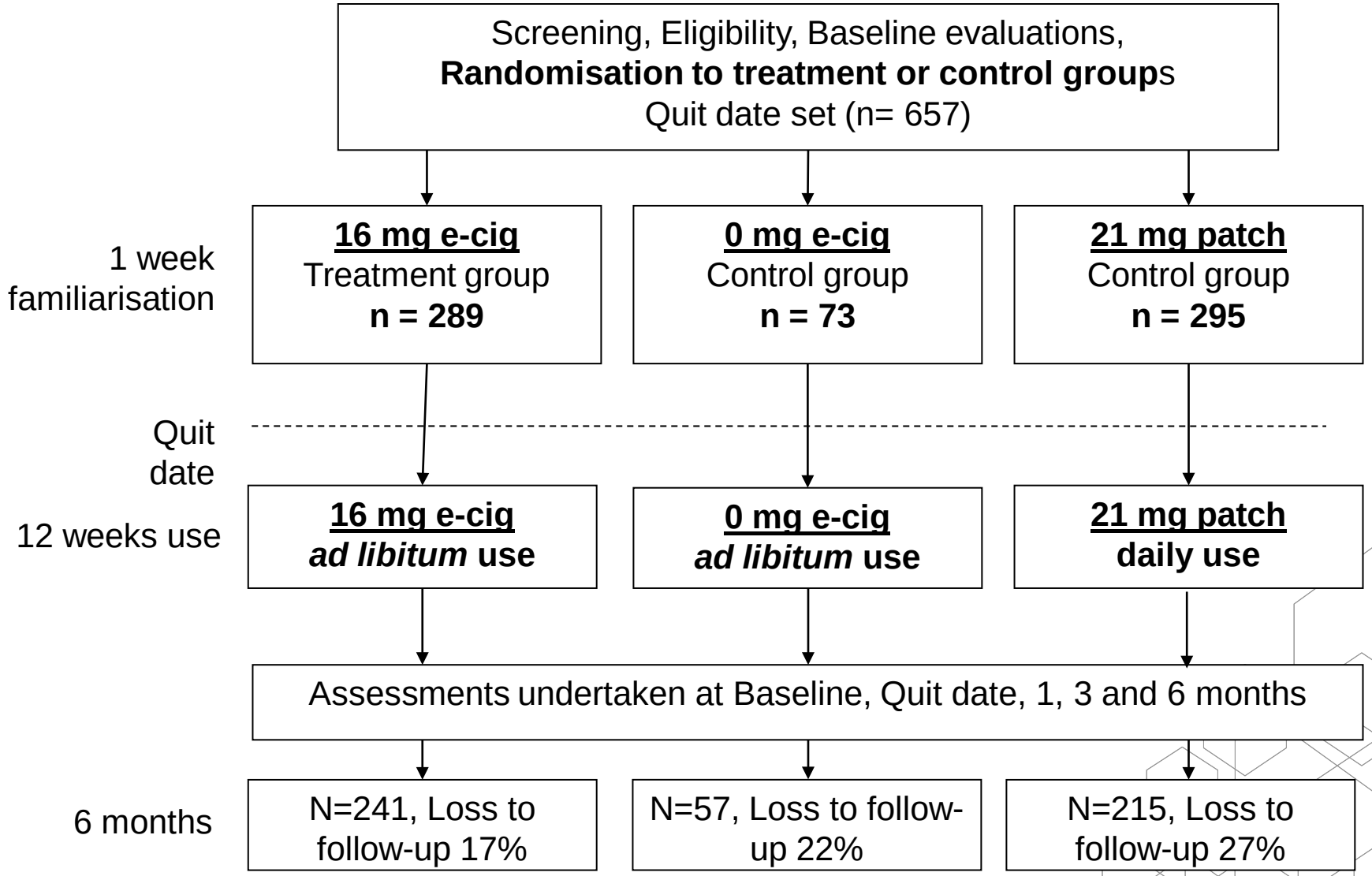
smokefree AOTEAROA NEW ZEALAND 2025



Ikeda et al. Tobacco Control (in press).

