THE UK ELECTRONIC CIGARETTE
RESEARCH FORUM

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Electronic Cigarette Research Briefing – June 2018

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 text below provides a critical overview of each of the selected studies then puts the study findings in the context of the wider literature and research gaps.

The studies selected and further reading list do not cover every e-cigarette-related study published each month. Instead, they include high profile studies most relevant to key themes identified by the UK Electronic Cigarette Research Forum; including efficacy and safety, smoking cessation, population level impact and marketing. For an explanation of the search strategy used, please see the end of this briefing.

Past research briefings can be found at www.cruk.org/UKECRF. If you would prefer not to receive this briefing in future, just let us know.

1. ['Real world' compensatory behaviour with low nicotine concentration e-liquid: subjective effects and nicotine, acrolein and formaldehyde exposure](#)

- **Study aims**

    This study examined 20 experienced exclusive e-cigarette users in England using four different combinations of e-cigarette power types and e-liquids ad libitum for 1 week each. The study aimed to compare low nicotine concentration (6 mg/mL) e-liquid and high nicotine concentration (18 mg/mL) e-liquid, with fixed or adjustable power devices.

    At the end of each condition, formaldehyde and nicotine intake were measured via urinary formate and salivary cotinine respectively. Participants self-reported subjective effects and vaping behaviour data from the device was also analysed.

- **Key findings**

    Urinary formate was higher in users following low nicotine conditions ($p = 0.05$) compared to high nicotine conditions, while salivary cotinine was significantly lower ($p = 0.001$).

    Average puff number and duration were significantly greater ($p = 0.001$ each) during the low nicotine conditions compared to high nicotine conditions. Within the low nicotine

conditions, puff duration was longer for those using fixed power devices compared to adjustable power (p = 0.006).

When using low nicotine e-liquid, participants reported significantly more frequent and stronger urges to vape (p = 0.001 each), and greater withdrawal symptoms (p = 0.04) compared to the high nicotine conditions.

Participants were significantly more likely to report negative effects (p = 0.03) and less likely to report positive effects (p = 0.05) when using fixed power devices compared to adjustable power. Within the fixed power condition, participants using low nicotine e-liquid were also less likely to report positive effects compared to high nicotine e-liquid (p = 0.008).

Self-reported adverse effects were very low across all conditions, but were significantly higher in the fixed power conditions compared to adjustable power conditions (p = 0.03).

On average a greater volume (mL) of e-liquid was used in the low nicotine conditions compared to the high nicotine conditions (p = 0.02).

- **Limitations**

Participants in this study had to switch between high nicotine concentration e-liquid to low nicotine e-liquid very rapidly, and each combination was used for an average of 6 days only. This may not represent transitions in real life, nor be applicable to more gradual transitions or longer-term use.

Users in this study experienced all conditions and were not blinded to power or nicotine combination. This may have influenced vaping behaviour and subjective reporting.

This study is vulnerable to unreported non-compliance (using non-study devices), which may make some results invalid.

Only one specific e-cigarette device was permitted to be used in the study. This may not be representative of the range of devices available.

This study only included a relatively small sample of experienced and exclusive e-cigarette users. This sample may not be representative of all e-cigarette users.

One researcher received funding from the pharmaceutical industry. This may introduce bias into the study.

Dawkins, L., Cox, S., Goniewicz, M., McRobbie, H., Kimber, C., Doig, M., Kosmider, L. (2018). 'Real world' compensatory behaviour with low nicotine concentration e-liquid: subjective effects and nicotine, acrolein and formaldehyde exposure. Addiction, doi: 10.1111/add.14271

2. [Patterns of e-cigarette use among youth and young adults: review of the impact of e-cigarettes on cigarette smoking](#)

- **Study aims**

This systematic review aimed to update the evidence on the association between e-cigarette use and later smoking behaviour in youth (up to 18 years) and young adults (18 – 29 adults).

The researchers identified 26 studies with a range of study designs and samples, and from a range of countries.

- **Key findings**

  This review identified 11 studies examining youth who had never smoked. All studies with the exception of one suggested a significant association between e-cigarette use at baseline and smoking uptake at follow-up.

  3 studies on young adults, and 1 study on youth and young adults combined, who had never smoked were reviewed. These all found a significant association between baseline e-cigarette use and smoking uptake at follow-up.

