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E-cigarettes versus nicotine replacement treatment as harm reduction interventions for smokers who find quitting difficult: Randomised controlled trial

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PH and HM have received research funding from and provided consultancy to Pfizer, a manufacturer of stop-smoking medications. DP has received research funding from Pfizer. All other authors having no conflicts to declare.

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Abstract

Background and aims The majority of smokers accessing the current best treatments continue to smoke. We aimed to test if e-cigarettes (EC) compared with nicotine replacement treatment (NRT) can help such smokers reduce smoking.

Design Randomised controlled trial of EC (n=68) vs NRT (n=67) with 6-month follow-up.

Setting Stop smoking service in London, UK.

Participants 135 smokers (median age=40, 51% males) previously unable to stop smoking with conventional treatments.

Interventions Participants received either NRT of their choice (8 week supply), or an EC starter pack and instructions to purchase further e-liquids of strength and flavours of their choice themselves. Products were accompanied by minimal behavioural support.

Measurements Participants who reported that they stopped smoking or reduced their daily cigarette consumption by at least 50% at six-month follow-up were invited to provide a carbon monoxide (CO) reading. The primary outcome was biochemically validated reduction in smoke intake of at least 50% at 6 months and the main secondary outcome was sustained validated abstinence at 6 months. Drop-outs were included as 'non-reducers'.

Findings Validated smoking reduction (including cessation) was achieved by 26.5% vs 6.0% of participants in the EC and NRT study arms, respectively (relative risk (RR)=4.4, p=0.005, 95% confidence interval (CI):1.6 to 12.4). Sustained validated abstinence rates at 6 months were 19.1% vs 3.0% (RR=6.4, p=0.01, 95%CI: 1.5 to 27.3). Product use was high and equal in both study arms initially, but at 6 months allocated product use was 47% in the EC arm vs 10% in the NRT arm (chi(1)=22.0, p<.001), respectively. Adverse events were minor and infrequent.

Conclusions In smokers unable to quit using conventional methods, e-cigarettes were more effective than nicotine replacement therapy in facilitating validated long-term smoking reduction and smoking cessation, when limited other support was provided.

Key words: Smoking cessation, tobacco dependence, e-cigarettes, harm reduction, randomised controlled trial, nicotine replacement treatment

INTRODUCTION

Among smokers seeking help, most do not achieve smoking cessation even with intensive treatments. Some 80% of smokers treated in clinical trials where various selection criteria apply (1, 2), and over 80% of those receiving intensive treatment in routine care (3, 4), smoke one year later.

A question arises as to whether smokers unable to quit with the current best treatments could benefit from approaches that offer a means to reduce the harm from smoking without ceasing nicotine use, with an option to stop nicotine use as well later on. The idea is not new. Nicotine replacement treatments (NRT) have been licenced for the 'cut down to quit' use for over 10 years, and several studies reported that such use can facilitate a significant reduction in smoke intake, as well as quitting smoking altogether at a later date (5, 6). The approach, however, is costly, the quit rates that it generates are low and achieved only with regular behavioural support and monitoring (7) and it is seldom used. The rise of e-cigarettes (EC) has now provided a new impetus to explore this issue further. EC have been shown to provide help to smokers attempting to quit (8). Regarding effects of pro-active provision of EC to smokers not intending to quit, an early randomised study examined effects of EC with low or no nicotine content in such smokers (9). There was a significant reduction in objectively measured smoke intake in both study arms and 9% smoking cessation rate at one year, but there was no control group not receiving EC.

We examined whether smokers unable to quit with licensed stop smoking medications can benefit from using EC to reduce or quit smoking, compared to using NRT, which is the most common treatment offered by the UK stop-smoking services. In contrast to a previous trial that has shown EC to be more effective than NRT when accompanied by intensive face-to-face counselling (10), both products were provided with only brief advice. This was included because standard counselling is not geared to smoking reduction; and we also aimed to assess how the products compare when less intensive support is provided.

