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.

1. E-cigarette use and associated changes in population smoking cessation: evidence from US current population surveys

- **Study aims**
  This study assessed the relationship between e-cigarette use and smoking cessation in the US population using the largest representative sample of smokers and e-cigarette users available to date (2014-15 Current Population Survey-Tobacco Use Supplement, n = 161,054).

  The study investigated whether e-cigarette users in 2014-15 had higher rates of quit attempts and quit success than non-users. It also compared 2014-15 quit attempt and cessation rates with 2010-11 and earlier, to see if smokers today are quitting at a higher rate.

- **Key findings**
  In 2014-15, 8.5% of US adults had ever tried e-cigarettes and 2.4% were current users. But only 2% of never smokers had ever used an e-cigarette, and only 0.3% of never smokers were current users.

  In 2014-15, smokers that had used e-cigarettes within the past year were more likely to have made a quit attempt than those that had stopped using or had never used an e-cigarette.

They were also more likely to have successfully quit smoking for at least three months than those that had stopped or had never used an e-cigarette.

The overall quit attempt rate in 2014-15 (45.9%) is significantly higher than in any of the other survey waves included.

When splitting those that made quit attempts in 2014-15 into past-year e-cigarette users and non-users, the non-users' quit attempt rate was similar to overall results from previous surveys. While the quit attempt rate among e-cigarette users was significantly higher.

The overall cessation rate in 2014-15 was significantly higher than in previous years. As with quit attempts, there was significantly higher quit success among e-cigarette users, while non-users' success remained similar to results from previous years.

- **Limitations**
  Population trends cannot control for all potential factors that may have led to an increase/decrease in quit attempts and success rate. It is possible that other external factors (e.g. an increase in tobacco tax and national media campaigns) may have contributed to the increasing quit attempts/success rate.

  All data were self-reported and the survey response rates were as low as 54.2% to 64.0% across survey waves.

  The study doesn't compare e-cigarette use to other quit methods (e.g. behavioural support and prescription medication), so cannot demonstrate how effective e-cigarettes are as a smoking cessation method. Similarly, the e-cigarette user population is different to non-users, meaning that e-cigarettes can't be causally associated with higher quit attempts or success without controlling for other influencing factors.

  The study doesn't assess any relationship between e-cigarettes and changes in population smoking prevalence.

Zhu Shu-Hong, Zhuang Yue-Lin, Wong Shiushing, Cummins Sharon E, Tedeschi Gary J. E-cigarette use and associated changes in population smoking cessation: evidence from US current population surveys BMJ 2017; 358 :j3262

2. Prevalence of population smoking cessation by electronic cigarette use status in a national sample of recent smokers.

- **Study aims**
  This US study uses 2014 and 2015 data from the National Health Interview Survey to examine relationships between smoking cessation and e-cigarette use in a group of current and former smokers (n = 15,532). The study population was selected so that all former smokers had quit after 2010, when e-cigarettes were more widely available. The study focuses on patterns of e-cigarette use and any effects on smoking cessation.

- **Key findings**
  The majority of former smokers (58%) hadn't tried e-cigarettes, but daily e-cigarette use was more common in former smokers (10.7%) than current smokers (3.3%).

Over half of daily e-cigarette users (52.2%) had quit smoking, which was a higher prevalence than in any of the other demographics or subgroups examined. After adjustment (for sociodemographics, psychological distress and health insurance status), daily e-cigarette users were around 3 times more likely to have quit smoking than never users (aPR = 3.15, 95% CI: 2.66-3.73). Across all demographics and subgroups analysed, daily e-cigarette use was consistently the strongest predictor of having quit smoking.

However, those that used e-cigarettes on some days or had previously tried an e-cigarette were significantly less likely to be former smokers than never e-cigarette users (aPR = 0.38, 95% CI: 0.32-0.47, and aPR = 0.67, 95% CI: 0.61-0.75 respectively).

- **Limitations**
  The study can't assess whether participants used an e-cigarette to quit smoking. It may be that some e-cigarette users had previously stopped smoking and were using their device to control cravings and prevent relapse. Likewise, it can't examine whether e-cigarette use is more or less effective than any other cessation methods.

  The study didn't control for all factors that may affect smoking cessation e.g. motivation to quit, nicotine dependence, additional support to quit. Neither did it take into account whether participants were using nicotine-containing e-cigarettes or not, or the generation of devices used.

