

THE UK ELECTRONIC CIGARETTE RESEARCH FORUM

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Electronic Cigarette Research Briefing – February 2016

This research briefing is part of a series of monthly updates aiming to provide an overview of new studies on electronic cigarettes. The briefings are intended for researchers, policy makers, health professionals and others who may not have time to keep up to date with new findings and would like to access a summary that goes beyond the study abstract. The briefing also aims to provide a critical overview of individual studies and put them in the context of what we already know from previous research.

The studies selected in these briefings do not form an exhaustive list of every e-cigarette related study published each month. Instead they include those most relevant to key themes identified by the newly formed UK Electronic Cigarette Research Forum. This includes mechanisms and safety, cessation, population level impact, marketing and unintended consequences. For an explanation of the search strategy used, please see the end of this briefing.

The text below provides an overview of the aims, key findings and limitations of each of the highlighted studies. The briefing concludes with a section that puts the study findings in the context of the wider literature and what we know about existing research gaps.

If you would prefer not to receive this briefing in future, just let us know by emailing tobacco control at tobaccocontrol@cancer.org.uk.

1. The efficacy and short-term effects of electronic cigarettes as a method for smoking cessation: a systematic review and a meta-analysis.

- **Study aims**

This Canadian review assessed the efficacy of e-cigarettes for smoking cessation by summarising and combining observational and randomised controlled trials (RCTs) where nicotine-containing e-cigarettes are compared to placebo e-cigarettes or other nicotine replacement therapy. All e-cigarette use is included, whether or not users were trying to quit. 5 studies were included in the review, including 840 participants, 581 of whom received nicotine e-cigarettes and the rest placebo e-cigarettes. Desire to smoke, withdrawal symptoms, and adverse events in adult smokers are also summarised.

- **Key findings**

A meta-analysis combining the two studies which measured long-term smoking cessation with participants using nicotine-containing e-cigarettes compared to placebo e-cigarettes found no significant difference between groups (RR 2.02; 95 % CI 0.97, 4.22).

Confidence intervals for the objective impact measures (desire to smoke, irritability, restlessness, poor concentration, depression and hunger) were wide and all results were non-significant. There was also no significant difference in incidence of adverse events.

- **Limitations**

This review includes comparative studies rather than all prospective studies, so measures are similar enough to perform a meaningful meta-analysis for smoking cessation. However there are only the two small RCTs, which have been reviewed previously, and so the overall quality of evidence is low. E-cigarette products, use and attitudes have changed significantly since these studies were conducted in 2010-2013, so it's not clear how representative these results are of e-cigarette use in the UK today.

Khoudigian S, Devji T, Lytvyn L, Campbell K, Hopkins R, O'Reilly D. The efficacy and short-term effects of electronic cigarettes as a method for smoking cessation: a systematic review and a meta-analysis. *Int J Public Health*. 2016. doi: [10.1007/s00038-016-0786-z](https://doi.org/10.1007/s00038-016-0786-z)

2. A randomized trial comparing the effect of nicotine versus placebo electronic cigarettes on smoking reduction among young adult smokers.

- **Study aims**

This US RCT investigated whether daily smokers aged 21-35 given nicotine-containing e-cigarettes were more likely to reduce smoking by 50% compared to those given non-nicotine e-cigarettes. Participants interested in reducing cigarette consumption were recruited through leaflets and Craigslist. Those currently using any smoking cessation medications or e-cigarettes were excluded. 3 weeks supply of tobacco flavoured disposable cig-a-likes was given to participants and they were also provided with telephone counselling.

- **Key findings**

Both groups significantly reduced cigarette consumption. At week 3 (but not week 1) those using nicotine e-cigarettes were smoking significantly fewer cigarettes per day on average. After adjusting for e-cigarette consumption and baseline readiness to quit, those using nicotine e-cigarettes were twice as likely to have achieved 50% reduction in smoking at week 3. However exhaled CO was not different between the groups at any time point.

Both groups reported using the same number of e-cigarettes per day and there was no significant difference in satisfaction ratings between the groups. There was also no difference in reported side effects.

- **Limitations**

This study used a specified cig-a-like model for consistency and real-world use may differ, for example when people are able to use different types of devices and

flavour choices or when they don't have the behavioural support session. Reduction in smoking was self-reported.

There was no non-e-cigarette arm so although a benefit in smoking reduction was seen with both nicotine and non-nicotine e-cigarettes, it may be that trial participation or the behavioural support given played a role.

It's not clear how smoking reduction with e-cigarette use translates to cessation. In this small study 2 participants in the nicotine containing group were abstinent at week 3 and only 1 in the control arm.

