THE UK ELECTRONIC CIGARETTE RESEARCH FORUM

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Electronic Cigarette Research Briefing – November 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.

Research Call from The Tobacco Advisory Group (TAG)

The funding call for June 2020 is open, for which Cancer Research UK's TAG are accepting proposals **themed around the impact of electronic cigarettes (ECs) on youth**. Applicants within the UK are eligible to apply for funding of around £400k, and this call would provide a funding for up to three years. A guidance document containing some further information can be found on the TAG webpage here.

1. The Relationship Between Electronic Cigarette Use and Conventional Cigarette Smoking Is Largely Attributable to Shared Risk Factors

- **Study Aims**

This US study examined the correlations between current and ever use of electronic cigarettes and current and ever use of cigarettes. Data were collected from 12,421 12-15-year olds who completed the Monitoring the Future (MTF) study questionnaire between 2015-2016. Results were adjusted for 14 different risk factors relating to likelihood of smoking using two different techniques: standard regression and Inverse Propensity Weighting (IPW).

- **Key Findings**

After standard adjustment, current e-cigarette use was associated with ever-smoking (OR=3.79 95%CI 2.53-5.68, p<0.001), but not current smoking (p=0.403).

After standard adjustment, ever e-cigarette use was associated with both ever-smoking (OR=5.63, p<0.001) and current smoking (OR=4.45, p=0.002)

After using IPW adjustment, ever and current e-cigarette use still significantly increased the risk of ever smoking a cigarette (OR=2.49, p<0.001; OR = 2.32, p<0.001). However, neither increased the risk of current cigarette smoking (p=0.228; p=0.849, for ever and current e-cigarette use respectively).

In the adjusted IPW model, shared risk factors accounted for 45% and 42% of variation in lifetime and current e-cigarette smoking, respectively. E-cigarette use explained an additional 1-7% of variation.

- **Limitations**

It was assumed that adolescents who reported use of both e-cigarettes and cigarettes initiated with e-cigarettes. As the order of use was not confirmed, causality cannot be determined.

IPW analysis assumes that there are no unmeasured confounding variables, but data on some known risk factors, such as parental smoking, were not available. This may have affected the associations observed in the IPW analyses, and other analyses may also be influenced by other confounders not included.

The study used self-reported data meaning that results could be subject to bias.

The study only considered data from 2015-2016 so cannot tell us how the association might vary over time. It also only included certain school age groups, so results may not be generalisable to all adolescents.

Kim S, Selya AS. (2019) The Relationship Between Electronic Cigarette Use and Conventional Cigarette Smoking Is Largely Attributable to Shared Risk Factors. Nicotine Tobacco Research.; doi: 10.1093/ntr/ntz157

2. A Combination of Factors Related to Smoking Behaviour, Attractive Product Characteristics, and Socio-Cognitive Factors are Important to Distinguish a Dual User from an Exclusive E-Cigarette User

- **Study Aims**

This Dutch study examined differences in characteristics between dual users and exclusive e-cigarette users. Data were collected via an online survey in 2016, from 36 and 80 adult (18+) exclusive vapers and dual users, respectively. Researchers looked at four clusters of characteristics: smoking and/or vaping behaviour, product characteristics, attitudes to smoking and vaping and socio-cognitive factors. The analysis used a machine learning algorithm to determine which factors were most significant in distinguishing the two groups.

- **Key Findings**

The quantity of tobacco smoked (in the past or currently) was a distinguishing characteristic. 38.9% of exclusive e-cigarette users smoked over a packet of cigarettes a day previously, compared to 6.3% of dual users currently.

The perception of cigarettes was also identified as a distinguishing factor between dual and exclusive e-cigarette users. Exclusive e-cigarette users found cigarettes more unattractive than dual users both in terms of smell and cost (58.3% vs 35% and 66.7% vs 43.8%, respectively).

Five socio-cognitive factors significantly impacted prediction accuracy. Dual users reported greater social ties with people who smoked – this was the most important distinguishing factor in the model. Dual users also had more negative attitudes towards e-cigarettes than exclusive users. Although dual users reported greater intention to quit vaping than exclusive e-cigarette users, they reported lower self-efficacy and to do so and more barriers to accessing e-cigarettes.

No product characteristics were identified as significantly different between dual users and exclusive users.