  With no follow-up after the survey, it's not possible to know if the former smokers may have gone on to relapse in future. And by only including those that had quit after 2010, some early e-cigarette adopters may not be included or people who previously quit through other methods.

Daniel P. Giovenco, Cristine D. Delnevo, Prevalence of population smoking cessation by electronic cigarette use status in a national sample of recent smokers, Addictive Behaviors, Volume 76, 2018, Pages 129-134, ISSN 0306-4603, http://dx.doi.org/10.1016/j.addbeh.2017.08.002.

3. Relationship between trying an electronic cigarette and subsequent cigarette experimentation in Scottish adolescents: a cohort study.

- **Study aims**
  This Scottish study uses a prospective cohort survey to examine whether young never smokers in Scotland who have tried an e-cigarette are more likely than those who have not to try a cigarette in the following year. The analysis was restricted to 11-18 year old never smokers (n = 3001/3807 surveyed) from four Scottish secondary schools. Results are from the 2015 and 2016 surveys.

- **Key findings**
  At baseline, 8.6% of never smokers who completed both the initial survey and follow-up had tried an e-cigarette.

  Of those that had tried e-cigarettes at baseline, 40.4% had tried smoking at follow-up. This compares to 12.8% of baseline never e-cigarette users having tried smoking at follow-up.

But, 22.9% of those that tried cigarettes at follow up had previously tried an e-cigarette, compared to 77.1% who had never used an e-cigarette at baseline.

The fully adjusted model showed that having tried an e-cigarette at baseline was significantly associated with trying cigarettes in the following year (OR = 6.64, 95% CI: 3.60-12.26).

Susceptibility to smoking in 2015 was significantly associated with subsequently trying cigarettes (OR = 5.19, 95% CI: 3.74-7.21), as was having a family member who smokes (OR = 1.83, 95% CI: 1.37-2.44), and having "at least some" friends who smoke (OR = 1.51, 95% CI: 1.07-2.14).

Having tried an e-cigarette at baseline had a bigger impact on someone's likelihood of having tried a cigarette at follow-up in those that were not susceptible to smoking at baseline, compared to those that were. Similarly, e-cigarette use at baseline had a bigger impact on people who had no friends who smoked at baseline than those who did have friends who smoked.

- **Limitations**
  This study cannot prove a causal link between e-cigarette use and later smoking. It can only show that those who try e-cigarettes are also likely to try cigarettes. The study was not able to control for all factors that may affect likelihood of trying smoking e.g. susceptibility for other risky behaviours, exposure to smoking in the media or surrounding environment etc.

  Smoking status was defined by a binary variable that included people who have only had "just one or two puffs." Similarly, due to low numbers of regular e-cigarette use, participants were split into ever and never users only for analysis.

  Smoking and e-cigarette use were self-reported, and none of the measures analysed in this study are able to predict regular e-cigarette use or smoking.

  The response rate was 87% at baseline and 70.4% of the original cohort completed the follow-up survey. The schools surveyed were selected based on having different socioeconomic and urban/rural characteristics, but may not be representative of the Scottish population. The study didn't appear to use the latest iteration of the Family Affluence Scale to control for sociodemographic differences.

  The study didn't record what type of e-cigarette or e-liquid was used, and whether participants were using nicotine-containing fluids or not.

Best C, Haseen F, Currie D*, et al.* Relationship between trying an electronic cigarette and subsequent cigarette experimentation in Scottish adolescents: a cohort study. Tobacco Control Published Online First: 22 July 2017. doi: 10.1136/tobaccocontrol-2017-053691

4. Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke.

- **Study aims**
  This UK study uses existing data to compare e-cigarette vapour, heat-not-burn (HNB) tobacco vapour, and nicotine inhalers and tobacco smoke from a range of products, in order to estimate cancer potency from their usage.

  The study uses a novel procedure to compare previously incompatible emissions data sets, and then uses a single variable from multiple individual compounds measured, to assess cancer potency from these devices.

- **Key findings**
  With tobacco smoke cancer potency set as a reference value of 1.0, HNB products had a considerably lower average cancer potency ratio ($2.01x10^{-2}$), e-cigarettes were lower still ($1.81x10^{-3}$), and the nicotine inhaler had the lowest ($1.02x10^{-4}$).

