Electronic Cigarette Research Briefing – December 2017 & January 2018

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.

Past research briefings can be found at www.cruk.org/UKECRF. If you would prefer not to receive this briefing in future, just let us know.

1. Relationship between spending on electronic cigarettes, 30-day use, and disease symptoms among current adult cigarette smokers in the U.S.

- **Study aims**

  This US study explored associations between spending on e-cigarettes and disease symptoms, and compared them to any associations between past 30-day e-cigarette use and disease symptoms. Data were taken from 533 respondents over 24 years old, who were current smokers and ever e-cigarette users in August 2015.

- **Key findings**

  When comparing respondents with any past 30-day e-cigarette use to non-users, there were no significant differences in any disease symptoms.

  For each $100 increase in amount spent on e-cigarettes in the last month, the odds of reporting a disease symptom were significantly increased for four symptoms. These were: chest pain (AOR = 1.25, 95% CI: 1.02-1.52), noticing blood when brushing teeth (AOR = 1.23,

95% CI: 1.02-1.49), having sores or ulcers in the mouth (AOR = 1.36, 95% CI: 1.08-1.72), and having more than one cold (AOR = 1.36, 95% CI: 1.05-1.78).

Increases of 10 cigarettes per day were significantly associated with reporting two symptoms (wheezing and shortness of breath).

- **Limitations**

  The study population assessed were all current cigarette smokers, so it isn't possible to entirely separate the effects of e-cigarette use from that of smoking. The study cannot demonstrate whether there are any differences between exclusive e-cigarette users and smokers or dual users.

  Increases of $100 expenditure per month may represent a greater intensity of e-cigarette use, but because of the range of products available, different prices and sources, this cannot be an exact proxy for e-cigarette use and intensity of use.

  The only other e-cigarette measures used in this study were comparing past 30-day e-cigarette ever use to non-use, which do not describe intensity. Other measures may be more appropriate to ascertain any effects.

  The study has a relatively small sample size and did not control for pre-existing health conditions that may be associated with the diseases symptoms described or for other factors such as nicotine dependency.

  This is a cross-sectional survey and all data were self-reported and could be subject to bias.

Yao, T., Max, W., Sung, H.-Y., Glantz, S. A., Goldberg, R. L., Wang, J. B., … Cataldo, J. (2017). Relationship between spending on electronic cigarettes, 30-day use, and disease symptoms among current adult cigarette smokers in the U.S. *PLoS ONE*, *12*(11), e0187399. http://doi.org/10.1371/journal.pone.0187399

2. A longitudinal study of the relationship between receptivity to e-cigarette advertisements and e-cigarette use among baseline non-users of cigarettes and e-cigarettes, United States.

- **Study aims**

  This US study used a nationally representative online panel to explore any relationships between receptivity to e-cigarette advertisements at baseline and e-cigarette use at 5-month follow-up. There were 2,191 respondents to both survey waves and all of these were adults who did not smoke or use e-cigarettes at baseline. The survey was conducted in 2014.

- **Key findings**

  At 5-month follow-up, 2.7% of those that were previously exposed to e-cigarette adverts had become e-cigarette users. This compares to 1.1% of those that hadn't previously been exposed to e-cigarette adverts. This equates to an attributable risk percentage of 59.3% in those that were exposed.

  Receptivity to e-cigarette adverts at baseline was significantly associated with e-cigarette use at follow-up (aOR = 1.57, 95% CI: 1.04-2.37).

Other variables that were associated with e-cigarette use at follow-up were, being a former smoker (aOR = 4.30, 95% CI: 1.47-12.61) and living with someone who smokes (aOR = 6.48, 95% CI: 2.47-16.97). Men were also less likely to use e-cigarettes at follow-up than women (aOR = 0.35, 95% CI: 0.14-0.90).

- **Limitations**
  This study can only explore associations between receptivity or exposure to e-cigarette adverts and later e-cigarette use. It cannot claim causality for these relationships.

