THE UK ELECTRONIC CIGARETTE RESEARCH FORUM

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Electronic Cigarette Research Briefing – May 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. [Changes in Use Patterns Over One Year Among Smokers and Dual Users of Combustible and electronic cigarettes.](#)

- **Study aims**

    This U.S. study analysed how patterns of product use varied between 117 exclusive smokers and 205 dual users over one year and examined predictors of continued dual use. Data on patterns of use were collected via in-person assessments at 4, 8 and 12 months from smokers and dual users who had no intention to quit smoking in the next 30 days. Abstinence from cigarettes was self-reported and 7-day abstinence was biochemically verified.

- **Key findings**

    At 1-year follow up, biochemically confirmed 7-day cigarette abstinence was significantly different (p=0.03) among baseline dual users (8.0%) from baseline smokers (1.9%). There was no significant difference (p=0.7) between these groups for self-reported 30-day abstinence.

After one year, less than half of baseline dual users were still dual users (n=100, 48.8%). 90 (43.9%) reported being exclusive smokers, 12 (5.9%) being exclusive vapers and 3 (1.4%) being abstinent from both products. Among baseline smokers, although there was some experimentation with e-cigarettes at intermediate follow up points, the majority (92.3%) returned to exclusive cigarette use.

Among those still smoking after one year, there was no significant difference between baseline dual users and baseline smokers in the mean change in number of cigarettes smoked between baseline and 1-year follow up.

In statistical modelling, baseline dual users were more likely to continue dual use if they were white, had lower cigarette dependency according to the Wisconsin Inventory of Smoking Dependence Motives (WISDM) and a higher e-cigarette dependence (e-WISDM).

- **Limitations**

  No adjustment was made for differences in baseline demographic variables between dual users and smokers, so confounding may have accounted for the differences in cessation outcomes. No causal associations between dual use and cessation outcome can be made.

  Sub-group sample sizes were small which increases the uncertainty of estimates and meant it was not possible to model significant predictors of quitting smoking.

  Participants had no interest in quitting and dual users may be people who have already failed in their quit attempts. This means that the participants may be more resistant to quitting, which may have impacted cessation outcomes.

  Participants were recruited via television and social media only and only those who were not interested in cessation were recruited. The dropout rate at 1-year follow-up was high (23.7%). Therefore, the participants and results may not be generalisable to the wider vaping population.

Piper ME, Baker TB, Benowitz NL, Jorenby DE. (2019). Changes in Use Patterns Over One Year Among Smokers and Dual Users of Combustible and electronic cigarettes. Nicotine Tob Res; doi: 10.1093/ntr/ntz065

2. [Perceptions, Knowledge, and Use of Electronic Cigarettes: A Survey of Mental Health Patients.](#)

- **Study aims**

  This U.S. study surveyed 110 out-patients with a psychiatric disorder (including depression, schizophrenia, anxiety and bipolar disorder) attending an adult mental health office to examine their perceptions, knowledge and use of e-cigarettes. Differences in knowledge and perceptions between younger (≤ 30 years) and older (>30years) patients were considered.

- **Key findings**

Most respondents learnt about e-cigarettes from friends or family (74.3%) and the internet (54.1%). This did not vary between age groups. Few (13.8%) had asked their healthcare providers opinions about e-cigarettes. Younger patients were more likely to learn about e-cigarettes from TV and social media websites compared to older patients (p values<0.021).

The majority of respondents (67.0%) across both age groups thought e-cigarettes help people quit tobacco and 60.4% of respondents agreed that e-cigarettes are socially acceptable.

Most participants believed e-cigarettes to be less harmful than smoking (56%). This percentage was higher among younger patients than older patients (62.7% vs 48.0%) but the difference was not significant (p=0.123).

The most commonly reported reasons for using e-cigarettes by all respondents were because they were less harmful than cigarettes (41.3%), to quit using tobacco (41.3%) and they are more socially acceptable than smoking (21.1%). Older patients were more likely to use ENDS on the recommendation of a healthcare provider (14.0% vs 1.7%, p=0.014).

- **Limitations**

Analyses were not adjusted, so differences between older and younger patients are subject to confounding. It's also not possible to determine whether knowledge and perceptions of e-cigarettes are different in mental health patients compared to the general population.

As participants were mostly white, had a bachelor's degree or higher and were only recruited from one outpatient mental health office in the U.S. results are unlikely to be generalisable.

Participants were not asked about their psychiatric diagnoses and may have very different illnesses, or potentially have no mental illness at all as surveys were left unattended in outpatient waiting rooms for people to complete. Therefore, e-cigarette use, and outcomes could not be compared to specific disorders.

This was a cross-sectional study, so it cannot tell us about perceptions and patterns of use over time.

