Electronic Cigarette Research Briefing – July 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. **Patterns and predictors of e-cigarette, cigarette and dual use uptake in UK adolescents: Evidence from a 24-month Prospective Study.**

   **Study aims**

   This study examined how demographic and behavioural factors might predict e-cigarette and cigarette use among 13-14 year olds (n=3210) in the UK. Data from a randomised control trial of a school-based smoking initiation intervention were used, looking at young people who had never used e-cigarettes or cigarettes. Product use after 24 months was examined. The model included all study variables and was additionally adjusted for the effects of the trial intervention.

   **Key findings**

   The majority (71.5%) of the participants remained never users at follow up. 13.3% had exclusively used e-cigarettes, 11.9% had used both products and 3.4% had exclusively used cigarettes. Of those who had used both products more participants reported using cigarettes first (n=108) than using e-cigarettes first (n=93), but most couldn’t recall which they’d used first (n=183).
Ever users of both products who reported using cigarettes first had significantly higher rates of regular smoking (at least one cigarette a week) than all other smoking groups (all p values < 0.034). Rates of regular e-cigarette use (using at least once a month) were significantly lower among ever e-cigarette users than those who had used both products (all p values < 0.001).

Males were significantly more likely to have only ever used e-cigarettes at follow-up, whereas females were more likely to have ever used cigarettes or both products.

Those with higher levels of impulsivity at baseline were more likely to have ever used e-cigarettes only at follow-up than be never users of both products (OR=1.26 95%CI 1.18-1.35). Higher levels of impulsivity were also a positive predictor for ever cigarette and ever use of both products.

Participants were more likely to report ever use of e-cigarettes only compared to never product use, if at baseline they had friends who smoked (OR= 1.48 95%CI 1.21-1.82) or family who smoked (OR = 1.17 95%CI 1.07-1.28). Similar trends were seen for ever cigarette use and ever use of both products.

### Limitations

This paper did not adjust for all factors that might influence product uptake, such as perceptions of e-cigarettes and whether family or friends used e-cigarettes. Therefore, a causal relationship cannot be determined.

Although the effect of the intervention was adjusted for there could be residual effects on outcomes of smoking and vaping uptake, which could alter results.

Although data on patterns of e-cigarette and cigarette use were recorded, this paper did not distinguish between factors that predict regular use of each product and those that predict experimentation.

Data were only collected from schools in two English counties and only from 13-14 year olds and sub-group sample sizes were small, therefore findings may not be generalisable to all adolescents.

Data were self-reported which may be subject to bias.


### Study aims
This U.S study aimed to determine how dual users’ perceptions of the harmfulness of e-cigarettes compared with cigarettes might influence patterns of use of both products, one year later. Data on the perceptions and patterns of product use were collected from 2,211 dual users from the PATH study between 2014-2016. Analyses were adjusted for demographic factors. 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

59.4% of participants perceived e-cigarettes as less harmful than smoking at baseline compared to 41.9% at follow-up.

Compared to all other participants, those that perceived e-cigarettes as less harmful than smoking at baseline were more likely to switch to exclusive e-cigarette use (OR=2.9 95%CI 1.7-4.8) and less likely to be exclusive cigarette users (OR=0.6 95%CI 0.5-0.7) at 12-month follow-up.

Those who perceived e-cigarettes as less harmful than smoking at baseline and reported continued smoking at follow up, were more likely to increase the number of days smoked in the last month (difference between baseline and follow-up +1.1 days 95%CI 0.2-1.9).

Those who perceived e-cigarettes as less harmful than smoking at baseline and reported vaping at follow up were also more likely to decrease the number of days vaped in the last month (difference between baseline and follow-up -2.8 days 95%CI -5.2--0.3).

Limitations

Those that did not perceive e-cigarettes as less harmful than smoking were grouped together. No distinction was made between those that thought e-cigarettes were somewhat less harmful and those that thought they were substantially less harmful. Separate analyses on these groups may show different associations.