METHODS

Study design

Randomised controlled trial comparing the effects of EC and NRT on the reduction in smoke intake and on smoking cessation with 6-months follow-up.

The study was approved by the Queen Mary Ethics of Research Committee (QMERC2016/65).

Participants
Smokers were included if they were aged ≥18 years, had a history of unsuccessful quitting with stop smoking medications, and had no preference to use or not to use NRT or EC. Exclusion criteria included pregnancy and current use of EC or stop smoking medications.

The trial was conducted at Queen Mary University of London, which provides a community stop-smoking service. Clients who did not manage to stop smoking with routine treatment were invited to take part. We also recruited eligible smokers seeking help with quitting via social media.

Randomisation and masking
Randomisation sequences (1:1 ratio in permuted blocks of 20) were produced by an independent statistician using computer generated randomisation codes. Codes were sealed in opaque envelopes and marked with a unique randomisation number. Study staff allocated randomisation numbers sequentially. Staff opened the next envelope and entered the allocation onto the clinical record form (CRF) and randomisation log. Data analysis was completed blind by an independent statistician.

Procedures
Interested participants were invited to a baseline visit where eligibility was confirmed and informed consent was collected. Participants were then randomised to either the EC or NRT arm and instructed on how to obtain their products (see details below).

Those wishing to stop smoking altogether were asked to set a target quit date (TQD) around the time of the second visit, typically a week later.

Participants were asked to bring their products along to the second visit to confirm that they had obtained the product/s, to try the product and to rate their experience. They were asked to start using the products only after this visit. Participants received brief instructions on product use and were advised to use their product as much as possible instead of smoking. Those opting for smoking cessation also received the standard advice on coping with urges to smoke (11). To limit contamination between study arms, participants signed a commitment form that they would not use the non-allocated product for at least the first four weeks of the study.

Participants received phone calls one and four weeks later to monitor product use and smoking status and to provide brief support. The calls took on average 10 minutes. The final follow-up took place over the phone at six months. Follow-up data were collected using a standard protocol to ensure that the same effort was used to contact all participants who did not respond initially. Participants received up to three phone calls, a text, an e-mail or postal questionnaire sent with self-addressed return envelope, and a final call two weeks later if there was no response.

At four weeks and six months, participants who reported stopping smoking or reducing cigarette consumption by at least 50% compared to baseline were invited to provide a carbon monoxide (CO) reading. Participants received £10 for their time and travel at both visits.

Study arms

NRT arm: At the baseline visit, participants selected an NRT product or product combination. A letter of recommendation (LOR) was provided as per standard practice to collect the product/s at local pharmacies (two-week supply). The choice of products included nicotine patch, chewing gum, nasal spray, microtab, inhalator, and mouth spray. Participants paid a prescription charge of £8.60, unless exempt (those over 60 years old, on benefits, or with eligible medical conditions). LORs were provided for up to eight weeks as per standard practice at the time, posted to the participants or picked up from the clinic, as required. Participants could switch to a different NRT product/s if required.

EC arm: At the baseline visit, participants were shown three different refillable EC products (Innokin T18E, Smok, and TECC mini with variable voltage) and explained the principles of their use. They were instructed to obtain one of these, or another product of their choice, together with initial samples of e-liquid with the strength and flavour of their choice, either via a voucher for up to £40 at a local vape shop that agreed to provide this service, or via other suppliers, and claim a refund against their receipt of up to £40. Participants paid for further supplies themselves. They were encouraged to try e-liquids of different strengths and flavours if the initial purchase did not meet their needs.

Note: For regular users of NRT and EC, prescription charges for NRT (estimated £17.20) would be about half of the costs of e-liquid (estimated £10).

Measures

The following measures were collected at baseline: demographic details, smoking history including Fagerstrom Test of Cigarette Dependence (FTCD) (12), Mood and Physical Symptoms Scale (MPSS) (13), expired-air carbon monoxide (CO) reading, respiratory symptoms checklist and whether participants had seen the GP or received treatment for the symptoms.

