Electronic Cigarette Research Briefing – March 2020

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.

You can find our previous research briefings at www.cruk.org/UKECRF.

If you would prefer not to receive this briefing in future, just let us know.

1. [Association of initial e-cigarette and other tobacco product use with subsequent cigarette smoking in adolescents: a cross-sectional, matched control study.](#)

- **Study Aims**

This cross-sectional US study of 78,265 adolescents (18+) compared the association between initiating e-cigarette or other tobacco products and ever, past 30 day or established smoking (30 day use and 100+ lifetime cigarettes). Propensity score matching was used to assess the association between initial e-cigarette/other tobacco use and subsequent smoking status with a matched synthetic control whilst adjusting for covariates including sociodemographic characteristics, smoking susceptibility and exposure to tobacco.

- **Key Findings**

In the comparative analysis, adolescents who had used e-cigarettes first were less likely to have ever smoked cigarettes, have smoked in the past 30 days or to be established smokers than those who had initiated with non-cigarette combustible tobacco (e.g. shisha, cigars) (OR=0.48,95% CI=0.40-0.57 p<0.05, OR=0.48, 95% CI = 0.36-0.62, OR=0.17, 95% CI = 0.10 – 0.30, p<0.05) and other non-combustible tobacco (e.g. snus) (OR=0.32, 95% CI= 0.26-0.39, p<0.05, OR=0.26, 95% CI = 0.19-0.3 p<0.05, OR=0.08, 95% CI = 0.04-0.13, p<0.05).

In the matched analysis, adolescents who had used an e-cigarette first were less likely than the control to have ever smoked a cigarette (OR=0.76, p<0.05), to have smoked a cigarette in the past 30 days (OR=0.71, p<0.05) or be an established smoker (OR=0.26, p<0.001).

Those who had used non cigarette combustible tobacco first were more likely than the matched control to have ever smoked a cigarette (OR= 1.32, p<0.001) but were less likely to be an established cigarette smoker (OR= 0.71, p<0.05). There was no significant difference observed for past 30-day cigarette use.

Those who had used other non-combustible tobacco were more likely than the matched control to have ever smoked a cigarette (OR= 1.29, p<0.05). No difference was observed for past 30 day cigarette smoking or established cigarette smoking.

- **Limitations**

As the study is based on cross sectional survey data, the order of product use may have been incorrectly reported. In addition, the statistical methods used are not optimised for cross-sectional data. Population level associations observed over an extended time period would be needed to confirm the associations.

Data on some covariates relating to smoking susceptibility, such as mental health problems were not available. Therefore, the results may be subject to some confounding.

The survey did not report differences in the types of e-cigarettes used. Therefore, it cannot be determined if use of different brands, for example Juul, affects the relationship with future smoking. Additionally, the nicotine concentration of e-cigarette used was not reported. Therefore, the relationship between nicotine use in e-cigarettes and subsequent smoking cannot be determined.

The study examines first product use without examining the extent of use. Therefore, it does not consider experimenting with the products versus regular use.

Shahab L, Beard E, Brown J. (2020). Association of initial e-cigarette and other tobacco product use with subsequent cigarette smoking in adolescents: a cross-sectional, matched control study. *Tobacco Control.* doi: 10.1136/tobaccocontrol-2019-055283

2. Is e-cigarette use in non-smoking young adults associated with later smoking? A systematic review and meta-analysis

- **Study Aims**

This study assessed the association between e-cigarette use in young people (≤30 years) who were never smokers at baseline and smoking at follow up. Unadjusted and adjusted pooled odds ratios were calculated from 17 studies in a random effects model. Further subgroup analyses explored the relationship between ever e-cigarette use and ever smoking, ever e-cigarette use and current smoking and current e-cigarette use and ever or current smoking.

- **Key Findings**

In the unadjusted analysis, e-cigarette use in non-smokers was associated with an increased odds of subsequent smoking (OR=4.59, 95%CI=3.6-5.85). In the adjusted analysis, a weaker positive association was seen (OR=2.93, 95%CI=2.30-3.71).

