Do electronic cigarettes impact on smoking cessation?

Elisabeth Quoix

15-18 April 2015, Geneva, Switzerland

Organisers

Partners

Electronic cigarette is a battery-powered vaporizer producing an aerosol thanks to a heating element that atomizes a liquid solution. E-liquids usually contain a mixture of propylene glycol, glycerin, various flavorings with or without nicotine

Components of e-cigarettes (1)

- All e-cigarettes contain a mouthpiece, a micro-electrical circuit, a vaporiser and a rechargeable lithium ion battery
- The solution (liquid) is in replaceable cartridges or used to fill a reservoir that contains propylene glycol and/or glycerin + flavourings +/-nicotine

Bullen C BMC Public Health 2013;13:210

Components (2)

- When the user draws air through the e-cigarette, the micro-electrical circuit activates an electric coil to heat and vaporise the liquid, creating a visible cloud of mist

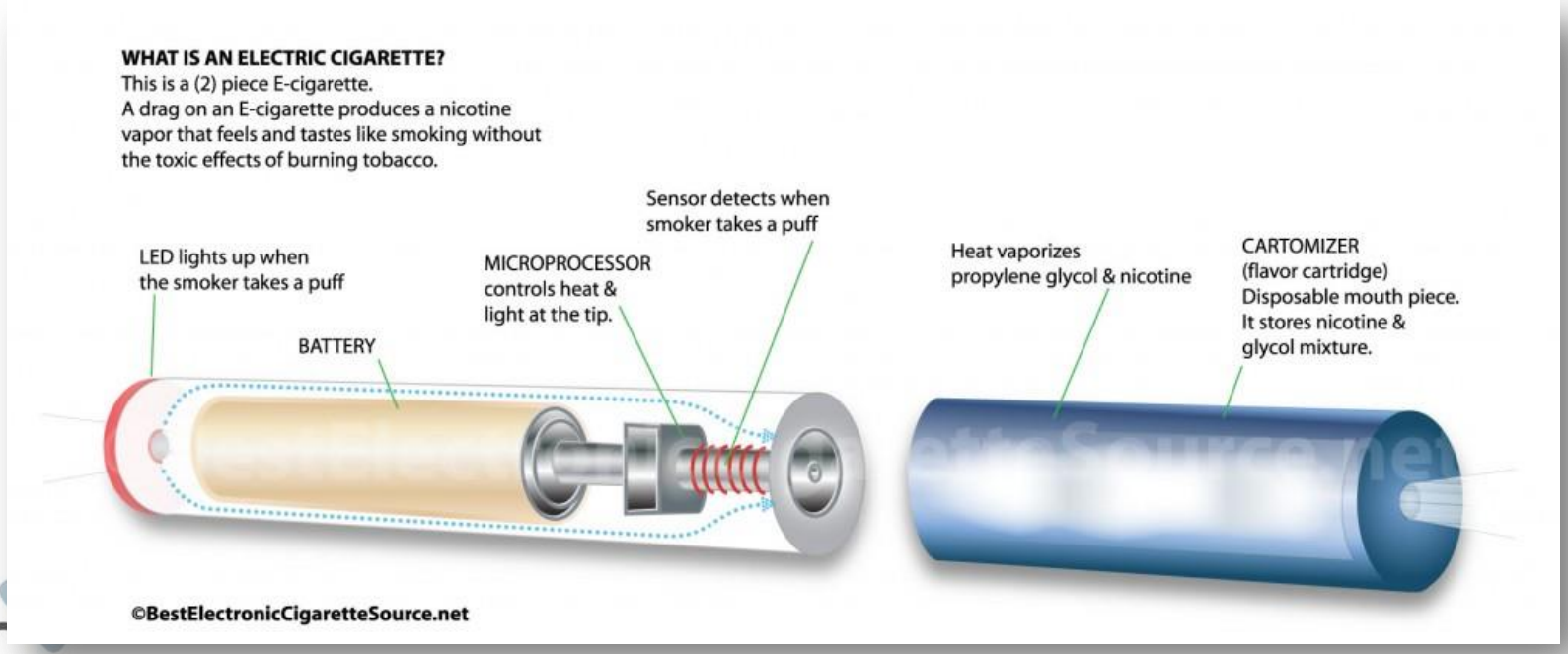


Table 2. Major Studies on Use of ENDS for Smoking Cessation

Author	Study Type and Population	Sample Size	Results
Etter and Bullen[42]	Online survey of e-cigarette users recruited from Web sites who were current or former combustible cigarette smokers	3,567	92% of users who were current smokers reported e-cigarettes helped them to reduce smoking; 96% of former smokers reported product helped them to quit smoking; 79% used e-cigarettes to deal with craving; 67% used e-cigarettes to deal with tobacco withdrawal symptoms
Brown et al[57]	Survey of adults in United Kingdom who tried to quit smoking in last year	6,000	e-cigarette users had higher quit rate (20%) than those who used NRTs (10%) or no smoking cessation aids (15%)
Adkison et al[5]	Four-country cross-sectional survey of current and/or former smokers	5,939	85% of current e-cigarette users reported using them to quit smoking; only 11% reported having quit, and there were no significant differences in quit rates between e-cigarette users and nonusers
Vickerman et al[58]	Survey of state telephone quit line participants registered for cessation services	2,758	e-cigarette users were less likely to quit smoking compared with never-users of e-cigarettes
Grana et al[59]	National sample of current US smokers recruited from Web-enabled panel	1,549	e-cigarette use at baseline did not predict smoking cessation 1 year later among smokers, regardless of whether they said they were using ENDS to quit or not
Polosa et al[60,61]	Observational study of smokers given access to e-cigarettes for 6 months	40	23% and 13% abstinence rates at 6 and 24 months, respectively; rates did not substantially differ from those found in similarly designed observational studies using NRT products[62,63]
Caponnetto et al[64]	Clinical trial of smokers assigned e-cigarettes with and without nicotine	300	No significant differences in abstinence rates were observed between smokers assigned e-cigarettes with and without nicotine; overall abstinence rates were similar to those found in trials where NRTs were provided for ≥ 6 months to reduce cigarette use[65-68]
Bullen et al[46]	Clinical trial of adult smokers randomly assigned to nicotine-containing e-cigarettes, nicotine patches, or non–nicotine-containing patches	657	No difference in abstinence rates among groups at 6 months; quit rates were lower than expected for NRTs, but authors concluded that trial was not sufficiently powered to make conclusions on effectiveness of e-cigarettes