  Only 2 studies were identified examining never- and ever- smoking youth combined that controlled for baseline smoking. One found a significant association between baseline e-cigarette use and follow-up smoking; the other found an association between using an e-cigarette with higher nicotine concentration e-liquid and regular smoking at follow-up.

  This review found mixed evidence in the 3 studies on youth and the 6 studies on young adults that smoked at baseline. This includes 2 studies on youths and 3 studies on young adults that found no significant association between baseline e-cigarette use and smoking behaviour at follow-up.

  Only one study examined youth and young adults combined who smoked at baseline. This found a significant association between baseline e-cigarette use and smoking cessation at follow-up, but not for quit attempts.

- **Limitations**

  This review is vulnerable to any limitations of the individual studies included. The majority of studies included did not control for confounding factors and only collected data at single time-points. Therefore, this review cannot establish causal relationships and patterns of use over time.

  The researchers of this study did not provide any new statistical analyses, nor did they provide study weightings based on quality appraisals.

  For most studies, information on regularity of e-cigarette use or smoking was not available. Therefore, it's not clear whether any associations reported relate to particular types of use.

  This review included studies from a range of countries, including many that were US-based. It's unclear how applicable these are to countries such as the UK.

  This review relied largely on self-reported data, which may be subject to bias.

Glasser, A., Abudayyeh, H., Cantrell, J., Niaura, R. (2018). Patterns of e-cigarette use among youth and young adults: review of the impact of e-cigarettes on cigarette smoking, doi: 10.1093/ntr/nty103.

3. [Second-hand aerosol from tobacco and electronic cigarettes: evaluation of the smoker emission rates and doses and lung cancer risk of passive smokers and vapers](#)

- **Study aims**

  This study measured the aerosols emitted by e-cigarettes and cigarettes when used in a naturally ventilated building with closed windows and doors to estimate the exposure of second-hand vapers and smokers.

Particle number, PM_{10}, and black carbon were measured from 3 separate smoking and vaping sessions by 10 volunteers each.

The researchers also used a model to estimate the theoretical median deposition of aerosol in the respiratory system, and the lung cancer risk to second-hand smokers or vapers.

- **Key findings**

Particle number peak concentrations were lower for the e-cigarette tests (3×10^4 part cm^{-3}) compared to the smoking tests, whilst concentrations of PM_{10} and black carbon did not peak during e-cigarette use, but did during the smoking tests.

Median particle number emission rates were lower for e-cigarettes (9.62×10^{10} part min^{-1}) compared to cigarettes (4.31×10^{11} part min^{-1}). E-cigarettes had negligible emission rates of PM_{10} and black carbon, while cigarettes had rates of 5mg min^{-1} and 66ug min^{-1} respectively.

Median particle emission factors were lower for e-cigarettes (5.51×10^{11}) compared to cigarettes (2.80×10^{12}). E-cigarettes had negligible emission factors for PM_{10} and black carbon, compared to 32mg and 430ug respectively for cigarettes.

The median maximum deposition in the respiratory system was calculated to be 3.4×10^5 particles for second-hand vapers, which decayed to background value in 52 minutes. The median maximum deposition for cigarettes was 2.3×10^6 particles, but after 52 minutes, the extra dose was still larger than 50% of this maximum value.

The median extra lung cancer risk due to second-hand exposure to one vaping session daily for a year was calculated to be 8.97×10^{-10}. This is a five order of magnitude lower than that for smoking (8.56×10^{-5}). For all second-hand exposure scenarios to e-cigarettes, the extra lung cancer risk is lower than 10^{-5}, the maximum tolerable risk defined by the US EPA.

- **Limitations**

This study measured the emissions of e-cigarettes and cigarettes, but did not directly measure exposure in humans. This may not be a valid representation of second-hand exposure in the real world. This study is also vulnerable to any limitations of the models and measuring instruments.

The volunteers in this study used the e-cigarette with the same behaviour as their smoking sessions, and were not required to be an experienced e-cigarette user. This may not be representative of patterns of e-cigarette use in real world situations.

This study assumed that the carcinogenic compound concentrations of second-hand aerosol were similar to mainstream aerosol. This may not be a realistic representation of the exposure of second-hand smokers and vapers.

This study examined a single laboratory-based exposure scenario only. It's unclear how applicable this may be to different real world exposure scenarios.

Only one specific e-cigarette device was used in this study. This may not be representative of the range of devices available.

This study did not look at the entire range of emissions possible.