Tseng TY, Ostroff JS, Campo A, Gerard M, Kirchner T, Rotrosen J, Shelley D. A Randomized Trial Comparing the Effect of Nicotine Versus Placebo Electronic Cigarettes on Smoking Reduction Among Young Adult Smokers. *Nicotine Tob Res.* 2016 Jan 17. pii: ntw017. doi: 10.1093/ntr/ntw017

3. [Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii.](#)

- **Study aims**

This Hawaiian study surveyed 14-16 year old children in schools and followed them up a year later (n=2338 and 2239) to explore e-cigarette and cigarette awareness, attitudes and use. They controlled for demographic characteristics as well as some predictors of smoking behaviour such as parental support, sensation seeking and rebelliousness. E-cigarette and cigarette use were measured on a 0-6 scale from never to use every day.

- **Key findings**

31% of participants used e-cigarettes and 15% smoked in the first sample and by a year later this has increased to 38% and 21% respectively. The majority of e-cigarette users had used them less than 4 times rather than more regularly.

Those who had only used e-cigarettes were more likely to have smoked a year later than those who hadn't used an e-cigarette. This was true at any level of e-cigarette use but regular (defined at yearly or monthly) smoking was only related to higher levels of e-cigarette use. Regular smoking was still rare at follow up with only 1% of respondents smoking every day.

Older age, Caucasian or Native Hawaiians ethnicity and high rebelliousness scores also predicted onset of ever smoking at follow-up.

- **Limitations**

It's not clear how representative this sample is of Hawaiian children or whether these results could apply to the UK. Regular cigarette and e-cigarette use was also low in this sample, making numbers for analysis quite small.

Although some potential confounders are controlled for, there may be other factors which influence both e-cigarette and cigarette use such as peer influence or parental smoking.

Wills TA, Knight R, Sargent JD, Gibbons FX, Pagano I, Williams RJ. Longitudinal study of e-cigarette use and onset of cigarette smoking among high school students in Hawaii.

Tob Control. 2016 Jan 25. pii: tobaccocontrol-2015-052705. doi: 10.1136/tobaccocontrol-2015-052705.

4. A longitudinal study of cotinine in long-term daily users of e-cigarettes.

- **Study aims**

This study followed 98 exclusive e-cigarette users in Switzerland, France and the US to track changes in cotinine levels and e-cigarette use. Vapers were sent a questionnaire and vial for saliva collection at baseline and again 8 months later.

- **Key findings**

Only 1% of participants were using cig-a-likes, 44% second- and 53% third-generation devices. Participants' cotinine levels were quite varied but were reported to be similar to levels observed in smokers.

Cotinine levels remained stable between assessments but self-reported concentration of nicotine used decreased (from 11mg/mL to 9.5mg/mL in second- and 6mg/mL in third-generation users). Reported number of puffs per day was stable but the volume of e-liquid used increased.

- **Limitations**

The participants were not representative of the population (or vapers) as they were almost exclusively daily exclusive e-cigarette users recruited through vaping websites and forums. There was a low response rate, with only 29% of those originally contacted completing both measurements.

Only two samples were taken to measure cotinine levels and e-cigarette use information relies on self-report and e-liquid volume and number of puffs may be difficult to estimate.

Etter JF. A longitudinal study of cotinine in long-term daily users of e-cigarettes. Drug Alcohol Depend. 2016 Jan 14. pii: S0376-8716(16)00010-7. doi: 10.1016/j.drugalcdep.2016.01.003.

Overview

This month we have included four papers examining e-cigarettes for smoking cessation and reduction, use over time in young people and the relationship with smoking, and a longitudinal study of non-smoking regular e-cigarette users. These studies were conducted by researchers in Canada, the USA and Switzerland.

The first study was another systematic review of e-cigarettes for smoking cessation, following on from a Cochrane review on this topic and other recent papers drawing on the same body of evidence. The main focus was a meta-analysis of the two small existing trials of e-cigarettes, one conducted in Italy and one in New Zealand which used now obsolete (and no longer available) first generation cig-a-likes. Readers may wonder why the inconclusive results were slightly different to the Cochrane review which indicated some promise for smoking cessation from e-cigarettes when compared with placebo. This is largely due to the fact that the Canadian authors chose to use the 6 month outcomes from the Italian trial (by Caponetto et al.) rather than the trial's primary outcome which was over a longer time period.

