Electronic Cigarette Research Briefing – August 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.

If you would prefer not to receive this briefing in future, just let us know.


- **Study aims**
  This study of 2,836 adolescents (aged 13-14 years at baseline) from two English counties, examined whether e-cigarette use was associated prospectively with initiation or escalation of tobacco cigarette use.

  Data were collected at baseline on self-reported e-cigarette and cigarette use in September-December 2014, and followed up after 12 months. Self-reported cigarette use was validated by breath carbon monoxide levels.

- **Key findings**
  At baseline, 61.5% of adolescents hadn’t tried either e-cigarettes or cigarettes. 16.0% had tried e-cigarettes but not cigarettes, 4.4% had tried cigarettes but not e-cigarettes, and 18.2% had tried both.

  After controlling for covariates, having tried e-cigarettes at baseline was significantly associated with having tried smoking at follow up (OR = 4.06, 95% CI: 2.94-5.60).

  In those that had tried smoking at baseline, there was no significant relationship between having tried e-cigarettes at baseline and subsequent increased smoking (OR = 1.89, 95% CI: 0.82-4.33).
• **Limitations**
  The study was not designed to look at e-cigarettes. It was a trial of a school-based smoking initiation intervention. Additional questions on e-cigarettes were added and were not the main focus of the trial.

  E-cigarette use was converted to a binary measure, but included those that had only tried the product once or twice, so likely included many that were only experimenting with e-cigarettes. The study didn’t assess extent of e-cigarette use at follow-up and whether those that tried e-cigarettes went on to become regular users.

  Likewise, smoking initiation included those that had only tried cigarettes once, so this study cannot demonstrate associations with regular cigarette use.

  The study wasn’t able to control for all factors that may affect smoking behaviour (e.g. tendency towards other risky behaviours, and other substance use), and cannot causally link e-cigarette use with later smoking.

  There was a small sample size for some measures, and high attrition between baseline and follow-up, which was significant for some of the characteristics measured (e.g. sex, intention to smoke, having friends/family who smoke).

  The description of e-cigarettes in the survey as “a tube that sometimes looks like a normal cigarette and has a glowing tip” likely only describes first generation e-cigarette devices.

  The study did not assess whether participants had used nicotine-containing e-cigarettes, or device types and flavours used.


2. [Young people’s use of e-cigarettes across the United Kingdom: Findings from five surveys 2015-2017](https://www.tobaccocontrol.com/doi/10.1136/tobaccocontrol-2016-053539)

• **Study Aims**
  This study reported ever and regular tobacco cigarette and e-cigarettes use amongst young people aged 11-16 in the UK. It drew on data from five surveys of young people in: the UK as a whole (Youth Tobacco Policy Survey n=1,213 in 2016); Great Britain (ASH Smokefree GB, n=1,205 in 2016 and 1,361 in 2017); Wales (Schools Health Research Network survey, n=32,479 in 2015); and Scotland (Scottish Schools Adolescent Lifestyle Survey, n=13,607 second year (13 year olds) and 11,697 fourth year (15 year olds) in 2015).

• **Key Findings**
  For the sample overall in terms of tobacco smoking, ever smoking ranged from 11-20%, in 11-16 year olds. The SALSUS Scotland survey of 15 year olds, found 31% had ever tried smoking. Regular smoking (defined as at least weekly) was much lower at 1-4% across 11-16 year olds, and 7% in the SALSUS Scotland survey of 15 year olds.
In terms of e-cigarette use, ever use ranged from 7-18%, with 32% having ever tried them in the SALSUS survey of 15 year olds. At least weekly use was between 1-3% across all surveys.

Young people who were regular smokers were far more likely to report ever e-cigarette use than never smokers (67-92% vs. 4-10%).

Among those who smoked at least weekly, regular e-cigarette was between 7% and 38%. While teenagers who had never smoked only reported very rare regular use of e-cigarettes at between 0.1% and 0.5%.