NOBODY SMOKES HERE ANY MORE

Study design



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Baseline

	16mg e-cig (n=289)	Patch (n=295)	0mg e-cig (n=73)
Age (years)	43.6 (12.7)	40.4 (13.0)	43.2 (12.4)
Women	178 (62%)	182 (62%)	45 (62%)
Maori ethnicity	95 (33%)	95 (32%)	23 (32%)
Education < year 12 or none	150 (52%)	123 (42%)	38 (52%)
Cigarettes per day	18.4 (7.2)	17.6 (6.0)	17.7 (5.6)
Age started smoking (years)	15.6 (4.7)	15.2 (3.8)	15.7 (5.1)
Years smoked	25.9 (13.1)	23.5 (12.9)	24.8 (13.7)
Type of tobacco smoked			
- Factory only	167 (58%)	167 (57%)	47 (64%)
- RYO only	92 (32%)	92 (31%)	21 (29%)
- Both	30 (10%)	35 (12%)	5 (7%)
Lives with other smokers	151 (52%)	149 (51%)	42 (58%)
>= 1 quit attempt in past 12 months	158 (55%)	169 (57%)	39 (53%)
FTND score	5.6 (2.0)	5.5 (2.0)	5.5 (2.0)
GN-SBQ Score	20.1 (7.9)	20.1 (8.4)	21.4 (8.6)
Self-efficacy	3.7 (1.0)	3.7 (0.9)	3.6 (1.0)
AUTOS	22.6 (7.2)	23.1 (7.6)	23.4 (7.3)

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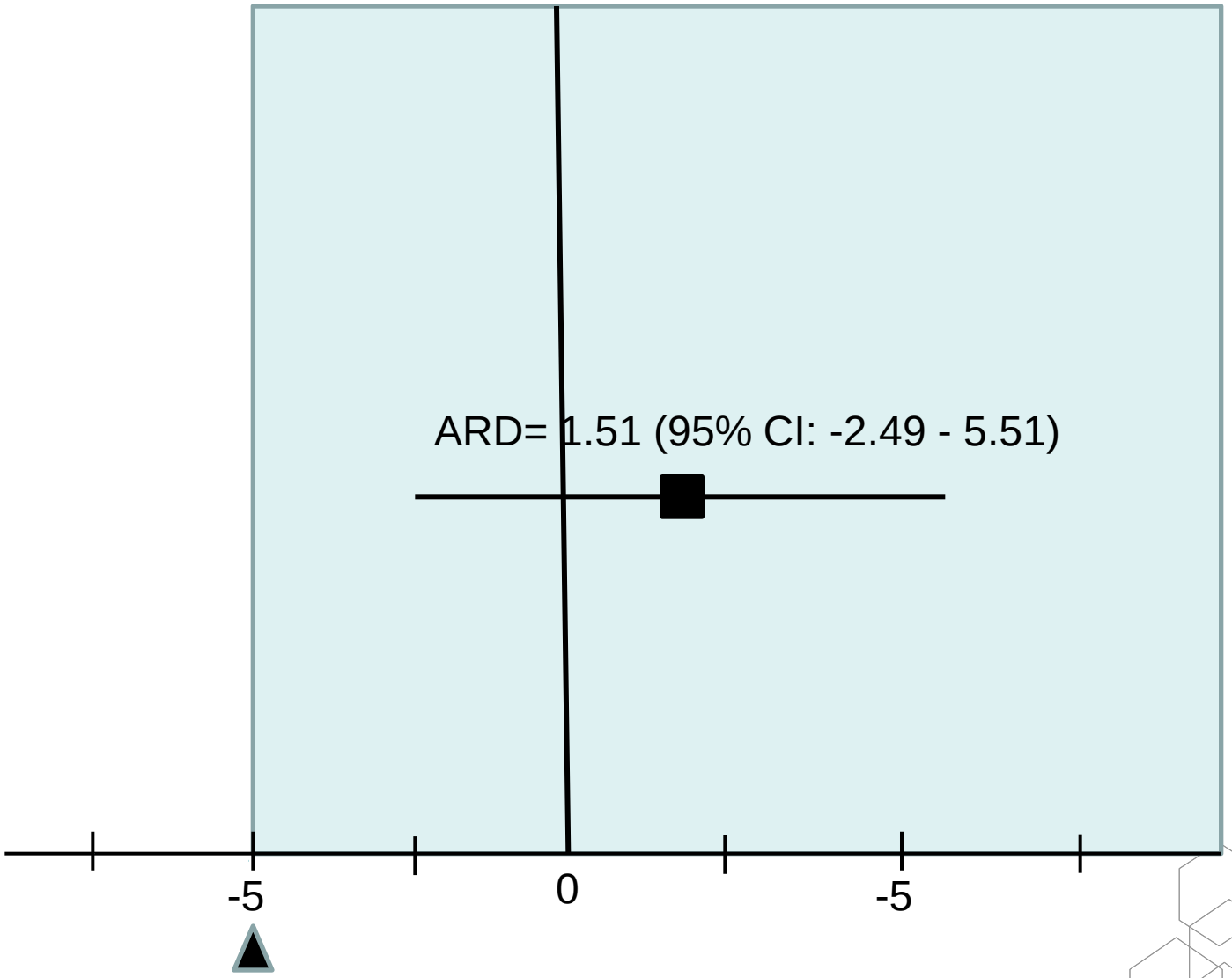
16mg e-cig versus patch