In the adjusted age-stratified analysis, the odds of subsequent smoking was greater in studies including ≤18 years old compared with excluding those ≤18 years (OR=3.01, 95%CI= 2.36 – 3.85 vs OR= 2.64, 95%CI = 1.12 – 6.24).

In the adjusted subgroup analysis, e-cigarette use in never smokers was associated with an increased odds of becoming a current smoker (OR=2.21, 95% CI=1.72 – 2.84).

In the adjusted subgroup analysis, past 30-day e-cigarette use was associated with an increased odds of becoming an ever or current smoker (OR=2.33, 95% CI = 1.84-2.96, OR=2.21, 95% CI=1.72-2.84).

- **Limitations**

The meta-analysis examined ever e-cigarette use at baseline and cigarette use at follow up. There was insufficient data to pool the results of regular cigarette use at follow - up. Therefore, the results cannot show that regular or occasional use of e-cigarettes leads to regular smoking.

Only six studies included in the meta-analysis adjusted for behavioural risk factors (e.g. alcohol and drug use) and confounders such as impulsivity cannot be easily adjusted for. As such, shared risk factors for e-cigarette use and other behaviours may have confounded the results.

The funnel plots indicated some risk of publication bias. Therefore, it is unclear if these studies are representative of all studies on the gateway effects of e-cigarettes.

There was high heterogeneity in both the unadjusted and adjusted meta-analyses (I^2= 88%, I^2=85%, respectively.) This could indicate methodological differences in the included studies, meaning that pooling of the data might not have been appropriate.

Data was self- reported in most studies. Therefore, the order of e-cigarette/ cigarette use could have been incorrectly reported.

Only one study considered the nicotine concentration of e-cigarettes. Therefore, the results do not show the effect of nicotine exposure in e-cigarettes on subsequent smoking.

Khouja JN, Suddell SF, Peters SE. (2020). Is e-cigarette use in non-smoking young adults associated with later smoking? A systematic review and meta-analysis. *Tobacco Control*. doi: 10.1136/tobaccocontrol-2019-055433.

3. [Cost effectiveness of e-cigarettes compared with nicotine replacement therapy in stop smoking services in England (TEC study): a randomized control trial](#)

- **Study aims**

This English study randomised 886 adult smokers attending four UK Stop Smoking Services to either an e-cigarette (EC) starter pack (One Kit) with 18mg/ml e-liquid or nicotine – replacement therapy (NRT) products of their choice. Both groups received weekly support for at least 4 weeks

and abstinence was verified at 4, 26 and 52 weeks. [Analysis of the original trial can be found here.](#)

The additional cost per quality-adjusted-life-year (QALYs) gained in the EC arm compared with the NRT arm was analysed over the 12-month trial follow up. Analysis were performed for intention to treat and complete cases. A Markov model was used to predict long-term cost effectiveness, accounting for incidence of smoking related diseases and the cost of secondary care. Analyses were adjusted for sociodemographic characteristics, smoking dependence, baseline costs to the NHS and baseline QALYs scores.

- **Key Findings**

In the primary analysis, the additional cost per QALY gained for the EC arm compared with the NRT arm was £1100. Therefore, if the decision maker is willing to spend an additional £1100 per QALY gained, the EC treatment would be considered cost-effective.

In the complete case analysis (CCA), the additional cost per QALY was negative. This demonstrates that the EC arm was less costly and more effective.

In the primary analysis, it was predicted that the probability of the EC arm being cost effective at £20,000 and £30,000/ QALY was 87% and 90%, respectively. In the CCA, the probability of cost effectiveness was 75% at £20,000/QALY and 70% at £30,000/ QALY.

In the long-term model, the additional cost per QALY gained for the EC arm compared with the NRT arm was £65. The probability of the EC arm being more cost effective than NRT was 85% at 20,000 and £30,000 / QALY.

