The UK Electronic Cigarette Research Forum

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Electronic Cigarette Research Briefing – August 2022

This research briefing is part of a series of quarterly 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 do not cover every e-cigarette-related study published each quarter. 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.

Let's talk e-cigarettes – University of Oxford podcasts

Jamie Hartmann-Boyce and Nicola Lindson discuss emerging evidence in e-cigarette research. In the June 2022 episode they interview Dr Francesca Pesola about the trial comparing e-cigarettes to nicotine patches for smoking cessation in pregnant women.

This podcast is a companion to the Cochrane living systematic review of e-cigarettes for smoking cessation and shares the evidence from the monthly searches.

Subscribe with iTunes or Spotify to listen to regular updates or find all episodes on the University of Oxford Podcasts site.

This podcast series is funded by CRUK.

Cochrane Living Systematic Review of E-cigarettes for Smoking Cessation update

The latest update to the CRUK-funded Cochrane Living Systematic Review of E-cigarettes for Smoking Cessation was published in Sept 2021 and includes 5 new studies. Visit the website (https://www.cebm.ox.ac.uk/research/electronic-cigarettes-for-smoking-cessation-cochrane-living-systematic-review-1) for full information on the review, including briefing documents, and new studies found since the update which will be incorporated in a future version of the review.

Electronic cigarettes versus nicotine patches for smoking cessation in pregnancy: a randomized controlled trial – Hajek *et al.*

Study aims

This trial recruited 1,140 pregnant women who smoked from 23 hospital sites in England and one stop smoking service in Scotland who were on average 15.7 weeks pregnant and willing to use either trial product. Participants were randomised to either an e-cigarette or nicotine patches (NRT). Participants also received six phone calls from stop-smoking advisors. The primary outcome was prolonged abstinence from smoking at end of pregnancy (EOP) confirmed by testing saliva or breath samples. Secondary outcomes included self-reported abstinence at 4 weeks and EOP, reduction in cigarette consumption of at least 50%, adverse events and birth outcomes.

Key findings

- There was no significant difference in validated prolonged abstinence between the e-cigarette and NRT arm.

- When participants who had regularly used a non-allocated product (participants in the NRT arm using e-cigarettes) were excluded, prolonged abstinence rates were statistically significantly higher in the e-cigarette group than the NRT group (RR=1.93 (95% CI 1.14–3.26) P=0.02)).

- Among smoking cessation secondary outcomes, self-reported abstinence at 4 weeks (RR=1.45 (95% CI 1.07–1.97), p=0.02)) and at EOP (RR=1.51 (95% CI 1.16–1.96), p=0.002)) were significantly higher in the e-cigarette arm than in the NRT arm. Differences in self-reported prolonged and validated abstinence at EOP were not statistically significant.

- When participants who regularly used a non-allocated product (mainly those in the NRT arm using e-cigarettes) were excluded, all secondary cessation outcomes were statistically significantly higher in the e-cigarette group.

- There was no statistically significant difference in validated cigarette reduction of 50% or more between the study arms. The rate of self-reported reduction was significantly higher in in the e-cigarette group (RR 1.25 (95% CI 1.06- 1.48) p=0.007)).

- Among birth outcomes, there were significantly fewer cases of low birthweight in the e-cigarette arm than in the NRT arm (RR 0.65 (95% 0.47–0.90) P=0.01). All other differences were non-significant.

- Rates of adverse and serious adverse events were similar between the two study arms.

Limitations

- There was low provision of saliva samples and breath samples, which limited power to detect a difference in validated outcomes between groups. Use of non-allocated products further reduced ability to detect differences between the arms.

- Results were from within the context of a randomised controlled trial in which behavioural support was available and so may not generalise to real-world contexts.

- Continued smoking abstinence after pregnancy was not investigated.

- End of pregnancy follow ups took place from 35 weeks gestation to 10 weeks post-partum meaning there was a wide range of follow up points between participants.