	16 mg e-cig (N=289)	Patches (N=295)	P-value	Rel Risk (95% CI)	Risk Diff (95% CI)
Continuous abstinence					
One month	67(23.2%)	47 (15.9%)	0.03	1.46 (1.04-2.04)	7.25 (0.84-13.66)
Three months	38 (13.1%)	27 (9.2%)	0.12	1.44 (0.90-2.33)	4.00 (-1.10-9.10)
Six months (primary outcome)	21 (7.3%)	17 (5.8%)	0.46	1.26 (0.68-2.34)	1.51 (-2.49-5.51)
7-day point prevalence					
One month	69 (23.9%)	51 (17.3%)	0.05	1.38 (1.00-1.91)	6.59 (0.05-13.13)
Three months	62 (21.5%)	50 (17.0%)	0.17	1.27 (0.91-1.77)	4.50 (-1.88-10.88)
Six months	61 (21.1%)	46 (15.6%)	0.09	1.35 (0.96-1.91)	5.52 (-0.75-11.79)

Non-inferiority



16mg e-cig versus 0mg e-cig

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	16 mg e-cig (N=289)	0mg e-cig (N=73)	P-value	Rel Risk (95% CI)	Risk Diff (95% CI)
Continuous abstinence					
One month	67(23.2%)	12 (16.4%)	0.21	1.41 (0.81-2.46)	6.74 (-3.06-16.54)
Three months	38 (13.1%)	5 (6.8%)	0.14	1.92 (0.78-4.70)	6.30 (-0.68-13.28)
Six months (primary outcome)	21 (7.3%)	3 (4.1%)	0.44	1.77 (0.54-5.77)	3.16 (-2.29-8.61)
7-day point prevalence					
One month	69 (23.9%)	12 (16.4%)	0.17	1.45 (0.83-2.53)	7.44 (-2.38-17.26)
Three months	62 (21.5%)	12 (16.4%)	0.34	1.31 (0.74-2.29)	5.01 (-4.72-14.74)
Six months	61 (21.1%)	16 (21.9%)	0.88	0.96 (0.59-1.57)	-0.81 (-11.40-9.78)

Time to first lapse

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Summary of number of events and censored values	Total	Relapsed		Censored		Duration (days)			
	n	n	%	n	%	Median	Lower CI	Upper CI	Mean
16 mg ENDS	289	197	68.2	92	31.8	35	15	56	74.5
Nicotine patch	295	200	67.8	95	32.2	14	8	18	54.1

Log-rank test P-value = <0.0001

Summary of number of events and censored values	Total	Relapsed		Censored		Duration (days)			
	n	n	%	n	%	Median	Lower CI	Upper CI	Mean
16 mg ENDS	289	197	68.2	92	31.8	35	15	56	74.5
0 mg ENDS	73	51	69.9	22	30.1	12	5	34	69.8

Log-rank test P-value = 0.0957

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Change from baseline in CPD

	Nicotine e-cigarette		Patches		Difference (nicotine e-cigarette–patches)		
	Mean	(SE)	Mean	(SE)	Mean	(SE)	p value
Overall	11·1	(0·4)	9·1	(0·4	2·0	(0·5)	<0·0001
1 month	12·9	(0·4)	10·5	(0·4)	2·4	(0·6)	<0·0001
3 months	10·8	(0·4)	9·1	(0·4)	1·7	(0·6)	0·006
6 months	9·7	(0·4)	7·7	(0·4)	1·9	(0·6)	0·0017

*For those reporting smoking at least one cigarette in past 7 days.

Table 4: **Change from baseline in cigarettes consumed per day during follow-up period, nicotine e-cigarette and patches***

Reduced cpd by 50% at 6 months

- 16mg e-cig = 57% of smokers
- 0 mg e-cig = 45% of smokers
- Patch = 41% of smokers

Reduced cpd by 25% at 6 months

- 16mg e-cig = 71% of smokers
- 0 mg e-cig = 63% of smokers
- Patch = 55% of smokers

