THE UK ELECTRONIC CIGARETTE RESEARCH FORUM

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Electronic Cigarette Research Briefing – June 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. Moderators of real-world effectiveness of smoking cessation aids: a population study.

- **Study aims**

  This English study aimed to assess the real-world effectiveness of different cessation aids and their effectiveness among different groups. Data were collected via monthly surveys between 2006 and 2018, from 18,929 smokers that had smoked and had made at least one quit attempt in the 12 months prior to being surveyed. Analyses were adjusted for demographic factors, level of cigarette addiction, the nature of the quit attempt, time since quit attempt, month and year of the survey and cessation aid variables.

- **Key findings**

  12.7% of participants used e-cigarettes in their most recent quit attempt. Of these, 21.2% reported being abstinent at the time of the survey. E-cigarette users were nearly twice as likely to be abstinent than non-e-cigarette users. (OR= 1.95 95% CI 1.69-2.24).

  Use of an e-cigarette varied by age, sex, socioeconomic status, whether the attempt was planned and whether it involved cutting down (all p values <0.02). Similar associations were

observed across other cessation aids, but socioeconomic status was not associated with use of NRT OTC, varenicline or face-to-face behavioural support.

Strength of urges to smoke was not associated with use of e-cigarettes (p=0.74), though it was associated with use of other cessation aids such as NRT OTC, prescription NRT, varenicline and face-to-face behavioural support (p<0.001 for all).

The association of e-cigarettes with abstinence did not significantly differ with cigarette addiction, social grade or age. There was some evidence that the effectiveness of e-cigarettes varied with sex; the odds of abstinence among those using an e-cigarette compared to those not using one was 1.66 (95%CI 1.35-2.04) in women and 2.26 (95%CI 1.87-2.74) in men.

- **Limitations**

This paper did not examine the effectiveness of using a combination of cessation aids, such as using support with medication and the effectiveness of the cessation aids were only estimated in comparison to not using that aid rather than in comparison to cold turkey. Therefore, it does not give the full picture of the effectiveness of cessation aids in a real-world setting.

This paper only examines abstinence at one time point and there may have only been a short time elapsed since quit attempts at the time of survey. Therefore, this paper cannot tell us how relapse rates vary among users of different cessation tools.

Participants' adherence to their cessation aid was not measured, low adherence may skew results.

All data were self-reported and may be subject to bias.

Jackson S, Kotz D, West R, Brown J. (2019). Moderators of real-world effectiveness of smoking cessation aids: a population study. Addiction; doi: 10.1111/add.14656.

2. Mental Health Problems and Initiation of E-cigarette and Combustible Cigarette Use.

- **Study aims**

This U.S. study examined whether an association between self-reported mental health problems and e-cigarette and cigarette use exists among 7702 adolescents (12 - 17 years) from the PATH study with no prior product use. Baseline data on past year internalising and externalising problems and 12-month follow-up data on past 30-day product use were recorded. Internalising problems included anxiety, depressive and somatic symptoms and externalising problems included impulsive, disruptive conduct and substance use symptoms. Analyses were adjusted for demographic factors and past year marijuana and alcohol use.

- **Key findings**

Compared to reporting low internalising problems at baseline, reporting high internalising problems was significantly associated with exclusive past 30-day e-cigarette use at one year follow up (OR=1.61 95%CI 1.12-2.33) but was not associated with exclusive past 30-day smoking or dual use.

Compared to reporting low externalising problems at baseline, participants that reported high levels of externalising problems were significantly more likely at one year follow up to have used e-cigarettes and cigarettes in the past 30 days (OR=2.78 95%CI 1.76-4.40 and OR = 5.59 95%CI 2.62-11.90, respectively). As were those that that reported moderate levels of externalising problems (OR=2.22 95%CI 1.50-3.27 and OR=3.29 95%CI 1.56-6.93, respectively).

