Electronic Cigarette Research Briefing – April & May 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 US study used results from the National Youth Tobacco Survey (N = 101,011) to estimate the prevalence of past month use of e-cigarettes and nine different tobacco products amongst adolescents in grades 6-12 (ages 11-18). Trends were assessed over 5 years (2011-2015) and outcomes such as tobacco use and smoking intensity were compared with ever and past month e-cigarette use.

- **Key findings**
  From 2011-2015, past 30-day cigarette use declined among males and females, but past 30-day e-cigarette use increased. In 2014 and 2015, past 30-day e-cigarette use overtook cigarette use (in 2015: 9.4% e-cigarette use vs. 5.4% cigarette use for females, and 13.2% vs. 7.2% for males). Overall use of either cigarettes or e-cigarettes at least once in the past 30 days was somewhat greater in 2014 and 2015 than in any of the previous three years.

  Overall e-cigarette ever use rose 10-fold among females and 7-fold among males.

  In 2015, among those that had never previously tried e-cigarettes or tobacco, e-cigarettes had higher past 30-day use than any tobacco product. Between 2011 and 2015, this rose from 0.1% to 1.8% for females and from 0.2% to 2.9% for males.
Among past 30-day cigarette users, past month e-cigarette use rose from 2011-2015 (4.3% to 53.6% for females, and 9.7% to 59.5% among males).

Among all past month cigarette users from 2011-2015, there was no statistically significant decline in cigarette smoking intensity during the period that e-cigarette use increased. There were also no statistically significant associations for quit attempts or quit intentions with past month e-cigarette use.

- **Limitations**
  The measures for ever e-cigarette or tobacco product use and past 30-day use may include people that have only tried the product once, so does not necessarily equate to regular use.

  Frequency of e-cigarette use in the past 30 days was only available from 2014 onwards. These data were not presented, and therefore associations between regular e-cigarette use and smoking cannot be determined.

  This paper is unable to determine whether the rise in e-cigarette use alongside a decline in other tobacco product use is due to people replacing tobacco with e-cigarettes, or whether people are taking up e-cigarettes who wouldn’t have otherwise smoked. Nor can it assess whether e-cigarettes may be responsible for the decline in smoking or not.

  Changes in questionnaire phrasing on e-cigarette use over the years may have resulted in underestimations for e-cigarette use in the early phases.

  This paper does not assess motivations for e-cigarette use or determine whether e-cigarettes were being used to help people cut down or stop smoking.

  Each yearly survey was given to different populations, so it wasn’t possible to assess individual trends for the ordering between e-cigarette initiation and tobacco use. Neither did this analysis control for potential confounders, such as socio-demographics or participation in other risky behaviours.

  There is no data on the type of e-cigarettes being used, or whether these products were flavoured or contained nicotine.


2. **A comparison of nicotine dependence among exclusive E-cigarette and cigarette users in the PATH study.**

- **Study aims**
  This US study uses a nationally representative survey (Wave 1 Population Assessment of Tobacco Health (PATH) Study) to assess the relative level of nicotine dependence among adult, everyday users of e-cigarettes and cigarettes. The study used 156 exclusive e-cigarette users and 3430 exclusive cigarette smokers.
• **Key findings**

77% of e-cigarette users considered themselves addicted to their products, compared to 94% of smokers.

After adjustment for potential sociodemographic confounders, compared to e-cigarette users, cigarette smokers were significantly more likely to consider themselves addicted to their product (OR = 6.9, 95% CL: 4.5-10.7) and ever have strong cravings to use their product (OR = 2.9, 95% CL: 1.9-4.2).

They were also more likely to find it difficult to keep from using their product in places where it is prohibited (OR = 6.4, 95% CL: 2.9-14.3), and feel like they really needed to use their product (OR = 3.9, 95% CL: 2.4-6.4).

After adjusting for smoking/vaping rules in the home, cigarettes smokers had a significantly shorter mean time-to-first-use of the day compared to e-cigarette users – 20.0 minutes (95% CL: 18.7-21.5) vs. 29.2 minutes (95% CL: 24.4-34.9).

• **Limitations**

This study does not use a recognised, validated measure of nicotine dependence, and data are self-reported, so may be subject to bias.

Though the survey used a nationally representative sample, the restricted populations of exclusive e-cigarette users and cigarette smokers had different demographics.

The study did not adjust results for type of e-cigarette, nicotine concentration or flavour used, and cannot compare dependence across these variables.

As this study involved exclusive, daily e-cigarette users who do not use other products, this group likely represents those most dependent on their e-cigarette to satisfy their cravings, in comparison to other groups of e-cigarette users e.g. dual users, non-daily users or past users. Therefore the study can’t assess e-cigarette dependence in all users, including dual or poly-users (who make up the majority of past 30-day e-cigarette users in this survey).

