Electronic Cigarette Research Briefing – November 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.

Some of you have been in touch to report that you haven't received some recent UKECRF briefings. You can find our previous research briefings at www.cruk.org/UKECRF.

If you would prefer not to receive this briefing in future, just let us know.

1. Are smokers who are regularly exposed to e-cigarette use by others more or less motivated to stop or to make a quit attempt? A cross-sectional and longitudinal survey

- **Study aims**

  This English cross-sectional study of 12,787 smokers pooled monthly data from the Smoking Toolkit survey between November 2014 and May 2018. It aimed to analyse the associations between regular exposure to e-cigarette use by others, quit attempts and motivation to quit. assessed. It also used data from 6-month follow-up interviews from 1580 participants to assess the association prospectively. Bayes Factor analyses were used to assess the absence of a causal effect where non-significant associations were found.

- **Key findings**

  25.8% of smokers reported regular exposure to e-cigarette use by others. In unadjusted analyses smokers exposed to others using e-cigarettes were more likely to have made a quit attempt in the last year (RR=1.21 95%CI 1.11-1.31) and more likely to report high motivation to quit (RR=1.17 95%CI 1.05-1.30). However, no significant associations were found after adjusting for age, sex, social grade, exposure to cigarette smoking by others.

No significant prospective associations between exposure to e-cigarettes by others and quit attempts were detected, in either unadjusted or adjusted analyses (p=0.410 and p=0.627, respectively)

Bayes factor analyses based on a moderate effect size suggested that there is no effect of exposure to e-cigarette use by others and quit attempts or motivation quit, rather than the data being insensitive to detect an effect.

Smokers' who were regularly exposed to e-cigarette use by others were more likely to use e-cigarettes themselves (p<0.001). Smokers' use of e-cigarettes was the biggest predictor of past quit attempts (RR=2.14, 95%CI 1.97-2.33), high motivation to quit (RR=1.95 95%CI 1.75-2.18) and prospective quit attempts (RR=1.44 95%CI 1.14-1.83), after adjustment for other confounders.

- **Limitations**

Many analyses in this study were cross-sectional, so it has limited scope to determine causality. It's not clear whether exposure to e-cigarette use by others drives smokers to use e-cigarettes and attempt a quit, or whether individuals who use e-cigarettes are already motivated to quit and more likely to spend time around others who also use e-cigarettes.

This study didn't control for all possible confounders that could affect results, such as nicotine dependence.

The sub-sample of those who responded to 6-month follow-up were not representative of the baseline population. They were more likely to be older and from a high social grade which may have influenced the results.

This study didn't examine the influences of e-cigarettes in different environments, for example home, work or social exposure. It's therefore not clear whether the strength of relationship with the e-cigarette user could affect motivation to quit.

This survey relied on self-reported data and this could be subject to bias.

Jackson, S., Beard, E., Michie, S., Shahab, L., Raupach, T., West, R., and Brown, J. (2018) Are smokers who are regularly exposed to e-cigarette use by others more or less motivated to stop or to make a quit attempt? A cross-sectional and longitudinal survey. BMC Medicine 16 (206) doi.org/10.1186/s12916-018-1195-3.

2. GPs' and nurses' perceptions of electronic cigarettes in England: a qualitative interview study

- **Study aims**

Researchers performed qualitative semi-structured interviews with 15 GPs and eight nurses from the Midlands, West of England and Thames Valley in 2017. The study aimed to assess practitioners' beliefs on e-cigarettes, their attitudes towards cessation and harm reduction using e-cigarettes and support needed to advise on e-cigarettes.

- **Key findings**

Almost all practitioners reported ambivalence towards e-cigarettes, feeling that, while they were less harmful than cigarettes they were not harmless. Fears around unknown long-term health impacts, effects on allergies and the uptake of vaping by non-smokers were common concerns.

Many practitioners were unconvinced around the impact of e-cigarettes on cessation. They were concerned about swapping one addiction for another and the potential harm from long-term use of e-cigs.

There was discomfort around the harm reduction approach, with a preference for offering current treatments, and all practitioners wanted use of e-cigarettes to be focussed around eventual quitting of all nicotine.

Despite reservations, a theme of pragmatism was identified, understanding that smoking cessation is difficult and that e-cigarettes are a step in the right direction.

