Electronic Cigarette Research Briefing – November 2017

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.

Past research briefings can be found at www.cruk.org/UKECRF. If you would prefer not to receive this briefing in future, just let us know.

1. "They're thinking, well it's not as bad, I probably won't get addicted to that. But it's still got the nicotine in it, so...": Maturity, control and socialising: Negotiating identities in relation to smoking and vaping. A qualitative study of young adults in Scotland.

- **Study aims**
  This qualitative study from Scotland conducted interviews with 72 young adults aged 16-24 year olds to explore their understandings of and engagement with e-cigarettes. Interviews were split into 22 small friendship groups and 11 individual interviews. Participants were mostly smokers and ex-smokers from socio-economically disadvantaged backgrounds.

- **Key findings**
  Smoking was an almost ubiquitous behaviour in the lives of all participants, with 92% having ever-smoked and 61% being current smokers. Some noted starting smoking as young as 8 or 9 years old, and others said they were introduced to smoking by family members. 83% of participants had ever used an e-cigarette, but only 19% were current users.

  Smokers often rationalised their smoking as something they had control over, being able to stick to a number of cigarettes per day. This made it seem more acceptable to some compared to vaping, which was seen as less controllable as people can take puffs

continually. Similarly, some participants expressed their opinion that vaping could be initiating a new addiction.

Many described the use of cigarettes for relief in their stressful lives, with e-cigarettes often not being seen as a suitable replacement. Neither did many feel that they would be likely to use an e-cigarette to help them stop smoking at this point in their lives.

Four participants reported having quit smoking using an e-cigarette. Three of these four had used third-generation "box mod" e-cigarettes, but few others had used these devices. Those that had, believed them to be the most effective for smoking cessation.

For many, smoking while drinking alcohol or on a night out, was a key social activity. Vaping wasn't seen as an effective alternative by many in this situation, sometimes leading to a breakdown in smoking quit attempts. Although some noted positive aspects of using e-cigarettes, such as individuality of devices, and meeting others with an enthusiasm for vaping.

- **Limitations**
  The study sample was not selected to be representative of any wider populations, and is purely a representation of attitudes and opinions in disadvantaged areas of Central Scotland.

  The study looked to recruit people from disadvantaged backgrounds, but wasn't able to use a verified measure of socioeconomic status.

  Interviews were carried out at one time-point and cannot represent evolving or changing e-cigarette perceptions, use behaviours or smoking cessation attempts.

  This study was unable to make clear conclusions about experiences with different types of e-cigarettes and whether some models would be perceived or used differently.

M Lucherini, C Rooke, A Amos; "They're thinking, well it's not as bad, I probably won't get addicted to that. But it's still got the nicotine in it, so…": Maturity, control and socialising: Negotiating identities in relation to smoking and vaping. A qualitative study of young adults in Scotland., *Nicotine & Tobacco Research*, , ntx245, https://doi.org/10.1093/ntr/ntx245

2. Health impact of E-cigarettes: a prospective 3.5-year study of regular daily users who have never smoked

- **Study aims**
  This study from Italy explored the health impacts of regular daily e-cigarette use in never smokers. The participants were nine daily e-cigarette users, who had been using their product for at least 3 months, and then followed up for 3.5 years. The reference group was twelve never smokers. The key outcomes measured were: heart rate, body weight, lung function, respiratory symptoms, exhaled breath nitric oxide (eNO), exhaled carbon monoxide (eCO), and high-resolution computed tomography (HRCT) of the lungs. Measurements were taken at baseline, 12 months, 24 months and 42 months.

- **Key findings**
  There were no significant changes from baseline among the e-cigarette users, and no significant differences between the e-cigarette users and control group in terms of blood

pressure, heart rate and body weight. Similarly, there were no significant changes or differences between groups for measures of lung function, eNO and eCO.

No severe adverse reactions were reported in the e-cigarette user group. Two users reported having a cough, one at baseline and the other at the second follow-up. Though in the control group, three participants reported having a cough on three separate occasions.

The HRCT scans of all eight participants that took part showed no pathological findings. This included no early signs of COPD, lipoid pneumonia or popcorn lung disease.

Six of the nine e-cigarette users in the study were using nicotine-containing e-liquids at baseline as well as by the end of the study, although strengths used changed over this time. Three users used zero-nicotine e-liquid. Preferred flavours were consistent over the time-period, but some users switched to more advanced devices.