Safety – number of events

	16mg e-cig	Patch	0mg e-cig
Total	137 (in 107 people)	119 (in 96 people)	36 (in 26 people)
Event type - Serious - Non-serious	 27 (20%) 110 (80%)	 14 (12%) 105 (88%)	 5 (14%) 31 (86%)
Related to treatment - Definitely - Probably - Possibly - Unrelated	 0 1 (1%) 5 (4%) 131 (96%)	 1 (1%) 1 (1%) 4 (3%) 113 (95%)	 0 1 (3%) 1 (3%) 34 (94%)

16mg e-cig: 0.8 events/person/month
0mg e-cig: 0.9 events/person/month
Patch: 0.8 events/person/month

Incidence rate ratio = 1.05, 95% CI: 0.82-1.34, p=0.7

Autonomy over smoking (AUTOS)

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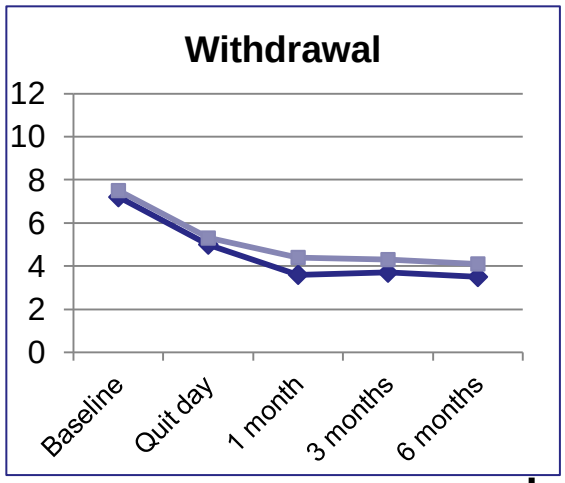