• **Limitations**

While the questions on tobacco and e-cigarette use in the surveys were comparable, the data were collected in different ways by each survey (in schools - SALSUS and SHRN; online - ASH Smokefree GB; and face to face in the home - YTPS). Each of these approaches to data collection has limitations which may have affected response rates or the representativeness of the samples.

While four of the surveys included young people aged 11-16 (YTPS, the two waves of ASH SmokefreeGB and SHRN), the SALSUS survey included only 13 year olds and 15 year olds, with results for each reported separately, which limits comparisons between the data for Scotland and the other surveys.

All the data were self-reported for both smoking and e-cigarette use. In addition, the surveys included were cross-sectional and could not explore any transition from e-cigarette use to smoking or vice-versa.

The study did not assess the types of e-cigarette used and whether they contained nicotine.


3. **A typology of vaping: Identifying differing beliefs, motivations for use, identity and political interest amongst e-cigarette users**

• **Study aims**

This UK study of 55 vapers, aimed to identify and differentiate the various accounts of e-cigarette use and identity among this group. 31 vapers were recruited from adverts in real-life venues (libraries, community centres and vaping shops), and 24 from online vaping forums. Material was collected in September/October 2014.

Participants were presented 70 statements on e-cigarettes, from media, academic and online discussions. These were then sorted by how much the participant agreed with each statement. Using Q-methodology, and qualitative interviews, similar accounts of e-cigarette use were identified from the participants and grouped into statistically significant factors.

• **Key findings**

Three accounts (or factors) of e-cigarette user were identified. The first two factors were associated with those that had quit smoking, whereas the third was associated with dual use.
Factor One was identified as “Vaping as Pleasure”. 19 participants were significantly associated with this factor. This group had a strong vaping identity, and were politically motivated to maintain vapers’ rights. They viewed vaping as enjoyable, and something they would continue in the long-term. The variety of flavours was seen as a core feature of vaping pleasure, alongside “being healthier”. They rejected a medical model of vaping as a medicine for smoking cessation. While nicotine addiction was not necessarily considered a bad thing among this group.

Factor Two was identified as “Vaping as Medical Treatment”. 14 participants were significantly associated with this factor. For this group, the primary reasons for vaping were to medicate their addiction to smoking, with the aim of ultimately reducing nicotine dependence. This group did not hold a strong vaping identity, and were more concerned about having stopped smoking and improving their health.

Factor Three was identified as “Ambivalent E-cigarette Use”. 6 participants were significantly associated with this factor. This group felt strongly about the vaping rights, but were ambivalent about their own use of e-cigarettes. They would switch between smoking and vaping for a variety of reasons. They were neutral about whether e-cigarettes increased their quality of life, and did not consider vaping to be a magic solution for stopping smoking. They had less certain ideas about the harms/benefits of vaping, and saw their e-cigarette use as temporary, with the intention of stopping using them.

- **Limitations**

Q-methodology is not designed to test any particular hypotheses, and can only present the identities that arise from factor analysis and qualitative interviews.

The participants were not selected to be representative of the vaping population e.g. 84% had quit smoking. Not all e-cigarette users’ views will have been sufficiently represented, so that there may be other factors not contained in these results. Similarly, the results excluded those participants that associated with multiple factors (n = 11), or none at all (n = 5).

The participants in this study are not necessarily fixed to any particular factor, and someone may switch their vaping identity over time. Similarly, there was reasonably high correlation between Factor One and Factor Two, suggesting that these factors may represent one wider viewpoint.

The study didn’t look to split participants by other variables and compare between them, e.g. smoking status, device type, e-liquid flavour or nicotine content.

4. **Characteristics and outcomes of e-cigarette exposure incidents reported to 10 European Poison Centers: a retrospective data analysis.**

- **Study aims**
  This study from 10 European Union Member States (EU MS), assessed whether intentional and accidental exposure to e-liquids may lead to adverse events. Data were taken from exposures reported to national poison centres from 2012 to March 2015.