Practitioners wanted further support and official guidance on e-cigarettes from public health bodies such as the National Institute for Health and Clinical Excellence, Public Health England or the British Medical Association. They suggested leaflets and decision aids would be useful to help facilitate discussion with patients and give them something tangible to take away.

- **Limitations**

  This was a small study and practitioners were sampled from certain regions in England. Practitioners with a particular knowledge or interest in cessation or e-cigarettes may have been more likely to volunteer for the study. Their views may not reflect the beliefs and attitudes of practitioners across the UK.

  The study didn't look at practitioners' behaviours regarding e-cigarettes, only their intentions and attitudes, which may differ.

  This was a cross-sectional study. Therefore, it cannot tell us about the views of health practitioners towards e-cigarettes over time.

  All qualitative studies rely on self-reported information, which may be subject to bias. Although this data can be used to generate hypotheses, it cannot be tested to determine significance.

Stepney, M., Aveyard, P. & Begh, R. (2018) GPs' and nurses' perceptions of electronic cigarettes in England: a qualitative interview study, British Journal of General Practice, doi.org/10.3399/bjgp18X699821

3. Pulmonary and other health effects of electronic cigarette use among adult smokers participating in a randomized controlled smoking reduction trial.

- **Study aims**

  This US study used interim data from 263 individuals participating in an ongoing randomised controlled trial which is looking at the effect of e-cigarettes on health indicators and tobacco product use. It compared two groups of smokers interested in reducing their tobacco consumption: one who received an e-cig of varying nicotine concentrations (0, 8 or 36 mg/mL)

and one who received a non-nicotine cigarette substitute (a plastic tube resembling a cigarette) without nicotine or an aerosol. They examined health outcomes including lung function, blood pressure and weight at 1 month and 3 months post randomisation.

- **Key findings**

  At 3 months follow-up, 69.2% of participants were dual users of cigarettes and their intervention product and a further 26.6% were exclusively cigarette smoking.

  Those randomised to an e-cigarette reduced the number of cigarettes smoked per day significantly more than those using a cigarette substitute at both 1 month and 3 months follow up. Adjusted mean cigarette dependence was decreased significantly more in the e-cigarette group at both follow up points (at 3 months PSCDI score = -3.9 in e-cigarette group vs -1.9 in cigarette substitute group, $p<0.001$)

  Most health outcomes showed no difference at any time point. Diastolic blood pressure and pulse were significantly lower in the e-cigarette group at 1 month, but these differences were no longer significant at 3 months. Forced expiratory time (FET - the time required to forcibly exhale a specified volume of air from the lung) was significantly better in the e-cigarette group at 3 months.

  No significant differences in any health outcome were found after additionally adjusting for demographics and product exposure (frequency of e-cigarette use/cigarette substitute use and cigarettes smoked per day).

  In a model analysing how the frequency of use of the e-cigarette/cigarette substitute affected health outcomes, no significant associations were found between e-cigarette times used and any health outcome.

- **Limitations**

  This was a small study and at three months over a quarter of participants had were exclusive cigarette smokers and therefore non-compliant with their intervention product. This would have impacted on the power to detect an effect on health outcomes.

  In this interim analysis there was no reporting of compliance within each intervention group and whether those in the e-cigarette group were more or less likely to relapse to exclusive cigarette use. There was no per protocol analysis to examine the effectiveness of using an e-cigarette compared to a cigarette substitute on the reported health outcomes.

  The study was not able to compare the health effects of using an e-cigarette to continued exclusive use of tobacco products. Both groups were aiming to reduce cigarette consumption and so this study could not analyse the relative health effects of using e-cigarettes compared to regular tobacco use.

  Due to the ongoing double-blinding of nicotine concentration in the e-cigarette arms of the trial, it was not possible to compare e-cigarette use or health outcomes across different nicotine concentrations in this analysis.

The follow-up time was short, so while this study can help shed light on the acute health effects of e-cig use it does not tell us about long term health effects of e-cigarettes or their efficacy as a quitting aid.