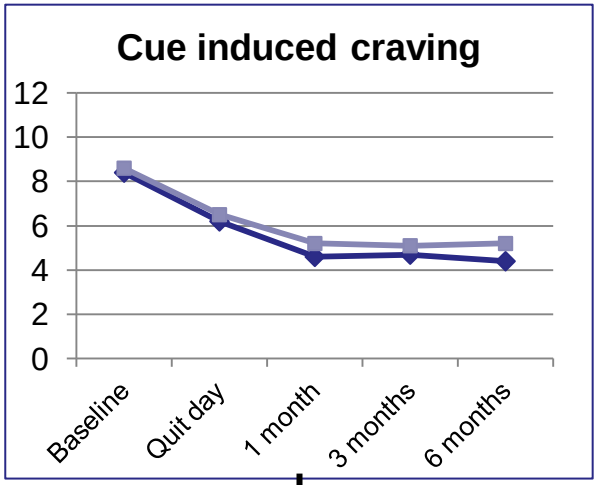

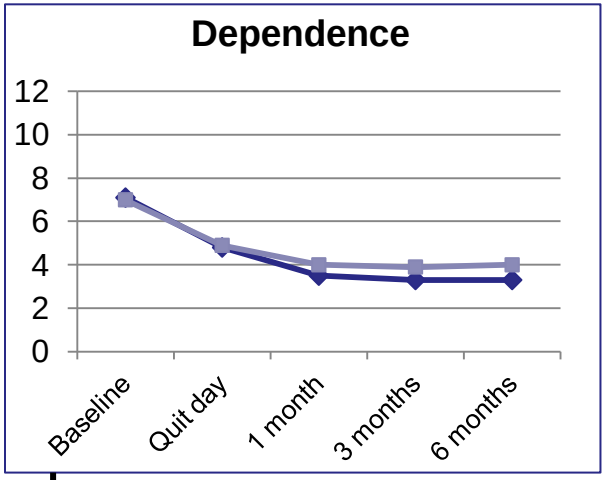

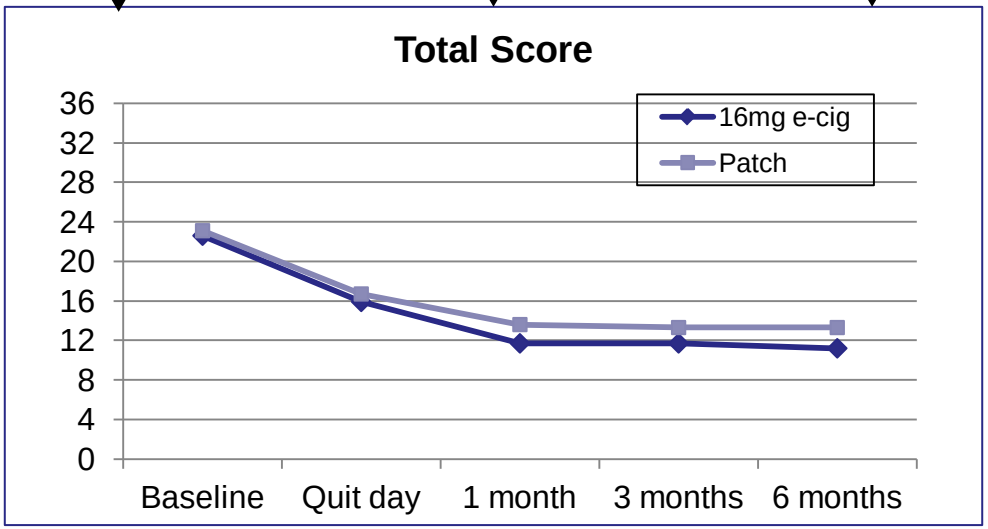

Change from baseline to six months for 16mg e-cig vs patch:

Withdrawal: p= 0.0424
Craving: p= 0.0378
Dependence= 0.0115
Total: p= 0.0181

Compliance

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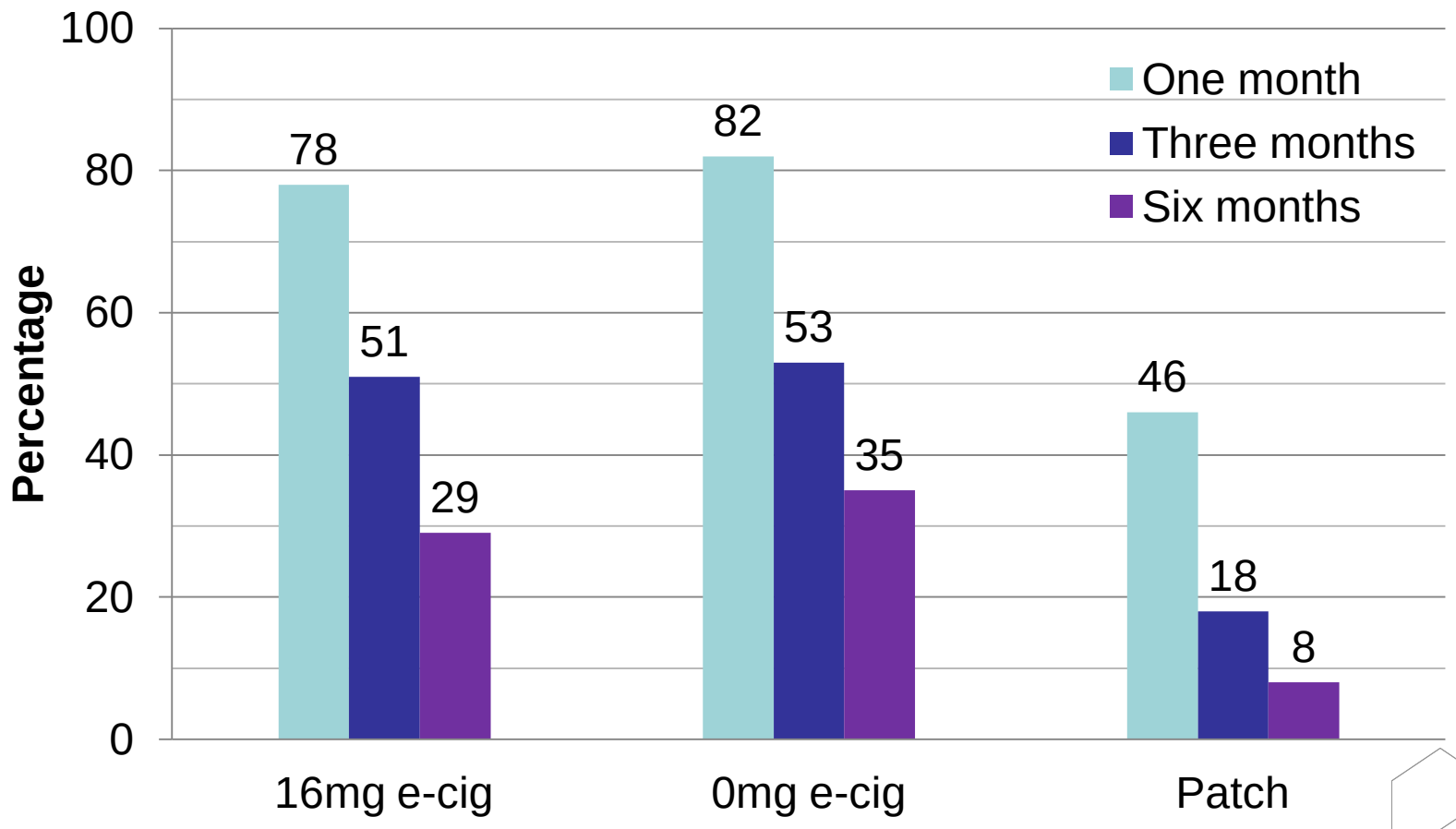

Poor compliance to NRT well known:

- Walker et al. Addiction 2011
- Etter et al. Nicotine & Tobacco Research 2013.