This paper only examined how harm perceptions affected patterns of use among dual users. Therefore, this paper does not give the full picture of how perceptions might affect uptake and cessation among non-users or exclusive smokers.

Results were not adjusted for all confounders that might affect changes in patterns of e-cigarette and cigarette use, such as nicotine addiction, reasons for use and the external policy environment. Therefore, a causal relationship cannot be determined.

Data were self-reported so may be subject to bias.

3. **E-Cigarettes are More Addictive than Traditional Cigarettes-A Study in Highly Educated Young People.**

- **Study aims**

  This cross-sectional Polish study collected data via in person questionnaires on cigarette and e-cigarette use from university students (mean age=22.4 years old) that were exclusive cigarette users (n=30), exclusive e-cigarette users (n=30) or dual users (n=30). It aimed to compare patterns of product use and nicotine dependency between these three groups. Dependency was calculated using the Fagerström test for nicotine dependency (FTND) and an adapted version for e-cigarettes.

- **Key findings**

  Dual users had used cigarettes significantly longer than exclusive smokers (M= 67.3 months vs M=50.0 months, p=0.03). 18.5% of the 60 e-cigarette users initiated nicotine use through e-cigarettes.

  There was no significant difference for average duration of e-cigarette use between exclusive e-cigarette users and dual users (M=29.0 months and M=27.7 months, respectively). The average nicotine concentration, amount of e-liquid, type of e-liquid and number of e-cigarette devices used by exclusive e-cigarette users and dual users did not differ significantly

  On average, dual users scored significantly higher on the e-cigarette FTND than the cigarette FTND (M=4.7 vs M=3.2, p=0.03). The mean FTND score was significantly higher for exclusive e-cigarette users than exclusive cigarette users (M=3.5 vs M=1.6, p=0.002).

  46.2% of dual users reported that smoking was more satisfying than vaping vs 23% who found vaping more satisfying. Smell and taste were reported as the primary advantages of e-cigarettes by 92.9% and 82.1% of dual users, respectively.

- **Limitations**

  Results were not adjusted for confounders that might affect nicotine dependency or patterns of product use. Therefore, differences in scores might be caused by other factors.

  It is not clear whether differences in satisfaction between cigarettes and e-cigarettes were significant.

  Sample sizes were small. Data were only collected from one region in Poland and participants were all university educated young adults. Therefore, results may not be generalisable to all e-cigarette users.

  This paper compared e-cigarette and cigarette FTND scores, which may not be appropriate.

  No definition of product use was given. Regularity of use may differ substantially between participants, which would affect results.
The study survey referred to ‘e-smoking’ habits and asked about ‘smoking satisfaction’ for e-cigarettes. This misrepresents the characteristic of e-cigarettes and may have biased results to questions.

This study is cross-sectional so cannot tell us how dependency on either product varies with time. All data were self-reported, which may be subject to bias. Exposure to nicotine was not biochemically verified, therefore results may not be accurate.


- **Study aims**

  This U.S study examined how urine and blood biomarker levels changed with number of cigarettes smoked per day (CPD) among different groups of daily cigarette users from the PATH study in 2013-2014. Participants were either exclusive cigarette smokers (n=1951), cigarette and e-cigarette users (e-cigarette dual users, n=648) or cigarette and smokeless tobacco users (smokeless tobacco dual users, n=110). Biomarkers analysed included total nicotine equivalents (TNE) – 2, tobacco specific nitrosamines (NNAL, NNN), polyaromatic hydrocarbons (1-HOP, 2-hydroxyflurone), volatile organic compounds (CYMA, HPMA, MHB3) and metals.

- **Key findings**

  Compared to exclusive cigarette smokers, e-cigarette dual users had higher levels of TNE-2, NNAL, 1-HOP, HPMA and lower levels of NNN (all p-values < 0.05).