- **Limitations**

General limitations of the original randomised control trial are discussed previously.

There was a 35% level of missing data which reduces the certainty of cost-effectiveness estimates. The CCA suggested an effect of missing data in the NRT arm. This makes the estimates of the NRT arm in the primary analysis less certain.

Participants self-reported their health care service use over a six-month period. Therefore, the results may be subject to recall bias.

The long-term model did not consider repeated quit attempts or the possible long-term health effects of ECs. Therefore, the long-term costs of EC use may have been mis-estimated.

The trial was conducted in three UK Stop Smoking Services and the predictions were based on a specific brand of e-cigarette. Therefore, the cost-effectiveness predictions may not be representative of the entire population.

The trial only compared e-cigarettes and NRT and did not examine the relative effectiveness of other quitting tools (e.g. prescription medication). Therefore, it cannot give an overall picture of which intervention may be the most cost-effective method of smoking cessation.

Li J, Hajek P, Pesola F, Phillips-Waller A et al. (2020) Cost-effectiveness of e-cigarettes compared with nicotine replacement therapy in stop smoking services in England (TEC study): a randomized controlled trial. *Addiction*. doi: 10.1111/add.14829

4.

- **Study aims**

This qualitative UK study investigated the factors influencing smokers' decisions to use e-cigarettes or behavioural support from Stop Smoking Services (SSS). It also examined the differences in perceptions of e-cigarettes and the support available at SSS between smokers and SSS stakeholders. Interviews of current or recent smokers who were users or non-users of SSSs (n=46) and SSS staff or stakeholders (n=12) were conducted at three sites in the UK. Findings were framed thematically according to the capability, opportunity, motivation and behaviour (COM-B) model.

- **Key Findings**

Several distinct groups were identified from interview responses. Interviewees with recent, regular e-cigarette use were split into "finite" and "forever" vapers. Forever vapers expressed no concerns about being addicted to e-cigarettes whereas finite vapers expressed a motivation to stop vaping. Non vapers were either "sceptical" about people vaping or were "supportive".

Finite vapers and sceptical non vapers expressed concern over a lack of evidence on e-cigarettes. Supportive non-vapers were more confident than sceptical non-vapers in assessing the relative risks of vaping versus smoking.

Vapers reported the importance of experimentation in finding e-cigarettes that matched personal preferences and mentioned that vape shops could offer valuable expertise. SSS staff also referred to vape shops as a source of expert advice.

Staff at all three sites described their SSS as "e-cigarette friendly". Concern among practitioners about the possible risks of long-term vaping varied across the sites. The ability for ex-smoking vapers to receive SSS support from the sites to stop vaping varied and was often subject to capacity. In contrast, smokers across all sites believed their SSS was reticent about vaping.

Finite vapers were concerned that vaping was prolonging or replacing an addiction rather than addressing it. Their perception of the evidence base was also important in informing their intention to quit vaping. Among both groups of vapers, interviewees perceived e-cigarettes as effective for cutting down or quitting smoking.

- **Limitations**

Data were collected from three research sites in the UK and socio-demographic characteristics of the participants were not reported. Therefore, the findings are not necessarily generalisable to the wider population.

The interviews were conducted at just one timepoint. Therefore, the results do not account for the possibility of perceptions of e-cigarettes/SSSs changing over time or interviewees transitioning between the identified groups.

The analysis did not consider the length of time participants had been smokers/ ex-smokers or vapers. Perceptions of e-cigarettes/ SSSs may vary in these subgroups.

Some of the themes identified involved multiple concepts so did not fit into the COM-B framework. This may have limited analysis of the interactions of these themes.

Hartwell G, Egan M, Petticrew M. (2020). Understanding decisions to use e-cigarettes or behavioural support to quit tobacco: a qualitative study of current and ex-smokers and stop smoking service staff. *Addiction.* doi: 10.1111/add.14844.

