Electronic Cigarette Research Briefing – January 2019

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.

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. **Attitudes to E-Cigarettes and Cessation Support for Pregnant Women from English Stop Smoking Services: A Mixed Methods Study**

   - **Study aims**

   This study examined the attitudes of Stop Smoking Service (SSS) managers across England on e-cigarettes and their role as a cessation tool for pregnant women. Researchers surveyed 72 SSS managers responsible for pregnant smokers between August and November 2015, and then used qualitative interviews (n=15) to further investigate beliefs, influences and barriers.

   - **Key findings**

   Of women who set a quit date, 2.2% were recorded as using e-cigarettes. This ranged from 1.4% in the South of England to 4.3% in London.

   56.9% of SSS were unlikely or very unlikely (20.8% and 36.1% respectively) to advise women to use e-cigarettes if asked by a pregnant smoker whether or not it would be a good idea to use them. 31.9% would be neither likely or unlikely, 8.3% would be likely and 0% would be very likely to advise using e-cigarettes.
Most SSS had, were beginning to or hoped to shift their positions towards being e-cigarette friendly. However, e-cigarettes were not usually seen as the first choice for pregnant women. While managers recognised the benefits of harm reduction, they would be more cautious about their use in pregnant women compared to the general population.

Local commissioning authorities were the most important factor in determining the e-cigarette stance of a SSS, with cases of this both facilitating and preventing the adoption of e-cigarette friendly SSS for pregnant women. National guidance, clinical experience and personal views were also reported to impact SSS stance.

Barriers to SSS becoming more e-cigarette friendly for pregnant women included a lack of evidence on e-cigarette use in pregnancy, the lack of a medically licensed e-cigarette, and the need for a consistent message on e-cigarettes across all antenatal services and specialist SSS.

- **Limitations**

The study didn’t record SSS advice given out regarding e-cigarette use and other nicotine replacement therapy in individual pregnant women, only overall provision of a service and intentions and attitudes. It did not compare willingness to advise e-cigarettes in comparison to NRT, so it’s not clear whether attitudes were influenced by concerns about recommending nicotine in general, or e-cigarettes specifically.

Not all SSS were invited to take part in the survey and of those asked 67.9% responded. Therefore, the themes and beliefs may not be representative of all SSS in England.

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

The survey and interviews relied on self-reported data on e-cigarette use and attitudes towards e-cigarette use in pregnancy which could be subject to bias.


2. **IQOS™ vs. e-cigarette vs tobacco cigarette: a direct comparison of short-term effects after overnight-abstinence**

- **Study aims**

This Belgian study randomised 30 smokers in a crossover design to use a cigarette, e-cigarette (3rd generation) or IQOS™ for five minutes following 12 hours of smoking abstinence. Exhaled carbon monoxide, cravings and withdrawal symptoms were measured prior to and after the five minutes and up to 55 minutes afterwards. Participants’ product preferences were surveyed at the end of the study.

- **Key findings**
Smoking a cigarette or IQOS™ increased carbon monoxide in the breath at all timepoints compared to the baseline of 12 hours abstinence (T0) (p values <0.001 and p<0.05 respectively). No increase in carbon monoxide was observed after using an e-cigarette at any timepoint compared to T0 (p values >0.06).

There was no difference in craving reduction between e-cigarettes and IQOS™ at any timepoint (p values >0.43). Both products were less effective than cigarettes at reducing cravings (p values <0.01).

After five minutes of product use, both smoking and using IQOS™ reduced nicotine withdrawal symptoms (p values <0.001). Vaping did not produce an immediate decrease in withdrawal symptoms (p=0.10). After 55 minutes, vaping produced higher withdrawal symptoms compared to smoking (p<0.05). There was no difference between the effect of smoking and IQOS™ on withdrawal symptoms.

After five minutes of product use, cigarettes were reported as the most satisfying product and using IQOS™ was more satisfying than vaping. Aversion was low across all products, and aversion to using IQOS™ was significantly lower than both smoking and vaping.