Amount of product used

16mg e-cig (mean)

- 1 month = 1.3 cartridges per day
- 3 months = 1.1 cartridges per day
- 6 months = 0.7 cartridges per day

0mg e-cig (mean)

- 1 month = 1.1 cartridges per day
- 3 months = 1.2 cartridges per day
- 6 months = 0.7 cartridges per day

Patches

- 1 per day as requested

Few used other cessation products

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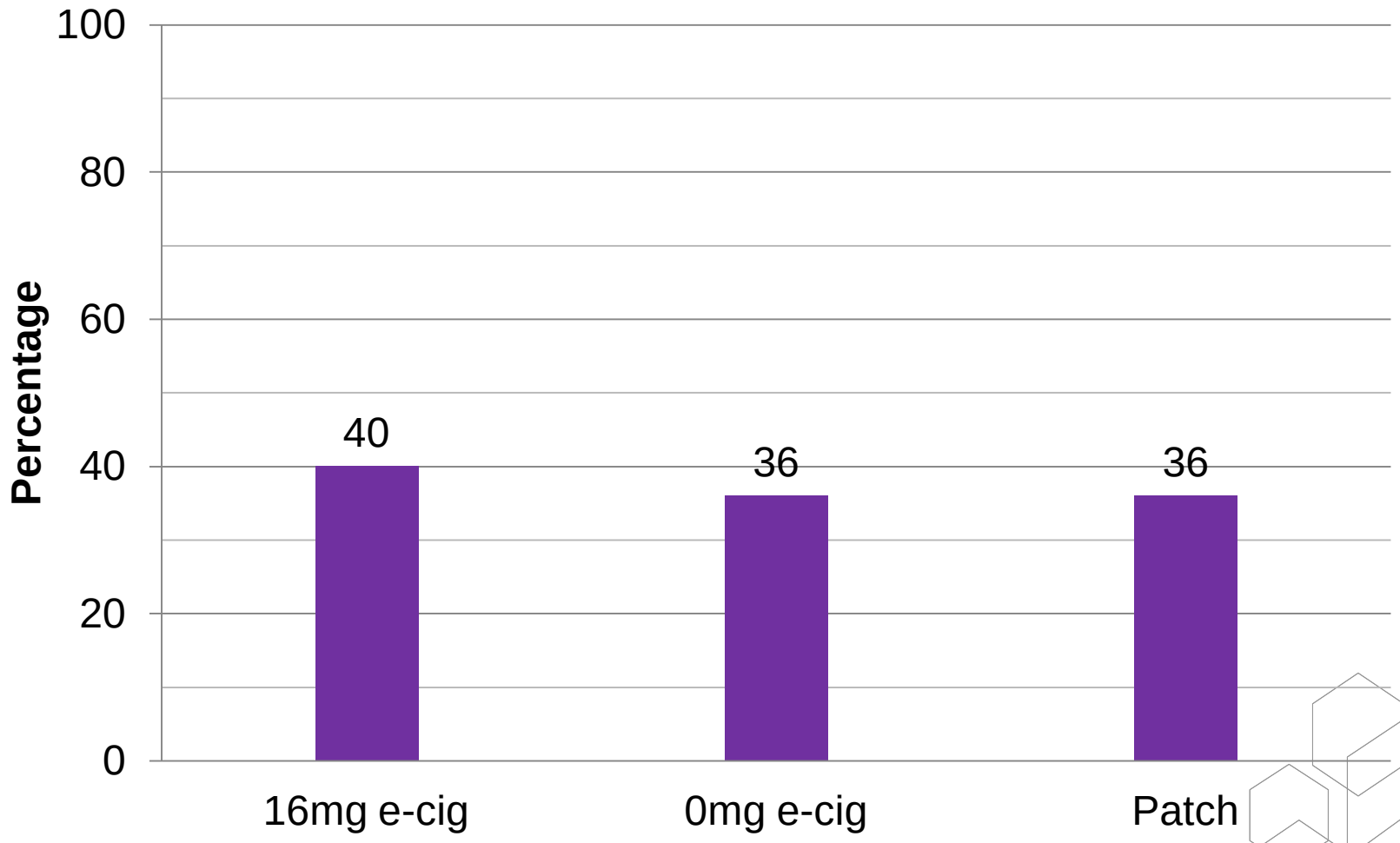
Accessed Quitline support