Overview

Hope all our readers are keeping safe and well in these challenging times. We will continue to produce the bulletin while we are all working from home, and hope you still find it useful.

Our four selected articles this month are all from research teams based in the UK. The first paper is from colleagues at University College London who conducted a secondary analysis of data from the [National Youth Tobacco Survey](#) (NYTS) in the USA (2014-2017). They were interested in examining any associations between e-cigarette and other tobacco product use and smoking at follow up. Most of the literature on this topic has come from longitudinal surveys where the authors use well-established statistical modelling techniques (regression analysis) to try and account for possible confounders when young people who report trying an e-cigarette at baseline are found to have smoked at follow up. But this type of analysis can't establish a causal association. To try a different approach, the authors used matched controls. This involves matching survey respondents in an 'exposure group' with 'behavioural controls'. Here this involved comparing ever, past 30 day or regular smoking young people (exposure group) who first used e-cigarettes with those who first used cigarettes or other tobacco products (controls). The study team then used propensity score matching (PSM) which is a statistical modelling technique that tries to mimic some of the characteristics of a randomised controlled trial and identifies 'synthetic' controls.

Overall, the study estimated that around one in four young people in the NYTS who tried e-cigarettes first subsequently went on to try smoking. Fewer than 1%, however, became established smokers by follow up. The conversion from trying smoking to regular smoking was lower among young people who started with vaping than those who started with other combustible tobacco products (i.e. cigars, waterpipe, bidis) or non-combustible tobacco products (i.e. chewing tobacco or snus). In other words, there might be a protective effect against regular smoking if the first product used was an e-cigarette. The analysis also found that the links between starting with an e-cigarette and subsequent smoking could be largely explained by 'shared vulnerability' to use either product. The authors concluded that over the period included in the analysis, vaping didn't appear to be an important gateway to smoking in young people in the USA, particularly in the context of a continued decline in cigarette smoking at the population level over the period. They argue that trying or initiating vaping may in fact have diverted some young people who might have become smokers in the absence of e-cigarettes. It should be noted, however, that the survey data used only went up to 2017 and vaping continued to rise amongst young people in the USA after that date. Future analysis of subsequent survey waves using similar methods should be able to assess if these findings remain consistent in a few years' time.

This month's second paper addresses more or less the same topic, but involved a systematic review of existing published studies on the link between vaping and subsequent smoking in young people and young adults under the age of 30. Conducted by researchers at the University of Bristol, the search strategy involved a replication and update of that used in a [previous review](#), but included an increased focus on potential bias in how study results were interpreted by authors. 17 studies were identified (three of these were from the UK) and data extracted to conduct a meta-analysis that pooled data to look at overall effects. All the studies included were longitudinal (with one cross-

sectional) and so have limitations of the type that the first study in this month's bulletin highlighted and tried to address.

Most studies focused on ever e-cigarette use and used ever smoking as an outcome at follow up. The meta-analysis found that reporting using an e-cigarette at baseline was strongly associated with smoking at follow up. Various follow up points were used, but one year later was common. There was a lot of heterogeneity (variation/differences) between studies in the pooled analysis. In addition, almost all the included studies relied on participants self-reporting smoking without any biochemical validation. The authors also noted that the methods used in the original studies couldn't establish whether the associations were causal (i.e. trying an e-cigarette caused subsequent smoking). They also didn't include information on the nicotine content of vaping products so it would be difficult to determine whether there was any link between nicotine exposure via vaping and subsequent smoking.

Our third study reports findings from an economic analysis conducted as part of the NIHR funded TEC trial. Readers will remember this trial, led by researchers at Queen Mary University of London, with the overall results published in the New England Journal of Medicine last year. The current research was led by economists at the University of York.

As a reminder, the TEC trial found that smokers randomised to stop with an e-cigarette and behavioural support (provided by stop smoking services - SSS) were around twice as likely to have quit at 12 months when compared to those accessing usual care (NRT plus behavioural support). The current study focused on the cost-effectiveness of e-cigarettes as a stop smoking aid when used in combination with SSS support. It used well-established methods to examine cost-effectiveness at 12 months and in the longer term.

