Electronic Cigarette Research Briefing – October 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. Potential deaths averted in USA by replacing cigarettes with e-cigarettes.

- **Study aims**
  This US study compares differing models of current smokers switching to e-cigarettes to predict effects on nationwide mortality.

  A Status Quo Scenario projecting smoking rates and health outcomes in the absence of vaping was compared to Substitution models, whereby smoking is largely replaced by e-cigarette use over a 10-year period. Both Optimistic and Pessimistic Scenarios were assessed, with different rates of smoking and different relative risks for e-cigarette use. The health outcomes from people switching over this 10-year period were then projected for 2016 to 2100.

- **Key findings**
  Under the Status Quo Scenario, a cumulative total of 26.1 million (18.8 million male and 7.3 million female) premature deaths and 248.6 million life years lost (LYL) from smoking are projected from 2016-2100.

  Under the Optimistic Scenario, a cumulative total of 19.5 million (14.0 million male and 5.5 million female) premature deaths and 161.9 million LYL are projected. This is a net gain of

6.6 million fewer deaths and 86.7 million fewer LYL compared to the Status Quo Scenario, representing 25% fewer premature deaths and 35% fewer LYL. The reduction in LYL translates to an increased average life expectancy of 0.33 years for the 2012 age 15 years and above population.

Under the Pessimistic Scenario, a cumulative total of 24.4 million (17.4 million male and 7.0 million female) premature deaths and 227.8 million LYL are projected. This is a net gain of 1.6 million fewer deaths and 20.8 million fewer LYL compared to the Status Quo Scenario, representing 6% fewer premature deaths and 8% fewer LYL. This translates to an increased average life expectancy of 0.08 years.

The analysis of the 2001 birth cohort, showed that there could be 82% fewer premature deaths and 79% fewer LYL in this group under the Optimistic Scenario.

- **Limitations**
  All trends in cigarette and e-cigarette use, cessation and associated risks follow assumptions based on existing data and technology. These data may not be easily extrapolated, and can only be considered to be estimates. We do not have evidence of the actual long-term health effects of e-cigarette use.

  The Status Quo Scenario was based on data up until 2012. Any tobacco control policy changes brought in after 2012 and in the future cannot be accounted for in this model.

  Risks associated with e-cigarettes were considered to be homogeneous across all products used, but there's likely significant variability in toxicant content, and the extent to which each is used.

  The study uses life years lost as an outcome to measure public health impact, but does not consider quality-adjusted life years lost.

  The study only considers cigarette and e-cigarette use, and no other tobacco or nicotine-containing products.

  The study does not provide an assessment of the likelihood of any of the scenarios being realised.

Levy DT, Borland R, Lindblom EN, et al. Potential deaths averted in USA by replacing cigarettes with e-cigarettes. Tobacco Control Published Online First: 02 October 2017. doi: 10.1136/tobaccocontrol-2017-053759

2. How do we determine the impact of e-cigarettes on cigarette smoking cessation or reduction? Review and recommendations for answering the research question with scientific rigor.

- **Study aims**
  This US study employs a systematic review to explore papers studying the impact of e-cigarettes on smoking cessation or reduction and assesses their quality against a hierarchy of methodological criteria.

  The measurements assessed include whether papers: 1) examine cigarette abstinence/reduction as an outcome, 2) assess e-cigarette use specifically for cessation as

the exposure of interest, 3) employ appropriate control/comparison groups, 4) ensure that the measurement of exposure precedes the outcome, 5) evaluate dose and duration of the exposure, and 6) evaluate the type of e-cigarette used.

After assessing papers against these criteria, the study then examines whether e-cigarette use leads to smoking cessation/reduction in those papers that meet the criteria.

- **Key findings**
  91 papers were identified relating to e-cigarette use and cigarette cessation. 67 of these were found to examine cigarette abstinence/reduction as the outcome of interest.

  After assessing whether studies explored e-cigarette use as a means for smoking cessation/reduction, and if they had appropriate study designs, so that remaining studies had appropriate controls or comparison groups, only 7 papers were left. Of these, only 4 papers met the remaining criteria on: exposure preceding outcome, dose and duration of exposure, and assessing type of e-cigarette used, and therefore met all 6 criteria.

