

Electronic cigarette research briefing – October 2016

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. Flavourings significantly affect inhalation toxicity of aerosol generated from electronic nicotine delivery systems (ENDS)

- Study aims**

This US study compared the effects of aerosols from different electronic nicotine delivery systems (ENDS), tobacco cigarette smoke and air on human bronchial epithelial cells in vitro. Different aspects of ENDS were explored, including device type, nicotine carrier, nicotine concentration, output voltage and flavour. Changes in cell viability, metabolic activity and levels of inflammatory mediators released were assessed.

- Key findings**

Exposure to ENDS aerosol generally resulted in decreased metabolic activity and cell viability and increased release of inflammatory mediators compared with air controls but cigarette smoke had a greater adverse impact than most of the ENDS products tested.

There was great variability across different ENDS products, for example the impact of aerosol from disposable and rechargeable products did not have a significantly different impact on cell viability to the air control however the tank style product was not significantly different to a cigarette.

Increasing battery output voltage resulted in significantly higher adverse outcomes across all measures. Different flavouring additives were found to significantly affect the potential toxicity of ENDS, with a strawberry-flavoured product showing the highest cytotoxicity.

Increasing the nicotine concentration did not have a significant cytotoxic effect on cells compared to the air control, but did induce the release of inflammatory cytokines. All tested nicotine carriers were significantly less toxic to cells than smoke from tobacco cigarettes.

- Limitations**

This study looks at cells directly exposed to aerosol (generated by a machine) in vitro so it's not clear how closely this could represent impact in users. A potentially unrealistic exposure time and intensity of three-second puffs every thirty seconds for thirty minutes was used.

This was chosen as this was the minimum exposure in which there were significant differences between ENDS aerosol and the air control.

This study did not look at which specific flavouring compounds caused the cytotoxicity and release of inflammatory mediators. Only one ENDS liquid product was tested for each flavour name (e.g. strawberry), so may not account for chemical differences between different products with the same flavour.

Leigh NJ, Lawton RI, Hershberger PA, Goniewicz ML. Flavourings significantly affect inhalation toxicity of aerosol generated from electronic nicotine delivery systems (ENDS). *Tob Control* 2016. pii: tobaccocontrol-2016-053205. doi: 10.1136/tobaccocontrol-2016-053205.

2. [Long-term e-cigarette use and smoking cessation: a longitudinal study with US population](#)

- **Study aims**

This longitudinal US study used a nationally representative sample of 2028 adult smokers to examine the effects of long-term e-cigarette use compared to short-term use and non-use. Participants were asked about e-cigarette use and quitting intentions and experiences in 2012 and again in 2014.

Participants were labelled as long-term e-cigarette users if they used e-cigarettes at both time points and short-term users if they were using at only one time point. Successful quitting was defined as not smoking for at least 3 months. The follow-up survey also asked about usage of approved cessation pharmacotherapies and beliefs on e-cigarette safety.

- **Key findings**

Long-term e-cigarette users had a significantly higher quit attempt rate (72.6%), than non-users (45.5%) and short-term users (53.8%).

Long-term users were significantly more likely to quit smoking successfully than non-users (OR=4.14), whilst quit success was not significantly different between short-term users and non-users.

Long-term e-cigarette users were more likely to believe that e-cigarettes are less harmful than cigarettes compared to short-term users, who in turn were more likely to believe that than non-users. Non-users generally held more negative beliefs about e-cigarettes than users did.

Overall more quit attempts were found to be aided by e-cigarettes than pharmacotherapy.

- **Limitations**

Long-term e-cigarette use was considered as those who used e-cigarettes in 2012 and in follow-up in 2014 rather than asking about prior use, between these time point or reflecting intensity.

Intention to quit was controlled for, however, long-term e-cigarette users may have different attitudes towards and experiences of trying to stop smoking.

The short-term use group was made up of those who used e-cigarettes only at baseline or only at follow-up. The study combined these sub-groups and doesn't assess how long they had been using e-cigarettes for.