At the second visit, participants were asked about their initial reactions to their product: ‘Was it pleasant to use?’, ‘Do you think it could be useful in helping you to quit smoking?’ and ‘Do you think you will use it regularly over the next few weeks?’ with responses 1=not at all to 10=extremely. They were also asked to rate the product compared to their normal cigarettes, with responses 1=much worse, 11=as good as normal cigarettes and 21=much better.

At one and four weeks and at six months, the following data were collected: Smoking status, cigarettes per day, use of allocated and non-allocated products since the last visit. Participants who stopped using their allocated product or who did not use it every day were asked for a reason. Participants also rated how helpful they found their allocated product with responses ranging from 1=not at all to 5=extremely, and whether they had any concerns about using their product/product related issues. At one and four weeks they were also asked how good the product tasted and how satisfying it was compared to normal cigarettes (1=much worse to 5= Much better). The MPSS was administered at all contacts apart from the six-month follow up. At the six month follow up participants were asked about the experience over the past six months of the same respiratory symptoms as at baseline. They were also asked whether any of the symptoms changed since they joined the trial.

At four weeks and six months, participants who reported stopping smoking or reducing their cigarette consumption by at least 50% compared to baseline were invited to attend the clinic to provide a carbon monoxide (CO) reading. Participants received £10 in compensation for their time and travel at both visits.

Outcomes

The primary outcome was reduction in cigarette consumption of at least 50% at six months, defined as self-reported reduction of ≥50% in the number of cigarettes smoked per day, confirmed by a reduction in end-expired CO levels of ≥50% compared to baseline.

Secondary outcomes included: Validated reduction in cigarette consumption at four weeks, defined as above; self-reported abstinence from smoking at four weeks, confirmed by CO reading of <8 ppm; sustained abstinence from smoking at six months, defined as self-report of abstinence at six months, with no more than five cigarettes smoked since the contact at four weeks, validated by CO reading of <8ppm at six months; use of and ratings of trial products; withdrawal severity at one and four weeks; product ratings; proportion of participants still using their allocated product at six months; adverse events; and changes in respiratory symptoms at six months compared to baseline.

Statistical analysis

Sample size: This was an early trial with no precedent, but we hypothesized a large effect, because apart from facilitating quitting, using EC also generates a significant reduction in smoking in non-quitters (10, 14, 15), while NRT has a more modest effect on smoke intake reduction (5), and use is normally only temporary (16). We allowed a recruitment period that was expected to generate a sample of at least 120 participants. The final sample size (N=135) provides 80% power to detect an RR of 3·6 (95%CI: 1·4 to 9·0), i.e. 25% of smokers using EC achieving CO-validated smoking reduction at six months compared to 7% of those using NRT.

Statistical analysis: Smoking cessation and reduction outcomes were analysed by regressing each smoking status on the intervention arm. Binomial regressions were conducted using the generalised linear model with binomial distribution and logarithmic link to estimate relative risk for EC vs NRT. Participants lost to follow up were classified as non-abstainers/non-reducers as per Russell standard (17). We present the relevant point estimates with 95% confidence intervals.

We estimated differences between study arms in product ratings and cigarettes per day using independent t-test or the Wilcoxon sign rank test, when the parametric assumptions were not met. We also explored differences in the proportion of participants who experienced changes in respiratory symptoms at follow-up compared to baseline using Fisher's exact test due to small cell size.

We conducted a sensitivity analysis of the primary outcome using multiple imputation by chained equation. The imputation model included auxiliary variables associated with CO readings and CPD at 24 weeks as well as their missingness, including baseline variables (FNTD, CPD, cotinine levels, education level, employment status and having tried EC) and CPD and CO levels at 4 weeks. We generated 50 completed datasets.

All tests of significance were two-tailed. Analyses were conducted in Stata version 15.
The analysis was not pre-registered and as such the results should be considered exploratory.