This study was not able to compare other quantitative measures, such as frequency of use per day, as these are not directly comparable across products within the PATH survey. Neither did it assess the length of time that people had been using their products.


3. **Correlates of Electronic Cigarettes Use Before and During Pregnancy.**

• **Study aims**

This US study surveyed 103 pregnant smokers who were entering a clinical trial for smoking cessation about their use of e-cigarettes and other cessation treatments. The study examined the characteristics of women using e-cigarettes and compared the frequency of e-cigarette use with that for medications approved by the US Food and Drug Administration (FDA).

• **Key findings**
14% of women (14 in total) reported previously using e-cigarettes during pregnancy. This group were more likely to have a history of substance abuse (p = 0.043), and have a greater number of quit attempts than non-users (p = 0.018). There were no significant differences for other characteristics, such as: number of cigarettes smoked before pregnancy, nicotine dependence, motivation to quit smoking, and history of anxiety or depression.

The most common reason for e-cigarette use during pregnancy was to stop smoking (57%), followed by to reduce smoking (36%), and curiosity (36%) (Participants were able to select more than one reason).

35% of all participants reported using an e-cigarette or FDA approved medicine during a previous quit attempt, either while pregnant or not. The most common aid used was an e-cigarette (15%), followed by nicotine patches (14%), nicotine gum (7%), varenicline (4%), bupropion (2%) and a nicotine inhaler (1%). No participants reported previous use of nicotine lozenges or nasal sprays.

- **Limitations**
  The study sample was a self-selected group of participants who volunteered to take part in a clinical trial for nicotine replacement therapy use for smoking cessation during pregnancy, so were likely more motivated to quit. They were recruited as they were unable to quit on their own, and the group was not selected to be representative of the pregnant smoker population. All results are self-reported.

  The study excluded current e-cigarette users, or those using medication to quit smoking, so may underestimate overall levels of e-cigarette or medication use during pregnancy. Any associations with e-cigarette use during pregnancy in this study are based on use prior to the study.

  The small sample size means many of the findings are non-significant.

  The reasons for e-cigarette use were selected a list of suggestive answers, so may not capture all reasons for use.

  The study did not capture whether participants used nicotine e-cigarettes, or nicotine concentration used. It also wasn’t able to provide analysis of the type of e-cigarettes used due to poor recall.


4. **A Comparative Health Risk Assessment of Electronic Cigarettes and Conventional Cigarettes.**

- **Study aims**
  This study from New Zealand assesses the comparative risks of e-cigarettes and tobacco cigarettes using the US Environmental Protection Agency (EPA) health risk assessment model (identifying hazards, exposures and risks based on pre-existing literature) and findings of a literature review of 96 articles. The study estimates the average and maximum hazard exposures for 12 toxicants in e-cigarettes and cigarettes, assesses potential health impacts from these, and then benchmarks each toxicant level against international guidelines.
Key findings
From reported levels in literature, four toxicants (acrolein, diethylene glycol, propylene glycol and cadmium) reported in e-cigarette emissions and eight toxicants (acetaldehyde, acrolein, formaldehyde, arsenic, cadmium, CO, NNK and NNN) reported in cigarette emissions had maximum exposure levels higher than guideline levels.

When taking mean exposures across products from reported literature, two toxicants (acrolein and propylene glycol) in e-cigarette emissions and seven toxicants (acetaldehyde, acrolein, formaldehyde, cadmium, CO, NNK and NNN) in cigarette emissions had average exposure levels higher than the guideline levels.

Limitations
The data related to e-cigarette emission hazards were taken from one paper first published in 2013 that tested 12 different e-cigarettes, and may not represent all e-cigarette products/liquids, or more recent products. Likewise, the data for cigarette emission hazards were taken from one study looking at 50 cigarettes.

Exposure levels were based on emission constituents, as opposed to real-world measures in humans.

Only 12 toxicants present in e-cigarettes or cigarettes, identified as the most significant hazards, were selected for analysis, meaning other potential toxicants were not included.

The exposure assessment was based on average cigarette use among current users in New Zealand (11 per day), and the reported equivalent level of e-cigarette puffs (165 per day). These may not be representative of real-world use of each product or directly comparable across products.

The health impact assessment in the paper was restricted to cancer, cardiovascular diseases and respiratory diseases, so other health risks cannot be evaluated from this study. Neither can this study predict long-term morbidity or mortality from using either product.


Overview
This month we include four articles, three from teams in the USA and the fourth from our colleagues at the University of Auckland in New Zealand.