Based on these factors, the algorithm predicted exclusive or dual e-cigarette or dual with 86.2% accuracy.

- **Limitations**

Sample sizes were small, particularly in the exclusive e-cigarette subgroup (n=36). Participants were recruited via an online panel. Therefore, the results may not be generalisable to the wider vaping population.

The number of cigarettes smoked per day before both groups used e-cigarettes was not measured – prior smoking in exclusive e-cigarette users was compared to current smoking in dual users. In addition, unlike smoking, vaping patterns were not measured. Therefore, the study does not give insight into the nicotine dependence of each group when only smoking combustible cigarettes or how these factors may affect likelihood of dual use.

The study was cross sectional so it cannot establish causal differentiating characteristics or tell us how the defining characteristics of each group may change over time.

Data on smoking and vaping were self-reported and may be subject to bias.

Romijinders KAGJ, Pennings JLA, van Osch L, de Vries H, Talhout R. (2019). A Combination of Factors Related to Smoking Behaviour, Attractive Product Characteristics, and Socio-Cognitive Factors are Important to Distinguish a Dual User from an Exclusive E-cigarette User. Int J Environ Res Public Health.; doi: 10.3390/ijerph16214191.

3. Prevalence and correlates of long-term e-cigarette and nicotine replacement therapy use: a prospective study in England

- **Study Aims**

This English study reviewed data collected from 40,933 people (aged 16+) between 2014-2016 in the Smoking Toolkit Study, and 733 were followed up for 12 months. Data was collected on the prevalence of all adults and within that, past year smokers, who reported long-term (≥1 year) use

of e-cigarettes or nicotine replacement therapy (NRT) at baseline and follow-up at six and 12 months. The sociodemographic and smoking related characteristics of long-term (≥1 year) e-cigarette and NRT users at baseline were compared.

- **Key Findings**

At baseline, long-term use of e-cigarettes and NRT did not differ significantly between current smokers and recent (<1 year) ex-smokers (p=0.747; p=0.724).

Long-term use of e-cigarettes did not differ significantly between long-term (≥ 1 year) ex-smokers and current smokers (p=0.274) however long-term use of NRT was significantly lower in long-term (≥ 1 year) ex-smokers compared to current smokers (OR=0.62, p=0.003).

At baseline, long-term use of e-cigarettes among past-year smokers was significantly lower among those without post 16-qualifications (OR= 0.63, p<0.001) and those from social grades C2DE (OR=0.66, p=0.001). Past-year smokers aged 35-54 or ≥55 years were more likely than those aged 16-34 to report long-term e-cigarette use (OR=1.90 p<0.001 and OR=1.55 p=0.008, respectively).

The weighted prevalence of long-term e-cigarette use assessed over the 12 months in past-year smokers was 13.4% (95%CI 10.9-15.9%) compared to 1.9% (95%CI 0.9-2.9%) for long-term NRT use.

- **Limitations**

The 12-month follow-up analysis did not consider differences in long-term e-cigarette/NRT use across sociodemographic and smoking related characteristics. Therefore, it cannot be determined whether the same trends exist as in the cross-sectional analysis.

The follow-up survey only included past year smokers so prospective analysis of the prevalence of long-term e-cigarette or NRT use in the entire population or long-term ex-smokers was not possible.

The loss to follow-up was high and the sample for the 12-month follow-up analysis was older, more affluent, reported more long-term use of e-cigarettes and NRT at baseline and were more likely to have quit recently. This may have influenced the prevalence of long-term e-cigarette use observed in the analysis and the results may not be generalisable.

Participants self-reported all data. Therefore, results could be subject to bias. Specifically, at baseline the use of cessation aids was reported retrospectively for the past 12 months which could be subject to recall bias.

Reasons for using e-cigarettes or NRT and the patterns of use were not considered.

Jackson SE, Hill E, Shahab L, Beard E, Michie S, Brown J. (2019). Prevalence and correlates of long-term e-cigarette and nicotine replacement therapy use: a prospective study in England. BMJ Open.; doi: 10.1136/bmjopen-2019-029252.

