

Electronic cigarette research briefing – March 2015

This research briefing is the first in 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.

We would really appreciate hearing your feedback on this first research briefing – please do share your thoughts during the next week. If you would prefer not to receive this briefing in future, just let us know by emailing tobaccocontrol@cancer.org.uk

1. Nicotine concentrations with electronic cigarette use: effects of sex and flavor.

- Study aims**

This study, conducted in the USA, aimed to explore the changes in blood nicotine concentration in smokers after using an e-cigarette for 5 minutes. 20 non-treatment seeking smokers were recruited via advertising and GP practices and instructed on the use of a second-generation of e-cigarette (Joye eGo-C with 18mg/mL). In a laboratory setting, users were allowed to use the e-cigarette *ad lib* for 5 minutes and were monitored for half an hour. Differences in gender and flavour (menthol and tobacco vs. tobacco alone) were explored.

- Key findings**

Nicotine concentrations significantly increased from baseline to 5 minutes by 4-5 ng/mL. The peak nicotine concentration reached varied significantly. In women using their non-preferred flavour significantly lower nicotine peaks were observed compared with women using their preferred flavour or either of the male groups.

Moderate adverse events were reported including cough, mouth/throat irritation, nausea and headache, with one subject discontinuing use due to more severe adverse events (itchy throat and cough).

- Limitations**

This study only explored the blood nicotine concentrations achieved with one e-cigarette brand in two flavours in a very small number of non-treatment seeking, reasonably healthy smokers, not all of whom had used e-cigarettes before, so is unlikely to be representative of the users in the USA as a whole.

Nicotine concentration was only measured at 5 minute intervals, it may be that the spike of peak nicotine concentration was sooner than this and higher than what was measured at

this point. The e-cigarette was also only used for 5 minutes; it could be that use over a longer period of time could achieve higher nicotine levels.

Oncken CA, Litt MD, McLaughlin LD, Burki NA. Nicotine concentrations with electronic cigarette use: effects of sex and flavor. *Nicotine Tob Res.* 2015 Apr;17(4):473-8. doi:10.1093/ntr/ntu232

2. Nicotine levels in electronic cigarette refill solutions: A comparative analysis of products from the US, Korea, and Poland

- **Study aims**

This study measured the nicotine concentration from 91 popular e-liquids sold online in the US, Korea and Poland and compared this to the stated content.

- **Key findings**

E-liquids from the US showed highest variability; 28% of products tested showed differences in nicotine content from the label by more than $\pm 20\%$ and nicotine was also detected (at trace levels) in three of the four liquids claiming to be nicotine free.

For Korea 28% of products tested showed differences in nicotine content from the label by more than -20% but no nicotine was detected in nicotine free liquids, however there was one sample which had nicotine at $150.3 \pm 7.9 \text{ mg/mL}$.

Only 10% of the Polish samples showed differences in nicotine content from the label by more than -20% and none of the nicotine free samples contained nicotine.

- **Limitations**

These products were selected based on online popularity and this may not reflect off-line e-liquids. It was also not possible to verify where each of the samples had originated from.

Although three repeats were conducted for each sample, only one sample was purchased so variability may exist between batches.

Goniewicz ML, Gupta R, Lee YH, Reinhardt S, Kim S, Kim B, Kosmider L, Sobczak A. Nicotine levels in electronic cigarette refill solutions: A comparative analysis of products from the US, Korea, and Poland. *Int J Drug Policy.* 2015. doi: 10.1016/j.drugpo.2015.01.020

3. Does Vaping in E-Cigarette Advertisements Affect Tobacco Smoking Urge, Intentions, and Perceptions in Daily, Intermittent, and Former Smokers?

- **Study aims**

This study, conducted in the USA, aimed to explore the effect of exposure to e-cigarette advertising on smokers (daily and intermittent) and former smokers. 884 participants were recruited through an online survey tool and shown either a selection of popular e-cigarette adverts showing vaping, a selection of these ads with the vaping visuals removed or no adverts.

