THE UK ELECTRONIC CIGARETTE RESEARCH FORUM

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Electronic Cigarette Research Briefing – April 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.

Thank you

A huge thank you to all those that responded to the survey in February, it was great to see that the vast majority of you rate the briefing highly and find it useful. We've taken on your feedback and suggestions for improvement, such as categorising the papers of interest by theme and aiming to be even more succinct and clear in our analysis. If you would like further information on results from the survey, please get in touch.

1. Have e-cigarettes re-normalised or displaced youth smoking? Results of a segmented regression analysis of repeated cross sectional survey data in England, Scotland and Wales.

- **Study aims**

  This British study aimed to assess whether the emergence of e-cigarettes in 2010 re-normalised cigarette smoking among 13 and 15-year olds (n=248 324) in Great Britain during

a period of limited regulation until 2015. The researchers used data from three national surveys to model changes in trends in smoking rates, acceptability of smoking and prevalence of alcohol and cannabis use between 1998-2015, adjusting for gender and school year.

- **Key findings**

  Between 1998 and 2015 the prevalence rates of ever and regular smoking declined among children aged 13 and 15 years by 41% and 14%, respectively. The acceptability of trying smoking and weekly smoking declined 43% and 22% respectively over the study period.

  There was no significant change in rate of decline after the 2010 intervention point (the emergence of e-cigarettes) for ever smoking (OR =1.01 95%CI 0.99-1.03).

  There was a 4% borderline significant slowing per year in the rate of decline of regular smoking after 2010 (OR=1.04 95%CI 1.00-1.08). Greater reductions in the rates of decline were seen in alcohol use (OR=1.17 95%CI 1.14-1.19) and cannabis use (OR=1.21 95%CI 1.18-1.25).

  There was a 12% and 18% acceleration per year in the rate of decline after 2010 for participants reporting that trying smoking is OK (OR=0.88 95%CI 0.86-0.90) and smoking weekly is OK (OR=0.82 95%CI 0.75-0.89), respectively.

- **Limitations**

  The surveys used in this paper differed in both methods used and interval time between surveys, thus results may not have been pooled appropriately.

  This study only considered population level trends. As it was not possible to examine other events and factors that may have contributed to smoking trends the causality between e-cigarette emergence and effect on smoking trends cannot be determined.

  This study relied on self-reported data which may be subject to bias.

  There were several non-prespecified analyses carried out which influenced the investigation of trends.

Hallingberg B, Maynard OM, Bauld L, Brown R, Gray L, Lowthian E, MacKintosh AM, Moore L, Munafo MR, Moore G. (2019) Have e-cigarettes renormalised or displaced youth smoking? Results of a segmented regression analysis of repeated cross sectional survey data in England, Scotland and Wales. Tob Control; doi: 10.1136/tobaccocontrol-2018-054584

2. Association of electronic cigarette vaping and subsequent smoking relapse among former smokers.

- **Study aims**

  This US study used data from the Population Assessment of Tobacco and Health (PATH) surveys to examine the association between e-cigarette use and subsequent smoking relapse. Data from 4,094 participants on e-cigarette use, time since smoking cessation and relapse outcomes after 1 year were analysed, adjusting for sociodemographic factors and patterns of tobacco product use. Baseline long term quitters (those who reported having stopped smoking for longer than 12 months, n=3,210) and recent quitters (reported quitting within the last 12 months, n=884) were considered separately.

- **Key findings**

  Most long-term quitters (91%) had no prior e-cigarette use at baseline. Over half (57.3%) of recent quitters had ever used or were using e-cigarettes in some capacity.

  Among recent quitters there was no significant association between relapse at one year follow up and any form of baseline e-cigarette use.

  Among long term quitters, those who were prior e-cigarette users and current regular users were more likely to have relapsed at 1-year follow-up compared to never users (OR=2.00 95%CI 1.25-3.20 and OR=3.77 95%CI 1.48-9.65 respectively). There was no significant association with current occasional e-cigarette use.

  Among all those who had relapsed by 1-year follow up (n=492), smoking frequency and intensity did not significantly differ according to e-cigarette use.

- **Limitations**

  This study did not examine how e-cigarette use varied among those who did not relapse, nor did it examine different trajectories of e-cigarette use and smoking. Thus, a causal relationship between e-cigarette use and relapse cannot be determined.

  There were small sample sizes for many of the patterns of e-cigarette use groups, which increases the uncertainty of effect estimates. Individuals who had only tried an e-cigarette once or twice were pooled with prior regular users for the prior use group which may not be appropriate for examining relapse.

  Data on confounders such as tobacco dependence were not available for the analysis of long-term quitters and other confounders, such as whether the participant used their e-cigarette to quit, or e-liquid nicotine strength were not included. This could have affected results.

  The dropout rate at 1-year follow-up was 16.9%. Therefore, the participants and results may not be generalisable to the wider vaping population.