- **Limitations**
  The study had small numbers, and low power to detect significant changes.

  There was no smoking control arm, so the study can't conclude how different these results might be compared to findings in smokers.

  The heaviest e-cigarette users were using 5ml/day of e-liquid. This is not representative of the heaviest levels of e-cigarette use in the wider population. While there was no analysis of how heavier use, or different liquids or flavours may have affected results.

  The study didn't use an exhaustive list of current health tests. Similarly, the study didn't look at some potential biomarkers of future harm e.g. the presence of carcinogens. Therefore, the results cannot be used to determine all possible future health risks, such as cancer.

  The participants may have included those who have tried cigarettes, as the eligibility requirement was having smoked less than 100 cigarettes in their lifetime.

Polosa, Riccardo & Cibella, Fabio & Caponnetto, Pasquale & Maglia, Marilena & Prosperini, Umberto & Russo, Cristina & Tashkin, Donald. (2017). Health impact of E-cigarettes: a prospective 3.5-year study of regular daily users who have never smoked. Scientific Reports. 7. 10.1038/s41598-017-14043-2.

3. The Relationship of E-Cigarette Use to Cigarette Quit Attempts and Cessation: Insights From a Large, Nationally Representative U.S. Survey.

- **Study aims**
  This US study uses data from the nationally representative 2014/15 Tobacco Use Supplement-Current Population Survey (TUS-CPS), in order to estimate the number of quit attempts and likelihood of quit success among smokers. Quit attempts were defined as having "tried to quit smoking completely" for those who smoked less than 12 days in the last month, and those who "stopped smoking for one day or longer because of trying to quit smoking" among those who smoked more than 12 days in the last month. Quit success was defined as having been abstinent for at least 3 months, among those that had at least one quit attempt.

Adjusted odds ratios (AORs) were calculated for the rate of quit attempts with frequency of e-cigarette use, and for the likelihood of quit success with frequency of e-cigarette use.

- **Key findings**
  Ever use of e-cigarettes was significantly associated with an increased rate of quit attempts (AOR = 2.31, 95% CI: 2.15-2.48). This likelihood increased with the frequency of use (AOR = 2.60 for current use, 3.39 for more than 5 days in the past 30 days, and 4.90 for more than 20 days). The linear use variable was significant, and the odds of a quit attempt increased by 5% with each additional day of use.

  Ever use of e-cigarettes was significantly associated with a decreased chance of quit success (AOR = 0.80, 95% CI: 0.69-0.92). But current use was significantly associated with an increased chance (AOR = 1.22, 95% CI: 1.02-1.46). This likelihood increased with the frequency of use (AOR = 1.59 for more than 5 days in the past 30 days, and 2.81 for more than 20 days). The linear use variable was significant, and the odds of quit success increased by 10% with each additional day of use.

- **Limitations**
  This is a cross-sectional study, and relies on significant recall, so results may be subject to bias and inaccuracies.

  Although the study adjusted for possible confounders, not all factors could be controlled for (e.g. the use of other cessation tools or behavioural support). The study cannot determine if e-cigarette use is causally associated with the results for quit attempts and quit success.

  The study wasn't able to adjust for intensity of e-cigarette use (puffs per day). Neither did it assess the types of devices used, flavours and whether e-liquids contained nicotine or not.

  The results do not include people that used e-cigarettes and then quit both smoking and e-cigarette use, potentially understating the impact of e-cigarettes.

  The study cannot account for potential relapse after having quit smoking for three months, and whether e-cigarette use makes this more or less likely.

David T Levy, Zhe Yuan, Yuying Luo, David B Abrams; The Relationship of E-Cigarette Use to Cigarette Quit Attempts and Cessation: Insights From a Large, Nationally Representative U.S. Survey, *Nicotine & Tobacco Research*, https://doi.org/10.1093/ntr/ntx166

4. Differences in adolescent e-cigarette and cigarette prevalence in two policy environments: South Korea and the United States.

- **Study aims**
  This study from South Korea and the United States, explores the use of e-cigarettes and cigarettes among adolescents in both countries. Using data collected between 2011 and 2015 from the Korean Youth Risk Behaviour Web-based Survey and the US National Youth Tobacco Survey, e-cigarette and cigarette prevalence were compared across years and between countries. The paper discusses how the differing policy environments may affect these numbers.