Data availability
The authors will make relevant anonymised patient level data available on reasonable request.

RESULTS

The first participant was randomised on 3 April 2017 and follow-up ended in August 2018. Figure 1 shows the flow of participants through the trial. Follow-up rates were 85% and 88% at 4 weeks and 88% and 70% at 6 months in the EC and NRT group, respectively.

Table 1 shows baseline characteristics of participants in the two study arms.

Significantly more participants achieved validated reduction in smoke intake of at least 50% at six months in the EC arm than in the NRT arm. The absolute risk reduction between arms at six months was 20.5 (95%CI: 7.7- 33.3); number needed to treat=5. Abstinence rates were also significantly higher in the EC arm (see Table

2). The result of the sensitivity analysis was consistent with the results of the primary analysis (RR=2.34; 95%CI: 1.36-4.04).

Table 3 shows changes in cigarette consumption over time in non-abstainers in the two study arms.

In the NRT arm, 65 (97%) of participants opted for NRT combinations, mostly a patch combined with one of the shorter acting products (most frequently inhalator and mouth spray). No EC arm participant switched from refillable to disposable or cartridge-based products within the six months of the study.

Most participants sourced their EC from collaborating vape shops. Fruit flavoured e-liquids were by far the most popular throughout the six months (Table 4).

Use of allocated products was similar in the two study arms at week one and at four weeks (Table 5). Use diverged substantially by six months (see Table 5). In the EC arm, 11 of the 13 verified abstainers (84·6%) and 15 of the 18 reducers (83·3%) were using EC at six months. One of the four reducers (25%) and none of the two verified abstainers (50%) in the NRT arm were using NRT at six months.

Amongst participants who reported EC strength at both baseline and at six months, the nicotine content of e-liquids was significantly reduced (see Table 4).

Regarding use of non-allocated products, three participants in the NRT arm reported using EC at week one, three at week four and seven at six months (none of these participants were abstainers or verified reducers). In the EC arm, nobody used NRT at week one and three used NRT at week four and at six months (none was an abstainer or verified reducer).

When tried initially, the ratings of NRT and EC did not differ (Table 6).

In participants who continued to use their products, by week four, EC were receiving higher ratings than NRT for helpfulness and taste, but the products continued to receive similar ratings for satisfaction (Table 7).

Only a few product concerns were raised in response to the question: ‘Have you had any product related issues since we last spoke?’ In the EC arm, these were battery life, harshness of aerosol and problems filling the tank (N=1 each). In the NRT arm, patch caused itching (N=5), fell off (N=1), and caused vivid dreams (N=1).

Regarding adverse events, in the EC arm there was a report of throat irritation (N=2) and nausea (N=1) at week one while in the NRT arm there was a report of cough (N=1), itchiness (N=4), vivid dreams (N=1) and hiccups (N=1). At week four, in the EC arm there were reports of cough (N=3) and cough/throat/chest irritation (N=4)

and dry throat (N=1) while in the NRT arm there was a report of dry throat (N=1), indigestion (N=2), itchiness/skin irritation (N=6), sleep problems (N=1), nausea (N=1), and sore glands (N=1). At week 24, in the EC arm there was a report of dry mouth (N=1) and cough/throat/chest irritation (N=3) while in the NRT arm there was a report of itchiness (N=1) and nausea (N=1).

Regarding the pre-specified respiratory symptoms, no significant differences were noted between the study arms or in participants who used EC at six months (N=31) and those who did not (N=60). E.g. the responses to the question about the overall change in respiratory symptoms since starting the study were: Better: 42% vs 30%; no change 56% vs 60%; worse 3% vs 10% in the EC and NRT arms, respectively (p=0·41).

DISCUSSION

In smokers with a history of unsuccessful quitting, EC were more effective than NRT both in terms of CO-validated reduction in smoking of at least 50% and in terms of smoking cessation.