  The study did not collect any data on past e-cigarette use, and may include former e-cigarette users, who may be more likely to try them again. Neither did the study control for other factors such as nicotine dependency and perception of e-cigarettes.

  Exposure to e-cigarette adverts at baseline was defined as having previously seen the individual advert that was shown to them. This will not capture exposure to all adverts as participants may have seen other adverts through other media that were not recorded.

  There was a reasonably high dropout before follow-up with a retention rate of 74.6%.

  Although further incentives were provided for those without internet access. This study population may not include those who are computer illiterate.

Agaku IT, Davis K, Patel D, et al. A longitudinal study of the relationship between receptivity to e-cigarette advertisements and e-cigarette use among baseline non-users of cigarettes and e-cigarettes, United States. *Tobacco Induced Diseases*. 2017;15:42. doi:10.1186/s12971-017-0145-8.

3. Predicting Short-Term Uptake of Electronic Cigarettes: Effects of Nicotine, Subjective Effects and Simulated Demand.

- **Study aims**
  This study from New Zealand used 35 adult daily smokers who had not tried e-cigarettes before, to explore how nicotine content affects subjective perceptions and use of e-cigarettes.

  Participants were followed for 8 weeks and given 0, 6, 12 and 18mg e-cigarette cartridges to use for a period of two weeks in a randomised, blinded order. Each was instructed to use their device *ad libitum* in an attempt to substitute their cigarette use as much as possible, but without motivations or incentives for smoking cessation. Smoking and e-cigarette use were reported daily via SMS, and perceptions were recorded every two weeks by questionnaire.

- **Key findings**
  During the trial periods, when e-cigarettes were made available, the mean cigarettes per day decreased from 9.69 at baseline to 6.09, representing a 37% reduction. There was a significant effect of e-liquid nicotine level on reducing cigarettes smoked per day; however, there was no significant difference when comparing the nicotine-containing e-cigarettes to zero nicotine ones.

There was no overall relationship between increasing e-liquid nicotine content and intensity of e-cigarette use. But daily use of the three nicotine-containing e-liquids was significantly higher compared to the one with zero nicotine.

There was a significant decrease in use of e-cigarettes over time across the 8-week period.

Craving Reduction was found to be significantly higher when using the nicotine-containing cartridges compared to the zero nicotine one.

When assessing whether subjective perceptions affected e-cigarette uptake, it was found that Psychological Reward (withdrawal symptom alleviation) and Satisfaction (taste and enjoyment) were both significant predictors of e-cigarette use, across nicotine levels.

- **Limitations**
  The study uses a small sample size and was not representative of the wider population of smokers. The sample size also reduced through attrition, with only 51% of participants completing all four two-weekly trials. Consequently, it might not have sufficient power to pick up some effects.

  The relatively short time period of the study means it cannot predict any further changes in cigarette or e-cigarette use e.g. smoking cessation, or giving up use of e-cigarettes.

  This study does not reflect real world use of e-cigarettes by imposing regular switching of e-liquids as part of the trial. Also, by encouraging e-cigarette use as part of a sustained experiment, this may have affected motivation to reduce or stop smoking that would not be experienced in real world settings.

  This study used second-generation e-cigarettes and one flavour of e-liquid, so the results might not reflect those from different devices or e-liquids.

  All data were self-reported and not validated by other measures.

Tucker M R, Laugesen M, Bullen C, Grace R C; Predicting Short-Term Uptake of Electronic Cigarettes: Effects of Nicotine, Subjective Effects and Simulated Demand, *Nicotine & Tobacco Research*, ntx269, https://doi.org/10.1093/ntr/ntx269

4. Trajectories of E-Cigarette and Conventional Cigarette Use Among Youth.

- **Study aims**
  This US study used the results from 3 waves of surveys in 2013, 2014 and 2015 to assess longitudinal associations between past-month cigarette and e-cigarette use among 808 students in Connecticut.

- **Key findings**
  Past-month e-cigarette use in earlier surveys was significantly associated with past-month cigarette use in future surveys (OR = 7.08, 95% CI: 2.34-21.42 for waves 1-2, and OR = 3.87, 95% CI: 1.86-8.06 for waves 2-3).