After 55 minutes, participants were willing to continue use for a further five minutes when given IQOS™ significantly more than e-cigarettes (p<0.05). There was no difference between IQOS™ and e-cigarettes in willingness to consider using them to quit smoking, or intention to go and buy the product.

- **Limitations**

The study participants were young (average age 22), 93% were students and they had low-moderate cigarette dependence. Therefore, the results may not be generalisable to the wider smoking population.

Participants had never used either e-cigarettes or IQOS™ and were only given brief instructions on how to use the devices. This may have affected their experiences and preferences. This study only examined reaction to product use on one occasion, and therefore the study couldn’t assess how perceptions and usage may adjust over a longer time period.

This was a small study which may have limited power to detect differences in effects between products.

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


3. Predicting vaping uptake, vaping frequency and ongoing vaping among daily smokers using longitudinal data from the International Tobacco Control (ITC) Four Country Surveys

- **Study aims**
This study combined survey data from 2008-2016 to examine factors that were associated with trying e-cigarettes, frequency of e-cigarette use and prolonged e-cigarette use in 6,296 daily smokers across Australia, the US, Canada and the UK. Analyses were adjusted for demographic variables and smoking related variables (including intention to quit, time to first cigarette, cigarettes per day) alcohol use, smoking perceptions, and health variables.

**Key findings**

The US had the highest absolute proportion of ever-e-cigarette use (38%), followed by the UK at (19%), then Canada (15%) and Australia (8%). After adjustment, those from the UK were most likely to try e-cigarettes (OR=3.18 95%CI 2.37-4.28, compared to Australia).

Compared to respondents who smoked 0-10 cigarettes per day, those who smoked 21-30 or 31+ cigarettes per day were more likely to have tried e-cigarettes (OR=1.41 95%CI 1.12-1.78, OR=1.69 95%CI 1.19-2.39, respectively). They were also more likely to vape more frequently; OR=1.46 95%CI 1.12-1.91 for 21-30 cigarettes, OR=1.97 95%CI 1.36-2.85 for 31+ cigarettes.

Smokers who intended to quit were more likely to vape more frequently, (p<0.001, OR=1.48 95%CI 1.21-1.82), but they were not more likely to try vaping.

Participants who reported daily alcohol use in the past year were more likely to use their e-cigarettes less frequently compared to non-drinkers (p<0.05, OR=0.72 95%CI 0.52-0.99).

Non-daily smokers at follow-up were more likely than daily smokers to be ongoing vapers (OR=4.99 95%CI 2.39-10.42). Ex-smokers were less likely to have continued vaping (OR=0.48 95%CI 0.29-0.80).

**Limitations**

This study only tested for pair-wise differences in stratified variables and did not examine trends across groups. This would have provided additional evidence for associations and detail on dose-dependent effects.

This study didn’t control for all possible confounders that could affect results, such as reasons for e-cigarette use.

In 2016 the method of data collection changed for the survey, from telephone-based to web-based. The proportion of participants lost between survey years was high (60%) when the switch occurred which could have affected the results.

This study did not test for interactions between any of the variables, which could have affected the results.

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


4. **E-Cigarettes May Support Smokers With High Smoking Risk Awareness to Stop Smoking in the Short Run: Preliminary Results by Randomized Controlled Trial**
• Study aims

This Italian double blinded randomised control trial randomised 210 long-term smokers to receive one of the following: an e-cigarette (2nd generation) with nicotine, an e-cigarette without nicotine (placebo) or no e-cigarette (control). All groups received behavioural support through telephone counselling for 12 weeks. The researchers examined the effectiveness of e-cigarettes for cessation and reduction in smoking as well as their safety over 3 months of follow-up.

• Key findings

After 3 months, 25.4% of those using e-cigarettes with nicotine and 23.4% of those using e-cigarettes without nicotine had successfully stopped smoking compared to 10.34% of those in the control arm (p=0.044).