Hajek P, Przulj D, Pesola F, Griffiths C, Walton R, McRobbie H, Coleman T, Lewis S, Whitemore R, Clark M, Ussher M, Sinclair L, Seager E, Cooper S, Bauld L, Naughton F, Sasieni P, Manyonda I, Myers Smith K. Electronic cigarettes versus nicotine patches for smoking cessation in pregnancy: a randomized controlled trial. Nat Med. 2022 May;28(5):958-964. doi: 10.1038/s41591-022-01808-0. Epub 2022 May 16. PMID: 35577966; PMCID: PMC9117131.

Differences in cigarette smoking quit attempts and cessation between adults who did and did not take up nicotine vaping: Findings from the ITC four country smoking and vaping surveys – Gravely *et al.*

Study aims

This longitudinal study analysed data from waves 1-3 (2016-18) of the ITC Four Country Smoking and Vaping surveys in England, the USA, Canada and Australia. It investigated associations between initiating daily or non-daily vaping and smoking cessation attempts and/or cessation (stopping smoking) in adults (18+) who smoked at baseline with no history of regular vaping (n=3,516). Results were adjusted for sociodemographic variables, cigarette dependence, quit attempts prior to baseline, past use of nicotine replacement therapy and time in sample (to reflect that not all participants were recruited at the same time and this could affect outcomes).

Key findings

- People who initiated any vaping or daily vaping were significantly more likely than those who did not to make a quit attempt (aOR = 1.60, 95% CI:1.25–2.06, p<0.001). There was no statistically significant difference in rates of quit attempts between those who initiated non-daily vaping and those who did not initiate vaping.

- Among all participants (regardless of whether they made a quit attempt), those who initiated any vaping were significantly more likely to have quit smoking by follow-up than those who did not (aOR = 1.76; 95% CI: 1.27–2.44, p<0.001). Cessation rates were also significantly higher among people who initiated daily vaping compared to those who did not initiate vaping (aOR = 3.00, 95% CI: 2.08–4.33, p<0.001). However, there was no statistically significant difference in cessation rates between those who initiated non-daily vaping and those who did not initiate vaping.

- Among people who made a quit attempt, those who initiated daily vaping were significantly more likely to have stopped smoking than those who did not initiate vaping (aOR = 1.95, 95% CI:1.29–2.94, p=0.001). There was no statistically significant difference in cessation rates between those who initiated non-daily vaping and those who did not initiate vaping. There was also no significant difference between those who initiated vaping at any frequency and those who did not.

- Compared with people who did not initiate any vaping, those who were vaping daily at follow-up were significantly more likely to have made a quit attempt (aOR = 4.19; 95% CI: 2.58–6.82). Those who were vaping daily at follow-up and made a quit attempt were also more likely to have quit at follow-up ((aOR = 4.42; 95% CI: 2.60–7.52)). Quit rates were also higher among all respondents who were vaping daily at follow-up, whether or not they made a quit attempt (aOR = 6.77; 95% CI: 4.27–10.75).

- The positive association between initiation of daily vaping, quit attempts and smoking cessation was found in all four countries.

Limitations

- The underlying cohort study relied on self-reported data which were not biochemically verified and so are subject to recall and social desirability biases.
- The order in which people initiated vaping and made any attempt to stop smoking was not elicited, so causality cannot be inferred.
- Respondents were not asked about any use of other smoking cessation aids such as nicotine replacement therapy between surveys, which could affect quit attempts and cessation rates.
- Some of the subgroup sample sizes were small, which may limit the accuracy of estimates.
- The inclusion criteria means that people who had successfully stopped smoking by vaping or tried to stop by vaping were excluded. This could bias outcomes.
- Respondents who reported vaping daily at follow-up were not asked about their vaping frequency between surveys, so their pattern of use over time is unclear.

Gravely S, Meng G, Hammond D, Hyland A, Michael Cummings K, Borland R, Kasza KA, Yong HH, Thompson ME, Quah ACK, Ouimet J, Martin N, O'Connor RJ, East KA, McNeill A, Boudreau C, Levy DT, Sweanor DT, Fong GT. Differences in cigarette smoking quit attempts and cessation between adults who did and did not take up nicotine vaping: Findings from the ITC four country smoking and vaping surveys. Addict Behav. 2022 Sep;132:107339. Doi: 10.1016/j.addbeh.2022.107339. Epub 2022 Apr 28. PMID: 35605409; PMCID: PMC9202449.