  Compared to breathing ambient air, the excess cancer risk for a lifetime of smoking 15 cigarettes per days was estimated to be $2.4x10^{-2}$, compared to $5.7x10^{-4}$ for 15 HNB sticks per day, $9.5x10^{-5}$ for vaping 30L from e-cigarettes at normal power, and $8.9x10^{-6}$ for inhaling 30L from the nicotine inhaler.

  Compared to the nicotine inhaler, the relative risks for cancer are 11 for e-cigarettes, 64 for HNB and ~2700 for cigarettes.

  E-cigarette cancer potencies were widely ranging. Converting the results from Goniewicz 2014, which assessed the majority of anticipated carcinogens in e-cigarette vapour (including nitrosamines, metals, carbonyls and volatile organic compounds), gave results clustering around ~10^{-3} of the potency of tobacco smoke.

  Higher levels of carbonyls found in some vapours extended the cancer potencies to similar levels to tobacco smoke. These higher levels were mostly associated with coils being subjected to the highest applied voltages. However, there was no consistent relationship between cancer potency and device power at the coil.

  The highest ranked carcinogens in e-cigarette vapour were cadmium and formaldehyde. Cadmium was not detected in all samples, and in others was found to be very close to the blank level.

- **Limitations**
  The study provides an estimate of cancer risk using emissions data from devices, but cannot provide data on what's actually happening in people. Neither has this model been validated to be an accurate representation of risk. Aggregating the effects of individual carcinogens may not equate to overall risk from use or account for different mechanisms e.g. synergistic or antagonistic interactions. The study didn't look at potential harms other than cancer.

  The range of devices and e-liquids tested are not necessarily representative of all devices currently on sale. The Heat Not Burn device was a prototype, so may not exactly represent what's currently available to the public. The emissions data used is also industry funded for the HNB device and some of the cigarette and e-cigarette results. Limitations from these data also apply, and may over/underestimate the risk.

When assessing mean cancer potency and average lifetime cancer risk for e-cigarettes, these include first and second generation devices only. Third generation devices were only used for variable voltage tests. This also meant that higher voltage tests weren't included for the mean cancer potency and lifetime cancer risk results.

Unit risk values were not available for all compounds (e.g. metals), so could not be included, potentially underestimating overall risk. Only the data from the Goniewicz study includes most of the relevant carcinogens for analysis in e-cigarettes.

The high levels of carbonyls under high power usage may not be replicated in real world use.

Unit risk was assumed to be linearly proportional to the dose with no threshold, potentially overestimating the risk. Neither did the study take into account particle size, which may affect overall risk.

Stephens WE. Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke. Tobacco Control Published Online First: 04 August 2017. doi: 10.1136/tobaccocontrol-2017-053808

Overview

In this month's bulletin we include two studies from the US and two from the UK. The first two address the theme of e-cigarette use and smoking cessation, the third youth use of e-cigarettes and tobacco, and the final paper examines the cancer potency of emissions from cigarettes, e-cigarette and heat not burn tobacco.

The first article includes data from the five waves of the nationally-representative CPS-TUS survey in the USA. The authors aimed to examine trends in the use of e-cigarettes and tobacco and any relationship between them at the population level. As in the UK, e-cigarette use in the USA began to be picked up in surveys from around 2010. This analysis compared rates of e-cigarette use and self-reported smoking cessation between a recent CPS-TUS survey (2014-15) and four previous surveys (2001-02, 2003, 2006-07 and 2010-11).

The authors found that during the period when e-cigarette use was rising amongst adult smokers in the USA, there was a significant increase in smoking cessation rates at the population level. The overall smoking cessation rate for the final year's survey included (2014-15) was significantly higher than for all the other survey years including 2010-11. In addition, e-cigarette users (defined as having used an e-cigarette sometime in the past year) were more likely than smokers who hadn't used e-cigarettes to report having made a quit attempt (defined as having stopped smoking for at least 24 hours). They were also more likely to have succeeded in stopping smoking (defined as having stopped smoking for at least three months).

The study didn't attempt to look at whether trends in e-cigarette use were associated with declines in smoking prevalence in the US population. It also relied on weak measures of e-cigarette use and all the data were self-reported. It's also possible that other tobacco control measures (like cigarette prices, use of quitlines/other aids to stop smoking, or media campaigns, for example) might have affected the frequency or success of quit attempts. Despite these and other limitations, the study provides data about any potential relationship between the rise of e-cigarette use by smokers in the USA and smoking cessation at the level of a national population.