Avino, P., Scungio, M., Stabile, L., Cortellessa, G., Buonanno, G., Manigrasso, M. (2018). Second-hand aerosol from tobacco and electronic cigarettes: evaluation of the smoker emission rates and doses and lung cancer risk of passive smokers and vapers. The Science of the Total Environment, 9; 642: 137-147, doi: 10.1016/j.scitotenv.2018.06.059

4. [Perceptions and reasons regarding e-cigarette use among users and non-users: a narrative literature review](#)

- **Study aims**

  This narrative review aimed to provide a summary of perceptions of e-cigarettes and reasons for use among adult and youth e-cigarette users, cigarette smokers, dual users, and non-users.

  The researchers reviewed 65 quantitative and qualitative studies with a range of study designs and samples, and from a range of countries.

- **Key findings**

  Adult e-cigarette users and smokers were found to commonly report health benefits and positive experiences as perceived benefits of e-cigarettes. Adult e-cigarette users also identified benefits to bystanders.

  Dual users and non-users generally did not identify health benefits or positive experiences in studies. Instead, they tended to note safety for the user, reduced cravings for cigarettes, and benefits to bystanders as perceived benefits of e-cigarettes.

  Young people of all user groups tended to perceive e-cigarettes as safe for users and fashionable.

  Other perceived benefits reported by different user groups included social acceptability and attractiveness, use as a smoking cessation aid, and avoidance of smoking restrictions.

  The reasons for e-cigarette use identified by this review included smoking cessation, expected and experienced benefits, avoidance of smoking restrictions, convenience, curiosity and social influences.

  Among adults in all user groups, smoking cessation was the most commonly reported reason for e-cigarette use.

- **Limitations**

  This review is vulnerable to any limitations of the individual studies used.

  The variability of studies in the current literature meant the researchers were unable to synthesise studies or perform statistical analyses, such as comparing different user groups or changes in perceptions over time.

  This review reported user groups as they were classified in the original study. However, some studies reported current use of e-cigarettes among current smokers without categorizing this group as dual users. Therefore, this review may be prone to misclassification bias.

The user groups in this study were not differentiated by past use of tobacco or e-cigarettes, not e-cigarette users by frequency of use. This may obscure more nuanced findings, including perceptions of former e-cigarette users that have chosen to stop using them.

49 of the 65 studies included in this review were US-based. It's unclear how applicable this is to other countries such as the UK.

This study did not compare the perceptions and reasons for use of e-cigarettes with other stop smoking methods.

Romijnders, K.A.G.J., van Osch, L., de Vries, H., Talhout, R. (2018). Perceptions and reasons regarding e-cigarette use among users and non-users: a narrative literature review. International Journal of Environmental Research and Public Health. 6; 15(6). pii: E1190.

Overview

This month we include four articles authored by research teams based in different countries: the UK; the USA; Italy and the Netherlands.

The first study was funded by Cancer Research UK and aimed to compare the effects of high nicotine (18 mg/ml) versus low nicotine (6 mg/ml) concentration e-liquid with fixed or adjustable power devices. The authors were particularly interested in whether compensatory puffing behaviour occurred with the lower nicotine e-liquid and how this affected a range of outcomes including toxicant exposure.

Participants were twenty experienced vapers recruited in the south east of England. They were asked to vape freely (ad libitum) for four weeks, were provided with a tank e-cigarette and e-liquid, and reported to the researcher five times (baseline followed by once a week). Each week involved a different condition: i) low nicotine fixed power; ii) low nicotine/ adjustable power; high nicotine fixed power; high nicotine/adjustable power. Participants were randomly assigned to start with either low or high nicotine concentration e-liquid. At follow up visits the researchers assessed: puffing behaviour; product use; subjective effects (including urge to vape, nicotine withdrawal); nicotine delivery and acrolein and formaldehyde exposure.

They found that the two different levels of nicotine affected the average number of puffs, puff duration, the amount of e-liquid consumed, urge to vape, withdrawal symptoms, nicotine intake and formaldehyde (but not acrolein) exposure. Overall, when vapers were provided with the lower nicotine concentration e-liquid, particularly in the non-adjustable power setting, the researchers identified more compensatory behaviour (more frequent and longer puffs). The lower nicotine condition also resulted in vapers consuming more e-liquid, experiencing stronger urges to vape and higher levels of formaldehyde exposure. The main implications of the study were that using lower nicotine concentration e-liquids may have unintended consequences including that it may affect how much formaldehyde users are intaking. Formaldehyde is a carcinogen, and while exposure levels from vaping are a small fraction of those that occur from smoking tobacco, additional exposure should be avoided. The findings on urges to vape and withdrawal symptoms with the lower nicotine e-liquid may also be relevant for smoking cessation. Smokers trying to quit with an e-cigarette with levels of nicotine that are not high enough for their cravings may find it does not adequately satisfy their cravings to smoke, which may affect the success of any quit attempt with e-cigarettes.