Abbreviations: ENDS, electronic nicotine delivery systems; NRT, nicotine replacement therapy.

The first randomized trial ECLAT

Figure 2. Image of the product tested in the study. The "Categoria" electronic cigarette is a three-piece model consisting of a disposable inhaler/mouthpiece (the cartridge), an atomizer and a rechargeable battery (the cigarette body). Disposable cartridges used in this study looked like tobacco cigarette's filters containing an absorbent material saturated with a liquid solution of propylene glycol and vegetable glycerin in which different concentrations of nicotine or an aroma were dissolved. The cigarette body contains a rechargeable 3.7 V-90 mAh lithium-ion battery that activates the heating element in the atomizer.
doi:10.1371/journal.pone.0066317.g002

- Prospective 12-month double blind controlled RCT
- To evaluate smoking reduction, smoking abstinence and adverse events in 300 smokers from Catania not willing to quit
- Recruitment June 2010-February 2011
- Inclusion criteria : >= 10 cig/day, for at least the past 5 years; age 18-70; good health; not attempting or wishing to quit during the next 30 days

Caponnetto P PLoS ONE 2013;8;e66317

The ECLAT study design

300 participants, Age 18-70

Smokers >= 10 cig/d

Not willing to stop smoking

No use of smoleless tobacco or NRT

No respiratory , cardiovascular no history of alcohol abuse

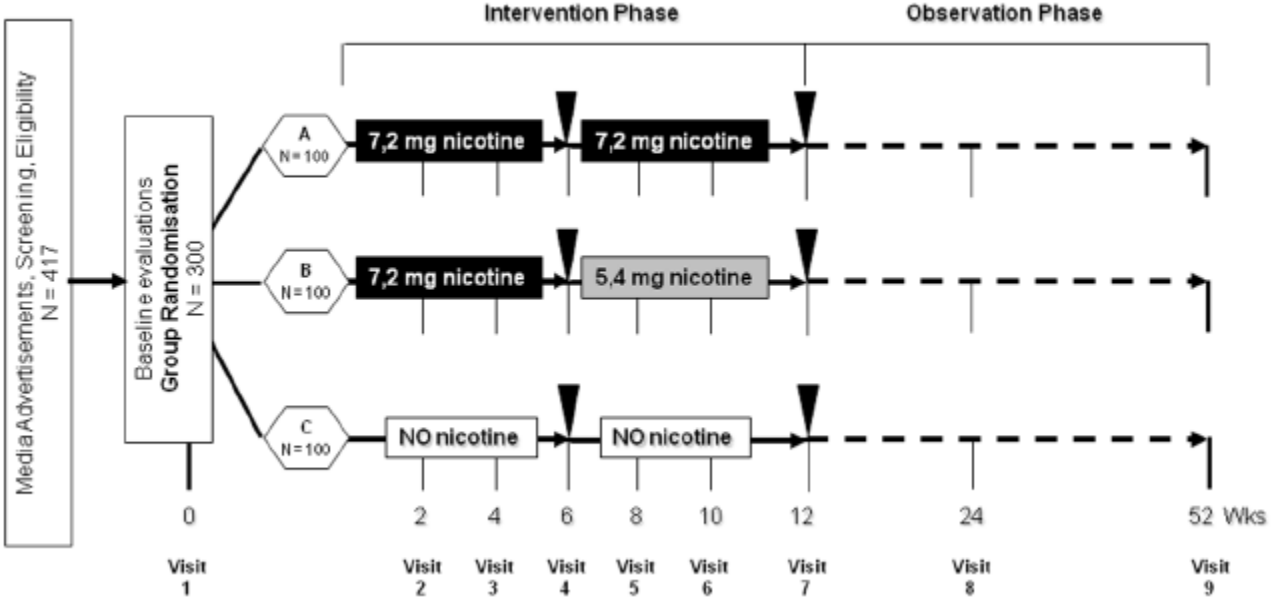
No pregnancy or breastfeeding

A: E-cig + 7.2 mg nicotine
12-weeks supply

B: E-cig with 7.2 mg
6-week supply then,
5.4 mg nicotine
6-week supply

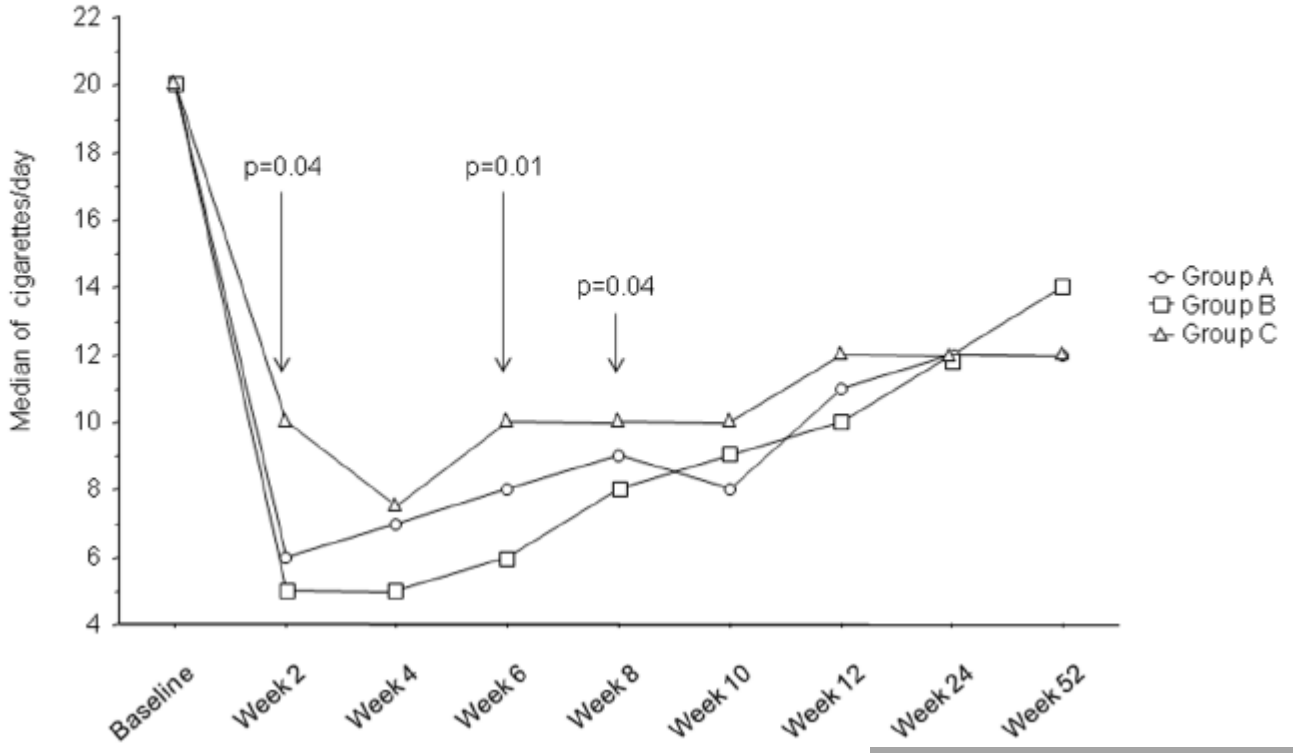
C: E-cig with 0 mg nicotine
Sweet tobacco aroma
12-weeks supply

Caponnetto P PLoS ONE 2013;8;e66317


Intervention Phase
Observation Phase
Media Advertisements, Screening, Eligibility
N = 417
Baseline evaluations
Group Randomisation
N = 300
A
N = 100
7,2 mg nicotine
7,2 mg nicotine
B
N = 100
7,2 mg nicotine
5,4 mg nicotine
C
N = 100
NO nicotine
NO nicotine
0
2
4
6
8
10
12
24
52 Wks
Visit 1
Visit 2
Visit 3
Visit 4
Visit 5
Visit 6
Visit 7
Visit 8
Visit 9

Time-course of changes in the median number of cig/day use from baseline

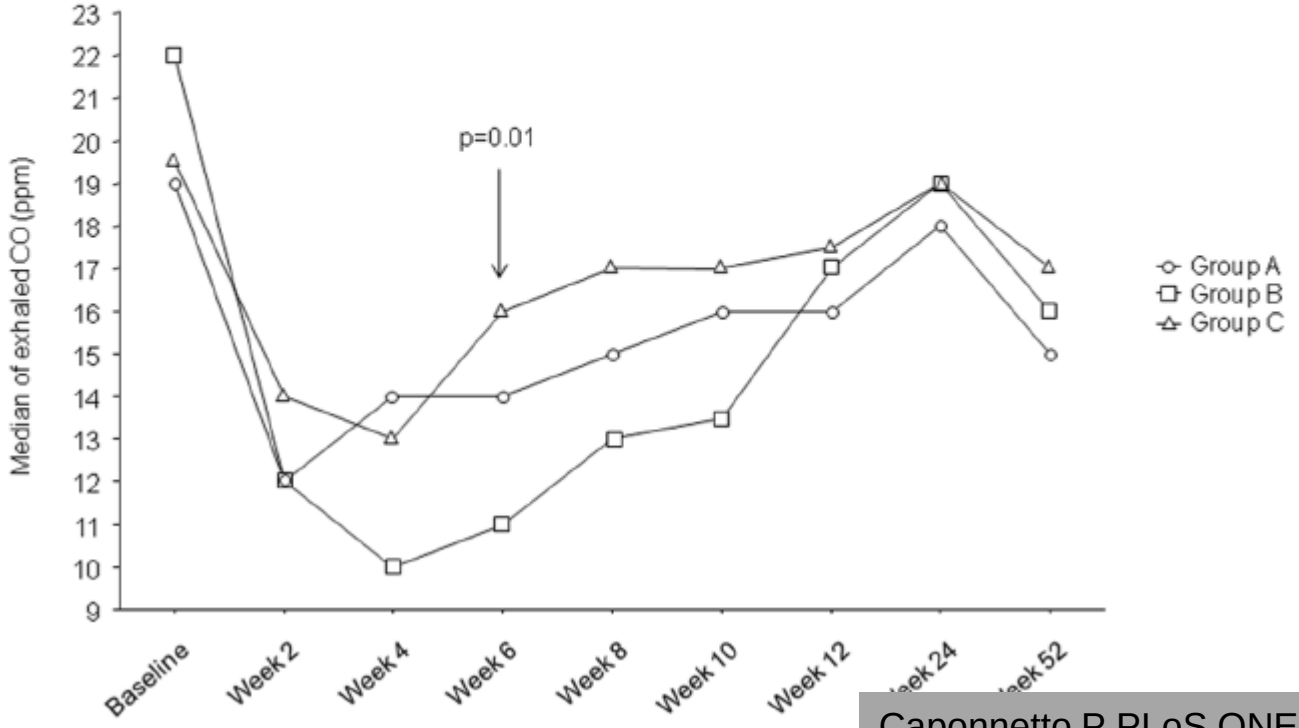
	No.	No.	No.	No.	No.	No.	No.	No.	No.
Group A	100	75	73	65	57	59	76	73	65
Group B	100	78	71	60	59	55	79	75	63
Group C	100	77	64	55	52	51	70	63	55