Zhuang Y, Cummins SE, Sun JY, Zhu S. Long-term e-cigarette use and smoking cessation: a longitudinal study with US population. *Tob Control* 2016;25:i90-i95 doi:10.1136/tobaccocontrol-2016-053096.

[3. Association Between Electronic Cigarette Marketing Near Schools and E-cigarette Use Among Youth.](#)

- **Study aims**

This US study explored whether there was an association between e-cigarette availability and promotion in tobacco retailers near schools and e-cigarette use in pupils. Results from the representative New Jersey Youth Tobacco Survey of nearly 4,000 students from 41 schools in 2014 were compared to an audit conducted at tobacco retailers in a half-mile radius. Demographic characteristics were taken into account and also the e-cigarette availability and promotion in comparison to tobacco.

- **Key findings**

24.1% of New Jersey high school students had ever tried an e-cigarette and 12.1% had used one in the last month. E-cigarettes were available in 57.7% of tobacco retailers and 32% had some e-cigarette advertising. The mean number of e-cigarette retailers near each school was 2.7, ranging from 0 – 16, and there were 6.4 e-cigarette adverts.

E-cigarette retailer density was linked to ever e-cigarette use, but advertisement volume was not. The association was stronger for past-month e-cigarette use; for every additional e-cigarette retailer within a half-mile of a school, the probability of a student at that school being a past-month e-cigarette user increased by 4% and for every additional e-cigarette advertisement, the probability of past-month e-cigarette use increased by 1%.

When density was weighted to take into account the proportion of tobacco retailers selling and advertising e-cigarettes, the association between e-cigarette retail measures and use was stronger.

- **Limitations**

This study was limited to the retail environment around schools and does not capture other exposure to e-cigarette advertising including online, print or billboards as well as other possible retail exposure e.g. near their home. Tobacco retailers were identified through the retail register and researchers also looked online for any specialist vape shops however none were identified near any of the schools. It's not clear whether any other shops could be selling e-cigarettes nearby.

Frequency of e-cigarette use and type of e-cigarette used (e.g. nicotine or non-nicotine) was not included. Prevalence ratios were close to 1 in all models for association between e-cigarette retail environment and e-cigarette use, suggesting any impact is small.

Giovenco DP, Casseus M, Duncan DT, Coups EJ, Lewis MJ, Delnevo CD. Association Between Electronic Cigarette Marketing Near Schools and E-cigarette Use Among Youth. *J Adolesc Health*. 2016. pii: S1054-139X(16)30249-X. doi: 10.1016/j.jadohealth.2016.08.007.

[4. Adolescent Awareness and Use of Electronic Cigarettes: A Review of Emerging Trends and Findings.](#)

- **Study aims**

This UK review summarises worldwide reports of e-cigarette awareness and use in under 18s from January 2014 - January 2016, to complement previous reviews which cover papers published before this time. Use was separated into ever use, current (reported past 30 day use) and regular use.

- **Key findings**

Awareness of e-cigarettes is almost complete, varying between up to 90.1% in the United States and 76.6% in Canada, with the UK at 83.2%. Awareness has increased over time.

Ever use was highest in Romania (38.5%) and lowest in Germany (4.7%), with UK results at 8.2% and 12.3% and US between 6.5% and 31%. Past 30 day use was lower at 2-14% in the US and very low in Hong Kong at 1.1%. Regular use was again lower, at 1.5% in the UK (not asked in the US). Regular use was 24% in Switzerland but this included both “regular use” and used “several times”.

Only one study reported why awareness may have increased, finding that 53.2% of adolescents heard about e-cigarettes from TV ads. Two studies looked at why adolescents might use e-cigarettes and found that a higher proportion of users viewed e-cigarettes as less harmful than tobacco.

When surveys have asked if the e-cigarettes used contain nicotine, prevalence of nicotine containing e-cigarettes tends to be lower and use of nicotine-containing e-cigarettes is more likely in tobacco smokers. A significant positive association was found between e-cigarette use and tobacco use but the directionality was not explored. Recent tobacco use trends in the US show a decline in tobacco use in adolescents.