  Compared to exclusive smokers, e-cigarette dual users were more likely to be female (p=0.01). Among e-cigarette dual users there were significant differences between males and females in levels of biomarkers, including TNE-2, NNAL and 1-HOP but not NNN. Similar patterns were seen among exclusive cigarette users.

  Smokeless tobacco dual users had higher levels of NNAL and NNN and lower levels of 2-hydroxyfluorene, CYMA, MHB3 and cadmium than exclusive smokers (all p-values < 0.05).

  The median CPD was 14.5 for exclusive smokers, 14.7 for e-cigarette dual users and 18.1 for smokeless tobacco dual users.

- **Limitations**
Biomarker levels of e-cigarette users were not analysed so no comparison could be made between smokers, dual users and exclusive e-cigarette users. Therefore, this paper does not give the whole picture of how biomarker levels might be affected by vaping.

This paper did not analyse differences in the levels for all biomarkers that were measured as part of this study. It’s not clear whether the choice in biomarkers reported was systematic.

Differences between groups for all biomarkers were only adjusted for CPD. Therefore, differences in scores might be caused by other factors, such as demographic differences.

Some sub-group sample sizes were small which may reduce certainty of estimates.

Patterns of use of e-cigarettes and smokeless tobacco were not clearly reported and may vary considerably between participants, which might skew results.

This study was cross-sectional so cannot tell us how biomarker levels vary with time.

Cigarettes per day were self-reported which may be subject to bias.


Overview

The four articles included in this month’s bulletin were authored by research teams from England, the USA and Poland.

The first study aimed to assess prevalence and predictors of e-cigarette and cigarette patterns of use in young people in two English counties. This research follows a 2017 paper from the same team that we’ve reviewed in a previous bulletin. The researchers added questions on e-cigarettes to surveys being conducted as part of a randomised controlled trial of a school-based smoking prevention intervention. In the current paper they examined differences between baseline (late 2014, when the participants were aged 13-14) and follow up at 24 months (late 2016 to early 2017, 15-16 year olds). None of the participants were vaping or smoking at baseline.

At two year follow up, the vast majority had still not tried vaping or smoking. After never users, the most common category of use was those who had tried vaping (13%) followed by those who had tried both products (12%) and then those who had tried cigarettes only (3.3%). Of those who had tried both products, the researchers asked which came first, trying smoking or trying vaping and it was slightly more common to try smoking than vaping first, although for many in this group it wasn’t clear which came first. They also examined potential predictors of use and found that having family and friends who smoked, plus measures of impulsivity were associated with both smoking and vaping. Exclusive vaping was more common in boys and smoking and dual use among girls. Regular smoking was higher in dual users than exclusive smokers suggesting that vaping didn’t decrease smoking in this group. However, using e-cigarettes first was associated with lower rates of progression to regular smoking. In addition, a higher proportion of young people who tried
cigarettes became regular smokers by follow up, compared to the transition from ever trying e-cigarettes to regular vaping.

Our second study analyses data from waves two (2014-15) and three (2015-16) of the PATH survey in the USA. In this paper the researchers were interested in determining whether harm perceptions comparing e-cigarettes and cigarettes affected product use, in particular any evidence of switching products from baseline to follow up. They focused their analysis on people who were dual users at baseline. The harm perceptions question asked whether e-cigarettes were less harmful, about the same, more harmful or don’t know.

In terms of harm perceptions, just under 6 in 10 (59.4%) of participants thought vaping was less harmful than smoking at baseline. This had changed by follow up one year later, when only four in ten (42%) thought vaping was less harmful. This is similar to other surveys in the USA that have found more adults believe e-cigarettes to be just as or more harmful than smoking in recent years. These harm perceptions may affect whether people stop smoking and switch to vaping, as this study found that dual users who perceived e-cigarettes as less harmful than cigarettes were more likely to become exclusive e-cigarette users one year later and less likely to become exclusive smokers. Harm perceptions didn’t seem to affect the odds of whether someone completely stopped using either product. The authors estimated that approximately 205,000 more dual users could have become exclusive vapers by 2015-16 in the USA if they had accurate perceptions of the relative harms of e-cigarettes compared to cigarettes.