Compared to the recent TEC trial that used the same study products (10) but included intensive multisession face-to-face behavioural support, the limited behavioural support and the more challenging clientele resulted in lower quit rates, but regarding EC efficacy compared to NRT, the effect size was larger.

This finding was not unexpected. NRT is effective in clinical trials where support and CO monitoring is always provided (18), but when bought over the counter, its efficacy is limited (19, 20). NRT's helpfulness seems dependent on advisors ensuring sufficient product use and effort on the part of smokers. EC use seems to require less effort, possibly because EC are better than NRT in providing what smokers seek (10). The higher rate of ongoing EC use compared to NRT use is consistent with this hypothesis. Behavioural support is thus likely to enhance the effects of NRT more than the effects of EC.

The inclusion of smokers who were finding quitting difficult could have further contributed to the large effect size. If EC provide some of the rewards that smokers seek, they can be expected to be especially helpful to those for whom such perceived benefits are particularly important and/or particularly hard to forfeit. If this line of argument is correct, EC superiority compared to NRT should be more marked in smokers with high tobacco dependence and/or mental health problems. Further trials are needed to test this assumption.

As in the TEC trial, smokers were more likely to persevere with EC use than with NRT use. Some switch to using EC as a smoking replacement (21) rather than as a

temporary aid. Long-term EC use is likely to carry some health risks (22), but this needs to be seen in the context of hard-to-reach smokers who would otherwise be subjected to much higher health risks from smoking. In this group, continuing use of nicotine is unlikely to pose any major harm. Ex-smokers who start using EC or oral tobacco, after a period of abstinence accompanied by no such use, have an increased risk of relapse back to smoking (23). It is not clear whether such use is an attempt by those concerned about relapse or already lapsing to avert return to smoking, or the cause of the relapse. In our sample, abstainers using EC at 4 weeks had a lower rate of relapse than those who did not, though not significantly so (46.3% vs 65.21%, RR=0.71, 95%CI: 0.43- 1.17). Interestingly, as in the previous study, smokers were reducing nicotine content of their EC over time, and 19% were using nicotine-free EC. Regarding flavour preferences, only a minority opted for tobacco flavoured e-liquid. Fruit flavours were the most popular.

The trial had several limitations. Participants could have had a preference for EC compared to NRT. If they received the less desirable treatment, they may have been more likely to drop out, not attempt quitting, or use the product less. We tried to mitigate this potential bias by only including participants who had no strong preferences and were willing to use either product; and we monitored closely both attendance and treatment adherence. It is reassuring that early attendance and product use were similar in the two study arms. Retention rates differed at six months, but in smoking cessation studies that include no incentives for responding, this normally reflects differences in efficacy, as treatment successes are more likely to maintain contact (17). More participants also attended for validation from among the EC arm than from the NRT arm. A related concern is that NRT could have been a less promising treatment than EC for participants who had tried NRT before, because they returned to smoking. Two issues mitigate this concern. Re-use of licensed stop smoking medications by smokers who are prepared to re-engage with these treatments have been shown to generate the same outcome as in first-time users (24, 25). In addition, almost a third of the participants in the EC arm had tried EC earlier, but stopped use and continued to smoke. Even if we were to assume that participants' preferences or their lack of previous success with NRT reduced the efficacy of NRT to such an extent that the NRT arm treatment was equivalent to a placebo, the study results still show that with this group of clients, EC are an effective tool for harm reduction and smoking cessation.

The level of behavioural support was much lower than in the TEC trial, but there were two face-to-face sessions. A question remains as to whether EC would be effective with no clinician involvement.

The sample size was relatively small. Although it was sufficient to detect treatment effects, there is an imprecision regarding the effect sizes, and we also had limited power for some of the sub-analyses that could only use reduced samples. NRT was provided for up to two months, while participants had to source and buy their e-liquid refills from early on themselves. This, however, should reduce rather than enhance

treatment effects that we detected. Similarly, EC arm participants had to collect their EC from collaborating vape shops or source them online and present their receipts, while NRT arm participants collected their NRT from their local pharmacies, which was likely to be more convenient. The cost of EC refills was higher than the cost of the NRT prescription charge, and there was no cost for the 24% of NRT arm participants entitled to free prescriptions.