4. Impact of non-menthol flavours in tobacco products on perceptions and use among youth, young adults and adults: an updated systematic review

- **Study Aims**

This systematic review assessed the impact of non-menthol flavoured e-cigarettes on perceptions and use among adults and youth. The review included 51 quantitative studies that examined harm perceptions, willingness to try, initiation of use, product appeal and role in smoking cessation. QATSDD, a quality assessment tool, was used to examine the quality of studies and data were extracted and grouped into age categories.

- **Key Findings**

Four studies examined taste, appeal and risk perceptions among young people (ages defined by individual study authors). Overall fruit flavours were perceived as less harmful. Eight studies of adults were identified, including several experimental studies, and they consistently found that e-cigarette flavours increase product appeal and enjoyment.

Nine studies in adults (all US based) and two studies in young people looked at reasons for use. Results were varied – from under 10% to a majority reporting flavours as a reason for using e-cigarettes.

Seven studies examined susceptibility, intention to try or initiation of e-cigarettes among youth. Six reported positive associations between flavours and e-cigarette use intentions. The one UK study (n=256) reported that cigarette smokers and non-smokers were more willing to try flavoured e-cigarettes than tobacco flavoured e-cigarettes (90% vs 73% and 34% vs 12%).

The role of flavours in quit intentions and quitting behaviour was inconclusive. The one study exclusively in young people found that US students who reported using flavoured e-cigarettes were less likely to quit than those not using e-cigarettes or using non-flavoured ones. Seven studies with conflicting outcomes in adults were found.

The QATSDD quality validation tool revealed deficits in the existing literature, particularly in consideration of sample size or assessment of measurement tools. It was also noted that the literature does not have a consistent and standardised way to categorise flavours.

- **Limitations**

This review is vulnerable to any limitations of the individual studies included. 90% of studies were cross-sectional in design and there was no indication of how well studies adjusted for confounding factors. Therefore, this review cannot establish causal relationships.

A minimum threshold of quality was not set and the quality of each study was not weighted in the analysis.

Due to heterogeneity in the data, a meta-analysis was not performed. Therefore, common effects of the studies cannot be statistically verified.

Industry-funded papers were not excluded, and the review included three studies which were funded or promoted by the e-cigarette industry. It was unclear whether these were e-cigarette manufacturers independent of the tobacco industry or also included tobacco industry funders.

This review included studies from a range of countries, but the majority (73%) were US-based. It's therefore unclear how applicable these are to countries such as the UK.

Baker HM, Meernik C, Kowitt SD, Ranney LM, Goldstein AO. (2019). Impact of non-menthol flavours in e-cigarettes on perceptions and use: an updated systematic review. BMJ Open.; doi: 10.1136/bmjopen-2019-031598.

Overview

This month's papers include studies from the USA, the Netherlands and England as well as a systematic review.

Our first paper examines the topical issue of the relationship between vaping and smoking among young people in the USA. The authors obtained data from the 2015-16 wave of the Monitoring the Future survey with 12-15 year olds (8th to 10th graders). They aimed to examine risk factors for both behaviours and the extent to which they were the same or different. Their rationale was that there is an ongoing debate about the extent to which vaping 'causes' smoking and that existing studies have been unable to establish this. To try and shed more light on the issue, they used a statistical method called propensity score matching. This approach is useful when examining issues where it is not possible or ethical to randomise individuals to receive or not receive a particular intervention or treatment (in this case, using an e-cigarette).

Just over 12,000 young people were included in the sample. The outcomes of interest were lifetime and current vaping and smoking, defined as using at least once (lifetime) or regular use at the time of the survey (current). Use of either product was relatively low (unsurprising given the age of the respondents) lifetime vaping 25% (smoking 14%), and current vaping 9% (smoking 6%). Fourteen risk factors were included in the analysis, based on demographic, substance use and behavioural/attitudinal variables available in the survey. The propensity score matching found that lifetime and current vaping increased the risk of ever smoking but this was not the case for current, continued smoking. In other words, the relationship that some previous studies have found between using an e-cigarette and progressing to regular smoking was fully explained in this study by shared risk factors. This is consistent with the 'common liability' theory - that some young people have characteristics, circumstances or beliefs/behaviours that put them at risk of both smoking and vaping and thus the relationship between the two is not necessarily causal.

This month's second study aimed to examine differences between adults who vape and those who both smoke and vape (dual users). Although the majority of vapers in the UK have now stopped smoking, this is not the case in some other countries where vaping is permitted. As dual use confers few if any health benefits, understanding the factors that might distinguish dual users from those who switch completely to vaping might be helpful for designing information campaigns or interventions involving e-cigarettes for smoking cessation.