Impact of vaping introduction on cigarette smoking in six jurisdictions with varied regulatory approaches to vaping: an interrupted time series analysis – *Wu et al.*

Study aims

This study investigated the effects of the introduction of e-cigarettes on cigarette smoking in six high-income jurisdictions (four Canadian provinces, the UK and Australia) with varying regulatory approaches to e-cigarettes. Jurisdictions were classified from less to most restrictive based on factors including permitted nicotine levels and restrictions on advertising and sales. Interrupted time series analysis was used to compare the trends for annual cigarette consumption per adult and prevalence of cigarette smoking among youths and young adults before and after the introduction of e-cigarettes in each jurisdiction. Analyses were adjusted for major tobacco control measures introduced and tobacco tax increases.

Key findings

- *Jurisdictions classed as less restrictive:* In Ontario the number of cigarette sticks sold per adult following the introduction of e-cigarettes declined significantly by 90.39 (95% CI −170.82 to −9.95, p=0.037). In Alberta there was no significant change in the number of cigarette sticks sold per adult, and smoking prevalence among young men aged 18-24 decreased significantly by 3.21% (95% CI −5.74 to –0.69, p = 0.027). There were no other statistically significant findings.

- *Jurisdictions classed as somewhat restrictive:* In Quebec, sales of cigarette sticks per adult per year reduced significantly following the introduction of e-cigarettes by 116.72 (95% CI -172.05 to -61.37, p=0.007), whereas they had previously been significantly increasing. Smoking prevalence also decreased significantly among young men (-4.47%, 95% CI −6.72 to −2.21, p = 0.024) and women (-5.62%, 95% CI−8.47 to −2.77, 0.008) aged 18-34. There were no other statistically significant findings. In British Columbia, there was no statistically significant change in any outcome measure.

- *Jurisdiction classed as more restrictive:* In the UK, there was no significant change in cigarette retail sales value per adult following the introduction of e-cigarettes. Smoking prevalence among young men aged 16-24 increased significantly by 1.88% (95% CI 0.33 to 3.42, p = 0.031). Among young men aged 25-34, smoking prevalence also increased significantly by 2.07% (95% CI 1.46 to 2.68, p= 0.002), continuing an underlying significant trend. There were no other statistically significant findings.

- *Jurisdiction classed as most restrictive:* In Australia, cigarette chain volume (a reflection of changes in sales quantity not affected by price) per adult increased significantly following the introduction of e-cigarettes by 119.91 (95% CI 55.64 to 184.18, p=0.015), slowing the underlying rate of decline. Smoking prevalence among young men aged 18-24 also increased significantly by 3.77% (95% CI 0.23 to 7.32, p = 0.044). There were no other statistically significant findings.

Limitations

- Not all countries collected data in the same way, so some comparisons were not exactly equivalent. For example, cigarette consumption per adult was calculated differently for Canada, the UK and Australia and the age ranges varied.

- The intervention period is defined based on the time following the start of data capture on e-cigarette use in national surveys in each country, so there may be a delay before the effects of the introduction of e-cigarettes become apparent.

- The outcome data are based on legal sales of tobacco products and do not include contraband.

- The data on age- and sex-specific tobacco use are based on surveys using self-reported data and as such are subject to recall and social desirability biases.

- The analysis did not control for other influences on cigarette sales and smoking prevalence, such as tobacco control measures and underlying long-term trends.

In some countries, the trend prior to the introduction of e-cigarettes was not statistically significant, and so changes could not be verified. Wu DC, Essue BM, Jha P. Impact of vaping introduction on cigarette smoking in six jurisdictions with varied regulatory approaches to vaping: an interrupted time series analysis. BMJ Open. 2022 May 2;12(5):e058324. Doi: 10.1136/bmjopen-2021-058324. PMID: 35501081; PMCID: PMC9062808.

Action on Smoking and Health (ASH). Use of e-cigarettes (vapes) among young people in Great Britain. 2022

Study aims

This report uses data from the ASH Smokefree GB Youth Survey carried out annually among young people in Great Britain since 2013 to examine trends in tobacco and e-cigarette use. The analysis focuses on 11-17-year-olds and the data are weighted to produce a representative sample.