Those who received e-cigarettes (either with nicotine or without) had a significantly greater reduction in daily cigarettes smoked at both 1 month and 3 months (p<0.010 and p<0.022, respectively).

The reported reduction in mean number of daily cigarettes smoked was highest amongst those who used nicotine e-cigarettes (-11.644) compared to those who used e-cigarettes without nicotine (-10.763) and those in the control group (-9.138). However, when restricted to those who did not quit smoking, there was no significant effect of using an e-cigarette (either with nicotine or without) on mean cigarette reduction.

Across all participants, there was a significant reduction in coughing, mucus and breathing problems after 3 months (21.5%, 18.5% and 14.5% of participants reported reductions for each symptom respectively).

After 1 month, 22.9% of those using an e-cigarette with nicotine and 4.3% of those using one without nicotine reported a burning throat. After 3 months this reduced to 5.7% and 2.9%, respectively. 11.4% and 10% of participants reported a cough after 1 month in each group respectively, and this reduced to 10% and 2.9% in each after 3 months.

• Limitations

The researchers did not analyse how cessation differed according to compliance and patterns of e-cigarette use. They did not measure use of other cessation tools during follow up so are not able to determine whether groups who did not receive a nicotine e-cigarette substituted with other nicotine-replacement.

These are preliminary results and the follow up period is short. They cannot tell us about the effectiveness of e-cigarettes as a cessation tool over longer periods of time.

This study only compared side effects in the two groups using e-cigarettes and not to the control group. Therefore, it’s not clear whether these side effects are attributable to e-cigarette use.

The sample size is relatively small, and no data is provided on the demographics of those involved in the study, so they may not be representative of the wider smoking population. The setting of a randomised control trial may also not be generalisable to real-world quitting behaviour.
The dropout rate in the control arm was higher than in both e-cigarette arms. This could indicate that willingness to participate in the study was related to desire to use e-cigarettes.

The number of cigarettes smoked, and continuous smoking cessation were self-reported which could be subject to bias.


Overview

For the first bulletin of 2019 we’ve selected articles from the UK, Belgium, Australia and Italy.

Our first paper reports results from a study that aimed to describe the types of support offered to pregnant women by stop smoking services in England in 2015, including attitudes and approaches to vaping in pregnancy. Most of the Stop Smoking Services invited (68%, n=72 managers) took part in the survey and then a sub-sample of 15 managers were interviewed to explore key issues in more depth.

The study found that over 90% of services said they would welcome pregnant smokers who were vaping to the service, with some (n=44) also including those who had recently quit smoking while vaping. Some services (n=40) were able to provide data on the number of women they had treated who were vaping and this was very small - averaging just over 2% at the time. In terms of providing active advice on vaping, a significant proportion of services, around a third, were unclear on what advice to offer and stated that they were neither likely nor unlikely to advise pregnant smokers to take up or continue vaping for smoking cessation during pregnancy. Just 8% of managers indicated that their service was likely or very likely to advise women who were smoking during pregnancy to try e-cigarettes. Key factors that were mentioned as influencing the stance of services were: lack of national guidance and the constraints of local commissioning policies; clinical experience; personal opinions or views; the need for more research evidence; the absence of a licensed product that could be recommended; and the need for consistent messages and training for staff. Since the research was conducted some practical advice on vaping during pregnancy has been produced by the Smoking in Pregnancy Challenge Group and a large trial of e-cigarettes for smoking cessation in pregnancy is now underway. Future research could assess any changes in attitudes and practice following these and other developments.