Caponnetto P PLoS ONE 2013;8;e66317

Time-course of changes in the median exhaled CO levels from baseline

	No.	No.	No.	No.	No.	No.	No.	No.	No.
Group A	100	75	73	65	57	59	76	73	65
Group B	100	78	71	60	59	55	79	75	63
Group C	100	77	64	55	52	51	70	63	55



Caponnetto P PLoS ONE 2013;8;e66317

Comparative reduction and quit rates

Table 2. Reduction and quit rates at different time points, shown separately for each study group (intention-to-treat analysis).

	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

*p values are relevant to the differences in frequency distribution in reduction and quit rates among groups at each Study Visits (χ^2 test).

doi:10.1371/journal.pone.0066317.t002

At week 52, 26.9% of the quitters still using their device

Caponnetto P PLoS ONE 2013;8;e66317

Adverse events

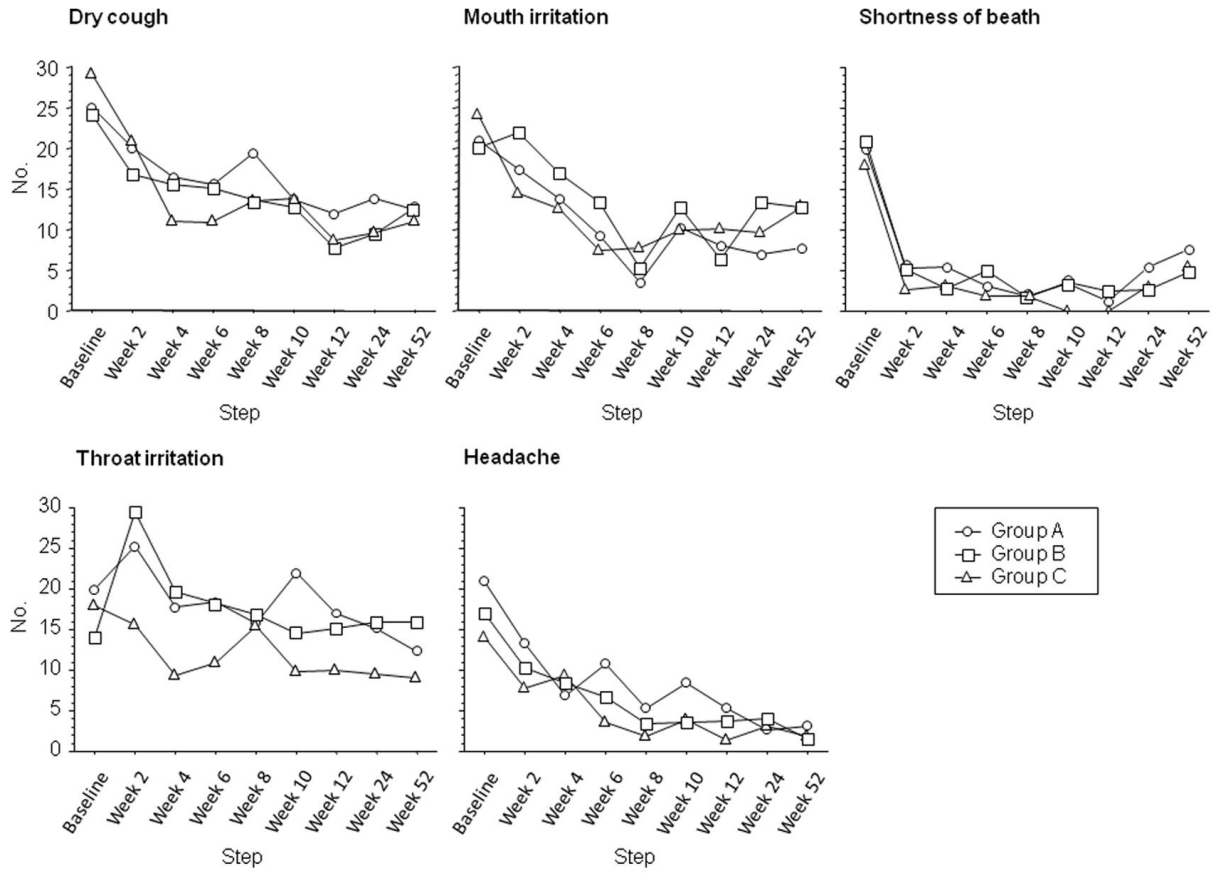


Figure 8. Time-course of changes in the frequency of the five most commonly reported adverse events (AEs) from baseline, separately for each study group. On Y-axis, the number of subjects reporting AEs is depicted. Compared to baseline, a significant reduction in frequency of cough, dry mouth, shortness of breath, and headache was observed at each study visits in all three study groups (per-protocol evaluation, $p<0.001$, χ^2 test). No difference was found in frequency distribution of AEs among study groups (χ^2 test).