Overall, the study found that e-cigarettes were more cost-effective for smoking cessation than NRT in the context of a quit attempt with SSS support. Providing an e-cigarette starter pack and initial supply of e-liquids cost on average £105 per participant. This compared with £201 for NRT, keeping in mind that more than one NRT product (combination therapy) was available to participants in the NRT arm. The researchers also examined the cost per Quality Adjusted Life Year (QALY) gained, which is a measure used to examine whether a treatment might meet the threshold for value for money as defined by the National Institute of Health and Care Excellence (NICE). There was an 87% probability this would be reached at 12 months and 85% probability for lifetime costs. These findings support the cost-effectiveness of e-cigarettes for smoking cessation in the context of SSS support in the UK.

Finally we include a qualitative study involving current and ex-smokers and stop smoking service staff, conducted by researchers at the London School of Hygiene and Tropical Medicine. The team were interested in examining the factors that influenced current and former smokers' decisions to use e-cigarettes and/or local stop smoking services, and any differences between these individuals and stop smoking service staff. Face to face interviews were conducted with 29 current/recent smokers and 17 SSS staff in three sites (North, Central, South England). A topic guide was developed for the interviews that drew on the COM-B behaviour change model.

Findings were organised around the main elements of COM-B: Capability, Opportunity, and Motivation. In terms of capability, the findings from interviews with smokers and ex-smokers were similar to previous studies that have identified differing views about the relative risks of vaping compared to smoking and that harm perceptions influence whether smokers try vaping or not. The researchers pointed to the need for clear and consistent information about relative risks, particularly

for smokers who had not tried e-cigarettes and were not accessing stop smoking services. For opportunity, there were mixed findings about the extent to which SSS were welcoming clients who chose to use e-cigarettes, and that this was influenced not just by policies at the service level but the individual views of SSS staff about vaping. This has also been found in previous studies but seems to persist. There was also lack of clarity about whether established vapers could access SSS for support to cut down or stop vaping, something the smokers and ex-smokers interviewed for the study thought should be available. Readers might be interested to know that in Scotland, national guidance on this has recently been developed for SSS. A further finding relating to opportunity, however, was that both vapers and SSS staff highlighted the value of specialist vaping retailers in terms of offering advice about e-cigarettes and providing opportunities to try different products.

For motivation, participants expressed concerns about ongoing use of nicotine as part of a quit attempt and in the longer term. Misperceptions about nicotine, which have also been raised in other recent research, related to both vaping and licensed medicinal nicotine products like NRT. Finally motivation was also heavily influenced by past experience. This was the case both for motivation to vape (where smokers and ex-smokers had positive or negative experiences of vaping in the past) and willingness to access SSS for smoking cessation. The authors argue that the COM-B framework may be helpful as a tool to help assess the attitudes and goals of smokers regarding different options for smoking cessation and/or continued use of vaping products.

Other studies from February you might find of interest:

Patterns of use

Associations Between Nicotine Metabolite Ratio and Gender With Transitions in Cigarette Smoking Status and E-Cigarette Use: Findings Across Waves 1 and 2 of the Population Assessment of Tobacco and Health (PATH) Study.

Juul and the upsurge of e-cigarette use among college undergraduates.

A thematic analysis of smokers' and non-smokers' accounts of E-cigarettes.

Electronic Cigarette Use During Preconception and/or Pregnancy: Prevalence, Characteristics, and Concurrent Mental Health Conditions.

Electronic Cigarettes to Vaporize Cannabis: Prevalence of Use and Associated Factors among Current Electronic Cigarette Users in Germany (DEBRA Study).

Integrating Social Dynamics Into Modeling Cigarette and E-Cigarette Use.

Examining the relationship between impulsivity-related personality traits and e-cigarette use in adults.