  Of the four papers left (from three RCTs), these studies are consistent in the finding that e-cigarettes can help cessation in adult smokers – either through abstinence or reduction – regardless of motivation to quit smoking. The results of these studies showed rates of cessation with e-cigarettes that are comparable to those from nicotine replacement therapy.

- **Limitations**
  This study purely seeks to identify whether e-cigarettes can be effective as a cessation tool, when used specifically for this purpose. The study cannot assess the impacts and effect of e-cigarettes on overall population smoking levels.

  Though the selected studies met the criteria employed by this paper, there may be other limitations in the final selection. There was no further evaluation of study quality or bias beyond the selected criteria.

  RCTs don't necessarily reflect real-world use of e-cigarettes, so the final studies may not represent user experience outside of trials.

  The search for papers only included English-language papers published in PubMed and may miss other studies in the topic area.

Villanti, A. C., Feirman, S. P., Niaura, R. S., Pearson, J. L., Glasser, A. M., Collins, L. K., and Abrams, D. B. (2017) How do we determine the impact of e-cigarettes on cigarette smoking cessation or reduction? Review and recommendations for answering the research question with scientific rigor. Addiction, doi: 10.1111/add.14020.

3. The impact of restricting the use of e-cigarettes in public places: a systematic review.

- **Study aims**
  This study, produced by researchers from Public Health Wales, aimed to explore whether restrictions on e-cigarette use in public places deter smokers from switching to e-cigarettes for harm reduction purposes. The study also explored secondary questions around how much of a role restrictions in public places play in smokers choosing to use e-cigarettes, and smokers' and vapers' attitudes towards restrictions.

A systematic review identified 352 articles to be explored to answer these questions.

- **Key findings**
  No studies were found to answer the primary question on whether restrictions deter smokers from switching to e-cigarettes. 12 studies were found for the secondary question on choosing to use e-cigarettes, and 14 studies were found on attitudes

  Amongst current and former smokers, being able to use e-cigarettes in areas where smoking is restricted was a common reason for e-cigarette use. This reason was also commonly selected among specific groups, such as homeless individuals and those in a substance use treatment centre.

  Former smokers had mixed opinions on e-cigarette use in public places. Two studies found they were significantly more likely to support e-cigarette use in public places than never smokers. A separate two studies found they were significantly less likely to support this than current smokers.

  Three studies found that current smokers were significantly more likely to support the use of e-cigarettes in public places than never smokers. But there were still found to be between 15-35% of current smokers who did not support their use in public places.

  Seven studies reported a significant association between e-cigarette use and support for using them in public places. No studies reported that they did not find a significant association.

  Support for restrictions varied depending on the location they would be implemented (bars, restaurants, schools etc.).

- **Limitations**
  This study wasn't able to answer the primary review question on whether e-cigarette restrictions in public places would reduce the likelihood of smokers switching to e-cigarettes for harm reduction purposes.

  There was high variation between studies. Most were cross-sectional in design, but some were qualitative or used mixed methods. Former, current and never smoking status and e-cigarette use were also reported differently between studies. While other questions were also asked differently between studies.

  The studies looked at different populations across a number of countries, including specific groups (e.g. homeless individuals, or those calling smoking quitline services), so were not necessarily selected to be representative of the population.

  There was no quality assessment of the studies included in the review, only a risk of bias assessment.

K.F. Cann, K.D. Heneghan, T. Knight; The impact of restricting the use of e-cigarettes in public places: a systematic review, *Journal of Public Health*, https://doi.org/10.1093/pubmed/fdx122

4. A Cloud on the Horizon - A survey into the use of electronic vaping devices for recreational drug and new psychoactive substance (NPS) administration.

- **Study aims**
  This study examines the prevalence of electronic vaping devices use for recreational drug or new psychoactive substance (NPS) delivery in the UK.

  The study used a voluntary online survey with a convenience sample of adults (aged 16 and over), identified by a market research company. Data were collected regarding demographics, smoking history, electronic vaping device history, recreational drug/NPS use and route of administration.