The ASCEND trial

657 participants, Age > 18

Smokers >= 10 cig/d

Wanting to stop smoking

No use of smoking cessation medications

No respiratory , cardiovascular and/or psychiatric disorders

R

E-cig + 16 mg/ml nicotine cartridges *ad libitum*

E-cig with 0 mg nicotine cartridges *ad libitum*

21 mg nicotine patch daily

Time lines : -1 week = product familiarisation
day 0 to 3 months use of the device
6 months follow-up

Primary outcome : % of particpants who maintain sustained abstinence for 6 months

Bullen C BMC Public Health 2013;13:210

The Ascend trial

Abstinence at	e-cigarette with nicotine	Patch 21mg	p
N	289	295	
1 month (%)	67 (23,2)	47 (15,9)	0,03
3 months (%)	38 (13,1)	27 (9,2)	0,12
6 months (%)	21 (7,3)	17 (5,8)	0,46
Abstinence at	e-cigarette with nicotine	e-cigarette w/o nicotine	
N	289	73	
1 month (%)	67 (23,2)	12 (16,4)	0,21
3 months (%)	38 (13,1)	5 (6,8)	0,14
6 months (%)	21 (7,3)	3 (4,1)	0,44

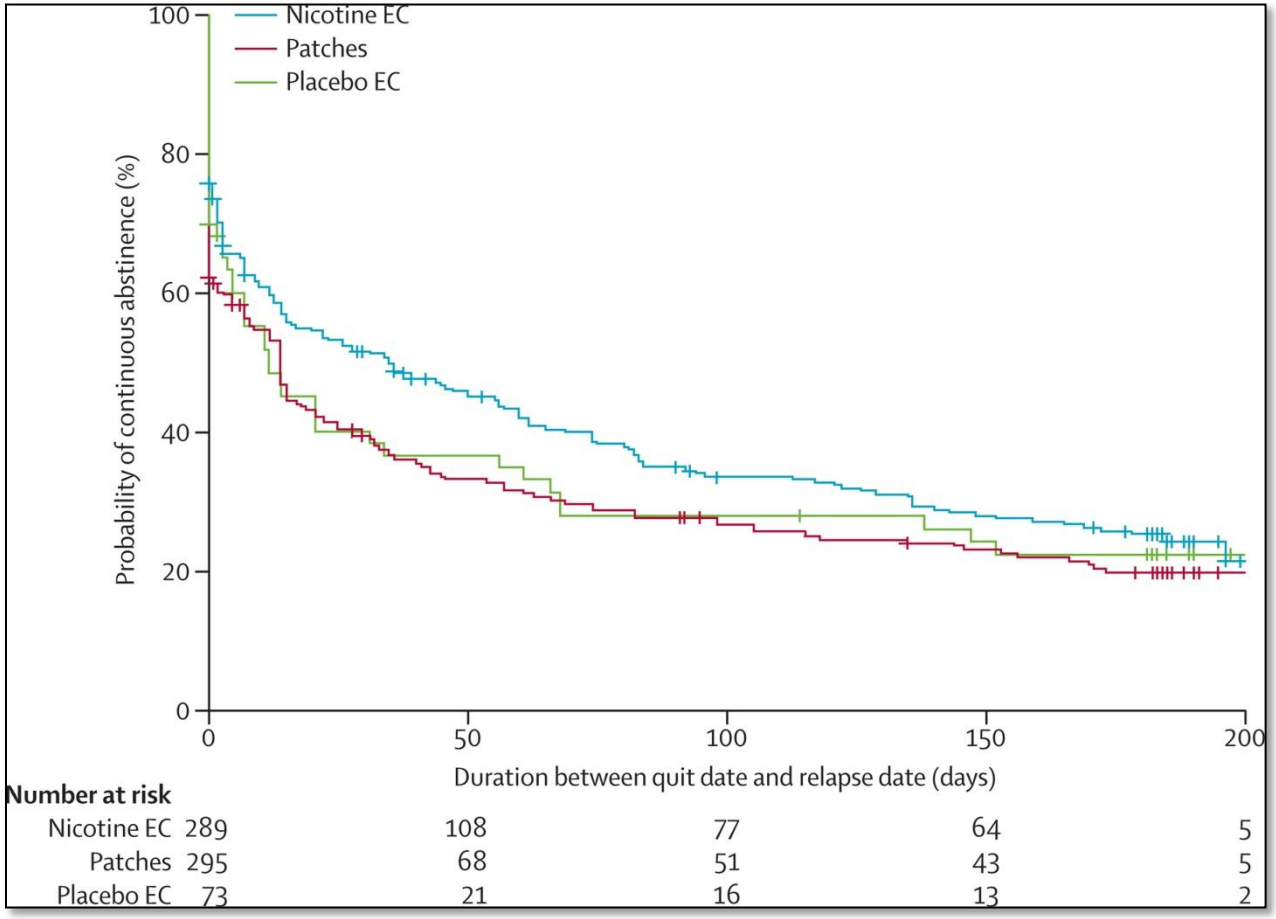
Bullen C, Lancet 2013; 382 : 1629-37.

% of participants reducing their consommation by at least half at 6 months

Reduction of consommation at 6 months (%)	**e-cigarette with nicotine**	**Patch**	**p**
	57	41	0.0002
	e-cigarette with nicotine	**e-cigarette w/o nicotine**	
	57	45	0.08

Bullen C, Lancet 2013; 382 : 1629-37.