The first paper examines data from five waves of the National Youth Tobacco Survey in the USA, examining trends in ever use and past 30 day use of e-cigarettes and a variety of tobacco products in 11-18 year olds. This analysis refers to e-cigarettes as a form of tobacco, which is a definition adopted in the USA but not other countries (because e-cigarettes do not contain tobacco). However, setting aside this difference in terminology, some clear patterns emerge. Experimentation (ever use) and recent (past 30 day) use of e-cigarettes rose consistently between 2011 and 2015. In the earlier years in this study, use was more common amongst males (who made up 74.7% of past 30 day users.
in 2011) but by 2015, recent use of e-cigarettes was fairly similar for males and females (59.8% males).

Experimentation and recent use of e-cigarettes were much more common among young people who had also recently smoked or used oral tobacco products or hookah. However, young people who had never used tobacco had tried e-cigarettes, 13.5% of females and 15% of males in 2015 who were past 30 day users of e-cigarettes had previously never used any other tobacco product. Over the same period, past month cigarette smoking rates fell significantly which is a positive finding and reflects other published data over the same period from the USA. The authors looked for any relationship between e-cigarette use and quitting behaviour in young people, but couldn’t find any. Their analysis found no association between past month e-cigarette use and quit attempts or considering quitting in past month smokers. However, other research has shown that most young people who report using an e-cigarette in the past 30 days vape only on a small number of days within that period, which is unlikely to change smoking behaviour.

The second study in this month’s bulletin looks at nicotine dependence amongst people who either vape or smoke (but don’t do both) in the USA. Data are drawn from Wave 1 of the PATH study which is nationally representative. In this analysis a relatively small sample (n=156) of vapers were included and a larger sample (n=3430) of smokers. The article is interesting because one of the concerns smokers express about vaping is that they would be ‘swapping one addiction for another’. This is a complex issue to explain in terms of addressing those fears (i.e. cigarettes contain nicotine, and some e-cigarettes also contain nicotine but it is not the nicotine that kills smokers, for example) but this article touches on some relevant data. Overall, it brings together a range of measures that are indicative of dependence including: whether users perceive themselves to be addicted to the product they use; have cravings to use the product; find it easy or difficult to avoid using it; and how quickly they use the product after waking. While the study has a range of limitations, highlighted by the authors and in our summary above, it does show a consistent pattern. Daily e-cigarette users were less dependent on vaping than daily smokers were on smoking. Other studies using different measures have drawn similar conclusions. These patterns may change as devices evolve, but providing information about relative differences in the ‘addictiveness’ of smoking and vaping may be important to include when communicating to smokers or the public about e-cigarettes.

E-cigarette use in pregnancy is the focus of this month’s third article. This is an under-researched area, but a number of surveys and qualitative studies are now available and this article provides the latest example. It involved just over 100 pregnant smokers in the USA who were participating in smoking cessation trial that did not involve e-cigarettes. The researchers took the opportunity to ask these women about vaping in a simple survey. Just over half the women had tried e-cigarettes prior to taking part in the study. 14% had used them during pregnancy, primarily to stop smoking. These women had a higher number of previous attempts to stop smoking than others in the study and also were more likely to have a history of drug or alcohol use. The authors suggest that these two factors are indicative of women who may find it more difficult to stop smoking. What is perhaps most interesting about this article is the thoughtful discussion on future research priorities in this area. The authors point out that given the acceptability of e-cigarettes amongst pregnant women who find it hard to quit, and the fact that stop smoking medications are either not licensed for use in pregnancy (varenicline, bupropion) or have not been shown to be effective (NRT), e-cigarettes could be useful for smoking cessation in pregnancy. While also pointing out the unknowns and possible risks, they recommend future trials on this topic.

The final study this month, from New Zealand, involves a comparative risk assessment of e-cigarettes and tobacco cigarettes. Previous studies that have made these comparisons have been
based on expert views examining the literature. This article extends that approach by explicitly estimating hazard levels from exposure to various toxicants and evaluates overall health risks by comparing exposure levels with international guidelines. The main focus was on toxicants such as acrolein, acetaldehyde, carbon monoxide and others present in tobacco cigarettes and the extent to which they are present in e-cigarette products. The authors aimed to answer two questions – Are e-cigarettes safe to use? Are e-cigarettes safer to use than cigarettes?

The study found that there were two toxicants (acrolein and propylene glycol) present in the emissions from e-cigarettes in the study that resulted in average exposure levels higher than guideline levels. At maximum exposure levels there were four toxicants identified in e-cigarettes that were higher than guideline levels. However, there were far more toxicants in tobacco cigarettes with both average and maximum exposure levels above guidelines. The authors conclude that the use of e-cigarettes presents a lower risk to health than smoking and that, overall, e-cigarette use is likely to present a low health risk to users. However, they also point to variability amongst e-cigarette products which results in varying toxicant levels in emissions. The authors point to the need both for regulations on e-cigarette manufacturing and quality and further research to develop standardised methods for assessing any toxicant exposure from e-cigarettes.