The second article this month draws on a different nationally representative survey from the USA, the National Health Interview Survey, and includes combined data from 2014 and 2015. The authors aimed to explore the factors that might have influenced whether cigarette smokers stopped smoking or not, with a focus on e-cigarette use. Before starting the study they had a hypothesis that they set out to test - using e-cigarettes at least daily would be significantly associated with stopping smoking.

The sample included current smokers and former smokers who had quit in 2010 or later. Current smokers were also asked if they'd made at quit attempt in the past year and had managed to avoid smoking for at least one day during that attempt. Questions on e-cigarettes included ever use and how frequent current use was at the time of the survey (resulting in four categories of use: daily; some days; had formerly tried; or had never used an e-cigarette).

The author's analysis estimated adjusted prevalence ratios for having stopped smoking by the four e-cigarette use categories. In doing this they controlled for some of the socio-demographic factors that other studies have found influence who quits smoking and who doesn't. They found that daily users of e-cigarettes were three times more likely to have stopped smoking than those who had never used an e-cigarette. Over half of daily e-cigarette users in the sample had stopped smoking in the past five years. People who used e-cigarettes less frequently, including just on some days, were less likely to have quit. The study has a number of limitations which we have described above, particularly the fact that e-cigarette users may have been vaping for relapse prevention rather than having used an e-cigarette during their successful quit attempt. However, the findings of this American study are similar to previous research from the UK conducted with a much smaller sample that found that daily e-cigarette users (using tank models) were more likely to stop smoking.

Our third article this month focuses on any relationship between trying an e-cigarette and subsequent use of tobacco cigarettes in young people in Scotland. The authors added questions on e-cigarette use to the NIHR funded DISPLAY study that was set up to assess the impact of the point of sale tobacco display ban in shops. This particular article asked young people aged 11-18 questions about smoking and vaping in the early spring of 2015 and followed them up one year later, focusing on participants who had never smoked at baseline.

A small proportion of the sample (8.6%, 183 young people) reported in 2015 that although they had never smoked, they had tried an e-cigarette at least once. One year later, 40% of this group (n=74) reported that they had tried a tobacco cigarette at least once. Amongst those who hadn't tried an e-cigarette when asked in 2015, a smaller proportion (just under 13%, 249 young people) went on to try smoking by one year later. The authors then conducted statistical modelling to try and determine if trying vaping might have contributed to trying smoking or whether other characteristics of the young people who went on to smoke might explain these differences. Even after taking into account susceptibility to smoking, having friends or family who smoke, socio-economic status and other factors, using an e-cigarette first still emerged as a predictor of smoking.

Findings from this study are similar to previous research in the USA, and in last month's bulletin we included a systematic review that summarised the results of this group of studies. All of them, including the new Scottish study, face similar limitations. Some of the most important are that the research can't fully control for the fact that young people who try either smoking or vaping may simply be more likely to experiment with a range of things (including alcohol or drugs, for example) and there may be an element of chance as to whether experimenting with either vaping or smoking comes first for these teens - particularly in countries like the USA and UK where tobacco remains widely available. In addition, 'ever trying' doesn't tell us about any transition to regular use of either e-cigarettes or tobacco. Population level data in both countries shows that smoking rates have

continued to decline in young people at the same time as ever use of e-cigarettes in teenagers has gone up. A useful overview of the challenges of assessing whether there is in fact any 'gateway' between vaping and smoking was published recently.

The final study in this bulletin focuses on assessing the relative harm from cigarettes compared with new nicotine delivery devices. Conducted by a researcher based in Scotland, it examined toxicants in vapour and smoke which can cause cancer, and estimated excess cancer risk over a lifetime from smoking cigarettes, vaping or using heat not burn tobacco compared to using none of these products. The author analysed data available from published studies which included the concentration of carcinogens in cigarettes, a prototype heat not burn device and a range of e-cigarette types, and converted these into comparable units. He also extracted available data on battery voltage and e-cigarette coil resistance. This results in 93 analyses. Comparisons were made with both ambient air and also published data on carcinogen emissions from an NRT inhaler which is licensed as a medicine. Bringing these data together from multiple different sources on this group of products, comparing them, and then assessing cancer potency has not been attempted before.