Past-month cigarette use was not found to be associated with past-month e-cigarette use in future surveys (OR = 2.02, 95% CI: 0.67-6.08 for waves 1-2, and OR = 1.90, 95% CI: 0.77-4.71 for waves 2-3).

- **Limitations**
  This study uses a small sample from Connecticut, and is not representative of the wider population. There was an attrition of over 40% of participants between the first and third waves.

  The study assesses the association between past-month e-cigarette and cigarette use and includes those that have only tried the product once in that time. These results do not necessarily translate to regular use.

  The study doesn't control for factors that may influence how likely someone is to smoke e.g. tendency towards risky behaviours, use of other substances, and exposure to adverts for tobacco or nicotine-containing products. Therefore, any associations cannot prove that trying one product leads to use of the other.

  The study provides no indication as to whether people were trying e-cigarettes with nicotine-containing e-liquids or not.

Bold, K. W., Kong, G., Camenga, D. R., Simon, P., Cavallo, D. A., Morean, M. E., & Krishnan-Sarin, S. (2017). Trajectories of e-cigarette and conventional cigarette use among youth. Pediatrics, e20171832.

5. User-identified electronic cigarette behavioural strategies and device characteristics for cigarette smoking reduction

- **Study aims**
  This US study of 72 current e-cigarette users, used concept mapping to explore e-cigarette use behaviours and device characteristics perceived to be associated with smoking cessation/reduction. Participants generated statements in response to a prompt on specific ways they have used an e-cigarette for smoking cessation/reduction, and then ordered these into groups to create a cluster map that could be interpreted thematically. Statements were also rated based on how much users agreed with them, with a score of 1 (Definitely NOT true for me) to 7 (Definitely true for me).

- **Key findings**
  Eight thematic clusters were identified: Convenience, Perceived Health Effects, Ease of Use, Versatility and Variety, Advantages of e-cigarettes over cigarettes, Cigarette Substitutability, Reducing Harms to Self and Others, and Social Benefits.

  The cluster with the highest mean rating was Convenience, with a score of M = 5.44. The lowest mean rating was for Social Benefits, with a score of M = 4.72.

  Former smokers rated Perceived Health Effects higher (M = 5.97) than those who smoked every day or most days (M = 5.01). Those that used 2nd and 3rd generation devices were also more likely to perceive health effects as a reason for smoking reduction (M = 5.52) compared to 1st generation e-cigarette users (M = 4.93).

Regular e-cigarette users, who used their device on at least 25 days of the past 30, rated Convenience, Advantages of e-cigarettes over cigarettes, and the Perceived Health Effects higher than those who reported e-cigarette use on only 1-29 days of the past 30.

Former smokers rated statements associated with stopping smoking completely rather than transitioning slowly higher than current smokers e.g. "I got rid of all of my cigarettes and lighters when I started vaping" and "I switched totally to electronic cigarettes the first day I started using electronic cigarettes".

- **Limitations**
  This study can only pull out the perceived reasons people think e-cigarettes may have helped them to stop or reduce their smoking. It cannot prove that these are successful quitting techniques.

  The participants were not representative of the entire vaping/smoking population, so results may not generalise.

  The majority of participants were still smokers and cannot provide valuable information on smoking cessation. Similarly, not all smokers were looking to give up tobacco entirely.

  Participants rated all the selected statements. The concept mapping process doesn't capture the frequency at which people would have selected these responses unprompted.

  The study does not take into account factors such as nicotine dependence and living with people who smoke, which may explain the behaviours exhibited and any cessation outcomes.

Soule E K, Maloney S F, Guy MC, Eissenberg T, Fagan P, User-identified electronic cigarette behavioral strategies and device characteristics for cigarette smoking reduction, Addictive Behaviors, Volume 79, 2018, Pages 93-101, ISSN 0306-4603, https://doi.org/10.1016/j.addbeh.2017.12.010.

Overview

This is the first UKECRF bulletin of 2018 and includes five articles, four from the USA and one from New Zealand.