Past year alcohol use was significantly associated with past 30-day e-cigarette and cigarette use at 12-month follow up compared to no past year alcohol use (0R=2.50 95%CI 1.62-3.86 and OR=2.13 95%CI 1.22-3.72, respectively).

Compared to no past year marijuana use, past year marijuana use was shown to have a significant positive association with cigarette use but not e-cigarette use ($p<0.05$).

- **Limitations**

The measure used to determine mental health problems was a screening tool and is not diagnostic. Analyses were not adjusted for all covariates that might influence uptake of e-cigarette use, such as susceptibility to vaping or smoking. Therefore, a causal relationship between diagnosed mental health problems and product use cannot be determined.

93% of the sample did not use any product at follow-up so the sample sizes of the subgroups of use of products might be small, which would make estimates less reliable.

The data on e-cigarette and cigarette use did not distinguish between experimental and regular use. Therefore, this paper does not give the full picture on how mental health problems could affect patterns of e-cigarette and cigarette use.

Only one time point was used to collect data on current product use therefore this paper cannot determine how mental health problems might have affected product use over time.

All data were self-reported which may be subject to bias.

Riehm KE, Young AS, Feder KA, Krawczyk N, Tormohlen KN, Pacek LR, Mojtabai R, Crum RM. (2019) Mental Health Problems and Initiation of E-cigarette and Combustible Cigarette Use. Pediatrics; doi: 10.1542/peds.2018-2935.

3. Impact of e-cigarette and cigarette prices on youth and young adult e-cigarette and cigarette behaviour: evidence from a national longitudinal cohort.

- **Study aims**

This U.S. study examined the effect of e-cigarette and cigarette prices on the use of both products among 11,578 young people aged 15-21 years. Data on e-cigarette and cigarette use were collected via biannual online surveys from 2014 to 2016. Quarterly price data were taken from Nielsen Company's retail store scanner database. Analyses were adjusted for age and state-level cigarette and e-cigarette policies.

- **Key findings**

The prices of e-cigarettes and cigarettes were not significantly associated with past 30-day e-cigarette use or with past 30-day smoking in the fully adjusted model.

State level e-cigarette minimum age sales laws significantly decreased the likelihood of past 30-day e-cigarette use (OR=0.77 95%CI 0.59-0.99).

For each one-year increase in age participants were 73% more likely to report past 30-day e-cigarette use and 161% more likely to report past 30-day cigarette use (OR=1.73 95%CI 1.40-2.14 and OR=2.61 95%CI 1.97-3.45, respectively).

- **Limitations**

This paper did not examine the change in price of all products related to e-cigarette use, such as device type or e-liquid refills. Therefore, this paper cannot determine causality between the cost of vaping and e-cigarette and cigarette use.

This study only looked at past 30-day use. This is likely to include people who might try vaping or smoking as well as those who buy a product, which would affect the associations. The measure of e-cigarette and cigarette use did not allow room to measure any reductions in the frequency of use that might be associated with product prices.

Data on e-cigarette prices were only taken from one database. It did not include data from common retailers such as vape shops and online e-cigarette stores. Therefore, this paper may not give the full picture of e-cigarette price trends and associated e-cigarette and cigarette use.

Prices of e-cigarettes, regulation and marketing vary nationally and internationally. The results of this study may not be generalisable to other countries, such as the UK.

Data on product use were self-reported and may be subject to bias.

Cantrell J, Huang J, Greenberg MS, Xiao H, Hair EC, Vallone D. (2019) Impact of e-cigarette and cigarette prices on youth and young adult e-cigarette and cigarette behaviour: evidence from a national longitudinal cohort. Tob Control; doi: 10.1136/tobaccocontrol-2018-054764

4. Adolescents' E-Cigarette Use: Increases in Frequency, Dependence, and Nicotine Exposure Over 12 Months.

- **Study aims**

This U.S. study aimed to examine how patterns of use, dependency on e-cigarettes and nicotine exposure changed over 12 months in a sample of 173 adolescents (13-18 years) that had used e-cigarettes at least 10 times in their lives and at least once in the past 30-days. At baseline, 6 and 12 months data on e-cigarette and cigarette use were collected via in person surveys and cotinine levels were recorded. Dependency was measured using the Electronic Cigarette Dependence Index. E-cigarette and cigarette use was defined as past 30-day use of each product only, dual use was defined as past 30-day use of both products.