The second study was an RCT from the US examining the extent to which use of nicotine and non-nicotine containing cig-a-like devices were associated with smoking reduction at one and three weeks in regular tobacco smoking young adults. Both groups reduced their cigarette consumption by three weeks. This suggests that even non nicotine containing e-cigarettes may be useful in this regard (perhaps for the behavioural aspects of e-cigarettes which mimic smoking) particularly when combined with some behavioural support as all participants received telephone counselling. However, reductions were greater in those who used the nicotine containing devices. CO levels were not lower, so we can't assume that participants reduced the harm from smoking (although exhaled CO is only one way to assess this). [Previous research](#) has suggested that smoking reduction with Nicotine Replacement Therapy (NRT) may lead to cessation in the longer term and this finding is the primary reason why cutting down with NRT is recommended for tobacco harm reduction. Future studies need to examine the effects of reduction using e-cigarettes over a longer period.

Thirdly we've included another longitudinal study of American teenagers (in Hawaii) aged 14-16 – a key age for smoking uptake. The authors found both e-cigarette and tobacco use increased one year after baseline. Those who had started with e-cigarettes only were more likely to be using tobacco at least occasionally at follow up. These young people had characteristics that previous research has found were predictive of smoking uptake although some key factors such as parental smoking were not included. Fortunately, regular smoking was still very rare at follow up, at just 1% of the overall sample.

Finally we've included a study of former smokers who had become exclusive e-cigarette users recruited from a stop smoking website with members in Switzerland, France and the US. This population is important for research in order to examine firstly levels of nicotine use over time as this study did but also exposure to toxicants from exclusive use of e-cigarettes as other ongoing studies are doing, including some in the UK. Participants were followed up over 8 months. Some reported cutting down the nicotine concentration in the e-liquids they were using, with the majority using later generation refillable e-cigarettes. However this was not reflected in cotinine samples which showed a fairly consistent level of saliva cotinine concentration between baseline and follow up. This was explained by increased consumption of lower nicotine concentration e-liquid to obtain the same level of nicotine as at the start of the study. The author speculates that consumption of more e-liquid could result in higher toxicant exposure and that taking fewer puffs using a higher strength liquid may be more desirable. This has interesting implications for any advice given to vapers about cutting down nicotine content over time. Further research should consider, for individuals, the best type of device and nicotine concentration needed to avoid any relapse to smoking while also taking into account user preferences.

Other studies from the last month that you may find of interest:

- [Effect of continuous smoking reduction and abstinence on blood pressure and heart rate in smokers switching to electronic cigarettes.](#)
- [Real-Time Chemical Analysis of E-Cigarette Aerosols By Means Of Secondary Electrospray Ionization Mass Spectrometry.](#)
- [Cigarette Smoking and Electronic Cigarettes Use: A Meta-Analysis.](#)
- [A Qualitative Approach to Understanding Real-World Electronic Cigarette Use: Implications for Measurement and Regulation.](#)

- [Protocol proposal for, and evaluation of, consistency in nicotine delivery from the liquid to the aerosol of electronic cigarettes atomizers: regulatory implications.](#)
- [Comparison between electronic cigarette refill liquid and nicotine on metabolic parameters in rats.](#)
- [E-cigarette regulation and policy: UK vapers' perspectives.](#)
- [Labelling of electronic cigarettes: regulations and current practice.](#)
- [E-cigarette use among US adolescents: secondhand smoke at home matters.](#)
- [Frequency of E-Cigarette Use and Cigarette Smoking by American Students in 2014.](#)
- [Noticing e-cigarette advertisements and associations with use of e-cigarettes, disapproval of smoking, and quitting smoking. Findings from the International Tobacco Control \(ITC\) Netherlands Survey.](#)
- [E-Cigarette Use and Intention to Initiate or Quit Smoking Among US Youths.](#)
- [Reasons for electronic cigarette use beyond cigarette smoking cessation: A concept mapping approach.](#)
- [Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapours.](#)
- [Vape, quit, tweet? Electronic cigarettes and smoking cessation on Twitter.](#)

Search strategy

The Pubmed database is searched in the middle of each month, for the previous month using the following search terms: e-cigarette*[title/abstract] OR electronic cigarette*[title/abstract] OR e-cig*[title/abstract] OR (nicotine AND (vaporizer OR vapourizer OR vaporiser OR vapouriser))

Based on the titles and abstracts new studies on e-cigarettes that may be relevant to health, the UK and the UKECRF key questions are identified. Only peer-reviewed primary studies and systematic reviews are included – commentaries will not be included. Please note studies funded by the tobacco industry will be excluded.

This briefing is produced by Nicola Smith from Cancer Research UK with assistance from Professor Linda Bauld and Kathryn Angus at the University of Stirling and the UK Centre for Tobacco and Alcohol Studies, primarily for the benefit of members of the CRUK & PHE UK E-Cigarette Research Forum. If you wish to circulate to external parties, do not make any alterations to the contents and provide a full acknowledgement. Kindly note Cancer Research UK cannot be responsible for the contents once externally circulated.