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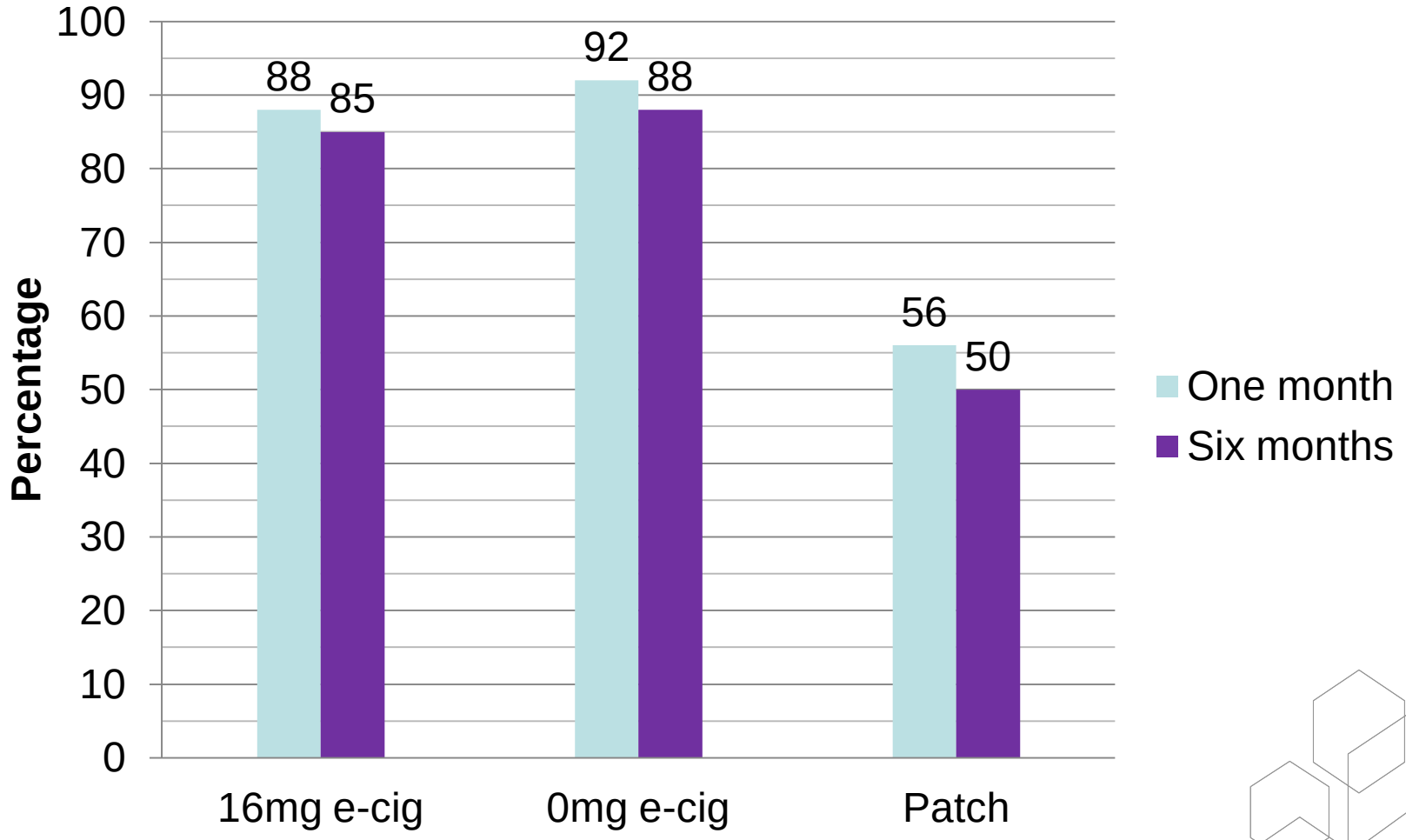
Would recommend to a friend



Trial strengths

- Largest trials conducted to date with cessation outcome
- Focus was on sustained abstinence
- Pragmatic trial looking at real-world effectiveness
- The low quit rate is similar to that seen in NRT trials with limited behavioural support

Stead et al. NRT for smoking cessation. *Cochrane Review* 2012

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Limitations, criticisms, comments

"…I'm so disappointed in you…. the trial was underpowered!"

- The trial was correctly powered to detect the chosen effect sizes
  - 10% for 16mg e-cig vs patch, 15% for 16mg e-cig vs 0mg e-cig; 15% QR in 0mg e-cig and 20% QR patch.
- Yes, the effect size and estimates of abstinence we used now appear overly optimistic
- At least we narrowed down the true difference
- Non-inferiority design may be a better choice.