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

- Other Tobacco Product Use Among Sexual Minority Young Adult Bar Patrons.
- Initiation of Electronic Cigarette Use by Age Among Youth in the U.S.
- The effects of electronic cigarette aerosol exposure on inflammation and lung function in mice.
- Electronic cigarette use was not associated with quitting of conventional cigarettes in youth smokers.
- Bans on electronic cigarette sales to minors and smoking among high school students.
- Elucidating challenges that electronic cigarettes pose to tobacco control in Asia: a population-based national survey in Taiwan.
- Effects of chronic inhalation of electronic cigarettes containing nicotine on glial glutamate transporters and α-7 nicotinic acetylcholine receptor in female CD-1 mice.
- Public reactions to e-cigarette regulations on Twitter: a text mining analysis.
- Negative Affect in At-Risk Youth: Outcome Expectancies Mediate Relations With Both Regular and Electronic Cigarette Use.
- Are Cigarette Smokers’, E-Cigarette Users’, and Dual-Users’ Health Risk Beliefs and Responses to Advertising Influenced by Addiction Warnings and Product Type?
- Exposure to advertising and perception, interest, and use of e-cigarettes among adolescents: findings from the US National Youth Tobacco Survey.
- Obesity and Cigarette Smoking: Extending the Link to E-cigarette/Vaping Use.
- Smokers making a quit attempt using e-cigarettes with or without nicotine or prescription nicotine replacement therapy: Impact on cardiovascular function (ISME-NRT) - a study protocol.
• Phenotypical changes in a differentiating immortalized bronchial epithelial cell line after exposure to mainstream cigarette smoke and e-cigarette vapor.
• Type of E-Cigarette Device Used among Adolescents and Young Adults: Findings from a pooled analysis of 8 studies of 2,166 vapers.
• Availability, price, and packaging of electronic cigarettes and e-liquids in Guatemala City retailers.
• Vape Shop Density and Socio-demographic Disparities: A U.S. Census Tract Analysis.
• E-cigarette use of young adults motivations and associations with combustible cigarette alcohol, marijuana, and other illicit drugs.
• Electronic nicotine delivery system (ENDS) use during smoking cessation: a qualitative study of 40 Oklahoma quitline callers.
• The Scottish adolescent e-cigarette user: profiling from the Scottish Schools Adolescent Lifestyle and Substance Use Survey (SALSUS).
• Prevalence of e-cigarette use among adolescents in 13 Eastern European towns and cities.
• Adolescents' behavioral and neural responses to e-cigarette advertising.
• Correlates of e-cigarette ad awareness and likeability in U.S. young adults.
• Aldehyde Detection in Electronic Cigarette Aerosols.
• E-cigarette Use, Cigarette Smoking, Dual Use, and Problem Behaviors Among U.S. Adolescents: Results From a National Survey.
• Flavored E-cigarette Liquids Reduce Proliferation and Viability in the CALU3 Airway Epithelial Cell Line.
• Claims in vapour device (e-cigarette) regulation: A Narrative Policy Framework analysis.
• Elements including metals in the atomizer and aerosol of disposable electronic cigarettes and electronic hookahs.
• The Southwest UK Burns Network (SWUK) experience of electronic cigarette explosions and review of literature.
• Nicotine, aerosol particles, carbonyls and volatile organic compounds in tobacco- and menthol-flavored e-cigarettes.
• Perceived Harms and Social Norms in the Use of Electronic Cigarettes and Smokeless Tobacco.
• MicroRNA expression profiling defines the impact of electronic cigarettes on human airway epithelial cells.
• Distinctive role of opinion leaders in the social networks of school adolescents: an investigation of e-cigarette use.
• A comparative study of electronic cigarette vapor extracts on airway-related cell lines in vitro.
• Temporal structure/function variation in cultured differentiated human nasal epithelium associated with acute single exposure to tobacco smoke or E-cigarette vapor.
• Use of Electronic Cigarettes Leads to Significant Beta2-Nicotinic Acetylcholine Receptor Occupancy: Evidence From a PET Imaging Study.
• A Prototypical First-Generation Electronic Cigarette Does Not Reduce Reports of Tobacco Urges or Withdrawal Symptoms among Cigarette Smokers.
• Flavored E-cigarette Liquids and Cinnamaldehyde Impair Respiratory Innate Immune Cell Function.
- **Point-of-Sale E-cigarette Advertising Among Tobacco Stores.**
- **Advertising exposure and use of e-cigarettes among female current and former tobacco users of childbearing age.**
- **Content analysis of age verification, purchase and delivery methods of internet e-cigarette vendors, 2013 and 2014.**

**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 UK ECRF 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 and Kathryn Angus 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.*