The first study is a cross-sectional of adults in the USA who were participating in the first wave of the national Tobacco and Attitudes Belief Survey (TABS). From the larger TABS sample, this study analysed data from 533 respondents who reported that they were current smokers and had tried an e-cigarette at least once. The study aimed to look at any relationship between reported spending on e-cigarettes and disease symptoms and recent (past 30 day) e-cigarette use and disease symptoms in smokers.

Smokers who reported spending money on e-cigarettes in the past month were significantly more likely to report disease symptoms than smokers who didn't buy any e-cigarettes (devices, component parts, accessories and/or liquids) after controlling for cigarettes smoked per day and participant characteristics. These symptoms included chest pain, blood when brushing teeth, mouth sores or ulcers and having more than one cold. The authors concluded that e-cigarette use involves adverse health effects even among smokers and that e-cigarette consumption needs to be reduced to improve health.

Some previous research has suggested that respiratory and other disease symptoms may be higher in dual users compared with those who smoke but don't vape. Other studies have found the opposite - that even in dual users, symptoms commonly associated with smoking can lessen when vaping. However, none of these studies have been able to adequately account for key issues such as duration of smoking or other co-morbidities that may explain why some smokers who vape experience more or less symptoms than exclusive cigarette users. In contrast, research with ex-smokers who have completely switched to vaping provides evidence of both reduced toxicant exposure and fewer disease symptoms, emphasising the importance of smoking cessation among e-cigarette users.

The second study is on the topic of e-cigarette advertising and involved longitudinal research with adults in the USA. Conducted a few years ago, in 2014, participants were included if they were neither smoking nor vaping at baseline (April to June) and were followed up three to six months later (Sept-November). The researchers showed participants a single e-cigarette advert at baseline and asked them if they had seen that particular advert either on TV or online in the past three months. If they had seen the ad, they were classified as having been exposed to e-cigarette advertising. At follow up, significantly more of those exposed to advertising reported having vaped at least once. The authors concluded that e-cigarette advertising exposure could increase the odds of using e-cigarettes and that efforts to address advertising are important, as advertising exposure may contribute to the initiation of e-cigarette use by non-smokers.

Previous research has suggested that e-cigarette advertising is appealing and may play a role in both smokers and non-smokers trying e-cigarettes. Concerns particularly about appeal to non-smokers have contributed to bans or restrictions on e-cigarette marketing including in the UK where broadcast, print and digital marketing is now prohibited. Similar restrictions are not in place in the USA where this particular study was conducted. A challenge for this type of research is that it can't establish causality, i.e., that it was the advertising that caused participants to try vaping. In addition, the inclusion criteria for participants in this study could not account for the fact that participants might have tried vaping in the past, or that very recent ex-smokers (who might try vaping for relapse prevention) could have been included amongst the former smokers in the sample.

The third study in our bulletin involved a small cohort of daily smokers in New Zealand who had never vaped and were asked to try e-cigarettes for eight weeks. All were provided with the same brand of second generation device and the same (tobacco) e-liquid flavour but nicotine content varied in random concealed order including 0,6,12 and 18mg cartridges. The researchers aimed to explore how nicotine content affects the use of e-cigarettes.

During the study, participants reduced the amount they smoked, by just over a third on average. Participants reported using the device more often, and experiencing fewer cravings, when cartridges containing nicotine were used. Fewer withdrawal symptoms and taste and enjoyment factors were significant in predicting e-cigarette use. Participants tended to use e-cigarettes less frequently as the study progressed.

This research adds to a growing number of studies that attempt to assess how device characteristics may affect perceptions and patterns of use, but also highlights the challenges of comparing study results when different products are involved. For example, existing published trials (including one from the same research team) haven't found significant differences in e-cigarette use by nicotine content, but these trials were conducted with now obsolete devices and the authors highlight the importance of replicating previous results with new technology as it emerges. The fact that smokers in this study used the e-cigarette less over the eight weeks is also interesting. This may suggest that

the devices were not a sufficient substitute for smoking - or simply that the fairly demanding requirements of the study (varying of nicotine levels every two weeks, frequent reporting) may have resulted in participant fatigue.

