Electronic Cigarette Research Briefing – February 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.

1. Nicotine, Carcinogen, and Toxin Exposure in Long-Term E-Cigarette and Nicotine Replacement Therapy Users: A Cross-sectional Study

- **Study aims**
  This UK study was the first study to measure the levels of key toxicants in long-term (average of around 17 months use) e-cigarette users compared to NRT users, smokers and dual users of cigarettes with e-cigarettes or NRT. By taking saliva and urine samples from 181 participants, metabolites of nicotine, tobacco-specific nitrosamines (TSNAs) and volatile organic compounds (VOCs) were measured.

- **Key findings**
  Measurements of urinary or salivary biomarkers of nicotine intake were broadly similar across groups.

  E-cigarette users had much lower metabolite levels of TSNAs in their body than the cigarette-only group. Similarly, many VOC biomarkers were found to be lower in e-cigarette users compared to smokers. The measured levels of toxicants were also broadly similar between e-cigarette users and NRT users, who acted as a control group in this study.
The toxicants measured were lower in exclusive e-cigarette or NRT users compared to dual users of cigarettes with e-cigarettes or NRT. Dual user levels were broadly similar to smoking only levels.

- **Limitations**
  The study purposively recruited participants into a relatively small sample of 36-37 people per group, and they may not be entirely representative of the user community or directly comparable across groups. Participants were recruited through diverse media, but the sample may reflect self-selection to some extent.

  There was no control group of non-smokers or non-vapers, so no conclusions can be drawn in comparison to toxicant levels in the general population. There was also no control for passive smoking or other potential sources of toxicants.

  The study did not select participants based on product, device, liquid or flavour used and therefore exposures were not compared across these characteristics.

  There are no comparisons within groups of different product usage patterns and the effect on exposure levels.

  This study measured the levels of toxicants, not actual harm caused by using the products.


2. **Cross-sectional study examining the prevalence, correlates and sequencing of electronic cigarette and tobacco use among 11-16-year olds in schools in Wales**

- **Study aims**
  This UK study is the largest to date in the UK to examine the prevalence and frequency of e-cigarette use among 11-16 year olds. Data was produced from a 2015 cross-sectional survey of school students (n = 32,479) across 87 secondary school in Wales.

  The study examined the associations of e-cigarette use with sociodemographic characteristics and with use of other substances (tobacco, alcohol, cannabis, mephedrone and laughing gas). It also looked to understand pathways into regular use of e-cigarettes or cigarettes by assessing what was tried first in those who had tried both.

- **Key findings**
  Students were nearly twice as likely to have ever used e-cigarettes (18.5%) than ever smoked (10.5%). At 15-16 years old, these numbers reached 37.3% and 26.5% respectively.

  But fewer students (2.7%) used an e-cigarette at least weekly than smoked at least weekly (3.3%). At 15-16 years old, these figures rose to 5.7% and 8.8% respectively.

  Only 0.5% of never smokers reported regular use of e-cigarettes. The majority (59%) of frequent smokers aged 15-16 regularly used e-cigarettes.
Ever smokers, alcohol drinkers, cannabis, mephedrone and laughing gas users were all significantly more likely to have tried e-cigarettes or used them at least occasionally.

Regular use of e-cigarettes was more prevalent in people from ethnic minority backgrounds or from poor families. Young males were more likely than young females to have tried an e-cigarette or used them more than once.

Of those that reported both tobacco and e-cigarette use, 66.4% reported that they tried tobacco first. The vast majority of weekly smokers (82.9%) reported that they had tried tobacco first.

- **Limitations**
  The sample was not chosen with the intention of being nationally representative, but comparisons suggest it is directly comparable to previous nationally representative samples.

  This is a retrospective study and all the responses in this survey are self-reported.

  “Occasional use” of e-cigarettes was defined as those that had “tried e-cigarettes more than once”, and used “less than once a week,” therefore including those that may have briefly experimented with e-cigarettes.

  Participants were not asked if they used nicotine-containing liquids in e-cigarettes.

  The study can’t confirm reasons for using e-cigarettes (e.g. to stop smoking), or whether e-cigarette use is affecting the number of regular smokers.