- **Key findings**

  At 12-month follow up 80.3% of participants had used e-cigarettes in the past 30-days. Between baseline and 12 months, frequency of use increased by 4.2 days per month (p=0.018) and the e-cigarette dependence score increased by 1.7 points (p=0.002). There was no significant change in these measures between baseline and 6 months. Cotinine levels increased significantly from both baseline to 6 months (p=0.019) and baseline to 12 months (p=0.0.13).

  At 12-month follow up, most baseline exclusive e-cigarette users were still using e-cigarettes only (n=56, 62%). Some reported using combustible cigarettes (n=19, 20.7%) and few reported no product use (n=17, 19%,).

  At 12-month follow up, 57% of baseline dual users were still dual users. Some had switched to using e-cigarettes only (n=11, 23%) and few were using only combustible cigarettes at 12 months (n=4, 11%).

  The proportion of participants reporting Juul as their most commonly used device significantly increased over time (p<0.001) going from the third most commonly used device at baseline and 6 months to the first at 12 months.

  The proportion of participants using e-cigarettes for enjoyment significantly increased from 35.7% at baseline to 63.3% at 12-months (p<.001). The proportion using e-cigarettes for social reasons did not change significantly.

- **Limitations**

  No adjustment for confounders was made when testing differences between outcomes at baseline and follow-up. Therefore, other factors may have influenced results.

  The measures of e-cigarette and cigarette use cannot differentiate between those who are experimenting and long-term users. Their patterns and reasons for use might be different, which would affect results.

  How use of e-cigarettes for smoking cessation varied between baseline and follow up was not reported. It was also not clear whether exclusive e-cigarette users at baseline were prior smokers, so we can't determine whether transitions to smoking were a relapse or a gateway effect.

  Cessation advice was offered but we don't have data on which participants used it so cannot be sure how much this influenced the changes seen.

  The sample size was small, participants were recruited from one area in the U.S., most were white and male, and loss to follow up was high (30.6% at 6 months and 26.6% at 12 months). Therefore, results may not be generalisable to the wider population of teenage vapers.

  Although data on dependency were measured no attempt was made to examine how this might effect changes in use.

  Most data were self-reported which may be subject to bias.

Vogel EA, Prochaska JJ, Ramo DE, Andres J, Rubinstein ML. (2019) Adolescents' E-Cigarette Use: Increases in Frequency, Dependence, and Nicotine Exposure Over 12 Months. J Adolesc Health; doi: 10.1016/j.jadohealth.2019.02.019.

Overview

This month's articles were authored by research teams in the UK and the USA and focus on: the effectiveness of e-cigarettes and other smoking cessation aids; mental health and e-cigarette use; pricing of e-cigarettes and cigarettes; and changing patterns of youth e-cigarette use over time.

The first paper uses the Smoking Toolkit study in England to examine the effectiveness of different smoking cessation aids and whether this varies depending on the characteristics of users. We've included several toolkit papers in past bulletins but it's worth mentioning again that this is a repeat cross sectional survey that gathers data every month from a representative sample of adults aged 16 and above. In this paper, a large sample of just under 19,000 participants is included, with data available from 2006-2018. Participants had smoked within the past year and made at least one attempt to stop smoking during that period. The main outcome was whether participants reported that they had successfully stopped smoking from quit date to survey.