The third article in this month’s bulletin aimed to assess patterns of e-cigarette use and compare nicotine dependence between smokers and vapers in a sample of young adults in Poland. Participants were recruited from a larger ongoing study and were all students at one University. The larger study had just over 3,000 participants and a small subgroup took part in the current study with 30 being exclusive e-cigarette users, 30 smokers and 30 dual users. As well as asking about smoking and vaping behaviour the researchers also aimed to assess nicotine dependence using the Fagerström test (FTND) and an adaptation that has tried to modify it to assess dependence in vapers.

There were some differences in patterns of use between the three groups in the study. Although both dual users and exclusive vapers had been using e-cigarettes for a similar length of time on average, the dual users had been smoking for significantly longer than the exclusive smokers, suggesting cigarette use was more established in this group. Dual users preferred smoking to vaping in terms of satisfaction, but acknowledged advantages to vaping including smell and taste. In terms of nicotine dependence, the researchers found that Fagerström scores were higher in exclusive vapers than smokers, and vapers were more likely to use the product within the first 30 minutes of waking. These findings should be treated with caution as the FTND was not designed to be used with vapers and there may be other reasons (i.e. ability to use indoors) that explain a shorter time to first use of an e-cigarette during the day. The researchers also found that nicotine dependence levels were higher among dual users when vaping rather than smoking and that dual users used more e-liquid at a higher nicotine concentration than exclusive vapers. However, the average nicotine strength used in the study was still low (6mg/ml) and dual users may need to vape more frequently to address cravings and withdrawal symptoms when they can’t smoke. Attempts to directly compare both behaviour and dependence between smokers and vapers are still at an early stage and further research is required, including with larger samples, to develop better measures to assess these issues.

Our final article this month is primarily about smoking, but included dual users as one group in the study. The authors were interested in finding out more about the relationship between the number
of cigarettes smoked per day and biomarkers of exposure to tobacco toxicants. A lot is already known about how the amount people smoke is related to health outcomes (such as lung cancer, heart disease and stroke) but less about how biomarkers reflect cigarettes per day. As with the second study above, this research drew on the PATH study in the USA, in this case involving 2,700 daily cigarette smokers enrolled in the first wave of the survey and who provided blood and saliva samples. These samples were tested for a very large number of biomarkers of nicotine, toxicants and carcinogens. The individuals in the study were grouped into three tobacco use categories: smokers, dual users of e-cigarettes and cigarettes, and dual users of smokeless tobacco and cigarettes. Detailed information was available on cigarettes per day but the extent of vaping or smokeless tobacco use wasn’t quantified in the analysis.

The main finding of the study was that biomarker concentrations increased with the number of cigarettes smoked per day. The dose-response relationship did vary by biomarker and variations were more difficult to detect for very heavy smokers. However, even those participants smoking just a few cigarettes per day had exposures at harmful levels, supporting previous research that even low levels of smoking can result in health effects. The authors found some evidence that dual users of e-cigarettes and cigarettes had higher levels of exposure to nicotine and some toxicants including NNAL, 1-HOP, HPMA (a metabolite of acrolein, linked to respiratory disease in particular) and MHB3 (a metabolite of 1,3-Butadiene, a carcinogen) than exclusive cigarette smokers. The authors pointed out that it wasn’t clear if this was due to exposures not captured by the analysis (perhaps compensatory smoking not reflected in the self-reported cigarettes per day) and a sensitivity analysis conducted between daily and non-daily vapers in the group wasn’t conclusive. That said, the extensive range of biomarkers tested for in the research, and the levels identified, could inform future studies that aim to compare toxicant exposure between smoking, vaping and the use of other nicotine-containing products.

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 04/08/2019 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

Current smoking habits in British IBD patients in the age of e-cigarettes.