Put simply, the results suggest that in terms of lifetime cancer risk, this is highest for smoking and significantly lower for any of the other products. Most e-cigarette emissions data suggested a cancer risk from vaping of below 1% that of smoking, but there were some exceptions. Cancer risks from heat not burn were also far lower, at less than 10% of the risks of smoking, but this was based on available data from only one prototype device.

Some of the e-cigarette emissions data showed higher levels of carcinogenic emissions. This was mostly due to the presence of carbonyls when device settings involved a high level of power being delivered to the atomiser coil. This excess power can be avoided and the author points to the need for increased user awareness of these conditions (which might, for example, result in the unpleasant 'dry puff' phenomenon which vapers can avoid by not overheating the coil) and user involvement in reducing risk. As the approach taken in this research is novel, the author also describes a wide range of limitations in the data. He also suggests lines of inquiry for future research, including more research on particle sizes from e-cigarette emissions, and studies focusing on the relative risks of smoking and vaping using similar methods to this article, but applied to cardiovascular and respiratory diseases.

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

- Risk Factors for Youth E-Cigarette "Vape Trick" Behavior.
- Second-hand smoke generated by combustion and electronic smoking devices used in real scenarios: Ultrafine particle pollution and age-related dose assessment.
- Patterns of and reasons for electronic cigarette use in primary care patients.
- Considerations and Future Research Directions for E-Cigarette Warnings-Findings from Expert Interviews.
- Transport phenomena governing nicotine emissions from electronic cigarettes: model formulation and experimental investigation.
- Impact of e-liquid flavors on nicotine intake and pharmacology of e-cigarettes.

- The association between electronic-cigarette use and self-reported oral symptoms including cracked or broken teeth and tongue and/or inside-cheek pain among adolescents: A cross-sectional study.
- The Experimental Tobacco Marketplace II: Substitutability and sex effects in dual electronic cigarette and conventional cigarette users.
- Current Use of E-Cigarettes and Conventional Cigarettes Among US High School Students in Urban and Rural Locations: 2014 National Youth Tobacco Survey.
- E-cigarette awareness, perceived harmfulness, and ever use among U.S. adults.
- Social Profile of Middle School-Aged Adolescents Who Use Electronic Cigarettes: Implications for Primary Prevention.
- Family Physicians' Perceptions of Electronic Cigarettes in Tobacco Use Counseling.
- Online Vape Shop Customers Who Use E-Cigarettes Report Abstinence from Smoking and Improved Quality of Life, But a Substantial Minority Still Have Vaping-Related Health Concerns.
- Electronic Cigarette Use Among Counseled Tobacco Users Hospitalized in 2015.
- Sequential determination of nickel and cadmium in tobacco, molasses and refill solutions for e-cigarettes samples by molecular fluorescence.
- [Do electronic cigarettes increase the risk of smoking among adolescents and young adults?]
- Susceptibility to cigarette smoking among middle and high school e-cigarette users in Canada.
- Use of electronic cigarettes in public and private settings in Barcelona (Spain).
- The effect of e-cigarette warning labels on college students' perception of e-cigarettes and intention to use e-cigarettes.
- Assessing the Association Between E-Cigarette Use and Exposure to Social Media in College Students: A Cross-Sectional Study.
- Electronic Nicotine Delivery Systems (E-cigarette/Vape) use and Co-Occurring Health-Risk Behaviors Among an Ethnically Diverse Sample of Young Adults.
- Knowledge, attitudes and beliefs towards e-cigarettes among e-cigarette users and stop smoking advisors in South East England: a qualitative study.

- Emissions from Electronic Cigarettes: Assessing Vapers' Intake of Toxic Compounds, Secondhand Exposures, and the Associated Health Impacts.
- Tobacco Marketing, E-cigarette Susceptibility, and Perceptions among Adults.
- Flavored e-cigarette liquids reduce proliferation and viability in the CALU3 airway epithelial cell line.
- The effects of electronic cigarette aerosol exposure on inflammation and lung function in mice.
- A Device-Independent Evaluation of Carbonyl Emissions from Heated Electronic Cigarette Solvents.
- Electronic Cigarettes and Awareness of Their Health Effects.
- Tobacco and nicotine delivery product use in a national sample of pregnant women.
- Gateway effects and electronic cigarettes.
- E-Liquid Autofluorescence can be used as a Marker of Vaping Deposition and Third-Hand Vape Exposure.
- Then and now: Consumption and dependence in e-cigarette users who formerly smoked cigarettes.

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 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.