Kaplan-Meier analysis of time to relapse



What about patients with mental illness in the ASCEND trial (of note: psychiatric disorders were an exclusion criteria)

Table 1 Baseline characteristics of mental illness participants by intervention

Characteristic	21 mg nicotine patch (n = 35)	16 mg e-cigarette (n = 39)	0 mg e-cigarette (n = 12)
Mean age	41 (11)	46 (11)	46 (14)
Female gender	69% (24)	67% (26)	59% (7)
Mean Fagerstrom score	6.5 (2.0)	6.6 (1.7)	5.1 (2.4)
Reported antidepressant use	69% (24)	77% (30)	83% (10)
Reported antipsychotic use	29% (10)	23% (9)	42% (5)
Reported anxiolytic use	6% (2)	13% (5)	8% (1)
Reported hypnosedative use	9% (3)	15% (6)	25% (3)
Reported drugs for addictive disorders use	3% (1)	3% (1)	8% (1)

Data are mean (SD) or % (n).

O'Brien B Tabacco Induced diseases 2015;13:5

What about patients with mental illness?

Table 2 Comparison of outcomes for participants with and without mental illness displaying both pooled and intervention level results for the three interventions (21 mg nicotine patch, 16 mg e-cigarette, 0 mg e-cigarette)

Outcome	Intervention	Mental Illness (n = 86, 13%) patch n = 35, 16 mg e-cigarette n = 39, 0 mg e-cigarette n = 12	No Mental Illness (n = 571, 87%) patch n = 260 , 16 mg e-cigarette n = 250, 0 mg e-cigarette n = 61	Difference (p value)
Biochemically verified continuous abstinence at six months % (n)	All interventions pooled	8% (7)	6% (34)	0.435
	21 mg nicotine patch	14% (5)	5% (12)	0.038[a]
	16 mg e-cigarette	5% (2)	7% (19)	0.750[a]
	0 mg e-cigarette	0% (0)	5% (3)	-
Relapse rate at six months % (n)	All interventions pooled	79% (68)	67% (380)	0.020
	21 mg nicotine patch	71% (25)	67% (175)	0.931
	16 mg e-cigarette	85% (33)	66% (164)	<0.0001
	0 mg e-cigarette	83% (10)	67% (41)	0.239
Mean reduction in CPD from baseline to six months in those that did not quit Mean (SD)	All interventions pooled	7.7 (6.7)	8.4 (7)	0.508
	21 mg nicotine patch	5.7 (6.3)	7.4 (7)	0.299
	16 mg e-cigarette	9.9 (7)	9.4 (7.1)	0.743
	0 mg e-cigarette	4.7 (3.5)	8.3 (5.9)	0.129[b]
Percentage reduction in CPD from baseline to six months in those that did not quit Mean (SD)	All interventions pooled	40% (30%)	46% (33%)	0.154
	21 mg nicotine patch	29% (30%)	41% (35%)	0.147
	16 mg e-cigarette	49% (28%)	51% (31%)	0.660
	0 mg e-cigarette	31% (26%)	47% (28%)	0.245[b]
Treatment compliance at three months % (n)	All interventions pooled	39% (30)	37% (167)	0.757
	21 mg nicotine patch	20% (6)	18% (34)	0.752
	16 mg e-cigarette	53% (19)	51% (107)	0.861
	0 mg e-cigarette	46% (5)	54% (26)	0.741

O'Brien B Tabacco Induced diseases 2015;13:5

What about patients with mental illness?

Table 3 Comparison of outcomes for mental illness participants who used 16 mg nicotine e-cigarettes, 0 mg e-cigarettes and 21 mg nicotine patches

Outcome	21 mg nicotine patch (n = 35, 40%)	16 mg nicotine e-cigarette (n = 39, 45%)	0 mg nicotine e-cigarette (n =12, 14%)	Difference (p-value)
Biochemically verified continuous abstinence at six months % (n)	14% (5)	5% (2)	0	0.245 (patch vs. 16 mg e-cig)[a]
				- (16 mg vs. 0 mg e-cig)
				0.115 (patch vs. combined e-cig)[a]
Relapse rate at six months % (n)	71% (25)	85% (33)	83% (10)	0.169 (patch vs. 16 mg e-cig)
				1.000 (16 mg vs. 0 mg e-cig)
				0.149 (patch vs. combined e-cig)
Mean reduction in CPD from baseline to six months in those that did not quit Mean (SD)	5.7 (6.3)	9.9 (7)	4.7 (3.5)	0.035 (patch vs. 16 mg e-cig)
				0.068 (16 mg vs. 0 mg e-cig)
				0.083 (patch vs. combined e-cig
Percentage reduction in CPD from baseline to six months in those that did not quit Mean (SD)	29% (30%)	49% (30%)	31% (30%)	0.025 (patch vs. 16 mg e-cig)
				0.153 (16 mg vs. 0 mg e-cig)
				0.049 (patch vs. combined e-cig)
Treatment compliance at three months % (n)	20% (6)	53% (19)	46% (5)	0.006 (patch vs. 16 mg e-cig)
				0.670 (16 mg vs. 0 mg e-cig)
				0.006 (patch vs. combined e-cig)