- **Key findings**

Adolescent e-cigarette use (including dual use) remained stable in South Korea between 2011 and 2015 at around 4%. Whereas in the US, this increased from 0.9% in 2011 to 11.2% in 2015. When looking at e-cigarette use alone (non-dual use), this remained stable at around 1% in South Korea, and increased from 0.2% to 7.4% in the US.

Cigarette use (including dual use) decreased from 12.1% to 7.8% in South Korea. While in the US, prevalence decreased from 11.2% to 6.1%. Cigarette only use decreased significantly in both countries, from 8.6% to 4.5% in South Korea, and from 10.3% to 2.7% in the US.

The combined prevalence of e-cigarette and cigarette use in South Korea decreased significantly from 13.2% to 8.5%. In the US, there was a non-significant increase from 11.3% to 14.0%.

- **Limitations**
  South Korea and the US are vastly different, and the study was unable to control for factors that likely would have affected the results e.g. cultural differences, policy regulations, tobacco industry activity, and knowledge, attitude and beliefs towards tobacco and health. In particular, the US had no national regulations on e-cigarettes until after the study period.

  There were large baseline differences between the two countries that could not be accounted for in analyses e.g. South Korea had a much higher prevalence of e-cigarette use in 2011 than the US. The trend comparison between countries may be strongly affected by these differences.

  The two samples used different age ranges. The US sample included people aged 9-21 years old, whereas the South Korean sample only included those ages 12-18. However, sensitivity analyses gave almost identical results when restricting the US sample to the same age range.

  Ever use of cigarettes in both surveys includes those that have only tried one or two puffs. This may not translate to regular use. This was different to the measure of e-cigarette use, which was only recorded for those that had used a device in the past 30 days. There were also slight differences in the ways this question was asked between countries.

  When the study displays trends in combined cigarette and e-cigarette use, this doesn't take into account the proportion of this group that are smokers compared to e-cigarette users.

  The study cannot make conclusions on transitions from e-cigarette use to cigarettes or cigarette use to e-cigarettes based on these data. Neither did it assess whether e-cigarette users were using nicotine-containing e-liquids or not.

H-J Cho, MD, PhD, L M Dutra, ScD, S A Glantz, PhD; Differences in Adolescent E-cigarette and Cigarette Prevalence in Two Policy Environments: South Korea and the United States, *Nicotine & Tobacco Research*, , ntx198, https://doi.org/10.1093/ntr/ntx198

Overview

This month we have included one paper from Scotland, one from Italy, one from the USA and a final paper comparing the USA with South Korea.

The first article describes finding from a CRUK funded qualitative study with 72 young adults from socio-economically disadvantaged backgrounds in Central Scotland. The authors aimed to explore the views of 16-24 year olds regarding their understanding of, and engagement with, e-cigarettes.

The majority were current smokers, followed by ex-smokers and a very small group of never smokers. Most had tried an e-cigarette at least once, a few were current vapers and some participants had never vaped. Because smoking and vaping status was explored during the interviews rather than through a questionnaire, the study couldn't directly assess whether any of the never smokers had vaped or were vaping, although the responses imply that vaping was an activity concentrated amongst those who currently smoked or had done so in the past.

Findings were organised around two main themes: how participants viewed their smoking identify in the light of e-cigarettes' emergence, and the social value of smoking compared with vaping. Overall, interviewees regarded e-cigarettes as at odds with the well-established place of smoking in their lives or those of family and friends in disadvantaged communities. Those who smoked viewed smoking as something 'controllable' and accepted, discussing their ability to 'smoke in moderation' and keep healthy in other respects as young people. This compared to accounts of older smokers who were often perceived as dependent on smoking and trying vaping because of concerns about their health. In contrast, some of the young adults viewed vaping as less controllable, particularly the fact that vaping didn't come to an end like smoking a single cigarette and vapers were perceived as using vaping devices more frequently or for longer periods than smoking. In addition, concerns were raised about vaping being more 'addictive' than smoking and confusion was expressed about why not all vapers want to cut down their use of an e-cigarette or stop vaping all together. For many, e-cigarettes didn't fit well into existing social situations where smoking had a value - i.e. the devices weren't seen as something to be shared, like smoking, or were not perceived to relieve stress in the same way that smoking did.