E-cigarettes were defined as electronic devices that deliver nicotine in a vapour and look like cigarettes. This may have been misleading since many e-cigarettes no longer look like combustible cigarettes.

All data were self-reported thus the results may be subject to bias.

Baltz GM, Lach HW. (2019) Perceptions, Knowledge, and Use of Electronic Cigarettes: A Survey of Mental Health Patients. Issues Ment Health Nurs; doi: 10.1080/01612840.2019.1579281.

3. Measuring e-cigarette addiction among adolescents.

- **Study aims**

This U.S study aimed to determine the most accurate self-reported measures for estimating nicotine exposure among adolescents (ages 13-18). Participants (n = 173) that had used an e-cigarette in the past month and had at least 10 lifetime uses, were asked about their frequency of use. Nicotine exposure was measured using salivary cotinine levels. Researchers evaluated three measures of e-cigarette dependency: The E-cigarette Addiction Severity Index (EASI), Heaviness of Vaping Index (HVI) and Penn State Electronic Cigarette Dependence Index (ECDI). Correlations between frequency of use and dependency measures, and cotinine levels were calculated.

- **Key findings**

Most (85.5%) respondents used their e-cigarettes less than daily, mean days per month = 15.4. When restricted to exclusive e-cigarette users, 89.6% used their e-cigarettes less than daily.

26.6% of participants reported smoking a cigarette in the past 30 days and 5.0% reported smoking a cigarette in the past 24 hours.

80.3% of participants reported that some or all their e-cigarette liquid contained nicotine (77.1% in exclusive e-cigarette users).

Sessions per month (SPM), days per month, sessions per day (SPD) all showed a moderate positive correlation with cotinine levels, r=0.59, r=0.58 and r=0.57, respectively. The three dependency measures, EASI (r=0.51), HVI (r=0.50) and ECDI (r=0.50) also showed moderate positive correlations.

All measures remained moderately positively correlated with cotinine levels when restricting to e-cigarette only users.

- **Limitations**

The study did not test whether correlations were significantly different from one another or significantly different across dual users and exclusive vapers. Therefore, we cannot determine whether one measure of e-cigarette dependence is better than the other or whether one might be better used among certain groups.

Biomarkers of nicotine and tobacco exposure were only taken once so do not give an indication of participants exposure levels over time.

While cotinine levels are a good indicator of recent nicotine exposure they may not be appropriate to measure addiction. High cotinine levels may reflect combustible cigarette use rather than e-cigarette use, and the researchers could only validate 24h tobacco abstinence among self-reported exclusive vapers.

The correlations may not be applicable outside the US setting because nicotine regulation of e-cigarettes differs across countries and therefore may affect nicotine exposure.

This was a relatively small sample size and participants may not be representative of the wider adolescent vaping population.

Vogel EA, Prochaska JJ, Rubinstein ML. (2019) Measuring e-cigarette addiction among adolescents. Tob Control; doi: 10.1136/tobaccocontrol-2018-054900

4. [The Health Risks of Electronic Cigarette Use to Bystanders.](#)

- **Study aims**

    This Dutch study aimed to assess the health risks of passive vaping. The exhaled breath of 17 adult e-cigarette users (≥ 18 years) was collected immediately post puff and analysed for levels of nicotine, propylene glycol, glycerol, tobacco specific nitrosamines (TSNAs), carbonyls and heavy metals. Local and systematic effects on bystanders were then modelled using estimates of harm from previous research for two different scenarios: a child in an unventilated car for one hour with two e-cigarette users and an adult in a ventilated office for four hours with one e-cigarette user.

- **Key findings**

    Glycerol, formaldehyde, acrolein, acetaldehyde and heavy metals were not detected in second-hand vapour or were below tolerable levels. Therefore, they were not estimated to cause any adverse health effects to bystanders.

    Propylene glycol was not predicted to cause any systemic effects in either bystander scenario. In the car scenario, mild local effects on the respiratory tract and eyes might be expected.

    The exposure to nicotine for both bystander scenarios was not expected to cause local effects on the respiratory tract. Systemic effects, namely increased heart rate and increased systolic blood pressure were predicted in the car scenario and potentially in the office scenario. The magnitude of the effects was estimated to be similar to the effects caused by drinking two to three cups of caffeinated coffee.

    Risk of increased tumour incidence from TSNAs could not be completely ruled out in the car scenario and could not be calculated with any certainty in the office scenario.

- **Limitations**

    The estimates of chemical concentrations in second-hand vapour were not directly measured in car or office scenarios. Many estimates were calculated by extrapolating harm found in animal studies and others used harm estimates from studies of similar compounds rather than of the chemical itself. All harm estimates had no specific effect size, therefore the actual harm to bystanders from chemicals in second-hand vapour cannot be determined.