- **Limitations**

The review is limited to the data available. 22 relevant studies were identified and there are many countries in which studies have not been conducted. The surveys have been cross-sectional rather than longitudinal and measures have been inconsistent, they rarely ask about frequency of use or whether the e-cigarettes used contain nicotine. Most studies did not explore regulatory or cultural environments which could have influenced these results or the relationship with tobacco smoking trends.

Greenhill R, Dawkins L, Notley C, Finn MD, Turner JJ. Adolescent Awareness and Use of Electronic Cigarettes: A Review of Emerging Trends and Findings. *J Adolesc Health*. 2016. pii: S1054-139X(16)30244-0. doi: 10.1016/j.jadohealth.2016.08.005. [Epub ahead of print]

5. Perceptions of emerging tobacco products and nicotine replacement therapy among pregnant women and women planning a pregnancy.

- **Study aims**

This American study explored perceptions of NRT and other alternatives to cigarettes (including snus, electronic nicotine delivery devices (ENDS) and dissolvables) in pregnant women (quitters and those currently smoking) or women planning to become pregnant in the next year. Focus groups were conducted in autumn 2013 with a total of 102 women in four US cities.

- **Key findings**

Participants were more familiar with ENDS and NRT than snus and dissolvables and had heard about them through advertising, family/friend use and personal past or current use.

ENDS seemed the most appealing products in terms of appearance. Other benefits mentioned were price compared to tobacco, no ash or unpleasant odours, option to use in smoke-free areas, appealing flavours, help to stop smoking and desirable similarities to cigarettes (the hand-to-mouth action and exhalation). Some mentioned ENDS as less harmful than cigarettes but others worried about excessive use. In contrast, NRT was seen as more medicinal, ineffective and with bad taste or side effects and reactions to snus and dissolvables were mixed. Some participants felt there was a stigma associated with smoking in pregnancy and that the discreet nature of snus and dissolvables could be exploited to avoid this.

Some pregnant smokers were considering trying to switch to ENDS but others wanted to quit cold turkey. There were concerns raised about the potential for overdosing with NRT and most women felt it was better to try and quit cold turkey than use NRT. Most women thought all products have at least some risks and some thought snus and/or dissolvables might be more harmful than cigarettes.

Some women expressed an intention to try a different product after delivery.

- **Limitations**

This was a convenience rather than representative sample, recruited in specific areas in the US so results cannot be generalised. Focus groups were conducted three years ago so results may be different now. It's not possible from this work to know how the reported perceptions translate into behaviours throughout pregnancy.

It's not clear which of the identified themes were developed *a priori* or whether any unexpected themes were explored or emergent codes used.

England LJ, Tong VT, Koblitz A, Kish-Doto J, Lynch MM, Southwell BG. Perceptions of emerging tobacco products and nicotine replacement therapy among pregnant women and women planning a pregnancy. *Prev Med Rep.* 2016; 4:481-5. doi: 10.1016/j.pmedr.2016.09.002. eCollection 2016.

Overview

This month our search identified a large number of studies, indicating that the literature on e-cigarettes continues to grow at a rapid pace. We've selected five papers for October, four by authors based in the USA and one by a British team which includes UKECRF members.

The first paper is a cell line study from an experienced team very active in e-cigarette research. Previous cell line studies have been criticised for not comparing how cells respond to e-cigarette vapour (aerosol) with tobacco smoke but this study does so and also includes cells (taken from the lining of human lungs) exposed only to air. The researchers looked at whether cells survived, metabolic activity and signs of inflammation. The worst results for all three types of outcomes were seen when cells were exposed to tobacco smoke, perhaps not surprisingly. However, compared to air alone, cells that were exposed to the vapour from e-cigarette products were less likely to survive, had less metabolic activity and showed signs of inflammation. The team used vapour from a variety of types of e-cigarettes and different e-liquid flavours and found a lot of variation in outcomes. Later

generation e-cigarette product vapour appeared more damaging in terms of cell life than vapour from first generation products, and some flavours - particularly the strawberry flavour tested - appeared more damaging to cells. As the authors point out, these results are useful for a number of reasons. First, they show that it is really not appropriate to treat e-cigarettes as a single product class when the devices are so variable. Secondly, they suggest that elements of product design (voltage and flavours) can affect the safety or any risks of using e-cigarettes. These product design features are modifiable either by user choice or regulation. The study faces the usual limitations of cell line studies, such as exposure regimes which may not always accurately reflect how the products are used, and questions about translation to humans, for example. However, the study provides useful data for those interested in better understanding of any risks from e-cigarette use, while also acknowledging that, consistent with previous studies, these risks are present at a lower level than for tobacco.