The study included four ex-smokers who had successfully quit through vaping - three with box mods. These participants demonstrated a deeper understanding of the devices and had positive accounts. However, overall, fears about e-cigarette addictiveness, the up-front cost of later generation vaping devices, and perceptions about e-cigarettes being products for older, dependent smokers were potentially deterring use of e-cigarettes by young disadvantaged smokers. The authors discuss how some young people in the study were rationalising continued smoking and many were uncertain about the value or acceptability of e-cigarettes as a less harmful alternative.

Our second article covers a new issue not yet explored in the literature, and as such it is novel. This is the health effects of vaping amongst never smokers. Surveys from a number of countries, including the UK, show that regular e-cigarette use is uncommon among young people or adults who are not smokers or ex-smokers. Thus finding never smoking vapers to participate in research is very challenging. However, Italian academics and clinicians who have been studying vaping for many years did manage to recruit and retain a cohort of nine daily e-cigarette users who had never smoked and followed them up for 3.5 years. The team assessed a range of health outcomes for these participants and compared them with a reference group of 12 never smokers.

Vaping participants were initially recruited from vape shops, had vaped daily at baseline for at least three months or more, and were on average just under 30 years of age. No significant differences were observed between the never smokers who vaped or didn't vape at baseline and at each follow up point in relation to: blood pressure; heart rate; body weight; lung function; respiratory symptoms; exhaled breath nitric oxide; exhaled CO and high-resolution computed tomography of the lungs. Some vaping participants reported a cough at follow up points, but so did some of the never smokers who did not vape. This research has a number of limitations beyond the very small sample size. In particular, only some types of health outcomes were assessed, and any adverse health effects from regular vaping may occur after years of use beyond the follow up point for this study. There would be merit in conducting a similar study with a larger sample, perhaps recruited

from a number of countries, and assessing a wider range of health outcomes. However, identifying large samples of never smoking regular vapers from any country is likely to be difficult to achieve.

The third article this month is the latest study using a large representative survey in the USA to assess possible relationships between e-cigarette use and smoking cessation, in this case quit attempts and success in stopping smoking for at least three months. Survey data were supplemented with information on tobacco control policies in US states to assess whether environmental (regulatory) factors might affect outcomes. These were limited to the retail price of cigarettes (reflecting tobacco taxes, which vary between states) and smoke-free workplaces and, where data were available (just three states), 'vape-free' workplace ordinances.

Smokers who reported using an e-cigarette were more likely to have made an attempt to stop smoking in the past year but, overall, were less likely to have stopped smoking. However, this depended on frequency of e-cigarette use. Occasional use did not appear to assist with smoking cessation. In contrast, success in stopping smoking for at least three months was significantly higher among those who had used e-cigarettes more frequently, with success rates increasing as frequency of use went up. For the regulatory factors, no significant differences were found for the final set of results (using logistic regression) but there was some indication that higher cigarette prices may increase the number of people making a quit attempt.

The findings of this study support that of previous research, which suggests that frequency of e-cigarette use makes a significant difference to smoking cessation outcomes. This is not surprising if we consider the large body of evidence on medicinal nicotine containing products (NRT) which suggest that smokers are more likely to quit if products are used correctly and for long enough. Clearly assessing frequency of e-cigarette use, as well as other factors not assessed in this study (nicotine content of e-liquids, for example) are important variables to include in any studies of e-cigarettes for smoking cessation.

Finally we include a study which involved a collaboration between researchers in South Korea and the USA. It compared results from nationally representative cross sectional surveys of young people in South Korea and the USA between 2011 and 2015. The main comparative measure was any use of an e-cigarette in the past 30 days, which is a commonly employed but not very specific measure of use, as other studies have explained. Encouragingly, youth smoking declined in both countries during the study period. However, trends in e-cigarette use, including dual use of tobacco and e-cigarettes, varied. The proportion of young people using e-cigarettes in the past 30 days but not smoking remained stable at very low levels in South Korea but rose from less than 1% to just over 7% in the USA. E-cigarette use including dual use also remained stable over the period in South Korea but increased significantly in the USA.

The authors argue that the reasons for these differences lie in the policy context, where e-cigarettes are fairly extensively regulated in South Korea but less so in the USA. Important differences do exist, and Johns Hopkins University provides a very useful overview of policy differences between countries including the two in this article. Their country list confirms, as do the study authors, that policy measures like age of sale, health warnings on e-cigarette packaging and restrictions on advertising, taxes on the products and a ban on use in public places are in place in Korea. Some but not all of these measures are also in place in the USA and some policies vary between states in contrast to a more uniform national approach in Korea. The data sources used in the article can't provide any causal link between trends in use and the regulatory environment. Other factors may explain the differences, as we describe in the article summary above. However, the study adds to

the growing literature comparing patterns of e-cigarette use in different populations between countries.