  The study reports on: age, gender, route of exposure, source of exposure, management of incident, reported clinical outcome, and reason of exposure.

- **Key findings**
  A total of 343 incidents were reported, with 277 from 8 EU MS having sufficient detail for analyses. There was an increase in reported exposures during the reporting period (10 in 2012, 85 in 2013, and 140 in 2014).

  Most exposures were unintentional (71.3%), followed by intentional (17.8%), abuse/misuse (7.7%), and suspected suicide (1.1%, n = 3).

  E-cigarette refill vials were responsible for the majority of reported incidents (87.3%). Poisoning through ingestion was the most frequent exposure route for all age groups (67.5%), followed by respiration (16.6%).

  Exposure through ingestion was significantly more likely for children ≤5 years old than adults (aOR = 4.36, 95% CI: 1.87-10.18).

  More than half of incidents only had a minor clinical effect (53.8%), with 39.4% being recorded as having no effect, 6.3% reported moderate effects, and 1 case (0.5%) reported a major clinical outcome. No deaths were recorded.

  Incidents involving children aged ≤5 years old were less likely to lead to clinical effects (aOR = 0.41, 95% CI: 0.21-0.82) than those aged ≥19 years old.

  The most commonly reported symptoms were: vomiting (20.3%), dizziness (14.5%), nausea (13.8%) and throat conditions (9.1%).

- **Limitations**
  This study is limited to data reported to poison centres and does not cover all adverse events that could be related to e-cigarettes e.g. burns. Neither can it assess longer term health outcomes from e-cigarette use.

  The study did not capture the type of e-liquid used, so adverse events cannot be linked to specific e-liquid constituents. Adverse events may not be due to nicotine poisoning.

  The results cannot be generalised to other EU MS not included in this study. Three countries were only able to provide summary statistics for some of the incidents reported. These 66 incidents from Ireland, Croatia and Estonia were excluded from the statistical analyses.

  The number of incidents reported was not proportional to country population, suggesting there may be differing reporting procedures, usage patterns or products used, that may affect the results presented.
The small sample size for a number of exposure characteristics led to wide confidence intervals for some analyses.

The study doesn’t compare e-cigarette exposure incidents with those from tobacco cigarettes or other nicotine-containing products.


5. **E-cigarettes emit very high formaldehyde levels only in conditions that are aversive to users: A replication study under verified realistic use conditions.**

- **Study aims**
  This study from Greece, replicated a study from 2015 that identified 5 to 15-fold higher formaldehyde levels in emissions from an older generation e-cigarette compared to tobacco cigarettes.

  The experiments were repeated with the same e-cigarette equipment and e-liquid. But this time, checked for the generation of dry puffs by using the reports of experienced e-cigarette users testing the product at different voltages. Formaldehyde levels were then measured in the aerosol for a range of different voltages, and compared to tobacco emissions.

- **Key findings**
  88% of participants identified dry puffs at ≥4.2V. The upper limit of realistic use without dry puffs was defined at 4.0V.

  The levels of formaldehydes detected ranged from 3.4 (SE = 2.2) µg/10 puffs at 3.3V, to 718.2 (SE = 58.2) µg/10 puffs at 5.0V. The differences between formaldehyde levels at increasing voltages were statistically significant.

  The formaldehyde levels detected at the maximum voltage of 5V, were 89% higher compared to the original study.

  The daily exposure to formaldehyde at 4V from consuming 3g of liquid with this device (1,005.4µg), was found to be 32% lower than the levels from smoking 20 tobacco cigarettes (1,480µg). At 5V, the exposure from 3g of liquid was as high as 27,151.5µg, which is 18.3-fold higher than the exposure from 20 tobacco cigarettes.

  E-liquid consumption ranged from less than 4mg per puff at 3.3V to around 8mg per puff at 4.6V and over. While liquid consumed increased linearly from 3.3V to 4.0V, the pattern was more erratic at higher voltages.