- **Key findings**

Although the abstract claims “visual depictions of vaping in e-cigarette commercials increase daily smokers’ urge to smoke cigarettes” – the post-test urges to smoke were higher in the cue condition compared to the two control conditions but the urges across all groups were lower after the test.

Former smokers in the cue condition reported lower intentions to abstain from smoking than former smokers in other conditions however this was not tested beforehand so we

cannot know if they had similar intentions going in or if there was any change. Self-efficacy and attitude towards smoking cessation did not vary significantly across groups.

- **Limitations**

The main limitation of this study is that participants were allowed to smoke during the test which will have influenced the ratings of urges to smoke and the other variables were not measured before and after. There were no significant differences between smoking activity across groups (the authors highlight that the daily smokers in the cue condition were more likely to smoke than the other two conditions but this is based on a “marginally significant” result $p=0.54$).

Although the selection of online adverts is a good approach, because of the fast-paced nature of this advertising it may already be out of date. The survey is also self-selected, non-representative and relies on self-report.

Maloney EK, Cappella JN. Does Vaping in E-Cigarette Advertisements Affect Tobacco Smoking Urge, Intentions, and Perceptions in Daily, Intermittent, and Former Smokers? *Health Commun.* 2015 Mar 11:1-10. doi: 10.1080/10410236.2014.993496

4. Electronic Cigarette Sales to Minors via the Internet

- **Study aims**

This study, conducted in one state in the USA, aimed to explore whether under-18s were able to purchase e-cigarettes online in a state in the US where sales to minors is banned. (North Carolina has an e-cigarette age verification law.) 11 14-17 year olds were supported in attempts to purchase e-cigarettes from 98 popular online suppliers.

- **Key findings**

76.5% of online purchase attempts were successfully delivered, with no attempt to verify age at delivery. Only 5 of the attempts were rejected due to age verification, 18 failed for other reasons. 83% of strategies used to verify age were highly ineffective (such as a check box) and 17% did not attempt to verify age at all.

- **Limitations**

It's not clear how generalisable these results would be outside of North Carolina.

Williams RS, Derrick J, Ribisl KM. Electronic Cigarette Sales to Minors via the Internet. *JAMA Pediatr.* 2015 Mar 2;169(3):e1563. doi: 10.1001/jamapediatrics.2015.63

5. Factors associated with dual use of tobacco and electronic cigarettes: A case control study.

- **Study aims**

This study is the second analysis of a multi-country e-cigarette survey, for which initial data was [published in 2014](#). A questionnaire to explore e-cigarette use was posted online in 10 different languages. This analysis aimed to explore the characteristics of tobacco and e-cigarette dual users, compared to those exclusively using e-cigarettes (all former smokers).

- **Key findings**

Of the original 19,441 survey respondents, 3682 were dual users.

Participants included: 85.1% from Europe, 9.6% from America, 2.0% from Asia, 0.6% from Australia, and 0.1% from Africa

In multivariate analyses, these dual users were more likely than the non-smoking users to:

- have higher educational attainment
- be occasional e-cigarette users
- use pre-filled cartomisers
- have used lower nicotine levels when starting e-cigarettes
- use first or second generation devices
- be less likely to claim they started using e-cigarettes to reduce smoke exposure to family members but more likely to want to avoid the smoking ban in public places
- have higher average perceptions of risk from e-cigarettes.

The risk perception scores were interesting; 14% of non-smoking vapers claimed e-cigarettes were absolutely harmless compared to 8.5% of dual users and less than 1% of both groups thought e-cigarettes were more harmful than smoking.

The dual users also claimed to now be smoking significantly less on average (previously smoking 20-a-day on average compared to 4-a-day currently).

- **Limitations**

Although this survey was large, the participants were self-selected e-cigarette users recruited primarily via e-cigarette user internet forums and so may not be representative of all e-cigarette users. This is highlighted by the fact that 94-97% of users in this study were daily e-cigarette users whereas the smoking toolkit study suggests 7 and 21% of ex-smoking users and dual users respectively use their e-cigarette less than daily.

This online survey had no biochemical verification so all results rely on self-report. And because of the cross-sectional nature of this study it is not possible to be confident about causality.