- **Key findings**
  Of the 861 people that had used an electronic vaping device, over one third (39.5%) had ever used them for recreational drug use (13.6% of total respondents). 236 people (27.4% of ever electronic vaping device users and 9.4% of the total sample) were currently using a device for this purpose.

  Only 1.6% of the non-cigarette smoker respondents had used electronic vaping devices for recreational drug use. This compares to 21.0% of current/ex-smokers.

  Of those currently vaping for recreational drug use, e-cigarettes were the device most frequently used (74.2%), followed by table-top vapourisers (20.3%), and then electronic nicotine delivery systems (ENDs) (5.5%).

  Among current recreational drug vapers, the most commonly vaped drug was cannabis (65.7% lifetime use, 38.6% within the last 30 days). This was followed by MDMA/ecstasy (42.8% lifetime use), cocaine powder (39.8%), mephedrone (30.9%), crack cocaine (30.5%), and synthetic cannabinoid receptor agonists (28.4%). Other reported drugs included heroin (25.8%), ketamine (24.6%), Magic Mushrooms (0.4%) and LSD (0.4%).

  The commonest reasons given for vaping recreational drugs were: “My friends do it” (60.6%), “Out of interest” (53.8%), and “Thought it was a safer way to take drugs” (46.6%).

  Of the respondents who had never used an electronic vaping device for recreational drug use, 28.8% were aware that these devices could be used for this purpose.

- **Limitations**
  The study population was a convenience sample from a survey panel of research respondents used by a market research company, and are not representative of the population. In particular, the reported smoking and vaping prevalence was higher than in national surveys.

  The study is cross-sectional in nature and cannot determine any gateway effects or long-term usage patterns. All data were self-reported.

  Reasons for using e-cigarettes in general and using them for recreational drug delivery were selected from a range of pre-defined response categories. These may not capture all possible reasons for use.

  Questions on electronic vaping device use defined e-cigarettes, ENDs, and table-top vapourisers as different products, which may confuse some of the terminology typically used by consumers, potentially leading to misreports.

M Blundell, P Dargan, D Wood; A cloud on the horizon–a survey into the use of electronic vaping devices for recreational drug and new psychoactive substance (NPS) administration, QJM: An International Journal of Medicine, https://doi.org/10.1093/qjmed/hcx178

Overview

This month we include four articles, the first two from the USA and the second two from the UK.

The first study builds on well-developed approaches to simulation modelling in tobacco control led by Professor David Levy (the SimSmoke model). In this instance, a group of authors collaborated with Levy to try and predict the smoking and health outcomes of smokers switching to e-cigarettes from tobacco cigarettes over the next ten years from 2016. The study then projects the health effects from the switch during this period over the next 74 years, to determine public health impacts until 2100.

The model includes three scenarios. The first of these is a Status Quo Scenario which projects forward current, former and never smoker rates and health outcomes (total premature deaths and life years lost) from 2016 in the absence of vaping. An Optimistic Scenario is then modelled, assuming that most smokers would switch to e-cigarettes rather than smoking but there would be a residual smoking rate of 5% prevalence. The Optimistic Scenario also assumes that using e-cigarettes confers 5% of the risk of smoking. A Pessimistic Scenario assumes that e-cigarettes carry 40% of the risk of smoking and there would be a residual smoking rate of 10%, and also that vaping is taken up by more never smokers than is currently the case in the USA.

The study found that a significant number of premature deaths would be prevented, and life years saved, if more smokers in the USA switched to e-cigarettes. This was the case for both the Optimistic and Pessimistic Scenarios. For the former, there would be 25% fewer premature deaths and 35% fewer life years lost than in the Status Quo Scenario. For the latter, there would be 6% fewer premature deaths and 8% fewer life years lost. The gains were greatest for younger cohorts and the authors also suggest that health inequalities would be reduced because of smoking rates being higher in less affluent groups.