- **Limitations**
  This study was a replication of previous experiments and only looked at one outdated e-cigarette device and one e-liquid. This is not representative of all e-cigarettes, e-liquids, nicotine concentrations and flavours available.
The study cannot prove a causal link between formaldehyde emissions and dry puff detection. It’s possible that other compounds may be responsible for dry puff detection. Neither did the study measure the levels of other potentially harmful chemicals in emissions.

Dry puff is a subjective phenomenon, and some e-cigarette users may still potentially vape at the higher voltages associated with dry puff in this study.

The levels of formaldehydes were measured in the vapour using a puffing machine and impinger set up, and may not detect all formaldehydes in the vapour, or represent exposures to these chemicals in humans under real world use.

When comparing to tobacco cigarettes, 3g of e-liquid may not be equivalent to the consumption of 20 cigarettes per day.

Konstantinos E. Farsalinos, Vassilis Voudris, Alketa Spyrou, Konstantinos Poulas, E-cigarettes emit very high formaldehyde levels only in conditions that are aversive to users: A replication study under verified realistic use conditions, In Food and Chemical Toxicology, Volume 109, Part 1, 2017, Pages 90-94, ISSN 0278-6915, https://doi.org/10.1016/j.fct.2017.08.044.

Overview

Five articles are included in this month’s bulletin. The first three are from research teams based in the UK, with the remaining two papers from academics in Greece.

Our initial two articles focus on e-cigarette use in young people. A team led by academics at the University of Leeds conducted the first study, in which questions on e-cigarette use were added to surveys conducted as part of a larger study on smoking initiation in schools. Children aged 13-14 were asked about their use of e-cigarettes and tobacco cigarettes in late 2014 and the questions were repeated at follow up one year later. At baseline the sample included just over 2,800 young people and data was available for just over 2,000 at follow up. The article only reports data on trying an e-cigarette or trying smoking once or twice rather than any measures of regular use. Findings were similar to the study from Scotland that we summarised in last month’s bulletin. After controlling for a variety of variables that might be expected to contribute to susceptibility to smoking, having tried an e-cigarette at the time of the first survey was significantly associated with having tried a tobacco cigarette at least once by the time of the second survey. However, having tried an e-cigarette wasn’t a significant predictor of increased smoking at follow up amongst those who had already tried a tobacco cigarette at baseline.

The second study examined e-cigarette use among young people in five cross-sectional surveys from across the UK. These took place between 2015 and 2017 and included just over 60,000 participants between the ages of 11-16. The surveys were designed to be representative of young people in each of the jurisdictions covered. The first survey collected data from across the UK, another (two waves - 2016 and 2017) Great Britain, one in Scotland and one in Wales. The authors aimed to provide a comparative overview of the latest data on smoking and e-cigarette use in young people with a particular focus on frequency of use. They found that across 11-16 years old, ever use of e-cigarettes ranged from 4-10% but that regular use was lower at between 1-3%. Both experimentation and regular use were heavily concentrated amongst young people who also smoked tobacco cigarettes. Regular use of e-cigarettes among young people who had never smoked was very rare - between 0.1% and 0.5%.
This study included only cross-sectional data so could not look at trajectories of use or any relationship between smoking and vaping in young people, which was the focus of the Leeds study above. Both types of studies are useful in developing our understanding of how young people respond to the (still) relatively new technology involved in e-cigarettes. As both articles make clear, smoking rates amongst teenagers in the UK have continued to decline during the period when e-cigarette experimentation has increased. This suggests that, at the population level, there is no clear evidence that e-cigarettes are causing a rise in smoking. The second article above also provides reassurance that, so far, e-cigarettes are not attracting large numbers of never smokers into regular use of new nicotine containing products. However, the Leeds study (as with the study from Scotland that we featured last month) merit closer consideration. Although neither could control for all the factors that explain why young people try smoking, they did identify e-cigarettes as one possible feature. This merits further research and longer term follow up. The Scottish study has recently collected two year follow up data from the same young people and the results of this analysis will be awaited with interest. The issue of young people vaping and smoking is one that we will continue to return to in this bulletin, as the evidence grows from the UK and elsewhere.