Farsalinos KE, Romagna G, Voudris V. Factors associated with dual use of tobacco and electronic cigarettes: A case control study. *Int J Drug Policy*. 2015. doi: 10.1016/j.drugpo.2015.01.006

Overview

These five diverse studies highlight different aspects of e-cigarette use including nicotine delivery and content, advertising, user characteristics and sales to children. The first paper is a small study of just 20 users. It supports what has been found in previous studies, that nicotine delivery from e-cigarettes varies significantly – in this case this varied even when the same brand was used. It has been argued that to act as an effective smoking cessation aid, e-cigarettes need to consistently deliver enough nicotine for users to substitute their smoking and avoid nicotine withdrawal symptoms. Other studies have suggested the initial nicotine peak from using an e-cigarette is less than smoking a cigarette but with more sustained use, similar nicotine levels can be reached. An interesting finding from this paper is that amongst women at least, they took in less nicotine when they were not able to use their preferred flavour (menthol vs tobacco). This gives some indication that flavour may be one of a number of determinants of how e-cigarettes are used and how much nicotine users take in.

The second paper also confirms previous research (some of which has been conducted in the UK) illustrating that information on nicotine content in e-liquid containers may not be accurate. This study tested liquids from three countries which provides a useful addition to the existing literature. Only in one country, the USA, was nicotine detected in liquids that claimed to be nicotine free, but this was only at trace levels. In terms of consumer safety and assurance in terms of nicotine delivery, this study provides further evidence that better labelling and consistency of products would be

helpful. In Europe, some of this will be addressed by requirements to be introduced through the Tobacco Products Directive. Some commentators have suggested that labelling indicating no, low, medium or high nicotine content may be most useful to consumers.

The study on e-cigarette advertising and its possible impact on perceptions, urges and intentions to smoke in current and ex smokers provides some preliminary data on e-cigarettes marketing and smoking behaviour. However, the significant limitations of this paper make it very difficult to draw any firm conclusions. Examining the impact of e-cigarette advertising in the UK and elsewhere is an important area for research and future studies should examine this in more detail. Particular concern about the impact of e-cigarette advertising on children has been expressed, and the fourth study included here does suggest that children are able to buy these products online, at least in the US state where this research was conducted. Online purchasing will need to be considered when the UK bans the sale of e-cigarettes to minors and how this might be regulated. In addition, online purchase is likely to be preceded and accompanied by online advertising, and this is also a relevant area for research.

Finally, there is significant policy and research interest in the extent to which users of e-cigarettes are stopping smoking or continuing to smoke ('dual use') while using these products. We know in England, based on the [Smoking Toolkit study](#), that the majority of e-cigarette users are dual users (around 85%). One new multi country study summarised here provides useful evidence on the differences between dual users and people who have stopped smoking completely and are using e-cigarettes. The dual users in this study reported that they had significantly cut down their smoking since starting to use e-cigarettes, reducing from an average of 20 to 4 cigarettes per day. [Previous research](#) has suggested that smokers who reduce consumption while using nicotine replacement therapy are more likely to go on to stop in the future (rather than those who simply cut down and don't use NRT). Thus dual users may be on a pathway to becoming non smokers, but this requires further (ideally longitudinal) research, ideally with biochemical validation which this study did not include. It also sheds light on some of the characteristics of dual users which may help inform future interventions or studies – that they may be less confident that e-cigarettes are safer than smoking and that they may be less concerned about second hand smoke exposure to others.

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

- [The effects of electronic cigarette emissions on systemic cotinine levels, weight and postnatal lung growth in neonatal mice](#)
- [E-cigarette Marketing and Older Smokers: Road to Renormalization](#)
- [Factors associated with electronic cigarette users' device preferences and transition from first generation to advanced generation devices](#)
- [Perceived Characteristics of E-cigarettes as an Innovation by Young Adults](#)
- [The prevalence, correlates and reasons for using electronic cigarettes among New Zealand adults](#)

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 UKERCRC key questions are identified. Only peer-reviewed primary studies and meta-analyses 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.

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