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

- Early age of e-cigarette use onset mediates the association between impulsivity and e-cigarette use frequency in youth.
- The Impact of E-cigarettes on Smoking and Related Outcomes in Veteran Smokers with Psychiatric Comorbidity.
- Lung Toxicity of Condensed Aerosol from E-CIG Liquids: Influence of the Flavor and the In Vitro Model Used.
- Symptoms during Adolescents' First Use of Cigarettes and E-Cigarettes: A Pilot Study.
- E-Cigarette Use Causes a Unique Innate Immune Response in the Lung Involving Increased Neutrophilic Activation and Altered Mucin Secretion.
- Electronic cigarette user plasma nicotine concentration, puff topography, heart rate, and subjective effects: Influence of liquid nicotine concentration and user experience.
- Exposure to electronic cigarette vapors affects pulmonary and systemic expression of circadian molecular clock genes.
- The association of e-cigarette use with exposure to nickel and chromium: A preliminary study of non-invasive biomarkers.
- Electronic Cigarette Smoke Impairs Normal Mesenchymal Stem Cell Differentiation.
- Electronic cigarette use among individuals with a self-reported eating disorder diagnosis.
- The Surgical Impact of E-Cigarettes: A Case Report and Review of the Current Literature.
- Recall of Point-of-Sale Marketing Predicts Cigar and E-Cigarette Use among Texas Youth.
- Generally Recognized as Safe: Uncertainty Surrounding E-Cigarette Flavoring Safety.
- Content Analysis of US News Stories About E-Cigarettes in 2015.
- Examining Daily Electronic Cigarette Puff Topography Among Established and Non-established Cigarette Smokers in their Natural Environment.
- Changes in puffing topography and nicotine consumption depending on the power setting of electronic cigarettes.
- Associations of Electronic Cigarette Nicotine Concentration With Subsequent Cigarette Smoking and Vaping Levels in Adolescents.
- Perceptions of the Harm and Addictiveness of Conventional Cigarette Smoking Among Adolescent E-Cigarette Users.
- Burns caused by electronic vaping devices (e-cigarettes): A new classification proposal based on mechanisms.
- The effect of sucralose on flavor sweetness in electronic cigarettes varies between delivery devices.
- Content analysis of e-cigarette products, promotions, prices and claims on Internet tobacco vendor websites, 2013-2014.
- Examining the association between physical activity, sedentary behaviour and sport participation with e-cigarette use and smoking status in a large sample of Canadian Youth.
- Chronic exposure to electronic cigarette (E-cig) results in impaired cardiovascular function in mice.
- The impact of flavour, device type and warning messages on youth preferences for electronic nicotine delivery systems: evidence from an online discrete choice experiment.

- E-cigarette Use and Smoking Cessation Among South Korean Adult Smokers: A Propensity Score-Matching Approach.
- Electronic cigarette use and smoking initiation among youth: a longitudinal cohort study.
- E-cigarette marketing exposure and combustible tobacco use among adolescents in the United States.
- Social media e-cigarette exposure and e-cigarette expectancies and use among young adults.
- A Naturalistic, Randomized Pilot Trial of E-Cigarettes: Uptake, Exposure, and Behavioral Effects.
- Perceptions Related to Use of Electronic Cigarettes among California College Students.
- Examining College Students' Social Environment, Normative Beliefs, and Attitudes in Subsequent Initiation of Electronic Nicotine Delivery Systems.
- Electronic Cigarette Use in Students and Its Relation with Tobacco-Smoking: A Cross-Sectional Analysis of the i-Share Study.
- Relationship between spending on electronic cigarettes, 30-day use, and disease symptoms among current adult cigarette smokers in the U.S.
- Aldehyde levels in e-cigarette aerosol: Findings from a replication study and from use of a new-generation device.
- The effect of e-cigarette indoor vaping restrictions on adult prenatal smoking and birth outcomes.
- Internet-based Advertising Claims and Consumer Reasons for Using Electronic Cigarettes by Device Type in the US.
- Assessment of reactive oxygen species generated by electronic cigarettes using acellular and cellular approaches.

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 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 Carl Alexander from Cancer Research UK with assistance from Professor Linda Bauld at the University of Stirling 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.