Role of flavours in vaping uptake and cessation among New Zealand smokers and non-smokers: a cross-sectional study.

Does e-cigarette experimentation increase the transition to daily smoking among young ever-smokers in France?

An Analysis of Associations Between Electronic Nicotine Delivery System Users.

Perception

Knowledge and attitudes towards E-cigarette use in Lebanon and their associated factors.

Framing and scientific uncertainty in nicotine vaping product regulation: An examination of competing narratives among health and medical organisations in the UK, Australia and New Zealand.

High School Youth and E-cigarettes: The Influence of Modified Risk Statements and Flavors on E-cigarette Packaging.

Nicotine and marijuana attitudes among flavor-only vaping youth: New evidence from Monitoring the Future.

Cessation

Impact of e-cigarette use among a cohort of American Indian cigarette smokers: associations with cigarette smoking cessation and cigarette consumption.

Will Electronic Nicotine Delivery System (ENDS) use reduce smoking disparities? Prevalence of daily ENDS use among cigarette smokers.

Subjective sleep quality and electronic cigarette dependence, perceived risks of use, and perceptions about quitting electronic cigarettes.

Understanding decisions to use e-cigarettes or behavioural support to quit tobacco: a qualitative study of current and ex-smokers and stop smoking service staff.

Cost-effectiveness of e-cigarettes compared with nicotine replacement therapy in stop smoking services in England (TEC study): a randomized controlled trial.
Gender differences in relationships between sociodemographic factors and e-cigarette use with smoking cessation: 2014-15 current population survey tobacco use supplement.

Youth

Is e-cigarette use in non-smoking young adults associated with later smoking? A systematic review and meta-analysis.

E-Cigarette Use and Regular Cigarette Smoking Among Youth: Population Assessment of Tobacco and Health Study (2013-2016).

Prevalence of Electronic Cigarette Use and its Determinants among 13-to-15-Year-Old Students in Greece: Results from the 2013 Global Youth Tobacco Survey (GYTS).

Psychological well-being and dual-use of cigarettes and e-cigarettes among high school students in Canada.

Harms and harm reduction

A numerical investigation of the potential effects of e-cigarette smoking on local tissue dosimetry and the deterioration of indoor air quality.

Potential for release of pulmonary toxic ketene from vaping pyrolysis of vitamin E acetate.

Exposure to secondhand aerosol of electronic cigarettes in indoor settings in 12 European countries: data from the TackSHS survey.

Electronic cigarettes containing nicotine increase endothelial and platelet derived extracellular vesicles in healthy volunteers.

Cigarette smoke and electronic cigarettes differentially activate bronchial epithelial cells.

Ocular conditions and dry eye due to traditional and new forms of smoking: A review.

Smoking and use of electronic cigarettes (vaping) in relation to preterm birth and small-for-gestational-age in a 2016 U.S. national sample.

Electronic Cigarette Aerosol Modulates the Oral Microbiome and Increases Risk of Infection.

In Utero Exposures to Electronic-Cigarette Aerosols Impair the Wnt Signaling during Mouse Lung Development.

Comparison between in vitro toxicities of tobacco- and menthol-flavored electronic cigarette liquids on human middle ear epithelial cells.

Passive exposure of non-smokers to E-Cigarette aerosols: Sensory irritation, timing and association with volatile organic compounds.

Marketing

E-cigarette advertising expenditures in the United States, 2014-2018.

Online Pro-Tobacco Marketing Exposure Is Associated With Dual Tobacco Product Use Among Underage US Students.

Misc

The Effects of Cannabis Use: A Test Among Dual Electronic and Combustible Cigarette Users.

Exploring the Point-of-Sale Among Vape Shops Across the US: Audits Integrating a Mystery Shopper Approach.

Comprehensive Chemical Characterization of the Aerosol Emissions of a Vaping Product Based on a New Technology.

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 ecig[title/abstract] OR (nicotine AND (vaporizer OR vaping 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.