There are a large number of limitations involved in this type of modelling research as we outline above. A particular caveat is that all projections (both the status quo and the two scenarios set out by the authors) would be affected by policy changes which can't be predicted. For example, the Status Quo Scenario could be too conservative if further ambitious tobacco control policies (i.e a ban on all forms of tobacco marketing in the USA, not currently in place) were introduced. Likewise if policies on e-cigarettes are too restrictive, then fewer smokers would switch which would affect both the future scenarios set out in the article.

The second study is the latest output from a team of researchers in the USA who have been systematically reviewing the evidence on e-cigarettes related to a number of themes of policy interest. This particular paper focuses on those studies that report outcomes relevant to stopping smoking. During an earlier trawl of the literature in 2014, the researchers set out six questions which need to be addressed to answer the question of whether e-cigarettes help or hinder smoking cessation or reduction. These relate to whether: the primary outcome (cessation/reduction) is adequately measured; e-cigarettes are being used for cessation/reduction rather than other reasons; the study had control/comparison groups; e-cigarette use precedes cessation/reduction; the amount/timing of e-cigarette use is measured; the type and quality of e-cigarette is assessed.

In this paper, the authors then used these questions to review 91 eligible papers published up to February 2017. Studies needed to address all six questions to meet inclusion criteria for the review. From the 91 identified, studies dropped out after each question was considered and the team found only four studies that adequately addressed all six questions. These four papers came from three randomised controlled trials of e-cigarettes for smoking cessation. Two of these were trials included in last year's updated Cochrane review of e-cigarettes for smoking cessation, with the third trial published more recently.

These results may be slightly dispiriting for researchers examining e-cigarettes for smoking cessation in studies that don't employ a randomised controlled design (i.e. well conducted longitudinal research) as the findings suggest that you can't really 'prove' that e-cigarettes help people quit without conducting a trial. This isn't surprising, as there can be too many factors that may account for outcomes in non-randomised studies, but of course longitudinal research is still essential in demonstrating potential population effects. The criteria the authors have set out will be very helpful to teams contemplating future research - for example, aiming to see if e-cigarettes help particular populations of smokers to quit. They are also useful for critical appraisal of research that claims to prove e-cigarettes help people stop, or alternatively that they don't help. Critical appraisal is important for improving media reporting of e-cigarette studies, or supporting policy makers and practitioners to make best use of research findings. The final questions described by the authors are particularly insightful as they emphasise the importance of considering dose, duration and product type, aspects that have arguably been neglected in the literature so far.

Our third paper this month is authored by colleagues from Public Health Wales. They conducted a systematic review of the literature (including the grey literature, i.e. research reports) to examine a number of issued related to vaping in public places. Their primary research objective was to ascertain whether or not restrictions on the use of e-cigarettes in public places reduce the likelihood that smokers will switch to e-cigarettes. Secondary objectives were to examine: how much of a role smoking restrictions in public places play in smokers choosing to use e-cigarettes; and what smokers and vapers attitudes are towards restrictions on e-cigarettes in public places. The review was conducted a few months after the Welsh government confirmed that it would not be introducing a previously proposed ban on e-cigarettes in public places and workplaces. The authors describe this background and explain that, despite this decision, it is still useful to examine the literature to inform any future policy options.

The approach taken by the review is fairly comprehensive but no studies addressing the primary objective were identified. Given the number of jurisdictions in other countries that have banned vaping in public places, this means the review identifies an interesting research gap.

There was more literature focusing on the secondary objectives of the review. These illustrate that being able to use an e-cigarette in areas where smoking is banned is one reason why smokers try or continue to use e-cigarettes, and in some studies this was an important reason for choosing vaping rather than smoking. For example, one study involving homeless smokers and another involving smokers in substance use treatment (both important groups for tobacco harm reduction) found that a majority of participants indicated that they had chosen to use an e-cigarette rather than smoke because it was permitted at times/in places when they could not smoke (as one of a number of reasons for use). The review also examined attitudes towards e-cigarette bans in public places and identified mixed results, including that some current smokers were in favour of bans, and that opinions varied across groups depending on the types of public places (i.e pubs or schools).