The second paper reports results from a longitudinal study with smokers conducted in the USA. It compared longer term use of e-cigarettes with no use or short term use. Questions about e-cigarette use, intentions to quit and subsequent smoking cessation were asked first in 2012 and then two years later. Longer term use involved reporting e-cigarette use at both baseline and follow up, and short term use at only one time point. Participants who used e-cigarettes over the longer term were significantly more likely to have stopped smoking for at least 3 months (72.6%) compared with short term users (53.8%) and smokers who did not use e-cigarettes (45.5%). More quit attempts were reported by smokers who had used e-cigarettes than licensed stop smoking medications. The study had a number of limitations with the authors themselves acknowledge and which we've highlighted in the summary above. However, this study adds to [existing literature](#) that frequency and duration of use may be relevant to any success in stopping smoking when using e-cigarettes.

The third study builds on previous research that has found an association between the density of tobacco retail outlets near schools, awareness of point of sale tobacco marketing and tobacco use amongst teenagers. The researchers asked similar questions but related to e-cigarette availability and point of sale e-cigarette marketing using a survey of pupils in 41 schools in New Jersey, USA. They found that the density of e-cigarette retailers near schools was associated with pupils ever trying an e-cigarette or using one recently (in the past 30 days) but links between point of sale advertising exposure and e-cigarette use were less strong. However, these exposures were not as important a predictor of e-cigarette use as smoking status. Ever e-cigarette use was 6 times higher amongst pupils who had used at least one tobacco product compared to never smokers. An interesting finding from the study was that the weighted density and advertising measures found stronger associations than unadjusted measures. As the authors point out, this means the promotion or availability of e-cigarettes relative to other tobacco products may be important in terms of which products teenagers choose to use. This is an interesting area for future research, particularly if tobacco retailer density and tobacco promotion can be reduced in order to support ongoing declines in youth tobacco use.

A review of papers reporting e-cigarette awareness and use in young people under the age of 18 is the fourth paper in this month's bulletin. Conducted by colleagues from three UK Universities, it identified 22 studies (21 cross-sectional, 1 cohort) published between 2014 and 2016. This paper contains a useful synthesis of the evidence and also highlights a number of areas for future research. First, it demonstrates that in the countries where these studies have been conducted, almost all

young people are aware of e-cigarettes. This may suggest that including an awareness question at least in developed countries is no longer an essential survey measure. Secondly, during the period covered by the studies youth experimentation with e-cigarettes continued to rise but regular use, where assessed, was far lower than reported rates of ever use. This underlines the need to assess different patterns of use in youth studies. It also shows that where measures are comparable, levels of e-cigarette use amongst young people do vary significantly between countries, with ever use as high as 38.5% in one Romanian study and as low as 4.7% in one study in Germany. Thirdly, most studies did not ask young people about whether they were using an e-cigarette product that contained nicotine or not. This is an important question to include, although there are likely to be limitations with recall and also awareness. Finally, the authors point to priorities for future research with young people, including longitudinal studies that examine relationships between e-cigarette use and tobacco use, and qualitative studies examining young people's views in more depth. On this latter point, UKERC members are conducting studies with young people using qualitative methods, funded by CRUK and we look forward to reading the results of this research when available.