  This study relied on self-reported data which may be subject to bias. Neither relapse or continued abstinence were biochemically verified.

Dai H, Leventhal AM. (2019). Association of electronic cigarette vaping and subsequent smoking relapse among former smokers. Drug Alcohol Depend; doi: 10.1016/j.drugalcdep.2019.01.043.

3. How Does Smoking and Nicotine Dependence Change after Onset of Vaping? A Retrospective Analysis of Dual Users.

- **Study aims**

  This US study used baseline data from a smoking cessation trial of 2,896 dual users of cigarettes and e-cigarettes to examine the effects of vaping on the use of and dependence on cigarettes and nicotine. They also examined predictors of cigarette and nicotine dependency, modelling demographic factors, smoking history and current smoking and nicotine use.

- **Key findings**

  After the onset of vaping the mean number of cigarettes smoked per day reduced from 19 to 11 ($p<0.0001$), but the mean number of nicotine sessions per day increased from 19 to 29 ($p<0.0001$). Overall cigarette dependency decreased by 41% post vaping initiation, but total nicotine dependency increased by 33%.

  Current vaping frequency was the strongest predictor of cigarette dependency, with increased frequency associated with decreased dependency. In contrast, number of years smoking, cigarette dependency pre-vaping and nicotine concentration used were positively associated with cigarette dependence ($p<0.008$ for all associations).

  Current vaping frequency was the strongest predictor of nicotine dependency, showing a positive association. Cigarette dependency pre-vaping, number of puffs per e-cigarette session, nicotine concentration used, and time spent using e-cigarettes also all had a significant positive association with nicotine dependence ($p<0.008$ for all associations).

  The final model including demographic factors, smoking history and current smoking and nicotine use explained 27.9% of the variation in cigarette dependence and 23.3% of the variation in nicotine dependence.

- **Limitations**

  The nicotine dependence score for smoking and e-cigarette use was adapted from accepted cigarette dependency scores but was not a validated measure of nicotine dependency and its reliability is unknown.

  This study only considered dual users, which may exclude any e-cigarette users who had already successfully quit smoking. Therefore, the study may not provide a clear picture of the association between e-cigarette use and nicotine dependency.

  This study was cross-sectional so cannot tell us how patterns of vaping over time influenced nicotine and cigarette dependency.

The researchers did not consider all confounders, such as the use of other tobacco products. All data were self-reported, including recalling smoking habits over 24 months previously for some participants, thus the results may be subject to bias.

Martínez Ú, Martínez-Loredo V, Simmons VN, Meltzer LR, Drobes DJ, Brandon KO, Palmer AM, Eissenberg T, Bullen CR, Harrell PT, Brandon TH, (2019) How Does Smoking and Nicotine Dependence Change after Onset of Vaping? A Retrospective Analysis of Dual Users. Nicotine Tob Res; doi: 10.1093/ntr/ntz043.

Overview

This month we have three papers, two from the USA and one from the UK.

The first paper reports results from an ongoing NIHR funded study in the UK of smoking and vaping in young people. In this analysis, the researchers were interested in finding out whether smoking had been renormalised among young people during the period when e-cigarettes became available in the UK market and were relatively unregulated. That period was defined as 2010 to 2015, prior to the implementation of the measures in the EU Tobacco Products Directive and introduction of age of sale laws. The researchers pooled data from national surveys conducted in England, Scotland and Wales. The period covered as 1998-2015 to allow analysis of trends over a longer time. The final sample included just under 250,000 young people aged 13 and 15. These two age groups were chosen because the national youth survey in Scotland only includes pupils in their second and fourth year of secondary school (aged approximately 13 and 15) so data for comparable ages in the English and Welsh surveys was used. The researchers conducted interrupted time series analysis to see whether trends from 2010-2015 were different from the period before e-cigarettes.

Two types of outcomes were examined: smoking (both ever and regular) and attitudes to smoking. Attitudes were assessed using a survey question that assessed the extent to which pupils thought it was OK to try smoking. For smoking prevalence, data were available for all three UK nations, but for attitudes England and Scotland only. Overall the researchers reported that they found little evidence that there was any change in the continued downward trend in smoking prevalence during the period when e-cigarettes became available and were largely unregulated, compared with trends prior to 2010. There was no change in the rate of decline for ever-smoking, and a small borderline significant slowing in the rate of decline for regular smoking. For attitudes, there was an increased rate of decline in the extent to which young people thought trying smoking was acceptable. Overall these results suggest that concerns that the availability of e-cigarettes might renormalise smoking among young people in the UK don't seem to have been realised. However, the study could not examine the relationship between vaping and smoking for individual young people. Other studies in the UK have suggested that the two may be linked, with youth who try vaping being subsequently more likely to try smoking. The fact that the current paper only covered the period up to 2015 is also an important limitation, but the researchers are continuing with their study and future papers should provide more recent data.