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Limitations, criticisms, comments

“Did the e-cigarette you used deliver any nicotine?”

- Nicotine level was less than labelled
  - Liquid analysis: 10-16mg per mL
  - Vapour analysis: 300 puffs from one cartridge = 3-6 mg nicotine (about 1-5 cigarettes)
- But low levels of nicotine may be sufficient
  - VLNC cigarette have sufficient nicotine to occupy ~ 26% of the main receptors

Goniewicz M et al. Nicotine Tob Res 2013; 15: 158-66
Brody A et al, Neuropsychopharmacology 2009; 34: 282-9
http://www.healthnz.co.nz/HealthNZstandard_Ecigs.htm

Limitations, criticisms, comments

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"How generalisable are these findings?"

	Bullen (2013)	3 NZ Quitline trials	Caponnetto (2013)
	(n=657)	(n=3,900)	(n=300)
Age (years)	42	41	44
Women	62%	60%	37%
Māori ethnicity	33%	24-28%	-
Education: < 12 years or none	49%	53%	31% low
Cigarettes per day (mean)	18	20	20* (15-25)
Self-efficacy	3.7	4.2	-
≥1 quit attempt in past 12 months	55%	29%	51%**
Mean FTND score	5.5	6.2	5.8

* Medium (IQR)
**Past attempts to quit

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Limitations, criticisms, comments

"How many people in the study would have been current or previous users of e-cigarettes?"

- NZ survey (2011) of 840 current smokers and recent quitters
  - 7% had ever purchased an e-cigarette
  - More likely to be aged 18-24 years & have a medium level income
  - No difference by gender, ethnicity , education, or quit attempts
- Given demographics of trial population, previous use is likely to be < 7%

Li J et al, NZ Med J May 2013

Limitations, criticisms, comments

"Access to the intervention differed between the groups"

- E-cigs were posted and provided free
- NRT via posted Quitcard, visit to Pharmacy and not free (US$4)
- A NZ trial comparing free access to selection box of NRT vs Quitcard system found no effect on quit rates at six months
  - But did delay time to relapse (medium 70 days vs 28 days)

Walker et al, *Addiction* 2011

Limitations, criticisms, comments

“There was differential drop-out between the treatment arms”

- ❑ 27% in patch compared to 22% and 17% in E-cigs
- ❑Baseline characteristics: Those that withdrew/LTFU were no different to those that participated
  - But slightly younger and less educated in ‘patch’ group
- ❑16 withdrew in patch group
  - 5 because they wanted e-cigs
  - 8 for no reason
  - 3 other

Summary of trial evidence

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In smokers who use e-cigs for 12-13 weeks with little to no behavioural support

- Six month quit rates are low (5-12%)
- Quit rates are similar for nicotine vs nicotine-free e-cigs
- Cigarette consumption is reduced
- Mild, self limiting side effects are reported
- E-cigs are highly acceptable to users

- In those motivated to quit:
  - E-cigs are of similar effectiveness to nicotine patches
  - Nicotine e-cigs delay relapse back to regular smoking

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Registered unpublished trials

	Gartner (Australia)	Arouni (USA)	Hajek (UK, Spain, Czech Rep)
Population	Varying motivation to quit	Motivated to quit	Motivated to quit
Product	18.6 mg Vype Red	STAM CE4 eGo Clearmizer	Gamucci
Sample size	1600	240	220
Intervention	• NRT choice for short term use • NRT choice for short and/or long term use • Choice of NRT and 'cigarette like' nicotine products for short and/or long term use	• e-cig (strength unknown) • 2 and 4 mg NRT gum	• Standard care (Varenicline or NRT plus behavioural support) • Standard care plus e-cig (bold strength)
Intervention period	3 weeks free, 6 weeks discounted	? 12 weeks	4 weeks
Follow-up	12 months	12 weeks	24 weeks
Power	80%	?	80%
Primary outcome	Self-reported 12 month continuous abstinence	Verified 12 week continuous abstinence?	Verified 4 week continuous abstinence

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Cochrane review

[Intervention Protocol]

Electronic cigarettes for smoking cessation and reduction

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

The primary objective is to evaluate the efficacy of electronic cigarettes (ECs) for helping people who smoke to achieve long-term cessation.

The secondary objectives are to evaluate the efficacy of ECs for helping smokers to substantially reduce cigarette use and to assess potential adverse effects.

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E-cigarettes: A 21st Century Cessation Device?

Yes, for some people