Our third study this month provides a fascinating insight into the perceptions of adults who use e-cigarettes, using innovative Q-methodology which blends qualitative and quantitative methods. The author based at the University of Exeter collected data from 55 current e-cigarette users and explored how they described the experience of vaping and motivations for use. She then analysed and synthesised their accounts to develop a typology with three categories of users: those who vaped for pleasure and had strong and positive vaping identity; those who saw vaping as ‘treatment’, using e-cigarettes to replace the nicotine in smoking with a less risky alternative, to stop smoking and in some cases to reduce their perceived dependence on nicotine; and finally a group who were more ambivalent and switched between vaping and smoking. This article contributes to a small but growing literature on the ethnography or ‘lived experience’ of vapers and the cultural phenomenon that is e-cigarette use. In some ways it connects to a slightly older literature on smoking identity and the factors that might differentiate those who stop smoking and why, and those who continue to use tobacco. It also highlights the importance of looking beyond simple survey measures of motivations for particular behaviours. Some of the findings of the study may be useful for those considering measures to include in mixed methods studies (for example, trials with an imbedded process evaluation) to better understand why people start, continue or stop using e-cigarettes.

The fourth paper arises from the EU funded EUREST-PLUS study. It involved a secondary analysis of routine data on exposure to e-liquids reported to poison centres in EU member states. Only eight of 22 EU member states agreed or were able to provide data in the form that could be analysed by the research team and this did not include the UK. The research team aimed to assess the factors associated with e-liquid exposure incidents from 2012-March 2015. This is effectively a baseline study, as the relevant EUREST-PLUS work-package has been established to examine outcomes from the e-cigarette elements of the EU Tobacco Products Directive and the analysis was conducted before the TPD regulations came into force in member states.

There were 277 incidents reported in these eight countries over the study period. Most exposure was by accident. The most common type of incident was ingestion of e-liquid from a refill vial, with children being more highly susceptible to this route of exposure. Only one incident was reported that had a major clinical effect (although no details of what this was are provided in the article). Just 13 incidents had a moderate effect and the remainder had minor or no effects. The most common type of symptom was vomiting, which is consistent with a nicotine containing e-liquid being
ingested. Exposure routes also occurred through the skin, eyes and by breathing in e-liquids. Three incidents of suspected suicides were included in the records, but again no further details are mentioned regarding these cases in the article and no deaths were recorded. The study did not include any comparisons with other incidents reported to poison centres in the same countries (for example from household cleaning products, occupational exposures to toxicants etc). The authors point out that the EU TPD has since introduced requirements regarding size, labelling and child and tamper proof packaging for e-liquid containers which should prevent some of the most common incidents reported in the article, and it will be interesting to see if the EUREST-PLUS team publish a pre-post TPD analysis in due course.

Our final paper this month is a replication of a previous study. The issue of reproducible science has received considerable recent attention in some peer-reviewed journals, focusing on the need for clear standards in the conduct and reporting of studies which would allow the research to be replicated by others to determine if the original result was accurate. Of course not all studies are reproducible - particular phenomena may be time-limited and can only be studied once – but for lab-based and experimental research in particular, replicating an original study should be possible.

The current paper sought to replicate a study originally published as a letter in the New England Journal of Medicine (NEMJ) which found that one type of e-cigarette tested in a lab produced formaldehyde emissions higher than those produced by combustible tobacco. After contacting the authors of the NEMJ piece to obtain further details about their approach, the device, testing equipment and e-cigarette used, a team of researchers in Greece replicated the study. The Greek researchers had a hypothesis that the high voltage setting (5.0V) used in the original study would produce emissions, which in use by humans (rather than just lab testing), vapers would avoid because it results in a very unpleasant taste from overheating the e-liquid, known as ‘dry puff’.

