THE UK ELECTRONIC CIGARETTE RESEARCH FORUM

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Electronic cigarette research briefing – September 2015

We note that this month's bulletin is slightly longer than previous versions. We would welcome your feedback on the content. Are the summaries of articles sufficient? Is the commentary at the end detailed enough or perhaps too detailed? Please send any comments to tobaccocontrol@cancer.org.uk

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.

1. E-cigarette marketing in UK stores: an observational audit and retailers' views

- **Study aims**
  This Scottish study audited stores selling tobacco products to explore how e-cigarettes are being promoted at the point of sale 12 months apart, retailers experience with these products and how they perceive market trends. Four communities of differing levels of social deprivation were chosen and all stores selling tobacco (n=96) were audited between 2013 and 2014. Retailer perceptions were explored through 25 interviews.

- **Key findings**

The number of e-cigarette point of sale display units and number of brands displayed increased over time whereas the proportion of shops with external advertising for e-cigarettes did not differ, but was more common in more deprived areas. In 2014, only 23% of shops were not selling e-cigarettes, around a third were selling one brand and the maximum number of brands on sale in a single shop was 6.

E-cigarettes were displayed close to products of interest to children in 36% of stores – most commonly confectionary. However no retailers said that children had tried to buy e-cigarettes.

The reported appeal of e-cigarettes was high profit margins (up to 40% compared to 5 6% for cigarettes). However the diversity of brands was a source of confusion and the uncertainly of the market and initial outlay put some retailers off. Some customers were perceived to purchase e-cigarettes as cessation aids, and others, particularly low-income smokers, as a cheaper temporary alternative to tobacco.

- **Limitations**
  This is a snapshot of stores in Scotland but it's not clear how representative this may be of the UK. The stores in this sample were selling tobacco, which will exclude specialist e-cigarette stores or kiosks and pharmacies. Online sales will also not be captured.

  The timing of the rise in popularity of e-cigarettes has coincided with the tobacco point of sale ban in the UK which may limit the applicability of these findings to other countries.

Eadie D, Stead M, MacKintosh AM, MacDonald L, Purves R, Pearce J, Tisch C, van der Sluijis W, Amos A, MacGregor A, Haw S. E-cigarette marketing in UK stores: an observational audit and retailers' views. BMJ Open. 2015 Sep 11;5(9):e008547. doi: 10.1136/bmjopen-2015-008547.

2. Contexts of cigarette and e-cigarette use among dual users: a qualitative study

- **Study aims**
  This qualitative focus group study in Hawaii explored the contexts of cigarette versus e-cigarette use among dual users. 62 young adult e-cigarette users were split into 12 focus groups – there were a mixture of current and former smokers and 2 never smokers.

- **Key findings**
  Some of the key themes identified revolved around environmental stimuli or personal situations where cigarettes were deemed to be superior to e-cigarettes; for example when cravings were strong, when participants were particularly stressed or where there was a strong habit formed (like first thing in the morning or last thing at night). Cigarettes also seem to be preferred when others around them are smoking or as a treat when partying on a weekend. Finally cigarettes were sometimes used when e-cigarettes are not available for example when the battery runs out or between trialling different types of e-cigarette.

  E-cigarettes seemed to be preferred when cigarettes could not be used (such as during work or in the home) but also when exercising or for convenience when the user doesn't want to smell like cigarettes. One user also mentioned e-cigarettes as similar to hookah, but more convenient. Generally e-cigarettes were seen as a less social activity than smoking or hookah.

- **Limitations**

This was a small non-representative sample of young adults in Hawaii, so we cannot know how applicable these findings may be to UK users.

Some of the participants were no longer dual users and may not reliably remember only situations when they used to smoke as a dual user. Different types of dual users (former and current, light and heavy users) were not separated out so this study cannot show which of the themes were associated with successfully moving away from tobacco.