The next article in this month's bulletin is a longitudinal study of young people aged 13-17 years old attending three secondary schools in Connecticut, USA. Questionnaires were completed in 2013, 2014 and 2015. The authors aimed to examine recent (past 30 day) cigarette and e-cigarette use over time.

The study found that using an e-cigarette at least once in the past month was significantly associated with past 30 day cigarette use at follow up. Smoking at least once in the past month was not, however, associated with recent use of an e-cigarette in future surveys. On the basis of these results the authors suggest that prevention policies targeting youth e-cigarette use may be needed to reduce future conventional tobacco use among young people.

Three longitudinal waves of data collection were included in this study which is a significant strength, although the sample was small and around 40% of the school pupils participating in the first year couldn't be followed up to year three. The study adds to a now fairly substantial number of studies which suggest there is an association between trying an e-cigarette and subsequently trying smoking in teenagers, although this evidence needs to be viewed in the context of continued declines in youth smoking in the countries where these longitudinal studies have taken place.

Finally we include an article from the USA which uses a concept mapping approach to explore behaviour related to e-cigarette use and the device characteristics which may be associated with smoking cessation or reduction. Just over 70 current e-cigarette users were recruited from seven cities in the USA and asked to complete a range of tasks online. Initially they were asked to describe specific ways that e-cigarettes had helped them reduce smoking. Subsequently they sorted and rated the statements that the whole sample provided and the researchers then analysed these data. This resulted in a 'cluster model' or, put more simply, a number of key themes including: convenience; perceived health effects; ease of use; versatility and variety; advantages of e-cigarettes over cigarettes; cigarette substitutability; reducing harms to self and others; and social benefits.

Two thirds of the participants were dual users (68%). There were some interesting differences in the ratings given to different themes between these dual users and the ex-smoking vapers in the study. The main difference was for perceived health effects, which was the only theme cluster that former smokers rated more highly than dual users. Items within this theme included, among others: 'Vaping has made me feel healthier'; 'Even with nicotine, vaping doesn't feel as addictive as smoking'; 'Electronic cigarettes are healthier than cigarettes'; 'Vaping makes me feel better and I can be more active'; 'I don't cough uncontrollably anymore since using an electronic cigarette'.

This study adds to existing literature on how perceptions might affect e-cigarette use and also how they might differ between those who have stopped smoking or continue to smoke. The paper provides further detail, for those interested, on how some of the concepts and themes addressed might inform future questions in surveys or studies using other designs.

Readers may also be interested in the new report from the National Academies of Science, Engineering and Medicine in the USA, which recently published a detailed report reviewing existing literature on e-cigarettes entitled "Public Health Consequences of E-cigarettes: Consensus Report" https://www.nap.edu/catalog/24952/public-health-consequences-of-e-cigarettes