There was no comparison to tobacco smoke and no tests of significance were carried out for the harm estimates. We cannot determine whether these predicted effects were significant and a result of e-cigarette vapour exposure or the relative harm of vapour compared to cigarette smoke.

The sample size was very small, the number of puffs were pre-specified, only one session per person was measured and the volume of exhaled air varied considerably between participants. Therefore, the estimated average volume and chemical concentrations of vapour in each scenario may not be reliable or reflect real-world vaping behaviour.

This study did not test differences in chemical concentration by specific devices or e-liquids. Only a small sample of e-cigarettes were included that are not necessarily representative of the range of devices and e-liquids available.

Visser WF, Klerx WN, Cremers HWJM, Ramlal R, Schwillens PL, Talhout R. (2019) The Health Risks of Electronic Cigarette Use to Bystanders. Int J Environ Res Public Health; doi: 10.3390/ijerph16091525.

Overview

This month we include four articles, three from the USA and one from the Netherlands. They focus on: dual use; perceptions and use of e-cigarettes among mental health patients; measures for e-cigarette dependence among young people; and passive vaping.

Our first study aimed to look at changes in vaping and smoking over time amongst a sample of smokers and dual users recruited from one US state who were not motivated to stop smoking. Previous research has found that smokers who use NRT are more likely to quit smoking at one year follow up than those who exclusively smoke. There is a great deal of interest in determining if this is also the case with smokers who vape.

The researchers recruited 117 smokers and 205 dual users for a two-year longitudinal study with multiple follow up points. The authors examined use patterns every four months and for the current paper, the final follow up was at one year. Almost one in four were lost to follow up by 12 months. Among the remaining sample, those who were smokers at baseline remained smokers in almost all cases (97.4%) despite a few experimenting with e-cigarettes during the study period. Among dual users, the patterns were quite different. More of them successfully stopped smoking (8%) than the exclusive smokers (1.9%). However, these higher levels of abstinence could be explained by differences in participant characteristics and the study couldn't prove that dual use over time helped them stop smoking. In addition, dual use was not sustained for the majority - in fact fewer than half of dual users continued to both vape and smoke and the vast majority (86%) of those who discontinued dual use went back to smoking. Some of this may be related to the fact that the sample were recruited on the basis that they didn't intend to quit smoking in the near future, or that the levels of dual use specified for study entry (vaping at least once a week) were low. The study is continuing for a second year of follow up so should provide further evidence in future.

This month's second paper aimed to examine the perceptions, knowledge and use of e-cigarettes amongst a small sample (n=110) of patients with a psychiatric disorder who were attending an out-patient clinic in the USA. Smoking rates are high in adults with mental health conditions and to date there have been relatively few studies focusing on vaping in this population. Among the current

sample, just over half were current smokers and eight in ten had smoked in the past. 59% had tried vaping at least once and two thirds of this group did so to try and cut down or quit smoking.

The authors were particularly interested in patient's views about the products and the role of health care professionals in providing information. Most participants thought e-cigarettes could help people stop smoking (67%) and just over half (56%) believed vaping was less harmful than smoking. The researchers compared older (over aged 30) and younger (18-29) respondents in their analysis and did find some differences, with vaping more common in the younger age groups, more accurate harm perceptions and younger respondents were more likely to report that flavours were an important factor in using e-cigarettes. Only a small proportion (14%) had ever asked a healthcare professional about vaping. Among this group of just 15 individuals, the advice received had been very variable, ranging from a recommendation not to use e-cigarettes at all (or indeed any nicotine product) to advice that vaping was less harmful than smoking, but more research was needed. The authors outline the need for better training and information for health professionals regarding e-cigarettes, as other studies previously included in this bulletin and elsewhere have done.

Our third study aimed to determine the most accurate self-report methods for assessing nicotine intake among young people who vape. The authors looked at the relationship between a range of measures of use and dependency, and saliva cotinine. To do so, 173 13-18 year olds who reported they had vaped at least once in the past month were recruited from one city in California. They were asked a range of questions about vaping behaviour and provided a saliva sample. The researchers employed three validated tools that aim to measure e-cigarette dependency - the E-cigarette Addiction Severity Index (EASI), the Heaviness of Vaping Index (HVI), and the Penn State E-cigarette Dependency Index (ECDI) - and looked at the relationship between patterns of use, cotinine levels and dependency.

The findings of this study are primarily useful for researchers interested in nicotine exposure or addiction among young people who vape, as they provide useful information on which measures and/or tools to include in future studies. The study did not focus on exclusive vapers, as just over one in four participants had smoked in the past month including 5% who had smoked in the past 24 hours. To account for this the authors did separate this group from the vaping only participants in some analyses. Overall, the authors found that all the measures used in the study, which were originally developed in research with adult vapers, were appropriate for use in studies with young people who vape. The measures also correlated significantly with nicotine exposure (as measured by cotinine) and so should be useful for assessing frequency of vaping and possible addiction to e-cigarettes. They also found that briefer measures such as days per month of vaping and the EASI tool performed just as well as longer or more complex indices.