O'Brien B Tabacco Induced diseases 2015;13:5

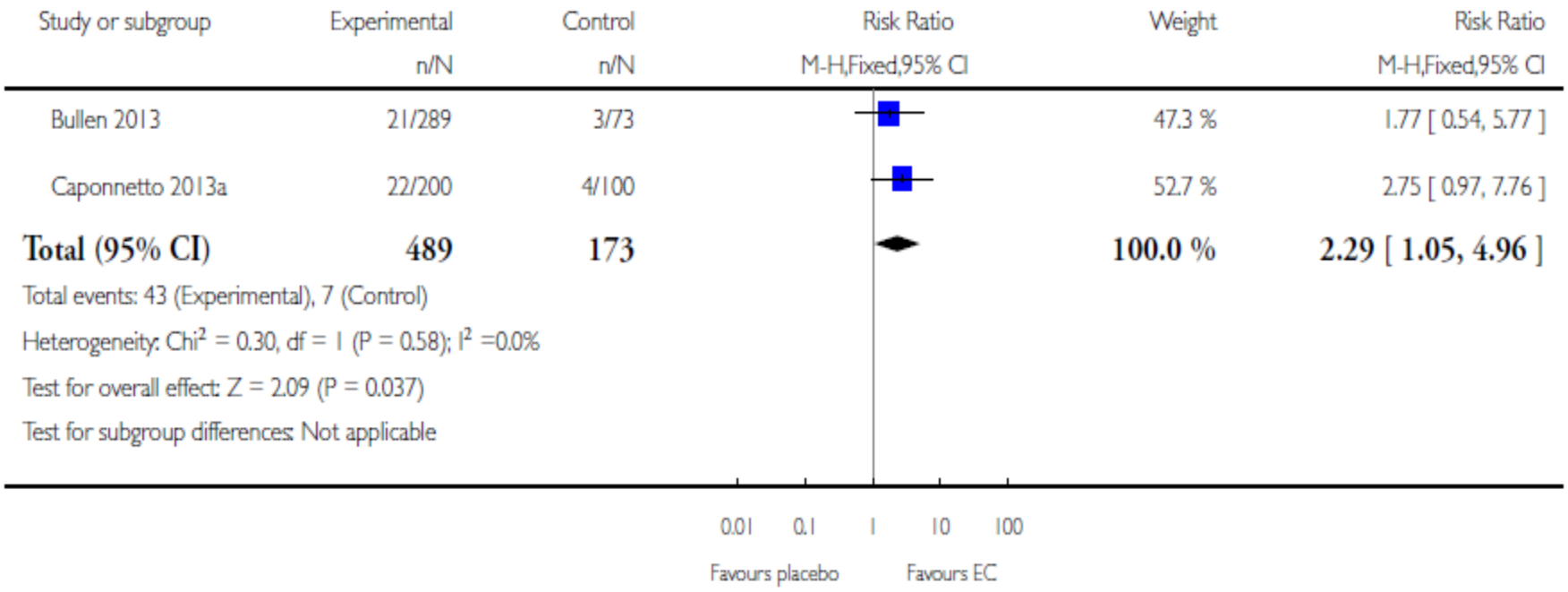
Cochrane meta-analysis

Analysis 1.1. Comparison 1 Smoking cessation, Outcome 1 Nicotine EC versus placebo EC.

Review: Electronic cigarettes for smoking cessation and reduction

Comparison: 1 Smoking cessation

Outcome: 1 Nicotine EC versus placebo EC



Cochrane meta-analysis

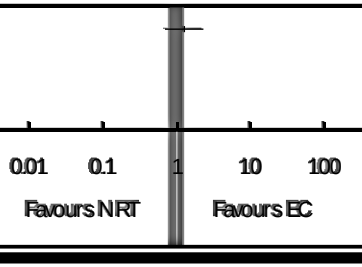
Analysis 1.2. Comparison 1 Smoking cessation, Outcome 2 Nicotine EC versus nicotine replacement therapy.

Review: Electronic cigarettes for smoking cessation and reduction

Comparison: 1 Smoking cessation

Outcome: 2 Nicotine EC versus nicotine replacement therapy

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Bullen 2013	21/289	17/295		1.26 [0.68, 2.34]



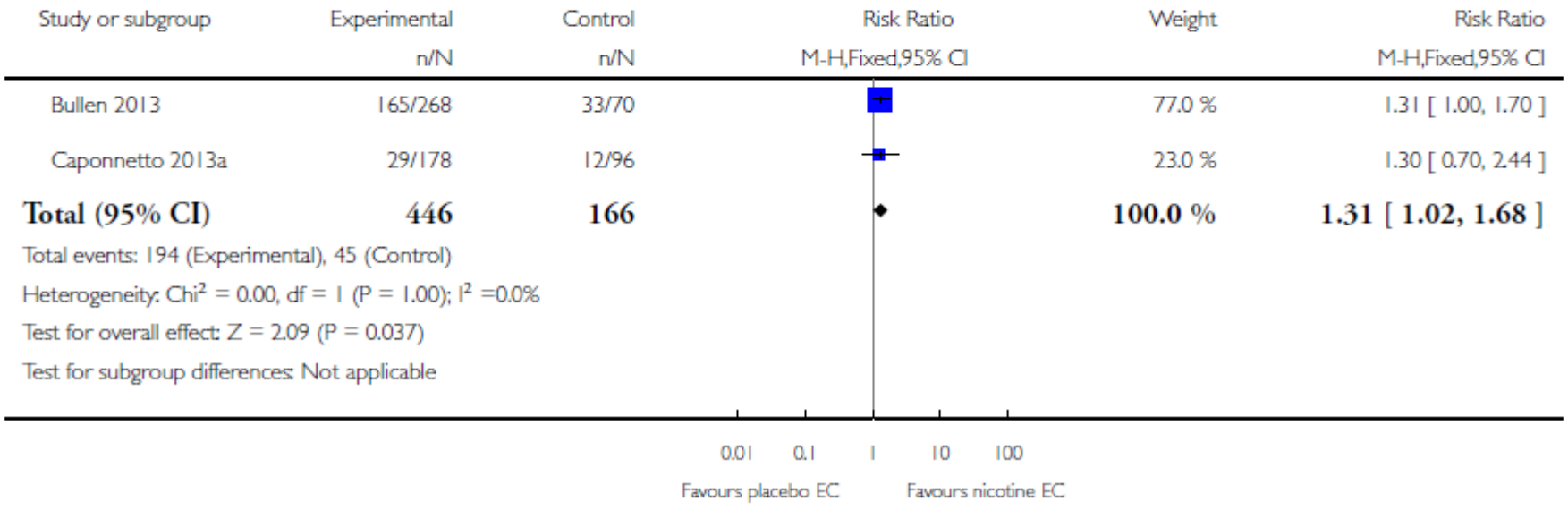
Cochrane meta-analysis

Analysis 2.1. Comparison 2 Smoking reduction, Outcome 1 Nicotine EC versus placebo EC (quitters excluded).