Veldheer, S., Yingst, J., Midya, V., Hummer, B., Lester, C., Krebs, N., Hrabovsky, S., Wilhlem, A., Liao, J., Yen, MS., Cobb, C., Eissenberg, T. & Foulds, J. (2018) Pulmonary and other health effects of electronic cigarette use among adult smokers participating in a randomized controlled smoking reduction trial. *Addictive Behaviours*. doi: 10.1016/j.addbeh.2018.10.041

4. Quitting behaviours among dual cigarette and e-cigarette users and cigarette smokers enrolled in the Tobacco User Adult Cohort

- **Study aims**

This US based study looked at differences in quitting behaviours between 88 dual users and 617 exclusive cigarette smokers over time. They examined association between dual use and cigarette smoking reduction, quit attempts, abstinence from cigarettes and abstinence from all products at 6 months, 12 months and 18 months follow-up.

- **Key findings**

Dual users reported higher interest in cessation (p=0.002, respectively) compared to smokers. There was no difference in nicotine dependence between the two groups.

There was no significant difference in number of quit attempts between dual users and smokers at any time point.

There was no significant difference in the change in number of cigarettes smoked per day between dual users and exclusive cigarette smokers at any follow-up point.

Dual users were more likely to have quit cigarettes at six months follow up (OR=2.54 95%CI 1.02-6.31, p=0.045), but this difference became non-significant at 12 months and 18 months. The majority of baseline dual users relapsed to exclusive cigarette use at follow-up interviews (57-66%). There was no effect of dual use on abstinence from all products at any time point.

- **Limitations**

This study did not examine patterns of e-cigarette use from initiation, only current e-cigarette use. This means that trajectories and length of e-cigarette use to cessation could not be examined. Any e-cigarette users who had already successfully quit smoking would be excluded from the analysis – looking at the dual user population may be selecting those who have already failed in their quit attempts.

This was a small cohort study which would have impacted the power to detect an effect of dual use on quitting behaviours.

Although measured at baseline, this study did not adjust for the effect of nicotine dependence in models of quitting behaviour, which could have affected the results.

The study did not report whether any of the exclusive cigarette smokers started using e-cigarettes during the follow up period, or whether participants were also using other cessation methods.

This survey relied on self-reported data on product use and abstinence which could be subject to bias.

Sweet, L., Brasky, TM., Cooper, S., Doogan, N., Hinton, A., Klein, E., Nagaraja, H., Quisenberry, A., Xi, W., Wewers, ME. (2018) Quitting behaviours among dual cigarette and e-cigarette users and cigarette smokers enrolled in the tobacco user adult cohort. *Nicotine & Tobacco Research*, doi: 10.1093/ntr/nty222

Overview

This month we include four articles, two from the UK and two from the USA

The first paper used data from the Smoking Toolkit study in England to examine whether there is any relationship between being exposed to other people's e-cigarette use and motivation to stop smoking or quit attempts in smokers. The researchers decided to examine this issue as concerns have been raised that seeing other people vaping might undermine cessation in continuing smokers.

The authors examined Toolkit data between 2014 and 2018 collected from adults aged 16 above who were smokers. They were asked if they regularly saw other people vaping, how motivated they were to stop smoking and whether they had tried to quit in the past year. A subsample of respondents were then followed up six months later to look at actual quit attempts. Using the baseline cross-sectional sample only, the researchers found that those regularly exposed to other people vaping were more likely to have made a quit attempt in the past year and had higher motivation to quit than those who did not regularly see others vaping. However, when looking at the six month follow up data these smokers were not more likely to have actually made a quit attempt since baseline. The authors then modelled responses to adjust for whether these smokers were using an e-cigarette or not (dual users). Those that were dual users had higher motivation to quit and past quit attempts but this was not observed in smokers who weren't dual users, suggesting the 'observation' effect may be being driven by participants being more likely to be vapers themselves.

Our second article is a small qualitative study involving interviews with 23 nurses and GPs in England in 2017. The researchers aimed to examine these health professionals' perceptions and attitudes towards e-cigarettes and their experience of discussing e-cigarettes with patients. The study found that nurses and GPs recognised that vaping is less harmful than smoking, but they had limited knowledge or understanding of the devices and were sceptical about their role in smoking cessation. They expressed concerns about: long term health effects; interactions with other medication; the risks of nicotine; uptake among young people; replacing 'one habit/addiction for another' and stories they had seen in the media, among other issues. That said, a theme of 'pragmatism' emerged with most practitioners recognising that some patients who smoke are trying these devices and that their use is preferable to continued smoking. Some interviewees felt reasonably confident discussing e-cigarettes with patients while others were unsure. GPs and nurses wanted more information on e-cigarettes, clear guidance from national bodies such as NICE and the Royal College of GPs (RCGP), and practical resources (official leaflets, booklets and webpages) that they could give to or discuss with patients.