Finally we include a fairly large qualitative study conducted with pregnant women or women planning a pregnancy in the USA. We chose this paper because e-cigarette use in pregnancy is a topic of considerable current policy and practice interest in the UK and elsewhere, but to date very few studies have been conducted. The current paper focused not just on e-cigarettes, but views regarding NRT, snus and dissolvables (tobacco pressed into small tablets, strips or sticks). 102 women took part in 15 focus groups in a number of US cities. 32 women were pregnant smokers, 27 were pregnant ex-smokers and 42 were smokers planning to become pregnant. The researchers were interested in how women perceive non-combustible tobacco and nicotine products and any health risks associated with using these products in pregnancy. Unfortunately, the paper did not report the number of women who had used or were using e-cigarettes but instead created a category of 'other tobacco products' (e-cigarettes, snus, chewing tobacco and hookah) and found that 28% of pregnant smokers, 19% of pregnant ex-smokers and 47% of smokers planning a pregnancy used these products. Overall in relation to views on e-cigarettes, participants regarded them as safer than tobacco cigarettes and that their use even during pregnancy could have advantages such as lower cost, appealing flavours, ability to be used in some smokefree areas, and could help with stopping smoking. However they were concerned about longer term use of e-cigarettes. NRT was not particularly positively perceived and women questioned its efficacy as a cessation aid and were concerned about any side-effects or indeed safety during pregnancy. Overall, despite most participants being smokers, women felt that use of any tobacco product, e-cigarettes or NRT could be harmful during pregnancy. These results perhaps need to be framed in the context of the country where the research was conducted. NRT is available for use in pregnancy in the USA but far less accepted than in the UK and can only be provided by doctor's prescription. Neither snus nor the dissolvable tobacco products discussed in the study are available in the UK. That said, the findings are interesting and potentially useful in informing the design or analysis of other qualitative research on e-cigarettes with pregnant women.

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

- [Association between Peer Cigarette Smoking and Electronic Cigarette Smoking among Adolescent Nonsmokers: A National Representative Survey.](#)

- [How Is the Effect of Adolescent E-Cigarette Use on Smoking Onset Mediated: A Longitudinal Analysis.](#)
- [Current and former smokers' use of electronic cigarettes for quitting smoking: An exploratory study of adolescents and young adults.](#)
- [Ever-Use and Curiosity About Cigarettes, Cigars, Smokeless Tobacco, and Electronic Cigarettes Among US Middle and High School Students, 2012-2014.](#)
- [Effects of sweet flavorings and nicotine on the appeal and sensory properties of e-cigarettes among young adult vapers: Application of a novel methodology.](#)
- [Basic science of electronic cigarettes: assessment in cell culture and in vivo models.](#)
- [Association between use of flavoured tobacco products and quit behaviours: findings from a cross-sectional survey of US adult tobacco users.](#)
- [Electronic cigarettes increase endothelial progenitor cells in the blood of healthy volunteers.](#)
- [Throat hit in users of the electronic cigarette: An exploratory study.](#)
- [Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users.](#)
- [Flavorings and Perceived Harm and Addictiveness of E-cigarettes among Youth.](#)
- [Week Long Topography Study of Young Adults Using Electronic Cigarettes in Their Natural Environment.](#)
- [Role of sweet and other flavours in liking and disliking of electronic cigarettes.](#)
- [Molecular impact of electronic cigarette aerosol exposure in human bronchial epithelium.](#)
- [Cigarette smoking and electronic cigarette vaping patterns as a function of e-cigarette flavourings.](#)
- [Flavour preferences in youth versus adults: a review.](#)
- [Distribution, quantification and toxicity of cinnamaldehyde in electronic cigarette refill fluids and aerosols.](#)
- [Adolescents' interest in trying flavoured e-cigarettes.](#)
- [Leading-Brand Advertisement of Quitting Smoking Benefits for E-Cigarettes.](#)
- [How do consumers perceive differences in risk across nicotine products? A review of relative risk perceptions across smokeless tobacco, e-cigarettes, nicotine replacement therapy and combustible cigarettes.](#)
- [Use of and reasons for using multiple other tobacco products in daily and nondaily smokers: Associations with cigarette consumption and nicotine dependence.](#)
- [Vaping on Instagram: cloud chasing, hand checks and product placement.](#)
- [E-cigarette use in adults: a qualitative study of users' perceptions and future use intentions.](#)

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 UKERCRC 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.