Among the various aids to stopping smoking asked about (medications including NRT, bupropion and varenicline; e-cigarettes; behavioural support; quitline; leaflets/materials; online; and hypnotherapy) people who used e-cigarettes or varenicline were significantly more likely to have quit. Results for NRT on prescription varied by age, with older (45+), but not younger smokers more likely to have stopped smoking using it. Stop smoking websites increased the odds of quitting for smokers from lower but not higher social grades. These results tend to support those from randomised controlled trials of both varenicline and e-cigarettes, providing recent 'real world' evidence that they are effective cessation aids. The findings for websites are particularly interesting but again align with other emerging evidence that suggests digital interventions may reduce barriers to support to stop smoking for less affluent groups.

Our second paper this month draws on the PATH study (which has also been covered in this bulletin in the past) a longitudinal study of youth and adults in the USA. In the current study, the focus was on young people and the researchers were interested in examining the association between mental health problems and e-cigarette use. They included just under 8,000 12-17 year olds who had not used tobacco or e-cigarettes at baseline who were followed up one year later. Mental health measures focused on 'internalising' and 'externalising' problems. Internalising symptoms include anxiety and/or depression, for example, and externalising impulsive and/or disruptive conduct and substance use problems. Past studies have suggested that internalising problems are associated with starting smoking and externalising problems with smoking at a younger age and lower odds of stopping smoking.

At one year follow up, the young people assessed as having high externalising problems were more likely to report that they had tried e-cigarettes, tobacco cigarettes or both. Young people with high internalising problems were more likely to have tried vaping but not smoking. The authors concluded that, as with smoking, young people at risk of mental health problems may be more likely to try vaping. This is consistent with other research suggesting that there may be a common liability among youth in terms of using nicotine products and indeed alcohol and/or drugs, although the latter was not the focus of the current paper. Given age of sale laws and policy measures to protect non-smoking youth from e-cigarette initiation in the USA, the UK and elsewhere, the paper

emphasises the importance of assessing mental health when considering risk factors and appropriate interventions for young people.

The third paper this month is more unusual in that it focuses on an under-researched topic to date – the relationship between the price of vaping products and cigarettes. The authors were interested in testing a new approach to assessing the impact of cigarette and e-cigarette prices on vaping and smoking in young adults in the USA. Data were drawn from a nationally-representative longitudinal cohort study of 15-21 year olds in the USA. Baseline data were collected in 2014 and there were then a further five waves of data collected every 6 months up to the autumn of 2016. Participants who had completed the survey over at least two waves (n=11,578) were included in the sample. Price data were drawn from Neilsen data of sales prices and volumes in retail outlets from 2014 to 2016. Price data was linked with past 30-day vaping and smoking and statistical modelling conducted to examine any associations.

There was some indication that when cigarette prices went up so did recent vaping, which would be in line with previous research that suggests tobacco taxes may encourage people to switch partially or completely to alternative nicotine products. However, the researchers couldn't find any clear relationship between e-cigarette prices and vaping or e-cigarette prices and recent smoking (i.e. that price rises on vaping products might increase smoking). The authors acknowledge, however, that the data had significant limitations – not least that young people who are able to buy vaping products (despite age of sale laws) are more likely to do so from vape shops in the USA than other retail outlets, and vape shop prices and volumes were not available from Neilsen data. That said, the study provides some proof of concept and would merit replication in other countries using alternative and potentially more comprehensive data sources.

Our final paper aimed to look at changes in patterns of e-cigarette use in young people over time. The authors drew on a small convenience sample of 173 participants aged 13-18, all recruited from San Francisco in the USA. To be eligible to participate, the young people needed to have vaped at least once in the past month and have used e-cigarettes on at least 10 occasions in their lifetime. Smoking was not excluded, so the sample included a mix of non-smokers and smokers, with one in four being dual users at recruitment. Data were collected at baseline, 6 months and 12 months and consisted of survey questions and collection of a saliva sample for cotinine testing.