Effects of E-cigarette Advertising Message Form and Cues on Cessation Intention: An Exploratory Study.

An Examination of Device Types and Features Used by Adult Electronic Nicotine Delivery System (ENDS) Users in the PATH Study, 2015-2016.

Perceived Relative Harm of Using E-Cigarettes Predicts Future Product Switching among U.S. Adult Cigarette and E-Cigarette Dual Users.
E-Cigarettes are More Addictive than Traditional Cigarettes: A Study in Highly Educated Young People.

Adverse childhood experiences and electronic cigarette use among young Australian women.

Patterns and Frequency of Current e-Cigarette Use in United States Adults.

Cessation

Effect of Electronic Cigarettes on Smoking Reduction and Cessation in Korean Male Smokers: A Randomized Controlled Study.

Electronic Cigarette Use and Cigarette Abstinence Over Two Years among U.S. Smokers in the Population Assessment of Tobacco and Health Study.

Perceptions

Impact of e-cigarette health warnings on motivation to vape and smoke.

Perceptions of Smoking and Vaping on Weight Control Among Adult American Indians Who Smoke.

'I Felt Welcomed in Like They're a Little Family in There, I Felt Like I Was Joining a Team or Something': Vape Shop Customers’ Experiences of E-Cigarette Use, Vape Shops and the Vaping Community.

The medium is not the message: A content analysis of public information about vaping product regulations in Australia.

Views of prison staff in Scotland on the potential benefits and risks of e-cigarettes in smoke-free prisons: a qualitative focus group study.

Survey of the effect of viewing an online e-cigarette advertisement on attitudes towards cigarette and e-cigarette use in adults located in the UK and USA: a cross-sectional study.

Promotion of Vape Tricks on YouTube: Content Analysis.

Reduced-Risk Warnings Versus the US FDA-Mandated Addiction Warning: The Effects of E-Cigarette Warning Variations on Health Risk Perceptions.

Youth use

Cigarette smoking, e-cigarette use, and sexual identity among high school students in the USA.

The Prevalence of Cigarette and E-cigarette Smoking Among Students in Central and Eastern Europe-Results of the YUPESS Study.

Patterns and predictors of e-cigarette, cigarette and dual use uptake in UK adolescents: Evidence from a 24-month Prospective Study.

Evidence that an intervention weakens the relationship between adolescent electronic cigarette use and tobacco smoking: a 24-month prospective study.

Substance Use Patterns Among Adolescents: A Latent Class Analysis.

Mechanisms of Social Media Effects on Attitudes Toward E-Cigarette Use: Motivations, Mediators, and Moderators in a National Survey of Adolescents.

Ethnic Differences in Patterns of Cigarette and E-Cigarette Use Over Time Among Adolescents.

Nicotine matters in predicting subsequent smoking after e-cigarette experimentation: A longitudinal study among Finnish adolescents.

Evidence of Nicotine Dependence in Adolescents Who Use Juul and Similar Pod Devices.

Adolescent Dual Use Classification and Its Association With Nicotine Dependence and Quit Intentions.

Exposure to multi-media tobacco marketing and product use among youth: A longitudinal analysis.

Tobacco Marketing and Subsequent Use of Cigarettes, E-Cigarettes, and Hookah in Adolescents.

Harms and harm reduction

[Exposure of vapers to formaldehyde and acrolein: A systematic review].

Comparison of cotinine levels in the peri-implant sulcular fluid among cigarette and waterpipe smokers, electronic-cigarette users, and nonsmokers.

Abuse liability of electronic cigarettes in men who are experienced electronic cigarette users.

E-cigarette use is associated with susceptibility to tobacco use among Australian young adults.

Comparison of cigarette, little cigar, and waterpipe tobacco smoke condensate and e-cigarette aerosol condensate in a self-administration model.


Gene Expression Alterations in the Bronchial Epithelium of Electronic Cigarette Users.

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.