The findings of this study are similar to other recent studies involving health professionals in the UK including dental professionals and those treating cancer patients. Taken together, these studies suggest there is still an 'information gap' among practitioners in relation to how they engage their smoking patients regarding e-cigarettes. Since this and other recent studies were conducted, NICE

guidance has been published that provides some recommendations with further additional guidance planned. Key organisations like the RCGP and Cancer Research UK have also produced new practical tools and sources of information for health professionals. Future research could assess the use of these resources and whether over time health professionals become more confident in addressing tobacco harm reduction, including the use of e-cigarettes, with their patients who smoke.

The third article is from a research team at two Universities in the USA who are conducting an ongoing randomised controlled trial examining the influence of e-cigarettes on health indicators, toxicant exposure and smoking. For the current study, 263 of the participants in the main trial provided data that allowed the researchers to assess key short term (at one month and three month post baseline) changes in blood pressure, lung function, pulse, exhaled CO and weight. The participants were all smokers when they were recruited, and were attempting to cut down their smoking. They were given either an e-cigarette (2nd generation device) with varying liquid nicotine concentrations or a cigarette replica without nicotine and asked to record their daily study product use. A range of data were collected for each participant including clinical data (i.e. blood pressure, lung function via spirometry etc).

At three months almost all of the participants were still smoking. This isn't surprising as the study was not a cessation trial but instead intended to examine health outcomes when cutting down using the e-cigarette or cigarette substitute. Only ten people had stopped smoking, the majority of which were in the e-cigarette arm . One in four had returned to exclusive smoking and the rest were dual users. Those in the e-cigarette arm cut down their smoking more than those using the cigarette substitute, and were recorded as less dependent on smoking at both one and three months. The e-cigarette group also had lower blood pressure and pulse at one month but no other significant differences (i.e. in lung function or other health outcomes) between the groups. These differences also became non-significant at 3 months. No significant differences were found between groups after adjusting for relevant confounders such as participant characteristics and frequency of product use. Overall, therefore, the researchers didn't find any clear evidence that cutting down smoking while vaping resulted in measureable short term changes in lung health or other health outcomes, but also no suggestion that using e-cigarettes concurrently with cigarettes confers additional acute health harms. These findings may be relevant to other research that has found dual use of cigarettes and e-cigarettes doesn't significantly reduce toxicant exposure, and that any health benefits from vaping are likely only to occur after stopping smoking.

Finally we include a further study from the USA that also focused on dual users. The researchers examined patterns of smoking cessation between adult smokers and those who were both smoking and vaping over an 18 month period. This relatively small study relied on self-reported information about product use, which may not always be accurate. Compared to smokers, dual users were more likely to report that they had stopped smoking by six months but this was not sustained at 12 or 18 months. In addition, the researchers didn't find that the dual users reduced their cigarette consumption by any significant degree over time, similar findings to those in a study in England that we included in a previous UKECRF bulletin this year. A potential challenge for the study was that the sample included non-daily users of e-cigarettes (but only daily smokers) in the dual user sample at baseline. Previous studies have found that frequency of vaping is important for smoking cessation and occasional use may have limited impact. Future longitudinal studies may be useful to untangle the complex relationship between concurrent smoking and vaping and any links with smoking cessation.

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

Trust of Information about Tobacco and E-Cigarettes from Health Professionals versus Tobacco or Electronic Cigarette Companies: Differences by Subgroups and Implications for Tobacco Messaging.

Perceived health risks of electronic nicotine delivery systems (ENDS) users: The role of cigarette smoking status.

E-cigarette use is associated with other tobacco use among US adolescents.

Sex and sexual orientation in relation to tobacco use among young adult college students in the US: a cross-sectional study.

Prevalence and Correlates of Electronic Cigarette Use Among a Clinical Sample of Polysubstance Users in Kentucky: Long Live the Cigarette?

Tobacco Product Use Among Adults - United States, 2017.

Youth Access to Tobacco Products in the United States: Findings from Wave 1 (2013-2014) of the Population Assessment of Tobacco and Health (PATH) Study.

Electronic Cigarettes and Smoking Cessation in the Perioperative Period of Cardiothoracic Surgery: Views of Australian Clinicians.

Adolescents have unfavorable opinions of adolescents who use e-cigarettes.