The month’s second paper responds to the need for more independent research on heated tobacco products and how they compare to e-cigarettes. This was a small trial involving 30 young adult (primarily male and students) smokers in Belgium who were randomised to use one of three products. These were: their own brand of cigarettes; a third generation e-cigarette with 18mg/ml and either tobacco or menthol flavour e-liquid; or iQOS™. Participants were asked to use the products for five minutes after overnight abstinence from smoking. The researchers measured exhaled carbon monoxide and assessed a range of psychological and behavioural outcomes via questionnaires (primarily using a range of well-validated measures) administered during and immediately after the experiment. Each participant attended on three occasions so that they were exposed to each of the conditions in the study.
The researchers found that breath carbon monoxide levels rose significantly after participants smoked, by a small amount after using iQOS™, and not at all in the vaping condition. Withdrawal symptoms were alleviated very quickly by smoking and also by using iQOS™, but took longer to decline when participants were vaping. Cravings for cigarettes were significantly reduced in all three conditions but the decline was stronger in the smoking condition. In terms of participant perceptions regarding the products (subjective reward, aversion and satisfaction), most preferred iQOS™ compared to the e-cigarette. A number of factors may explain these differences, but as the authors acknowledge, the fact that the study involved naïve users who were not heavy smokers may be particularly relevant. They only received basic instructions in how to use the products and previous research has shown that for e-cigarettes naïve users may take some time to become accustomed to vaping. This may also be the case for using heat not burn products. However, the results do seem to suggest that iQOS™ more closely mimicked smoking for this group of young adults. Further research is needed that compares this and other heated tobacco products with a variety of vaping devices and in different populations.

Thirdly we include a recent paper from the International Tobacco Control project. Members of the ITC team based in Australia analysed longitudinal data from smokers in the UK, USA, Canada and Australia collected over eight years (six survey waves 2008-2016). The authors aimed to examine factors that might affect vaping uptake, current vaping and vaping frequency among daily smokers. They conducted statistical modelling to examine the relationships between factors and vaping and smoking outcomes, and included data from smokers who had participated in ITC for at least two consecutive waves of the survey.

Vaping was more common both in terms of uptake and vaping frequency in the US and the UK compared to Australia. This undoubtedly relates to the policy environment (as previous ITC publications have argued) as vaping is far more heavily regulated in Australia. Policies vary between states but in general the sale and supply of e-cigarettes with nicotine is illegal and e-liquids have to be sourced from overseas. This means there are barriers to vaping in Australia that are not present in the UK or the USA. There were also differences across the sample a whole for gender (with women more likely to take up vaping and vape more frequently) education and income (those with higher education and/or income reported higher vaping frequency). In terms of the relationship between smoking and vaping, respondents who reported that they intended to quit smoking were more likely to vape at greater frequency at follow up. In addition, participants who smoked 30 cigarettes or more per day were more likely to be vaping at follow up and also to be vaping more frequently. In other words, whether someone takes up vaping and how often they vape appear to be influenced by motivation to quit and heaviness of smoking. The study also found that continuing to vape (between waves) was, perhaps unsurprisingly, related to smokers cutting down tobacco use or stopping smoking and also how frequently (i.e. at least daily) they vaped. These findings may be relevant for how advice and information on vaping for smoking cessation is developed and targeted.

Our fourth publication this month reports results from a randomised controlled trial in Italy to assess the effects of e-cigarettes on long-term smokers who were motivated to quit and who were taking part in a lung cancer screening programme. The authors assessed the effectiveness and safety of e-cigarettes for smoking cessation at three months. There were 210 smokers in the trial randomised into one of three groups. All received relatively brief counselling for smoking cessation and this was combined with either a) a 2nd generation e-cigarette (EC) with a 8mg/ml tobacco flavoured e-liquid b) the same device with no nicotine in the e-liquid or c) control (no EC, counselling alone).

Quit rates at three months were significantly higher in both the e-cigarette arms compared with controls (25% EC with nicotine, 23% EC without nicotine, 10% controls). Smokers in the EC with
nicotine arm were significantly more likely to cut down their cigarette consumption compared to those in the control group. However, after restricting the analysis to those who did not quit smoking, there was no significant difference in cigarette reduction between groups. The authors concluded that the e-cigarettes helped participants stop smoking but the lack of significant difference between the nicotine vs no nicotine arms was unusual, and at odds with previous trials. This could be related to the low nicotine concentration in the e-liquid provided. It may also suggest that the sensory and behavioural aspects of vaping alone helped with smoking cessation, irrespective of nicotine.