3. **E-Cigarettes and "Dripping" Among High-School Youth**

- **Study aims**
  This US study is the first to evaluate the prevalence rates and reasons for using e-cigarettes for dripping (which involves putting a few drops of e-liquids directly onto the atomizer coil in an e-cigarette and inhaling the produced vapour) among high school students. Students from 8 Connecticut high schools (n = 7,045) completed surveys in 2015, and those who reported e-cigarette use were asked about dripping.

  The study also examined whether dripping behaviour was associated with sex, age, race, number of other tobacco products tried and the frequency of e-cigarette use in the past month.

- **Key findings**
  26.6% of participants surveyed had ever used e-cigarettes. Among ever e-cigarette users that properly filled out the survey, 26.1% reported they had ever used dripping, 48.7% reported that they had never used dripping, and 25.2% did not know.

  Dripping was positively associated with being male (OR = 2.74), being white (OR = 1.84), having tried more tobacco products (OR = 1.34) and using e-cigarettes on a greater number of days in the past month (OR = 1.07). There was no association with age.
The top reasons for dripping were: “produces thicker clouds of vapour” (63.5%), “flavour tastes better” (38.7%), “a stronger throat hit” (27.7%), and “curiosity” (21.6%). 7.6% of students selected “other” and offered reasons such as “friends use it,” “tried it once,” and “don’t know”.

- Limitations

The results in this survey are only from high schools in Connecticut, so do not represent the country or international youth behaviours. Though they did attempt to collect results from a sociodemographically diverse range of schools.

A significant number (42.4%) of the 1,874 participants who said they had tried e-cigarettes were excluded from the survey for not providing complete responses (10.6%) or providing incongruent responses (31.8%). The survey questions were not tested for reliability or validity and a high number (25.2%) of e-cigarette users responded that they did not know if they had participated in dripping.

The study measured ever dripping in ever e-cigarette users, so may include those who only used dripping once or vaped only once. It also did not look at dripping behaviours, such as regularity, or assess the range of devices, liquids, flavours or nicotine content used for dripping.

The question on reasons for dripping provided suggested answers. This may have biased participants to select one of these over a more accurate response (though open-ended responses were also accepted).


- Study aims

This US study used data from the 2004-2014 National Youth Tobacco Survey to assess smoking prevalence and examine whether the decline in adolescent cigarette smoking changed after e-cigarettes entered the US market (around 2007).

They also used their own model of psychosocial predictors of cigarette use (such as ethnicity, living with a smoker, and likelihood of accepting a cigarette from a friend) to examine whether e-cigarette users were likely to smoke cigarettes.

- Key findings

Ever smoking decreased from 40% in 2004 to 22.1% in 2014. Over the same period, current smoking (defined as use on at least one day in the last 30 days) decreased by 15.8% to 6.4%.

There was a continuous linear decline of ever smoking (P = 0.009) and current smoking (P = 0.05) over this period, with no significant slope changes after the introduction of e-cigarettes in 2009.
Total ever-use of cigarettes or e-cigarettes (including dual use), slightly decreased from 29.8% in 2011 to 28.6% in 2014. But total current use of both products increased from 11.4% to 12.2% over the same period.

While ever and current cigarette smoking declined, there was an increase in e-cigarette ever use (3.3% to 19.9%) and current use (1.1% to 9.4%) between 2011 and 2014.

From 2011 to 2014 the predictive model correctly classified around 70% of ever smokers and around 76% of past-30-day smokers.

The predictive model suggested that only 11.0-23.1% of current e-cigarette only users were likely to be current smokers. While 40.7-52.2% of ever e-cigarette only users were predicted to be ever-smokers.

- **Limitations**

  This self-reported survey had school response rates as low as 75% in 2013 and student response rates as low as 88% in 2004. Up to 10.1% of participants (in 2009 and 2011) were excluded from the study for missing responses. The survey also doesn’t include high school dropouts, who may have higher tobacco use than students.

  Current use of cigarettes and e-cigarettes was defined as those who had used either on at least 1 day of the past 30 days, and may include people who only recently tried these products. The study did not give results examining any association of smoking intensity with e-cigarette use.

  The survey did not ask if students were using nicotine-containing e-cigarettes, so no conclusions can be drawn about e-cigarettes potential contribution to nicotine addiction.

  The cross-sectional nature of the study means they cannot conclude whether e-cigarettes actually caused a change in smoking prevalence or not.