Pokhrel P, Herzog TA, Muranaka N, Regmi S, Fagan P. Contexts of cigarette and e-cigarette use among dual users: a qualitative study. BMC Public Health. 2015 Sep 4;15:859. doi: 10.1186/s12889-015-2198-z

3. Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults

- **Study aims**
  This longitudinal US study aimed to explore how smoking and smoking susceptibility changed over a year in non-smokers not susceptible to smoking at baseline, and how this varied by e-cigarette use, demographic variables and personal/ environmental characteristics. Of 728 young people (aged 16-26) not susceptible to smoking, 507 were successfully followed up from 2012/13 to 2013/14.

- **Key findings**
  At follow up, 11 of 16 e-cigarette users (68.8%) and 128 of 678 of those who had not used e-cigarettes (18.9%) progressed toward cigarette smoking – this includes becoming more susceptible to smoking or having tried a cigarette.

  The 16 young people who had tried an e-cigarette were not significantly different to those who hadn't apart from the fact that they had higher 'sensation seeking' score (measured by items such as 'I like to do dangerous things').

- **Limitations**
  This non-representative sample only included a very small number of young people who had tried an e-cigarette and asked about ever having tried an e-cigarette or cigarette – these experimenters cannot be classified as "users" of either of these.

  The surveys did not ask what types of e-cigarettes were used or whether they contained nicotine. And because the baseline sample included non-smokers, the study could not reflect any positive impact of e-cigarettes helping smokers move away from tobacco.

Primack BA, Soneji S, Stoolmiller M, Fine MJ, Sargent JD. Progression to Traditional Cigarette Smoking After Electronic Cigarette Use Among US Adolescents and Young Adults. JAMA Pediatr. 2015 Sep 8:1-7. doi: 10.1001/jamapediatrics.2015.1742.

4. Electronic cigarette nicotine delivery can exceed that of combustible cigarettes: a preliminary report

- **Study aims**

This US study tracked plasma nicotine levels in relation to e-liquid nicotine levels in e-cigarette users and also measured puffing behaviour. 16 experienced e-cigarette users were given a tank-style e-cigarette and randomised to four different nicotine e-liquid concentrations (0, 8, 18 or 36 mg/mL) each two days apart, with a prescribed puffing regimen.

- **Key findings**
  After 5 minutes, until 30 minutes, users of 8, 18 and 36 mg/ml nicotine e-liquid concentration conditions showed significantly higher plasma nicotine levels than the 0 mg/ml condition. At 36 mg/mL, the nicotine boost from baseline was 24.1 ng/mL (SD=18.3). This is higher than a cigarette, assuming smoking raises plasma nicotine levels to 15 ng/mL.

- **Limitations**
  Only a very small number of non-representative users were included in the study and the confidence intervals for the data points were wide. Plasma nicotine levels were quite varied at baseline so it seems unlikely that all users adhered to the requested 12h prior abstinence. Unfortunately an abstinence measure (equivalent to CO monitoring for cigarette use) has not yet been established for e-cigarette use.

  A specific device was used for consistency – results may differ for different types of devices and e-liquids and users may be able to achieve higher levels with their usual device. Higher levels may also have been achieved if users were allowed to vape *ad lib* or outside of a lab setting.

Ramôa CP, Hiler MM, Spindle TR, Lopez AA, Karaoghlanian N, Lipato T, Breland AB, Shihadeh A, Eissenberg T. Electronic cigarette nicotine delivery can exceed that of combustible cigarettes: a preliminary report. Tob Control. 2015 Aug 31. pii: tobaccocontrol-2015-052447. doi: 10.1136/tobaccocontrol-2015-052447.

5. Effects of Switching to Electronic Cigarettes with and without Concurrent Smoking on Exposure to Nicotine, Carbon Monoxide, and Acrolein

- **Study aims**
  This UK study investigated exposure to carbon monoxide (CO), nicotine (by measuring cotinine in urine), and acrolein (by measuring its primary metabolite) in smokers given an e-cigarette for a quit attempt. 40 smokers, naïve to e-cigarettes, used a specific e-cigarette cig-a-like device (2.4% nicotine) along with behavioural support for 4 weeks.