Next month we expect to include results from a larger UK trial of vaping for smoking cessation due to be published very soon in the New England Journal of Medicine. Look out for the February 2019 UKECRF bulletin for this and other new studies.

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

Patterns of e-cigarette use, biochemically verified smoking status and self-reported changes in health status of a random sample of vapeshops customers in Greece.

The Impact of E-Cigarette Warnings, Warning Themes and Inclusion of Relative Harm Statements on Young Adults’ E-Cigarette Perceptions and Use Intentions.

Identification and quantification of electronic cigarette exhaled aerosol residue chemicals in field sites.

Exposure to and perceptions of health warning labels on nicotine vaping products: Findings from the 2016 International Tobacco Control Four Country Smoking and Vaping Survey

Where college students look for vaping information and what information they believe.

Cigarette Smoking and E-Cigarette Use by Pharmacy Students in Serbia

Attitudes to E-Cigarettes and Cessation Support for Pregnant Women from English Stop Smoking Services: A Mixed Methods Study.

Harm perceptions of e-cigarettes and other nicotine products in a UK sample.

E-Cigarette Social Norms and Risk Perceptions Among Susceptible Adolescents in a Country That Bans E-Cigarettes.

Cinnamaldehyde in Flavored E-Cigarette Liquids Temporarily Suppresses Bronchial Epithelial Cell Ciliary Motility by Dysregulation of Mitochondrial Function.

Electronic cigarette power affects count concentration and particle size distribution of vaping aerosol.

Cold Turkey and Hot Vapes? A national study of young adult cigarette cessation strategies.

E-cigarette nicotine dose and flavor: Relationship with appeal, choice, and tobacco use amongst veterans with comorbid psychiatric disorders.

Patterns of sustained e-cigarette use in a sample of young adults.

A conflict of interest is strongly associated with tobacco industry-favourable results, indicating no harm of e-cigarettes.

Vaporized E-Cigarette Liquids Induce Ion Transport Dysfunction in Airway Epithelia.
Predicting vaping uptake, vaping frequency and ongoing vaping among daily smokers using longitudinal data from the International Tobacco Control (ITC) Four Country Surveys.

IQOS vs. e-Cigarette vs. Tobacco Cigarette: A Direct Comparison of Short-Term Effects after Overnight-Abstinence.

Influence of electronic cigarette vaping on the composition of indoor organic pollutants, particles, and exhaled breath of bystanders.

To "vape" or smoke? Experimental evidence on adult smokers.

Predictors of E-cigarette Use Among Young Australian Women

Young adult e-cigarette users: perceptions of stress, body image, and weight control.

A Modeling Approach to Gauging the Effects of Nicotine Vaping Product Use on Cessation from Cigarettes: What Do We Know, What Do We Need to Know?

Discussions between health professionals and smokers about nicotine vaping products: Results from the 2016 ITC Four Country Smoking and Vaping Survey.

Electronic cigarette usage patterns: a case study combining survey and social media data.

Beliefs about E-cigarettes: A Focus Group Study with College Students.

E-cigarette use and respiratory disorder in an adult sample.

Laryngeal inflammatory response to smoke and vape in a murine model.

Stimulus effects of propylene glycol and vegetable glycerin in electronic cigarette liquids.

Acute effects of electronic and tobacco cigarettes on vascular and respiratory function in healthy volunteers: a cross-over study.

E-cigarettes May Support Smokers With High Smoking-Related Risk Awareness to Stop Smoking in the Short Run: Preliminary Results by Randomized Controlled Trial.

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 and Helen Callard 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
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