This was a small cross-sectional survey that recruited 80 dual users and 36 exclusive vapers via an online survey in the Netherlands. It examined smoking and vaping behaviour, products used, reasons for use and attitudes and beliefs. Using a machine learning algorithm, the authors identified some interesting differences between the two groups. Exclusive vapers had started smoking earlier and were heavier smokers before switching. Exclusive vapers were also more focused on the health benefits of vaping and had more negative attitudes towards smoking, while dual users were more likely to report that avoiding smoking restrictions, product appearance, flavours and novelty of vaping

were important to them. Dual users were more likely to report that they had partners, friends, family and colleagues who smoked and felt stronger social ties to smokers than exclusive vapers. Dual users also perceived fewer risks from smoking and had higher intentions to quit vaping (plus lower self-efficacy to quit smoking). On the basis of these findings, the authors include some key messages that could be developed for health communication to support dual users to quit smoking in the Netherlands and elsewhere.

The third paper is from the smoking toolkit study in England and aimed to examine the prevalence and characteristics of long term e-cigarette users compared with long term NRT users. Long term was defined as more than 12 months. Some studies have found that longer term vaping is more common in ex-smokers than continued use of NRT, and the authors intended to provide more information on this issue.

Cross-sectional data from around 41,000 adults aged 16 and over were included, plus a smaller sub-sample of smokers (n=733) who were followed up in a prospective study at 6 and 12 months. Long term use of either e-cigarettes or NRT was rare at the general population level (1.5% and 0.5% respectively) and almost completely absent (0.1% and 0.0% respectively) among never smokers. Even among past year smokers using either product for 12 months or more was unusual (3.9% e-cigarettes, 1.3% NRT). However, in the prospective study this was slightly more common, particularly for e-cigarettes (10.3% and 1.6% respectively), suggesting that people may forget or under-report what is used through time. Longer term use of NRT was much less common among long-term ex-smokers than continuing smokers, whereas longer term use of e-cigarettes was similar, suggesting that NRT used in a quit attempt is discontinued quite quickly whereas more people may continue vaping post smoking cessation. The study also identified some differences by age, socio-economic status and region of residence (north vs south England) that may be useful to inform policy and practice developments in the UK.

This month's final paper is a systematic review focusing on e-cigarette flavours. The authors (all based at the University of North Carolina in the USA) searched for published studies up to March 2018 that examined the effect of non-menthol flavours in e-cigarettes on perceptions and use among adults and young people. Fifty-one articles were identified that met the review's inclusion criteria, 30 with adults, 13 with young people and eight including both youth and adults. The vast majority (72%, 32 studies) were conducted in the USA and only one in a low or middle-income country (Malaysia). Studies examined: appeal; reasons for use; risk perceptions; intentions to try; initiation; preferences; current use; quit intentions and cessation.

Among adults, flavours increased the appeal of vaping and in some studies, were included as the primary reason why e-cigarettes were used. However, the specific role of e-cigarette flavours in smoking cessation was unclear, and this is an important area for future research. Among young people, flavours (particularly fruit and sweet flavours) contributed to the products being perceived as less harmful than smoking and increased willingness to try vaping. The review did not discuss in any detail the extent to which the participants in the original studies were current, ex or never smokers although some information on this is included in the Tables summarising the studies. The authors concluded that flavours attract both young people and adults to use e-cigarettes. They also point out that flavour bans may reduce uptake among youth, but this needs to be balanced with their role in the appeal of the products to adult smokers.

Other studies from November that you might find of interest

Patterns of Use

E-Cigarette Use Among Adult Primary Care Patients: Results from a Multisite Study.

Differences in nicotine intake and effects from electronic and combustible cigarettes among dual users.

Potential for non-combustible nicotine products to reduce socioeconomic inequalities in smoking: a systematic review and synthesis of best available evidence.

Electronic cigarettes: Ever use, current use and attitudes among alcohol and other drug clients.

Nearly 20 000 e-liquids and 250 unique flavour descriptions: an overview of the Dutch market based on information from manufacturers.

Prevalence of e-cigarette use from a nationally representative sample in New Zealand.