The trial concerned smokers who failed in previous treatment, a clientele that is also typical in stop smoking services. The results may not generalise to smokers in general, although failed quit attempts are generally common.

Future research may consider including arms receiving intensive behavioural support versus minimal support; and include extended follow-up periods to check on relapse rates among ex-smokers who do and do not use EC over long term.

The trial results suggest that when treating smokers who failed with stop-smoking medications previously, recommending a refillable EC with an e-liquid of strength and flavours of patient's choice is a more effective approach than prescribing combination NRT.

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Author Contributions

KMS, PH, APW, DP, MO and HM contributed to the planning, conduct, and reporting of the work described in the article. FP conducted the analysis and contributed to the reporting of the work.

Figure 1: Participant flow

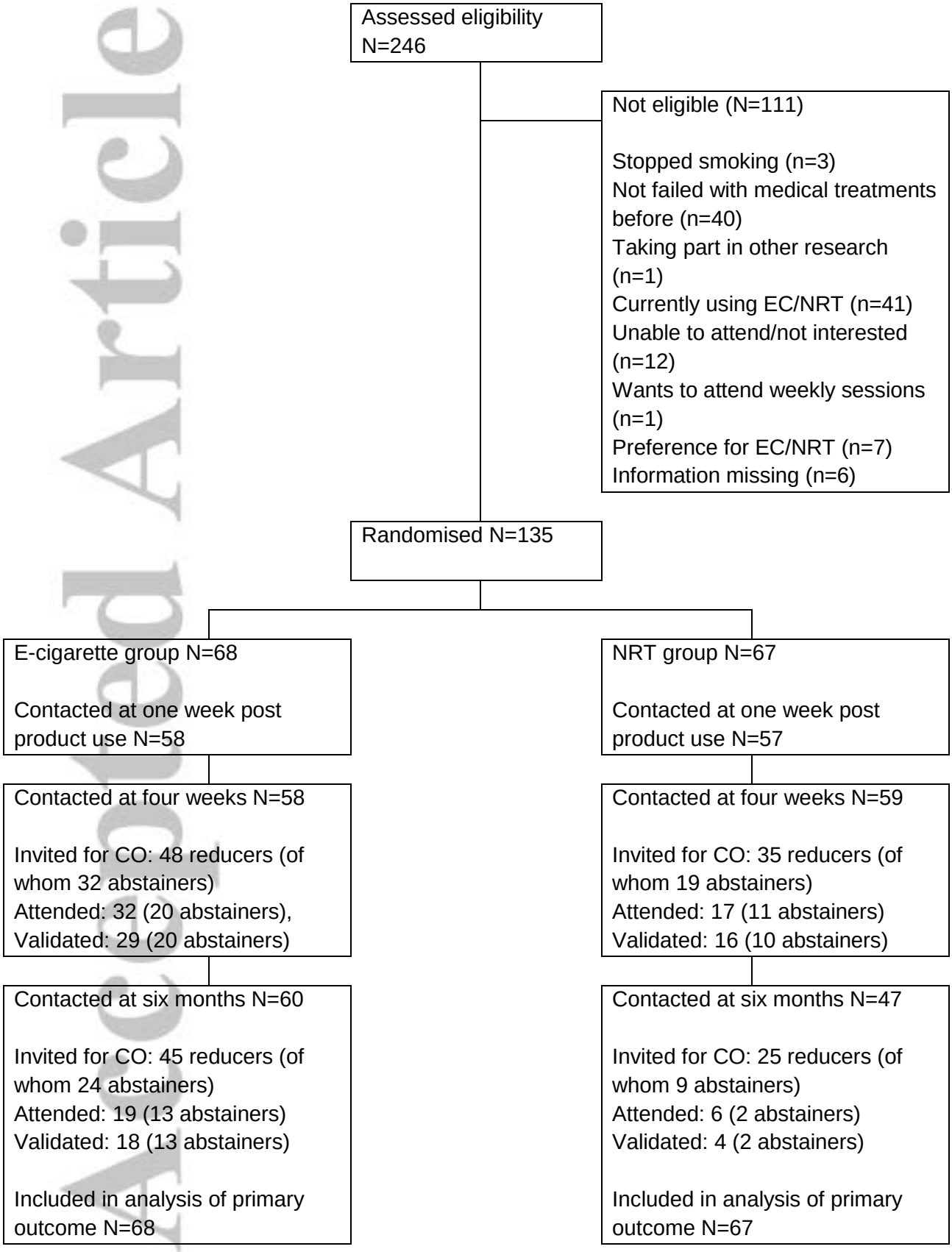

Table 1. Sample characteristics

	EC arm (N=68)	NRT arm (N=67)
Median age (IQR)	41 (16)	40 (19)
N (%) male	36 (52·9)	33 (49·3)
N (%) in paid employment	49 (72·0)	49 (73·1)
N (%) entitled to free prescriptions	23 (33·8)	16 (23·9)
N (%) white British	34 (50)	35 (52·2)
N (%) with higher/further education*	49 (72·1)	47 (70·1)
Treatments tried earlier N (%)**		
NRT	34 (65·4)	33 (63·5)