  The psychosocial model used was previously untested, and the test results in this study show it only ever reached around 70-76% accuracy. Any conclusions drawn from this model cannot be confirmed.


**Overview**

This month we have included four studies, two from the UK and two from the USA. The first two are studies published by teams who are members of UKECRF.

The first study was funded by Cancer Research UK and looked at toxicant exposure among long term users of e-cigarettes. This is novel research, as most existing studies have examined the effects of short term exposure either in cell-line or rodent studies or with humans. In this case, the e-cigarette users had been vaping for many months, either as ex-smokers who vape, or as dual users who combine e-cigarettes with tobacco. Urine and saliva samples were compared between these two groups, and also ex-smokers who use Nicotine Replacement Therapy, those who use NRT and smoke, and adults who smoke but don’t use e-cigarettes or NRT. The researchers found that all
groups were exposed to nicotine (not surprising, as all were using a nicotine product) and that levels were broadly similar, suggesting that even among the non-smoking vapers, reasonable levels of nicotine delivery were achieved. This is in contrast to some early studies of vaping where nicotine levels were lower, and suggest that current devices are better at delivering nicotine and that users can titrate levels to fend off withdrawal symptoms. E-cigarette only users and NRT users had significantly lower levels of exposure to toxins and carcinogens related to tobacco. However, levels were not significantly lower in dual users or smokers. This article adds to existing evidence suggesting that e-cigarettes are less harmful than tobacco, but also that if health benefits are to be realised, vapers need to stop smoking all together. The study had a number of limitations acknowledged by the authors but it’s also worth noting that the difference between the number of cigarettes smoked per day between the dual users (11.9) and smokers (13.9) was relatively small which may have contributed to the fact that toxicant exposure was not that different between these two groups. On the other hand, there have been concerns that dual use may actually increase toxicant exposure (compared to smoking alone) and this study did not find that. Many smokers who try to stop with e-cigarettes go through a transition period of dual use. This study suggests that dual use does not confer additional risks, but that smoking cessation remains the priority in terms of reducing harm.

The second study is a cross-sectional survey of 32,479 11-16 year olds in schools in Wales. Questions on ever and regular use of e-cigarettes were included in the survey in 2015 and the article reports associations between use, the characteristics of respondents and use of other substances. Consistent with other UK surveys conducted in the same year, ever use (85.9%) and regular (weekly or more use (20%) of e-cigarettes was highly concentrated amongst young people who had ever smoked. However, there was experimentation amongst never smokers (10.4%) but at least weekly use was very low in this group (0.5%) but higher than in a different survey in Wales in 2013. Regular use of e-cigarettes was higher in young people who also used other substances like cannabis and alcohol. There is another interesting finding somewhat buried in the article, that ex-smokers accounted for an increasing proportion of regular e-cigarette users every year the age of the young people increased, which might suggest that some young smokers are stopping smoking by using e-cigarettes, but this requires further investigation. It is worth noting that the team that led this study have just secured an NIHR grant to examine longer term trends in smoking and vaping amongst UK youth, using this survey and others from Scotland and England. We look forward to the findings of this future study.

This month’s third study also focuses on young people, this time from 8 high schools in Connecticut, USA. It focuses on ‘dripping’ which involves putting a few drops of e-liquids directly onto the atomizer coil in an e-cigarette and inhaling the produced vapour. One in four survey respondents had ever tried an e-cigarette, and amongst these 26% reported that they had tried dripping (with a similar proportion saying they simply did not know). The article is interesting in that it reports on a phenomenon not previously studied and about which we know little or nothing in terms of risks. Having tried dripping was more common amongst young people who were smokers, were male or white and were more frequent users of e-cigarettes. The main reported appeal of dripping was to produce thicker clouds of vapour and more flavour from e-liquids, and one in five also said they tried dripping out of simple curiosity. As we note above, a high proportion of respondents who had tried e-cigarettes were excluded from the survey because of providing incomplete or incongruent responses. There is also a lot of text in the article about nicotine, but the survey didn’t ask if the young people were using nicotine containing e-cigarettes or whether dripping was about obtaining more nicotine. This is important as some of the other reasons for dripping (producing more vapour and throat hit) can be achieved by different concentrations of propylene glycol and vegetable
glycerine in e-liquid, particularly increasing glycerine which involves dilution that may actually reduce nicotine strength. The article leaves a lot of questions which could be examined in future research and it is important to keep monitoring different ways that e-cigarettes are used, particularly as devices evolve.