- **Key findings**
  Only 6 participants were lost to follow-up. 33 of the remaining 34 were still using the e-cigarette and 16 participants achieved CO-verified abstinence at 4 weeks.

  In e-cigarette only users, there were significant reductions in CO (80% decrease) and acrolein (79% decrease) but not cotinine (17% reduction but not significantly different). For dual users there were significant decreases in all three biomarkers (CO = 52%, acrolein = 60% and cotinine 44% decrease). However measures for CO and cotinine were significantly lower at baseline in those who went on to quit, so 4 week exposure levels were lower in e-cigarette only users than dual users.

- **Limitations**

This was only a small non-randomised trial so there was not a control arm exploring the impact of adding behavioural support to this device or comparing it to a placebo. It's not clear whether participants could have been using other forms of quit aid (such as NRT) or how well participants adhered to the behavioural support sessions.

These results may not translate into similar real-world results as, on one hand, in addition to behavioural support users received their e-cigarette and cartridges and instructions, however the devise they were using was first generation and user preference may be for a different device.

McRobbie H, Phillips A, Goniewicz ML, Smith KM, Knight-West O, Przulj D, Hajek P. Effects of Switching to Electronic Cigarettes with and without Concurrent Smoking on Exposure to Nicotine, Carbon Monoxide, and Acrolein. Cancer Prev Res (Phila). 2015 Sep;8(9):873-8. doi: 10.1158/1940-6207.CAPR-15-0058.

Overview

This month we include five very varied studies from UK and the USA.

The first study in the list (Eadie et al, 2015) outlines the first example of research examining point of sale marketing and retailer attitudes to this marketing and the products in the UK. The study involved an audit of marketing in 96 retail outlets in Scotland and interviews with 25 retailers. In line with an increase in e-cigarette use in the UK over the 12 month period when the study was conducted, the researchers found a rise in marketing of the products at the point of sale, although more general marketing (in the front of shops, for instance) did not increase. The number of displays at the point of sale rose from 20 retail outlets to 47 during the study period, most commonly in display units. The most displayed brands were of first generation (cigalike) devices and just over a third were found to be near sweets, collectable cards or mints and gum at the point of sale, products potentially of interest to children. Perhaps the most interesting findings stem from their interviews with retailers, often of small high street shops who reported some benefit to selling e-cigarettes relative to tobacco (higher profit margins) but also confusion about the products. This stemmed from what the retailers described as their own lack of knowledge about the devices and also mixed customer experiences of using them. Interestingly, during the study period some retailers reported that customers now preferred refillable (2nd or 3rd generation) e-cigarettes with cigalikes having less appeal or being reported by customers to be less effective. Encouragingly no retailers reported that children were requesting the products despite age of sale laws not yet being in place in the UK at the time. Future research on point of sale marketing and customer and retailer views would be of interest, particularly as the study was conducted in Scotland where pending legislation proposes banning all forms of e-cigarette marketing not covered by the EU Tobacco Products Directive except point of sale displays. This means this form of marketing may become increasingly important and is a viable topic for further studies.

The second study (Pokhrell et al, 2015) involved detailed qualitative research with 62 young adults (18-35) in Hawaii, USA. We covered a previous article from a different element of the same body of work from this team last month (http://www.ncbi.nlm.nih.gov/pubmed/26074148). In this article, all the participants were e-cigarette users, and 84% were dual tobacco and e-cigarette users, with dual use being the focus of the study. The article provides a fascinating account of why and under what

circumstances the participants used each product. The narratives and direct quotes describe circumstances in which e-cigarettes did not provide the same perceived stimulation or benefits of tobacco cigarettes (particularly rapid nicotine delivery for relieving cravings, socialising with other smokers or maintaining particular routines associated with tobacco but not e-cig use). They also outline perceived benefits to e-cig use when tobacco smoking was unacceptable or not permitted – for example in workplaces, at home with family or to avoid smelling of cigarettes. The study did not focus on how dual users could be supported or encouraged to stop smoking and did not explore participant's perceptions of harms, both of which are important topics to understand amongst dual users. However, the descriptions of reasons for continued tobacco use do point to lessons for interventions that may involve e-cigarettes as smoking cessation aids, for example to provide insight for stop smoking advisers working with dual users. Similar research in a UK context would be welcome.