Varenicline	4 (7·7)	4 (7·7)
Both NRT and varenicline	14 (26·9)	15 (28·8)
N (%) who tried EC earlier	21 (31)	33 (49)
N (%) aiming to reduce smoking	13 (19·1)	16 (23·9)
Median cigarettes per day (IQR)	15 (10)	15 (10)
CO median (IQR)	16 (12.5)	16 (16)
FTCD median (IQR)	5 (3)	4 (3)

*Education after secondary school

** N=104 due to missing data

Table 2. Smoking reduction of at least 50% and smoking cessation in the two study arms

	EC arm (N=68) N (%)	NRT arm (N=67) N (%)	RR (95%CI)	p-value
CO-validated reduction in smoking				
At four weeks, CO validated	29 (42·7)	16 (23·9)	1.79 (1.07-2.97)	p=0·03
At six months, CO validated	18 (26·5)	4 (6·0)	4·43 (1·58-12·41)	p=0·005
Self-reported* reduction in smoking				
At four weeks, self-reported	48 (70·6)	35 (52·2)	1·35 (1·03-1·78)	p=0·03
At six months, self-reported	45 (66·2)	25 (37·3)	1·77 (1·25-2·53)	p=0·002
CO-validated smoking cessation				
At four weeks, CO validated	20 (29.4)	10 (14·9)	1.97 (1·00-3·89)	p=0·05
At six months, CO validated	13 (19·1)	2 (3·0)	6·40 (1·50-7·30)	p=0·01
Self-reported* smoking cessation				
At four weeks, self-reported	32 (47.1)	19 (28.4)	1·66 (1·05-2·62)	p=0·03
At six months, self-reported	20 (29·4)	6 (9·0)	2·82 (1.28-6·21)	p=0·01

*Self-reported groups include all participants reporting the given outcome, whether validated or not.
Note: A sensitivity analysis was conducted adjusting for previous use of EC at baseline. This did not change the results.