A group of experienced vapers were asked to take puffs at varying voltage settings and report on dry puffs. Formaldehyde emissions were measured at each voltage setting. The replication study found that the reporting of dry puffs was very common when the voltage on the device was above 4.2. They concluded that the high levels of formaldehyde reported in the NEMJ letter were the result of testing in unrealistic conditions that would not mirror use in humans. These findings may be relevant when interpreting other laboratory studies of e-cigarette aerosol content where realistic conditions (i.e. use by humans) have not been possible or not been attempted. The findings also highlight the need for ongoing testing and reporting of aldehyde emissions from e-cigarettes as devices evolve.

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

- A critique of the US Surgeon General’s conclusions regarding e-cigarette use among youth and young adults in the United States of America.
- Assessing electronic cigarette effects and regulatory impact: Challenges with user self-reported device power.
- Evaluating the Mutual Pathways among Electronic Cigarette Use, Conventional Smoking, and Nicotine Dependence.
- The association of e-cigarette use with exposure to nickel and chromium: A preliminary study of non-invasive biomarkers.
• “Knowledge, recommendation, and beliefs of e-cigarettes among physicians involved in tobacco cessation: A qualitative study”.

• Initial Development of an E-cigarette Purchase Task: A Mixed Methods Study.

• Do you vape? Leveraging electronic health records to assess clinician documentation of electronic nicotine delivery system use among adolescents and adults.

• E-cigarette use and support for banning e-cigarette use in public places in the European Union.

• Use of electronic cigarettes in public and private settings in Barcelona (Spain).

• Adolescent Sports Participation, E-cigarette Use, and Cigarette Smoking.

• Flavoring Chemicals and Aldehydes in E-Cigarette Emissions.

• The knowledge, concerns and healthcare practices among physicians regarding electronic cigarettes.

• Characteristics of Adults Who Switched From Cigarette Smoking to E-cigarettes.

• Comprehensive determination of flavouring additives and nicotine in e-cigarette refill solutions. Part II: Gas-chromatography-mass spectrometry analysis.

• Prevalence and correlates of smoking and e-cigarette use among young men who have sex with men and transgender women.

• Importance of Survey Design for Studying the Epidemiology of Emerging Tobacco Product Use Among Youth.

• Formaldehyde Hemiacetal Sampling, Recovery, and Quantification from Electronic Cigarette Aerosols.

• Electronic Cigarette Use in US Adults at Risk for or with COPD: Analysis from Two Observational Cohorts.

• To vape or not to vape? Effects of exposure to conflicting news headlines on beliefs about harms and benefits of electronic cigarette use: Results from a randomized controlled experiment.

• Electronic cigarette use behaviors and motivations among smokers and non-smokers.

• Use of Nicotine in Electronic Nicotine and Non-Nicotine Delivery Systems by US Adults, 2015.

• How Social Care Beneficiaries in Poland Rate Relative Harmfulness of Various Tobacco and Nicotine-Containing Products.
• Phagocytosis and Inflammation: Exploring the effects of the components of E-cigarette vapor on macrophages.

• Similar precipitated withdrawal effects on intracranial self-stimulation during chronic infusion of an e-cigarette liquid or nicotine alone.

• Comprehensive determination of flavouring additives and nicotine in e-cigarette refill solutions. Part I: Liquid chromatography-tandem mass spectrometry analysis.

• Effects of nicotine versus placebo e-cigarette use on symptom relief during initial tobacco abstinence.

• Studying the interactive effects of menthol and nicotine among youth: An examination using e-cigarettes.

• Electronic Cigarette Use among Mississippi Adults, 2015.

• Investigating the neural correlates of smoking: Feasibility and results of combining electronic cigarettes with fMRI.

• Activation of the "Splenocardiac Axis" by electronic and tobacco cigarettes in otherwise healthy young adults.

• Use of smoking cessation products: A survey of patients in community pharmacies.

• Exclusive e-cigarette use predicts cigarette initiation among college students.

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 UKERCRF 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 and Nikki Smith 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 members 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.