Our second paper is another output from the highly productive PATH survey in the USA. The researchers aimed to examine the relationship between vaping and relapse to smoking, as there is a lot of interest in the issue of whether vaping post cessation might be protective against going back to smoking or make relapse more likely. Data were drawn from the first two waves of PATH, conducted in September 2013-December 2014 (baseline) and October 2014-October 2015 (follow

up). For this analysis the researchers used data from PATH participants who reported being former smokers at baseline and divided them into two groups - those that had quit more than a year before the survey (long term quitters) or more recently (recent quitters). Data on e-cigarette use at baseline (in several categories from never to current regular use) was also available. One year later the former smokers were asked again about their smoking status. Those that reported they now smoked on some days of the week or every day were classified as having relapsed to smoking. The researchers then conducted logistic regression analysis to model the association between baseline e-cigarette use and smoking relapse at follow up.

The study didn't find any relationship between e-cigarette use at baseline and relapse to smoking among recent quitters. However among long term quitters, although vaping was rare (91% had not used e-cigarettes at baseline) relapse was associated with prior vaping and current regular vaping, but not current occasional vaping. In other words, the researchers found evidence that vaping more than a year after quitting smoking may be linked to increased risk of future relapse to smoking. In their discussion the researchers considered a number of potential reasons for this finding. For example, it is possible that continued use of a nicotine containing product after quitting, or taking up vaping some time after quitting, might make ex-smokers more vulnerable to going back to smoking even after a long period of smoking abstinence. Alternatively other explanations may apply, including that the association was caused by factors not examined in the research. Looking at the relationship between vaping and smoking relapse remains an important area for research and undoubtedly other studies will shed further light on this in the future.

This month's final study is also from the USA and focused on dual users to examine how vaping might influence how much they smoke and use nicotine, and how dependent they are on smoking and nicotine. Data were collected from just under 3,000 dual users who were taking part in randomised controlled trial of a self-help intervention for smoking cessation. For the current analysis, the researchers examined baseline trial data, including demographic information and smoking and vaping characteristics, collected between 2016 and 2017. They conducted statistical modelling to look at the relationship between smoking and vaping use and dependence. Many of the measures used in the study were fairly well established, but the researchers developed a new approach to assess overall nicotine dependency. This was a nicotine dependence score (HIS-nic) that combined time to first cigarette or use of an e-cigarette with number of 'nicotine sessions' per day (cigarettes per day plus vaping sessions per day). This approach would merit validation in other studies.

79% of smokers in the study reported that they smoked less after they started vaping, with the number of cigarettes per day decreasing by 42%. Cigarette dependence also declined with vaping. However total nicotine use increased - i.e. the combination of frequency of smoking or vaping, accounting for number of puffs and nicotine e-liquid content in the case of vaping. Total nicotine dependence as measured by the HSI-nic also increased with dual use. Other research has provided conflicting findings on the extent to which dual use actually results in smoking reduction. This study adds to the existing literature on that topic although the authors do make clear that continued dual use is unlikely to confer any health benefit. Clearly if dual use results in higher nicotine dependence this could make smoking cessation more difficult. However, recent studies, including some we have previously covered in this bulletin, do suggest that some dual users eventually stop smoking. Population surveys in the UK also now show there are more ex-smokers than dual users among vapers, a pattern that has gradually changed over time.

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:

Patterns of use

The Prevalence of E-Cigarette Use Among Adults in Malaysia: Findings From the 2016 National E-Cigarette Survey.

Associations between e-cigarette and combustible cigarette use among U.S. cancer survivors: implications for research and practice.

Youth use

Cigarette and e-cigarette use and social perceptions over the transition to college: The role of ADHD symptoms.

Offers of Cigarettes and E-Cigarettes Among High School Students: A Population Study from California.

Electronic Cigarette Use and Smoking Initiation in Taiwan: Evidence from the First Prospective Study in Asia.

Young adult perceptions of JUUL and other pod electronic cigarette devices in California: a qualitative study.

Harms and harm reduction

The toxic potential of a fourth-generation E-cigarette on human lung cell lines and tissue explants.

Acute Effects of Electronic Cigarette Inhalation on the Vasculature and the Conducting Airways.

E-cigarette nicotine deposition and persistence on glass and cotton surfaces.

Comparison of Free Radical Levels in the Aerosol from Conventional Cigarettes, Electronic Cigarettes, and Heat-Not-Burn Tobacco Products.

High Nicotine Electronic Cigarette Products: Toxicity of JUUL Fluids and Aerosols Correlates Strongly with Nicotine and Some Flavor Chemical Concentrations.

Dermatologic manifestations associated with electronic cigarette use.

Assessing the protective effect of rosiglitazone against electronic cigarette/tobacco smoke-induced blood-brain barrier impairment.

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.