Table 3. Smoking reduction and cigarette consumption in non-abstainers

Time point	EC arm	NRT arm	Difference
Smoking reduction at six months* (N, %)			
Self-reported^ (N=55 EC, N=65 NRT)	32 (58.2)	22 (33.9)	RR:1.7 (1.1-2.6) p=0.009
CO-validated (N=68 EC, N=67 NRT)	5 (9.1)	2 (3.1)	RR=3 (0.6–14.6) p=0.18
Cigarette consumption (Cigarettes per day)**			
Baseline N=68 EC, N=67 NRT Median (IQR)	15 (10-20)	15 (10-20)	*z*=-0·2[a], p=0·83
Four weeks N=35 EC, N=44 NRT Median (IQR)	2 (0-10)	5·5 (2-15)	z=-1·7[a], p=0·08
Six months N=44 EC, N=41 NRT Median (IQR)	0 (0-10)	7 (0-15)	z=-2·4[a], p=0·02
Six months – change from baseline N=44 EC, N=41 NRT Mean (SD)	-12·8 (8·9)	-8·1 (8·1)	t=-2·5[b], p=0·01

* Participants lost to follow-up are included as non-reducers

** Only participants providing the information are included

^ Self-reported groups include all participants reporting the given outcome, whether validated or not

[a] Wilcoxon rank-sum test; [b] Independent t-test,

Note: Smoking <1 cig/day was coded as 0

Table 4: EC product use by participants in the EC arm

	One week	Four weeks	Six months
E-liquid flavours (N)*	**N=49**	**N=52**	**N=31**
Fruit	21	30	18
Tobacco	13	14	6
Menthol/mint	8	6	5
Sweet	5	4	2
Energy/soft drink	2	2	2
Coffee	3	1	0
Other	6	5	2
E-liquid strength (mg) N (%)	**N=48**	**N=49**	**N=31**
N (%) using 0%	1 (2)	1 (2)	1 (3)
N (%) using 1-10% nicotine	26 (54)	29 (59)	25 (81)
N (%) using >10% nicotine	21 (43.8)	19 (38.8)	5 (16.1)
EC strength in those providing data at all time points (N=23) Median (IQR)[a]	10 (3-12)	6 (3-12)	6 (3-12)
Source of the initial EC product N (%)			
Collaborating vape shops	54 (79.4)		
Other vape shops	5 (7.4)		
Used EC they already had at home	2 (2.9)		
Information missing (did not attend preparation session)	7 (10.3%)		

* Some participants used multiple flavours; the N is based on the overall number of entries at each time point

[a] Friedman test p = 0·003

Table 5: Number (%) using allocated product at each timepoint

	EC arm (n=68)	NRT arm (n=67)	Difference
Week 1	50 (73.5)	52 (77.6)	$X^2(1)=0{\cdot}3$, p=0·58
Week 4	52 (76.5)	43(64.2)	$X^2(1)=2{\cdot}5$, p=0·12
Six months	32 (47.1)	7 (10.5)	$X^2(1)=22{\cdot}0$, p<0·001

Table 6: Product ratings at baseline, median and interquartile range (IQR)

	EC (N=60)	NRT (N=55)	Wilcoxon test
Pleasant to use (1-10 where 1=not at all; 10=extremely)	5 (3-8)	6 (3-8)	Z=-0·04,p=0·97
Will you use it regularly? (1-10 where 1=not at all; 10=extremely)	10 (8-10)	10 (9-10)	Z=-1·01, p=0·32
Rating compared to normal cigarettes (1-21 where 1=much worse, 11=as good, 21=much better)	11 (6-15)	11 (6-13)	Z = 0·80, p=0·42

Table 7. Product ratings at one and four weeks, median and interquartile range (IQR)

	EC (N=44-52)*	NRT (N=29-52)*	Wilcoxon test
Helpfulness (1=not at all; 5=extremely)			
Week one	4 (4-5)	4 (4-5)	z=-0·3, p=0·75
Week four	5 (4-5)	4 (3-5)	z=2·6, p=0·01
Taste compared to cigarettes (1=much worse; 5=much better)			
Week one	4 (3-5)	3 (1-5)	z=1·9, p=0·06
Week four	5 (2-5)	3 (2-4)	z=2·5, p=0·01
Satisfaction compared to cigarettes (1=much worse; 5=much better)			
Week one	2 (2-3)	2 (1-4)	z=0·01,p=0·99
Week four	3 (2-4)	3 (2-3)	z=0·8, p=0·45

* N varies due to missing data