Key findings

- 7% of young people currently vape, most of whom also currently smoke (55.4%) or used to smoke (29.7%) combustible cigarettes. This is compared with 3.3% in 2021 and 4.1% in 2020.
- 15.8% of young people have ever tried vaping, compared with 11.2% in 2021 and 13.9% in 2020.
- 92.2% of young people who have never smoked have either never used an e-cigarette or are unaware of them, and 7.5% have ever tried an e-cigarette.
- In 2022 the survey asked about awareness of e-cigarette promotions for the first time. 55.8% of young people were aware of some form of e-cigarette promotion. Among online sources of e-cigarette promotion, TikTok was the most common place to see promotions (45.4%), followed by Instagram (33.1%) and Snapchat (22.0%).
- 40.9% of young people incorrectly believe that e-cigarettes are as harmful as, or more harmful than, combustible cigarettes. This continues a long-term trend and follows findings of 40.9% in 2020 and 37.2% in 2021.
- Most young people who had ever used an e-cigarette (45.7%), including 65.4% of those who had never smoked, did so 'Just to give it a try.' Those who currently smoked and had also tried e-cigarettes were most likely to report that they did so because they liked the flavours (20.8%), because they enjoyed the experience (17.5%) or to stop smoking (10.7%).
- In terms of types of devices used, the prevalence of disposable e-cigarettes has risen from 7.7% in 2021 to 52% in 2022. This coincides with the introduction of 'puff bar' disposable vapes including popular brands such as 'Elf Bar' and 'Geek Bar.'

Helping the quitters quit: A systematic review and narrative synthesis of the barriers and facilitators to e-cigarette cessation and the support that is needed – Dyson *et al.*

Study aims

This is a systematic review of 10 studies (of which 8 were conducted in the US) on attitudes to barriers and facilitators to cessation of vaping and the impact of interventions. The 19,028 participants included people with different patterns of nicotine use, such as current smoking, dual use or vaping and having stopped smoking or ever tried an e-cigarette. The majority were adults and some were

adolescents. Where possible, results were combined to give an indication of the strength of influence of the factors. Potential interventions that could address particular barriers to stopping vaping were identified.

Key findings

- Three barriers to vaping cessation were identified: fear of returning to combustible tobacco (the main barrier cited in one study); dependency; and stress reduction as a consequence of vaping. The authors identified gradually reducing nicotine content of e-liquids and using nicotine patches or gum as potential support strategies to address the barrier of dependency.
- One facilitator to vaping cessation was identified: cessation support. This included gradually reducing nicotine concentration, switching to other flavours (e.g. using tobacco flavour to switch from cigarettes to e-cigarettes among people who smoke and then an alternative flavour to progress to vaping cessation), use of traditional nicotine replacement therapies, support from healthcare professionals and limiting e-cigarette use to places where someone would usually use tobacco.
- Four factors were identified which could be barriers or facilitators to vaping cessation, depending on context: health and hazard beliefs (such as beliefs about the relative harms of tobacco and e-cigarettes); degree of enjoyment (including flavour); social influences; and environment (such as price and being able to vape in places where smoking is not allowed).
- Of factors which could be barriers or facilitators, those most frequently cited were expense (mean 18.6%), health risks (mean 18.4%) and not liking the flavour/taste (mean 15.9%).
- People who had never smoked or formerly smoked were more likely to cite health concerns about vaping than people who currently smoked.
- Not liking the flavour of e-cigarettes was cited as a reason for stopping vaping in three studies, but may have influenced some participants to return to smoking, as in one study people who currently smoked were more likely to cite not liking e-cigarette flavours as a reason for vaping cessation.

Limitations

- Many of the papers were surveys in which respondents selected a response from a list and so did not allow for further exploration of the reasons for their responses.
- None of the underlying studies had vaping cessation or effects on smoking as an outcome. Therefore, the impact of certain barriers/facilitators on cessation of vaping or smoking behaviour cannot be determined. Some asked participants about intention to stop vaping, reasons for cessation or which interventions they thought would be helpful.
- The studies included varied in participant age, smoking and vaping experience. These characteristics may influence people's attitudes towards vaping cessation, so results cannot be generalised.
- Most of the studies were conducted in the US, which differs from the UK in its regulatory environment and public health messaging around e-cigarettes. None of the underlying studies were conducted in the UK, so the findings may not generalise to the UK population.
- Studies were cross sectional, so cannot determine changes in attitudes over time.