Young adult dual combusted cigarette and e-cigarette users' anticipated responses to a nicotine reduction policy and menthol ban in combusted cigarettes.

Tobacco Product Harm Perceptions and New Use.

E-cigarette Use and Subsequent Smoking Frequency Among Adolescents.

E-cigarettes, alcohol use, and mental health: Use and perceptions of e-cigarettes among college students, by alcohol use and mental health status.

A framework to investigate the impact of topography and product characteristics on electronic cigarette emissions.

Accuracy of commercial electronic nicotine delivery systems (ENDS) temperature control technology.

Querying about the Use of Specific E-cigarette Devices May Enhance Accurate Measurement of E-cigarette Prevalence Rates among High School Students.

The experimental tobacco marketplace: Narrative influence on electronic cigarette substitution.

Comparisons of the stages and psychosocial factors of smoking cessation and coping strategies for smoking cessation in college student smokers: Conventional cigarette smokers compared to dual smokers of conventional and e-cigarettes.

Impact of messages about scientific uncertainty on risk perceptions and intentions to use electronic vaping products.

Next generation media monitoring: Global coverage of electronic nicotine delivery systems (electronic cigarettes) on Bing, Google and Twitter, 2013-2018.

Metal emissions from e-cigarettes: a risk assessment analysis of a recently-published study.

Propylene glycol, a major electronic cigarette constituent, attenuates the adverse effects of high-dose nicotine as measured by intracranial self-stimulation in rats.

Tobacco product transition patterns in rural and urban cohorts: Where do dual users go?

Secondhand exposure to aerosol from electronic cigarettes: pilot study of assessment of tobacco-specific nitrosamine (NNAL) in urine.

Electronic Cigarette Themes on Twitter: Dissemination Patterns and Relations with Online News and Search Engine Queries in South Korea.

Use of Juul E-Cigarettes Among Youth in the United States.

Composition and chemical health hazards of the most common electronic cigarette liquids in nine European countries.

Electronic cigarette use is associated with depressive symptoms among smokers and former smokers: Cross-sectional and longitudinal findings from the Constances cohort.

Identifying behavioural characteristics of tobacco product and e-cigarette use clusters: A repeat cross-sectional analysis.

The effect of electronic cigarettes on dental enamel color.

A qualitative exploration of information-seeking by electronic nicotine delivery systems (ENDS) users in New Zealand.

Measurement of electronic cigarette frequency of use among smokers participating in a randomized controlled trial.

Dual Users Compared to Smokers: Demographics, Dependence, and Biomarkers.

Impact of cigarette smoking and vaping on the outcome of full-mouth ultrasonic scaling among patients with gingival inflammation: a prospective study.

Effects of Electronic Cigarette Liquid Flavors and Modified Risk Messages on Perceptions and Subjective Effects of E-Cigarettes.

Assessing the Impact of Conflicting Health Warning Information on Intentions to Use E-Cigarettes - An Application of the Heuristic-Systematic Model.

Acute pulmonary effects of aerosolized nicotine.

A qualitative assessment of business perspectives and tactics of tobacco and vape shop retailers in three communities in Orange County, CA, 2015-2016.

Missed Opportunities for Detecting Alternative Nicotine Product Use in Youth: Data From the National Dental Practice-Based Research Network.

Association of Electronic Cigarette Vaping and Cigarette Smoking With Decreased Random Flap Viability in Rats.

Smoking-related weight and appetite concerns and use of electronic cigarettes among daily cigarette smokers.

Free Radical, Carbonyl, and Nicotine Levels Produced by Juul Electronic Cigarettes.

Correlates of smoking status in cancer survivors.

Vapes, e-cigs, and mods: what do young adults call e-cigarettes?

Formation of flavorant-propylene Glycol Adducts With Novel Toxicological Properties in Chemically Unstable E-Cigarette Liquids.

Association between Smoking Behavior Patterns and Glycated Hemoglobin Levels in a General Population.

Regulation of Sox2 and stemness by nicotine and electronic-cigarettes in non-small cell lung cancer.

Electronic Cigarettes: Impact on Lung Function and Fractional Exhaled Nitric Oxide Among Healthy 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 vaping 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 Sophia Lowes from Cancer Research UK with assistance from Professor Linda Bauld at the University of Edinburgh and the UK Centre for Tobacco and Alcohol Studies, primarily for the benefit of attendees 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.