The second article reports results from a systematic review of studies focusing on the association between e-cigarette use and later smoking in teenagers and young adults. It follows two previous systematic reviews on this topic, and it included studies up to December 31st 2017. Twenty six longitudinal studies with young people or young adults up to the age of 29 were identified. All but five studies were conducted in the USA. These five were from Canada, England, the Netherlands, Mexico and Scotland. The English and Scottish studies have been included in previous UKECRF bulletins.

As with the two previous reviews, the current review found that, among teenagers and young adults who had never smoked, e-cigarette use at baseline was associated with trying smoking at follow up, with the follow up period varying between studies from six to 20 months. The association between e-cigarette use and subsequent smoking behaviour among teenagers and young adults who also smoked at baseline was unclear. Much of the current review focused on an examination of the measures and quality of the original studies. The authors conducted a critical appraisal of the quality of each study using criteria established by the National Heart, Lung and Blood Institute in the USA and also examined the studies in the context of guidelines for causal inference. This identified a number of limitations in the included studies. The authors argue that these mean firm conclusions cannot be drawn about any causal link between e-cigarette use and subsequent smoking in youth and young adults, based on the available evidence. They highlight in particular: small sample sizes in the original studies; the fact that studies measured recent or ever e-cigarette use only; and that studies could not control for factors that might provide alternative explanations for smoking at follow up (confounders). The article outlines suggestions for future research including a better understanding of the characteristics that put young people at risk of either vaping or smoking, and how product characteristics or the availability of products (both relevant issues for policy) are related to use.

The third study this month aimed to evaluate and compare passive exposure to e-cigarette aerosol and tobacco smoke. To do this, the Italian research team recruited 10 smokers and asked them to smoke as they normally would and, in separate sessions, vape (using a refillable tank system vaporiser with mint flavoured liquid with 18mg/ml nicotine) in a similar manner to smoking (trying to reproduce the same puff length and interpuff time as smoking - which may not reflect how e-cigarettes are normally used). They did this in a ventilated room and the researchers then performed a number of tests to assess the number of particles, the nature of particles (PM_{10}) and the presence of black carbon in the air.

The experiment found that, on average, the smoking sessions generated a 4.5 fold higher emission rate of particles compared to the vaping sessions. They found very low (negligible) emissions of PM_{10} and black carbon during the vaping sessions in contrast to the smoking sessions. The researchers then estimated how this would translate to human exposure and concluded that the deposition of particles into the respiratory system of a bystander would be 15 fold higher for smoking than for vaping. The implications of this for lung cancer risk were then modelled, based on bystander exposure to one vaping or smoking session per day for a year. The authors estimated that the lung cancer risk for passive smoking was five orders of magnitude higher than for passive vaping, and that the lung cancer risk from regular exposure to second-hand e-cigarette aerosol was below the acceptable risk level defined by the US Environmental Protection Agency for all exposure scenarios modelled.

Our final article this month involved a systematic literature review of studies examining risk perceptions, perceived benefits and reasons for e-cigarette use. Articles up to February 2018 were included. Only a narrative synthesis of results was possible, as the studies used a variety of different

study designs, primarily cross-sectional surveys and qualitative research. 65 studies from 72 separate articles were identified that met the review's inclusion criteria. The authors, based in the Netherlands, developed a series of themes relating to perceptions and reasons for use and extracted findings from the individual articles using this thematic framework.