Flavored ENDS Use among Adults Who Have Used Cigarettes and ENDS, 2016-2017.

Participation in electronic cigarette-related social media communities: Effects on attitudes toward quitting, self-efficacy, and intention to quit.

Electronic Cigarette Use and Related Factors among Active Duty Service Members in the U.S. Military.

Electronic Cigarette Use Among Populations of Women During Reproductive Years.

Perceptions

Communicating risk differences between electronic and combusted cigarettes: the role of the FDA-mandated addiction warning and a nicotine fact sheet.

Awareness, current use of electronic cigarettes and associated smoking factors in Zhejiang Chinese adolescents.

Motivations for using electronic cigarettes in young adults: A systematic review.

Acceptability of electronic nicotine delivery systems (ENDS) among HIV positive smokers.

Cessation

Tobacco Use among Recovery Home Residents: Vapers Less Confident to Quit.

Are electronic nicotine delivery systems (ENDs) helping cigarette smokers quit?-Current evidence.

Population level predictors of changes in success rates of smoking quit attempts in England: a time series analysis.

Youth Use

Association of Canada's Provincial Bans on Electronic Cigarette Sales to Minors With Electronic Cigarette Use Among Youths.

Flavored E-cigarette Use and Progression of Vaping in Adolescents.

Exploring the Bi-Directional Association between Tobacco and E-Cigarette Use among Youth in Canada.

Transitions Across Tobacco Use Profiles Among Adolescents: Results from the Population Assessment of Tobacco and Health (PATH) Study Wave 1 and Wave 2.

e-Cigarette Use Among Youth in the United States, 2019.

Flavors of e-Cigarettes Used by Youths in the United States.

Appeal of JUUL among adolescents.

E-Cigarette Use and Subsequent Cigarette Initiation and Sustained Use Among Youth, U.S., 2015-2017.

High school students' use of flavored e-cigarette e-liquids for appetite control and weight loss.

Predictors of E-Cigarette Use Susceptibility-A Study of Young People from a Socio-Economically Disadvantaged Rural Area in Poland.

Reasons for Transition From Electronic Cigarette Use to Cigarette Smoking Among Young Adult College Students.

Harms and harm reduction

Flavored E-liquids Increase Cytoplasmic Ca_{2+} Levels in Airway Epithelia.

Systemic toxicity evaluation of novel tobacco products in Caenorhabditis elegans.

Electronic Cigarette Vapor with Nicotine Causes Airway Mucociliary Dysfunction Preferentially via TRPA1 Receptors.

E-Cigarette Use Increases Susceptibility to Bacterial Infection by Impairment of Human Neutrophil Chemotaxis, Phagocytosis and NET Formation.

E-cigarette use is associated with a self-reported diagnosis of prediabetes in never cigarette smokers: Results from the behavioral risk factor surveillance system survey.

Does Nicotine-free Electronic Cigarette Vaping Affect Aortic Stiffness Independently of Heart Rate?

Levels of the Thiocyanate in the Saliva of Tobacco Smokers in Comparison to e-Cigarette Smokers and Nonsmokers Measured by HPLC on a Phosphatidylcholine Column.

Impact of electronic cigarette heating coil resistance on the production of reactive carbonyls, reactive oxygen species and induction of cytotoxicity in human lung cancer cells in vitro.

The association between e-cigarette use and asthma among never combustible cigarette smokers: behavioral risk factor surveillance system (BRFSS) 2016 & 2017.

Effects of Electronic Cigarette Constituents on the Human Lung: A Pilot Clinical Trial.

Adult E-Cigarettes Use Associated with a Self-Reported Diagnosis of COPD.

Marketing

A content analysis of the promotional strategies employed by e-cigarette brands on Twitter.

The Effect of E-cigarette Commercials on Youth Smoking: A Prospective Study.

E-cigarette Marketing Exposure and Subsequent Experimentation Among Youth and Young Adults.

Misc

What factors reliably predict electronic cigarette nicotine delivery?

Expenditure on smoking and alternative nicotine delivery products: a population survey in England.

Rapid Brain Nicotine Uptake from Electronic Cigarettes.

Evaluating tobacco retailer experience and compliance with a flavoured tobacco product restriction in Boston, Massachusetts: impact on product availability, advertisement and consumer demand.

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 ecig[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 Alice Davies and 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.