The researchers were particularly interested in duration and frequency of vaping, the relationship with smoking, and also product preferences. Given the small sample and some loss to follow-up between baseline and follow up points, their results are unlikely to be generalizable beyond this study nevertheless interesting patterns emerged. Most participants continued vaping during the study with 80% still reporting use one year later. There was also movement between products, as has been found in longitudinal studies with adults in the USA. 28% of those who were only vaping at baseline reported some cigarette use by 12 months. Among those who were dual users at baseline, 31% had switched to only e-cigarettes by 12 months. Frequency of vaping also increased, with daily use rising from 14% to 30% at final follow up. In terms of products, pod (i.e Juul) and mod devices became more popular at each follow up point but flavour preferences were stable with fruit flavours being most popular.

CRUK Funding Committee Call Dates

Population Research Committee

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 feasibility study with embedded pilot randomised controlled trial and process evaluation of electronic cigarettes for smoking cessation in patients with periodontitis.

Electronic cigarette use during a randomized trial of interventions for smoking cessation among Medicaid beneficiaries with mental illness.

Moderators of real-world effectiveness of smoking cessation aids: a population study.

Patterns of use

Bi-Directional Associations Between Young Adults' Reported Exposure to E-Cigarette Marketing and E-Cigarette Use.

Impact of e-cigarette and cigarette prices on youth and young adult e-cigarette and cigarette behaviour: evidence from a national longitudinal cohort.

Influence of Electronic Cigarette Characteristics on Susceptibility, Perceptions, and Abuse Liability Indices among Combustible Tobacco Cigarette Smokers and Non-Smokers.

The impact of e-cigarette price changes on vaping and smoking behaviors.

Electronic cigarette use among adults with asthma: 2014-2017 National Health Interview Survey.

Genetic Vulnerability for Smoking and Cannabis Use: Associations With E-Cigarette and Water Pipe Use.

Perceptions

E-Cigarette Outcome Expectancies among Nationally Representative Samples of Adolescents and Young Adults.

Youth use

US young adults' perceived effectiveness of draft pictorial e-cigarette warning labels.

Mental Health Problems and Initiation of E-cigarette and Combustible Cigarette Use.

Characteristics of Daily E-Cigarette Use and Acquisition Means Among a National Sample of Adolescents.

Adolescents' E-Cigarette Use: Increases in Frequency, Dependence, and Nicotine Exposure Over 12 Months.

College students' reasons for using different e-cigarette products: A mixed methods analysis.

Adolescents' first tobacco products: Associations with current multiple tobacco product use.

Associations between public e-cigarette use and tobacco-related social norms among youth.

Widespread use of flavored e-cigarettes and hookah tobacco in the United States.

Effects of E-Cigarette Health Warnings and Modified Risk Ad Claims on Adolescent E-Cigarette Craving and Susceptibility.

Harms and harm reduction

Prevalence and correlates of secondhand smoke exposure in the home and in a vehicle among youth in the United States.

Chronic Intermittent Electronic Cigarette Exposure Induces Cardiac Dysfunction and Atherosclerosis in Apolipoprotein E (ApoE) Knockout Mice.

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

Electronic Cigarette Use and Myocardial Infarction Among Adults in the US Population Assessment of Tobacco and Health.

Genotoxicity evaluation of tobacco and nicotine delivery products: Part Two. In vitro micronucleus assay.

Electronic Cigarettes Enhance Replication of *Mycobacterium abscessus* in Airway Epithelial Cells.

E-cigarettes and head and neck cancers: A systematic review of the current literature.

Modeling Cardiovascular Risks of E-Cigarettes With Human-Induced Pluripotent Stem Cell-Derived Endothelial Cells.

Effect of nicotine on human gingival, periodontal ligament and oral epithelial cells. A systematic review of the literature.

Common E-Cigarette Flavoring Chemicals Impair Neutrophil Phagocytosis and Oxidative Burst.

Sucralose-Enhanced Degradation of Electronic Cigarette Liquids during Vaping.

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 Helen Callard 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.