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

- A new form of nicotine retailers: a systematic review of the sales and marketing practices of vape shops.
- Quit Methods Used by American Smokers, 2013-2014.
- Weight Status and Cigarette and Electronic Cigarette Use in Adolescents.
- Nicotine delivery efficiency of first- and second-generation e-cigarettes and its impact on relief of craving during the acute phase of use.
- Patterns of E-cigarette Use Frequency-National Adult Tobacco Survey, 2012-2014.
- Oral mucosal lesions in electronic cigarettes consumers versus former smokers.
- Effects of Solvent and Temperature on Free Radical Formation in Electronic Cigarette Aerosols.
- Electronic cigarette vapor alters the lateral structure but not tensiometric properties of calf lung surfactant.
- Microglia Activation and Gene Expression Alteration of Neurotrophins in the Hippocampus Following Early Life Exposure to E-cigarette Aerosols in a Murine Model.
- Exposure to tobacco websites: Associations with cigarette and e-cigarette use and susceptibility among adolescents.
- Young adult e-cigarette use outcome expectancies: Validity of a revised scale and a short scale.
- E-cigarette Price Sensitivity Among Middle and High School Students: Evidence from Monitoring the Future.
- Sugar and Aldehyde Content in Flavored Electronic Cigarette Liquids.
- Measuring perceptions related to e-cigarettes: Important principles and next steps to enhance study validity.
- Dual- and Polytobacco/Nicotine Product Use Trends in a National Sample of High School Students.
- Exploring the Predictive Validity of the Susceptibility to Smoking Construct for Tobacco Cigarettes, Alternative Tobacco Products, and E-Cigarettes.
- Effect of Flavors and Modified Risk Messages on E-cigarette Abuse Liability.
- Using the Vape Shop Standardized Tobacco Assessment for Retail Settings (V-STARS) to Assess Product Availability, Price Promotions, and Messaging in New Hampshire Vape Shop Retailers.
- Electronic Nicotine Delivery Systems (ENDS): What Nurses Need to Know.
- Effects of E-cigarette Advertising Messages and Cues on Cessation Outcomes.
- Initiation of Traditional Cigarette Smoking after Electronic Cigarette Use among Tobacco-Naïve U.S. Young Adults.
- Just a Spoonful of Sugar Helps the Messages Go Down: Using Stories and Vicarious Self-Affirmation to Reduce e-Cigarette Use.
- Effects of e-Cigarette Advertisements on Adolescents' Perceptions of Cigarettes.
- Does Seeking e-Cigarette Information Lead to Vaping? Evidence from a National Longitudinal Survey of Youth and Young Adults.
- The Effects of Varying Electronic Cigarette Warning Label Design Features On Attention, Recall, and Product Perceptions Among Young Adults.
- Global sale of tobacco products and electronic nicotine delivery systems in community pharmacies.
- Community education by advanced pharmacy practice experience students: Increasing electronic cigarette awareness amongst teens.
- Electronic cigarette use, knowledge, and perceptions among health professional students.

- Associations of Electronic Cigarette Nicotine Concentration With Subsequent Cigarette Smoking and Vaping Levels in Adolescents.
- Reasons for Vaping among U.S. 12th Graders.
- Predicting Short-Term Uptake of Electronic Cigarettes: Effects of Nicotine, Subjective Effects and Simulated Demand.
- E-Cigarette Surveillance With Social Media Data: Social Bots, Emerging Topics, and Trends.
- E-cigarette and waterpipe use in two adolescent cohorts: cross-sectional and longitudinal associations with conventional cigarette smoking.
- Active, passive, and electronic cigarette smoking is associated with asthma in adolescents.
- Assessment of indoor air quality at an electronic cigarette (Vaping) convention.
- The Nicotine Content of a Sample of E-cigarette Liquid Manufactured in the United States.
- Electronic cigarettes for adults with tobacco dependence enrolled in a tobacco treatment program: A pilot study.
- Associations of ADHD Symptoms With Smoking and Alternative Tobacco Product Use Initiation During Adolescence.
- Favourable Perceptions of Electronic Cigarettes Relative to Cigarettes and the Associations with Susceptibility to Electronic Cigarette Use in Hong Kong Chinese Adolescents.
- Psychometric evaluation of the Patient-Reported Outcomes Measurement Information System (PROMIS) Nicotine Dependence Item Bank for use with electronic cigarettes.
- Preferring more e-cigarette flavors is associated with e-cigarette use frequency among adolescents but not adults.
- Association of Noncigarette Tobacco Product Use With Future Cigarette Smoking Among Youth in the Population Assessment of Tobacco and Health (PATH) Study, 2013-2015.
- Differences between Dual Users and Switchers Center around Vaping Behavior and Its Experiences Rather than Beliefs and Attitudes.
- Adolescents' Use of Basic, Intermediate, and Advanced Device Types for Vaping.
- Correlates of Allowing Alternative Tobacco Product or Marijuana Use in the Homes of Young Adults.
- E-cigarette use, dual use of e-cigarettes and tobacco cigarettes, and frequency of cannabis use among high school students.

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 attendees 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

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