The third article (Primack et al, 2015) adds to the existing literature on young people and e-cigarettes and adopts a similar longitudinal design to a study conducted in California that we summarised last month (https://jama.jamanetwork.com/article.aspx?articleid=2428954). The current study involved a national sample in the USA of 694 never smoking 16-26 year olds. It aimed to find out if ever use of e-cigarettes was associated with subsequently trying tobacco. It identified very few people at baseline who had ever used an e-cigarette (n=16) and then found that 6 of them went on to report that they had subsequently tried a tobacco cigarette by one year. Both e-cigarette and tobacco use were very broadly defined (having tried an e-cigarette at least once, having had at least one puff of a cigarette in a lifetime) and because of this and the very small sample engaged in the relevant behaviours, it is difficult if not impossible to draw conclusions about the implications of the study. However, these types of longitudinal studies following up young people and looking at the onset of e-cigarette and tobacco use are interesting and with larger samples could yield more meaningful results.

The issue of how much nicotine different types of electronic cigarettes can deliver has been the subject of a number of studies to date, and the latest (Ramoa et al, 2015) is from a team led by Tom Eissenberg at Virginia Commonwealth University. This was a small study of 16 experienced vapers conducted in a lab where blood samples were taken to test for nicotine levels following e-cigarette use (four sessions at least 2 days apart). The e-cigarettes provided contained e-liquids of differing strength (0, 8, 18 or 36 mg/ml). Perhaps unsurprisingly, the researchers found a relationship between the e-liquid strength and how much nicotine participants had in their blood, with higher strength resulting in more nicotine exposure. Some of those using the highest strength liquid (36 mg/ml) achieved higher blood nicotine levels than would be expected from a conventional cigarette. At least two important observations emerge that are relevant to the UK context. The first is that higher strength e-liquids (at least in this study) can deliver more nicotine which is important for smoking cessation – providing sufficient quantities to help with withdrawal symptoms in smokers trying to quit. Secondly, however, the highest strength e-liquid did appear to deliver more nicotine than in a cigarette, which the authors argue could results in more nicotine dependence, although it is likely that users would control intake by changing their puffing behaviour. The incoming EU Tobacco Products Directive will not allow e-liquid strengths above 20mg/ml to be sold, except as part of a licensed medicine.

The final article included in this month's bulletin is from a team who are members of the UK Centre for Tobacco and Alcohol Studies based at Queen Mary University of London (McRobbie et al, 2015). They looked at the important issue of toxicants in e-cigarette vapour with a focus on carbonyl compounds, in particular acrolein. Concern has been expressed that dual users of e-cigarettes and cigarettes may be particularly at risk of high levels of acrolein exposure, so this study focused on people who already smoke and had either stopped smoking entirely (4 weeks post quit date) using an electronic cigarette (n=16) or were dual users (n=17). The researchers found that people who used electronic cigarettes significantly reduced their acrolein exposure, including dual users. People who cut down their cigarette consumption using e-cigarettes also reduced their smoke intake as assessed by carbon monoxide and cotinine (a nicotine metabolite). The paper also contains some useful observations on quit rates in the study compared to previous work with NHS stop smoking services, and speculates why continuing 'dual' users may have found it difficult to stop smoking completely during the study. Interested readers could consult the full article for these findings.

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

- High School Students' Use of Electronic Cigarettes to Vaporize Cannabis
- Combined expectancies of alcohol and e-cigarette use relate to higher alcohol use.
- Modeling the Health Effects of Expanding e-Cigarette Sales in the United States and United Kingdom: A Monte Carlo Analysis.
- E-cigarette use in Canada: prevalence and patterns of use in a regulated market.

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.