- There was insufficient research to allow identification of any associations with sociodemographic factors.

Dyson J, Bhatnagar M, Skinner J, Crooks M. Helping the quitters quit: A systematic review and narrative synthesis of the barriers and facilitators to e-cigarette cessation and the support that is needed. Patient Educ Couns. 2022 Jun;105(6):1402-1410. doi: 10.1016/j.pec.2021.09.024. Epub 2021 Sep 17. PMID: 34579994.

Commentary

This quarter, we cover two papers on e-cigarettes for smoking cessation, using different approaches. Hajek *et al* report results from the first randomized controlled trial of e-cigarettes for smoking cessation in pregnancy. The main analysis did not show a statistically significant difference between e-cigarettes and nicotine replacement therapy (NRT). However, this analysis was underpowered due to low rates of biochemical validation, and a substantial number of participants assigned to NRT used e-cigarettes. When accounting for either or both of these factors, participants assigned to e-cigarettes were statistically significantly more likely to be abstinent from cigarettes at end of pregnancy than those using NRT, which is consistent with results from pooled Cochrane analyses. There was no indication of a difference in harms between the two interventions, but there were fewer cases of low birthweight in the e-cigarette than NRT arm. Low birthweight is a common pregnancy complication in people who smoke, and this warrants further investigation.

Gravely et al used observational data from four countries to investigate associations between vaping and smoking cessation. They included people who smoked but did not vape at study start, and found that people who began to vape daily during the study period were more likely to try to quit smoking and to successfully quit smoking than those who didn't vape at all, or vaped less frequently. Other observational studies looking at associations between vaping and quitting smoking have had mixed findings. It is possible that the positive association between vaping and quitting smoking found by Gravely et al is partly due to the fact the sample included only those who didn't vape at study start. The study also demonstrates the importance of specifying vaping frequency in analyses.

Whereas Gravely et al looked at associations between vaping and smoking in individuals, Wu et al looked at these associations at the population level, investigating the relationship between vaping introduction and cigarette smoking across six areas with different e-cigarette regulations using interrupted time series analysis. Findings were mixed, and depended on regulations. In most settings where policies enabled substitution of cigarettes with e-cigarettes, the introduction of vaping appeared to reduce smoking rates further than would have been expected without the introduction of vaping. However, in settings that restricted uptake of e-cigarettes or prohibited nicotine e-cigarettes, the introduction of vaping appeared to increase smoking rates compared to what would have been expected.

This quarter, we also wanted to include population data on young people's vaping from ASH's new report. These annual surveys are an important way to monitor trends in vaping in Great Britain, and have received considerable media attention over the previous weeks. The new data show that the rate of regular youth vaping has gone up, though as in former years the large majority of young people who don't smoke don't vape, either. Within young people who vape, there has been a striking increase in the use of disposable e-cigarettes, mainly attributed to the rise of Geek Bar and Puff Bar products. In response, ASH has echoed the Khan review's call for greater investment in enforcement, and called for strengthening of laws prohibiting child-friendly packaging and labelling of vaping products, and preventing promotion on social media.

Finally, Dyson et al conducted a qualitative systematic review of factors that impact quitting vaping. They found 10 studies, of which 8 were from the US. They identified cessation support as a facilitator for vaping cessation, as well as three main barriers to vaping cessation: dependency; perceived benefits of vaping for stress reduction; and fear of returning to combustible tobacco. The studies varied in their participants, including experience of smoking, and none were from the UK. More research is needed into vaping cessation, including further exploration of how to support people who have quit smoking through vaping, in order to avoid smoking relapse.

Search strategy

The Pubmed database is searched in the middle of every third month, for the previous three months 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 OR vaping)).

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 are not included. Please note studies funded by the tobacco industry are also excluded.

This briefing is produced by Julia Cotterill and Alice Davies from Cancer Research UK with assistance from Associate Professor Jamie Hartmann-Boyce at the University of Oxford, primarily for the benefit of attendees of the CRUK 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.