This month's final paper outlines results from a study that aimed to assess any health risks to bystanders exposed to e-cigarette emissions. The researchers, based in the Netherlands, collected exhaled vapour from 17 adult vapers (nine of whom were dual users) and analysed the samples for a range of toxicants and constituents. They then modelled the potential impact of exposure using two different scenarios. This first simulated use in a car for one hour where a child was present along with two vapers and no ventilation, and the second a ventilated office where one vaper was using their device over four hours.

The exhaled e-cigarette emissions contained propylene glycol and the researchers estimated that exposure could cause mild irritation to the eyes or respiratory tract of bystanders in an enclosed setting (i.e. a car) but not in the office scenario. The exhaled vapour contained nicotine, and while this was not expected to cause local (respiratory) effects in either scenario, it could increase heart

rate and blood pressure in bystanders in the car and possibly the office setting. Other toxicants and constituents that the researchers measured in the vapour included aldehydes and heavy metals but these did not reach levels that would be expected to have health effects. Possible cancer risks (tumour development) from exhaled tobacco specific nitrosamines (TSNA) in the car scenario couldn't be excluded, but the authors noted data were lacking to accurately assess the extent of risk. Overall the researchers stated that there were likely to be some health effects to bystanders exposed to e-cigarette emissions, particularly in very enclosed spaces, but that the effects in their study were relatively mild. They also pointed out that arguably the most worrying outcome - possible cancer risk from TSNA exposure, could be avoided if regulations are enforced (i.e. the EU TPD stipulates that e-liquids may not contain detectable amounts of TSNAs). The article also includes a call for more research on second hand vapour involving a larger number of participants and a wider range of devices and e-liquids.

CRUK Funding Committee Call Dates

Population Research Committee

Project Awards – deadline of 23/05/2019 for decisions in late Nov 2019

Postdoctoral Fellowship – deadline of 14/11/2019 for decisions in late July 2020

Contact: PRC@cancer.org.uk

Tobacco Advisory Group

Project Awards – deadline of 23/05/2019 for expressions of interest, for decisions in November 2019

Contact: TAG@cancer.org.uk

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

Cessation

A Pilot Study of E-Cigarette Naïve Cigarette Smokers and the Effects on Craving After Acute Exposure to E-Cigarettes in the Laboratory.

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

Are Electronic Cigarettes an Effective Aid to Smoking Cessation or Reduction Among Vulnerable Groups? A Systematic Review of Quantitative and Qualitative Evidence.

Patterns of use

Potential Country-level Health and Cost Impacts of Legalizing Domestic Sale of Vaporized NicotineProducts.

Use of Flavored E-Cigarettes Among Adolescents, Young Adults, and Older Adults: Findings From the Population Assessment for Tobacco and Health Study.

Changes in Use Patterns OVER ONE YEAR Among Smokers and Dual Users of Combustible and electronic cigarettes.

Impacts of Nicotine and Flavoring on the Sensory Perception of E-Cigarette Aerosol.

Perceptions

[Perceptions, Knowledge, and Use of Electronic Cigarettes: A Survey of Mental Health Patients.](#)

Youth use

[Self-Reported Use of Tobacco, E-cigarettes, and Marijuana Versus Urinary Biomarkers.](#)

[Measuring e-cigarette addiction among adolescents.](#)

Harms and harm reduction

[Impairment of testicular function in electronic cigarette (e-cig, e-cigs) exposed rats under low-voltage and nicotine-free conditions.](#)

[Acute exposure to e-cigarettes causes inflammation and endothelial oxidative stress in non-smoking healthy young subjects.](#)

[Chronic exposure to e-cig aerosols during early development causes vascular dysfunction and offspring growth deficits.](#)

[The Health Risks of Electronic Cigarette Use to Bystanders.](#)

[Clinical periodontal status and gingival crevicular fluid cytokine profile among cigarette-smokers, electronic-cigarette users and never-smokers.](#)

[High-Nicotine Electronic Cigarette Products: Toxicity of JUUL Fluids and Aerosols Correlates Strongly with Nicotine and Some Flavor Chemical Concentrations.](#)

[Sucralose-enhanced degradation of electronic cigarette liquids during vaping.](#)

[Metal concentrations in electronic cigarette aerosol: Effect of open-system and closed-system devices and power settings.](#)

[Experiences of women with cervical dysplasia and associated diagnoses using electronic cigarettes for smoking substitution.](#)

[The transfer characteristics of heavy metals in electronic cigarette liquid.](#)

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.