The final study this month examines the issue of whether, and to what extent, alternative nicotine delivery devices, including e-cigarettes, are being used to deliver recreational drugs (such as cannabis) or new psychoactive substances (NPS). This was a cross sectional survey using a convenience sample of vapers who volunteered to complete the questionnaire. Just over 2,500 adults in the UK did so. Just over a third had ever vaped – 861 of the respondents and 95% of these were smokers or ex-smokers.

Amongst the 861 ever vapers, just under four in ten had used them for recreational drug use, most commonly cannabis but a significant proportion (between less than 1% and 43% of those who had ever vaped recreational drugs) reported use of these devices to deliver other substances. Ever vaping to deliver recreational drugs was rare (1.6%) amongst non-smokers.

The rates of both vaping and smoking in the sample were higher amongst respondents than in general population surveys, which raises questions about the representativeness of the survey. As our summary above shows, there were also issues to do with how vaping devices were defined in the study which could have caused confusion amongst those participating. However, what the survey does suggest is that vaping to deliver drugs other than nicotine is occurring and may not be that unusual. An important priority for future research would be a more comprehensive assessment of how common this is in the UK and elsewhere, and also what health effects may occur as a result.

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

- Use of Nicotine in Electronic Nicotine and Non-Nicotine Delivery Systems by US Adults, 2015.
- "Juice Monsters": Sub-Ohm Vaping and Toxic Volatile Aldehyde Emissions.
- Direct Marketing Promotion and Electronic Cigarette Use Among US Adults, National Adult Tobacco Survey, 2013-2014.
- Influence of legislations and news on Indian internet search query patterns of e-cigarettes.
- Sympathomimetic Effects of Acute E-Cigarette Use: Role of Nicotine and Non-Nicotine Constituents.
- Adolescents and young adults' perceptions of electronic cigarettes as a gateway to smoking: a qualitative study in Switzerland.
- Do Current and Former Cigarette Smokers have an Attentional Bias for E-cigarette Cues?
- Biomarkers of exposure to new and emerging tobacco delivery products.
- Key issues surrounding the health impacts of electronic nicotine delivery systems (ENDS) and other sources of nicotine.
- Maternal E-cigarette Exposure in Mice Alters DNA Methylation and Lung Cytokine Expression in Offspring.
- A comparison of electronic and traditional cigarette butt leachate on the development of Xenopus laevis embryos.
- E-cigarette aerosol exposure can cause craniofacial defects in Xenopus laevis embryos and mammalian neural crest cells.
- Mists, vapors and other illusory volatilities of electronic cigarettes.
- Electronic cigarette awareness, use, and perception of harmfulness in Brazil: findings from a country that has strict regulatory requirements.
- Classification of Twitter Users Who Tweet About E-Cigarettes.

- Short-term respiratory effects of e-cigarettes in healthy individuals and smokers with asthma.
- Evaluating oral flavorant effects on nicotine self-administration behavior and phasic dopamine signaling.
- Effects of health-oriented descriptors on combustible cigarette and electronic cigarette packaging: an experiment among adult smokers in the United States.
- The Use of Substances Other Than Nicotine in Electronic Cigarettes Among College Students.
- The effect of sucralose on flavor sweetness in electronic cigarettes varies between delivery devices.
- Point of Sale Scanner Data for Rapid Surveillance of the E-cigarette Market.
- E-cigarette use and asthma in a multiethnic sample of adolescents.
- E-cigarette Use and Cigarette Smoking Cessation among Texas College Students.
- Influence of Risk Perception on Attitudes and Norms Regarding Electronic Cigarettes.
- Using Focus Group Interviews to Analyze the Behavior of Users of New Types of Tobacco Products.
- They're heating up: Internet search query trends reveal significant public interest in heat-not-burn tobacco products.
- The Prevalence and Characteristics of E-Cigarette Users in the U.S.
- The prevalence and marketing of electronic cigarettes in proximity to at-risk youths: An investigation of point-of-sale practices near alternative high schools.
- E-cigarette use among treatment-seeking smokers: Moderation of abstinence by use frequency.
- A longitudinal study of electronic cigarette use and onset of conventional cigarette smoking and marijuana use among Mexican adolescents.
- Assessing notions of denormalization and renormalization of smoking in light of e-cigarette regulation.

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 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.