The fourth study is a secondary analysis of the National Youth Tobacco Surveys cross-sectional surveys from 2004-2014. It used an interrupted time series analysis to examine any change in the decline in smoking amongst young people after e-cigarettes arrived on the US market from around 2007. The focus of the analysis was comparing the 2004-2009 period with 2011-2014. The authors chart the rise in experimentation (ever use) of e-cigarettes from 2011 onwards and found that this did not contribute to an accelerated decline in cigarette smoking. This is a difficult article to follow because of the US classification of e-cigarettes as a tobacco product. E-cigarettes do not contain tobacco, but this classification reflects the US regulatory environment. Thus statements in the article about overall increases in tobacco use amongst youth in the USA include e-cigarettes, which is inaccurate. A key finding from this paper is that use of smoked tobacco in young people continued to decline from 2004-2014 at a steady rate, which is good news for cancer prevention and public health. We can also see that this study didn’t present results for the frequency of e-cigarette use. It’s worth noting that most studies reporting this show that it is rare for non-smokers who only try nicotine products to become regular users.

On a final note, it’s worth taking a quick look at one of the articles listed below which involved a comparison of tweets on the social media site Twitter posted by medical professionals in the UK and USA. The authors reviewed tweets posted by doctors on e-cigarettes between June 2015 and 2016. Overall, they found doctors in the USA were more likely to emphasise any dangers of e-cigarette use by adolescents. In contrast, doctors in the UK were more likely to tweet on the subject of e-cigarettes for smoking cessation. Please feel free to tweet the link to our site where all the UKECRF bulletins (like this one) are stored, available here, so we can keep focusing on the evidence as it grows.

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

- **Identifying Topics for E-Cigarette User-Generated Contents: A Case Study From Multiple Social Media Platforms.**
- **Use of Electronic Cigarettes Among U.S. Adults With Medical Comorbidities.**
- **Electronic cigarettes and indoor air quality: a review of studies using human volunteers.**
- **Secondhand smoke exposure at home among middle and high school students in the United States - does the type of tobacco product matter?**
- **The Association between Sensation Seeking and E-cigarette Use in Texas Young Adults: A Cross-Sectional Study.**
- **Transgender Use of Cigarettes, Cigars, and E-Cigarettes in a National Study.**
- **E-cigarette specialty retailers: Data to assess the association between retail environment and student e-cigarette use.**
- **E-Cigarette Use, Perceptions, and Cigarette Smoking Intentions in a Community Sample of Young Adult Nondaily Cigarette Smokers.**
- **Thermal injury patterns associated with electronic cigarettes.**
- **Trace Metals Derived from Electronic Cigarette (ECIG) Generated Aerosol: Potential Problem of ECIG Devices That Contain Nickel.**
• **E-Cigarette Topics Shared by Medical Professionals: A Comparison of Tweets from the United States and United Kingdom.**
• **Use and Perceived Risk of Electronic Cigarettes Among North Carolina Middle and High School Students.**
• **Adolescent Risk Behaviors and Use of Electronic Vapor Products and Cigarettes.**
• **Factors associated with electronic cigarette use among current cigarette-smoking adolescents in the Republic of Korea.**
• **Electronic Nicotine Delivery Systems and Smoking Cessation in Arkansas, 2014.**
• **Increased Cardiac Sympathetic Activity and Oxidative Stress in Habitual Electronic Cigarette Users: Implications for Cardiovascular Risk.**
• **Subjective experiences at first use of cigarette, e-cigarettes, hookah, and cigar products among Texas adolescents.**
• **Evaluating nicotine dependence levels in e-cigarette users.**
• **E-cigarette use as a predictor of cigarette smoking: results from a 1-year follow-up of a national sample of 12th grade students.**
• **Measuring youth beliefs about the harms of e-cigarettes and smokeless tobacco compared to cigarettes.**
• **Delivery of nicotine aerosol to mice via a modified electronic cigarette device.**

**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 Nikki Smith and Carl Alexander 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._