Review: Electronic cigarettes for smoking cessation and reduction

Comparison: 2 Smoking reduction

Outcome: 1 Nicotine EC versus placebo EC (quitters excluded)



Cochrane meta-analysis

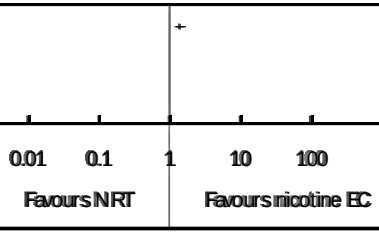
Analysis 2.2. Comparison 2 Smoking reduction, Outcome 2 Nicotine EC versus nicotine replacement therapy (quitters excluded).

Review: Electronic cigarettes for smoking cessation and reduction

Comparison: 2 Smoking reduction

Outcome: 2 Nicotine EC versus nicotine replacement therapy (quitters excluded)

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Bullen 2013	165/268	121/278		1.41 [1.20, 1.67]



McRobbie H, Bullen C, Hartmann-Boyce J, Hajek P

Electronic cigarettes for smoking cessation and reduction (Review)

Analysis 3.1. Comparison 3 Adverse Events, Outcome 1 Proportion of participants reporting adverse events: Nicotine EC versus placebo EC.

Review: Electronic cigarettes for smoking cessation and reduction

Comparison: 3 Adverse Events

Outcome: 1 Proportion of participants reporting adverse events: Nicotine EC versus placebo EC

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Bullen 2013	107/241	26/57		0.97 [0.71, 1.34]

Analysis 3.2. Comparison 3 Adverse Events, Outcome 2 Proportion of participants reporting adverse events: nicotine EC versus nicotine replacement therapy.

Review: Electronic cigarettes for smoking cessation and reduction

Comparison: 3 Adverse Events

Outcome: 2 Proportion of participants reporting adverse events: nicotine EC versus nicotine replacement therapy

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Bullen 2013	107/241	96/215		0.99 [0.81, 1.22]

Is e-cigarette as dangerous as cigarette?

Comparison of toxicants levels between conventional and electronic cigarettes.

Toxic compound	Conventional cigarette (μg in mainstream smoke) [35]	Electronic cigarette (μg per 15 puffs)	Average ratio (conventional vs. electronic cigarette)
Formaldehyde	1.6-52	0.20-5.61	9
Acetaldehyde	52-140	0.11-1.36	450
Acrolein	2.4-62	0.07-4.19	15
Toluene	8.3-70	0.02-0.63	120
NNN	0.005-0.19	0.00008-0.00043	380
NNK	0.012-0.11	0.00011-0.00283	40

Goniewicz ML Tob Control 2014;23:133-9

Ideological biases

- Whereas the combustion of cigarettes represents a public health disaster
- Recent innovations such as e-cigarettes without this combustion of tobacco may represent a less harmful product
- Unfortunately, the debate is now mainly ideological without scientific backgrounds
- For sure, the decisions of regulators should be based on science not ideology

JF Etter BMC Medicine 2015;13:32

So, between two evils, is there a good one or at least a lesser evil?

Pros and cons

EC advocates

- The product has a potential to reduce smoking and even stop cigarette use
- With switch to a safer product
- Achieving this goal requires little government expenditure and involvement
- Use of nicotine without tobacco toxic composants is by far less harmful (but not for pregnant smokers)

Commentators in favor of EC restrictions

- EC has a potential to increase cigarette use by re-normalizing smoking
- EC will result in reducing motivation to quit completely
- EC is a gateway to smoking for non-smokers especially the young
- Nicotine is addictive and health risks from longterm EC use may yet emerge

Hajek P Addiction 2014;1801-10

Statements of IASLC and ASCO

The International Association for the Study of Lung Cancer does recommend that research be done to evaluate the safety and efficacy of e-cigarettes as a cessation treatment in cancer patients to help guide clinical practice. For individual patients who are either using or planning to use e-cigarettes despite advice not to do so, they should be offered evidence-based stop smoking treatments while monitoring for any adverse effect of e-cigarette use.

Cummings KM JTO 2014;9:438-41

Rapid elimination of combustible tobacco products would dramatically reduce the burden of tobacco-related death and disease. The AACR and ASCO support every effort to reduce the use of combustible tobacco, and we support careful consideration of ENDS as a potentially harmful, and a potentially beneficial, product in this regard. The benefits and harms must be evaluated with respect to the population as a whole and take into account the effect on youth, adults, nonsmokers, and smokers. There are currently too few data on the safety of ENDS and their efficacy as cessation products to recommend their use for the general population or for patients with chronic diseases such as cancer. The AACR and ASCO recommend strategic research on the composition, uptake, biologic effects, behavioral patterns, and health effects of ENDS use, including abuse liability of ENDS; research on how ENDS use affects other tobacco product use patterns; and research on how ENDS use affects treatment and outcomes for patients with cancer. The AACR and ASCO encourage policymakers to review the rapidly evolving literature regarding ENDS regularly and make public health decisions based on scientific evidence.

Brandon T JCO 2015;33:952-63