The identified articles included diverse groups of participants (adults, youth, smokers, non-smokers, vapers, dual users) from a number of countries (USA, UK, New Zealand, Canada, France, Switzerland, Australia and Belgium). Because of this variation in populations and regulatory and cultural contexts, the results vary substantially between studies. That said, some key themes emerged. The authors found that the perceived harm of e-cigarettes compared to tobacco cigarettes seemed to have increased among users and non-users in a number of countries in more recent years, as we know is the case in the UK. Some articles asked about risk perceptions relating to e-liquid flavours and overall the review found that fruit or sweet flavours were perceived as less risky than tobacco flavoured e-liquid. Vapers in the included studies described benefits to e-cigarette use which included smoking cessation or cutting down on traditional cigarettes, and reported health benefits and positive features of the products (convenience, cost etc). However, continuing smokers who had tried e-cigarettes but did not continue vaping also pointed to less positive experiences and barriers to use, primarily due to the e-cigarette not providing a direct replacement for smoking. Young people in the included studies reported elements of product appeal and popularity, and generally did not tend to identify health benefits of e-cigarettes compared to adults in the included studies. The authors highlight in their discussion a number of implications of the findings for policy in order to strike a balance between protecting non-smokers and young people from taking up vaping while tailoring accurate risk communication to smokers who could benefit from switching from smoking to vaping.

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

E-cigarette advice to patients from physicians and dentists in the United States

The association of point-of-sale e-cigarette advertising with socio-demographic characteristics of neighborhoods

Altered lung biology of healthy never smokers following acute inhalation of e-cigarettes

Change and continuity in vaping and smoking by young people: a qualitative case study of a friendship group

Association of e-cigarette use with oral health: a population-based cross-sectional questionnaire study

Changes in electronic cigarette use among adults in the United States, 2014-2016

Positive expectancies for e-cigarette use and anxiety sensitivity among adults

Oral candida carriage among cigarette- and waterpipe-smokers, and electronic-cigarette users

Comparative study of the effects of cigarette smoke and electronic cigarettes on human gingival fibroblast proliferation, migration and apoptosis

Risky business: a longitudinal study examining cigarette smoking initiation among susceptible and non-susceptible e-cigarette users in Canada

Clinical and radiographic periodontal status and whole salivary cotinine, il-1β and il-6 levels in cigarette- and waterpipe-smokers and e-cig users

Weight concerns and use of cigarettes and e-cigarettes among young adults

Adverse events of smoking cessation treatments (nicotine replacement therapy and non-nicotine prescription medication) and electronic cigarettes in the food and drug administration adverse event reporting system, 2004-2016

Tobacco marketing and subsequent use of cigarettes, e-cigarettes and hookah in adolescents

Inhalation of electronic cigarette aerosol induces reflex bronchoconstriction by activation of vagal bronchopulmonary c-fibers

Systemic absorption of nicotine following acute secondhand exposure to electronic cigarette aerosol in a realistic social setting

Initiation of vaporizing cannabis: individual and social network predictors in a longitudinal study of young adults

Cigarette and e-liquid demand and substitution in e-cigarette-naïve smokers

Beliefs and behavior regarding e-cigarettes in a large cross-sectional survey

Exposure to the tobacco power wall increases adolescents' willingness to use e-cigarettes in the future

Comparison of urinary biomarkers of exposure in humans using electronic cigarettes, combustible cigarettes, and smokeless tobacco

Experimental analysis of behavior and tobacco regulatory research on nicotine reduction

More than half of adolescent e-cigarette users had never smoked a cigarette: findings from a study of school children in the UK

Discrimination of nicotine content in electronic cigarettes

An exploration of smoking-to-vaping transition attempts using a "smart" electronic nicotine delivery system

Tobacco product use among middle and high school students - United States, 2011-2017

Conventional and electronic cigarettes dysregulate the expression of iron transporters and detoxifying enzymes at the brain vascular endothelium: in vivo evidence of a gender-specific cellular response to chronic cigarette smoke exposure

Impact of e-liquid flavors on e-cigarette vaping behavior

Tobacco and electronic cigarette products: awareness, cessation attitudes, and behaviours among general practitioners

Practice patterns and perceptions of chest health care providers on electronic cigarette use: an in-depth discussion and report of survey results

The effect of electronic cigarettes on voice quality

[Co-occurring vulnerabilities and menthol use in U.S. young adult cigarette smokers: findings from wave 1 of the path study, 2013-2014](#)

[Representations of electronic cigarettes in Chinese media](#)

[Talking about tobacco on twitter is associated with tobacco product use](#)

[Flavorings in tobacco products induce endothelial cell dysfunction](#)

[Electronic cigarette use patterns and reasons for use among smokers recently diagnosed with cancer](#)

[Impulsivity and tobacco product use over time](#)

[The effect of flavor content in e-liquids on e-cigarette emissions of carbonyl compounds](#)

[Use of price promotions among U.S. adults who use electronic vapor products](#)

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 OR vaping))

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.