The UK Electronic Cigarette Research Forum

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Electronic Cigarette Research Briefing – February 2024

This research briefing is part of a series of quarterly updates aiming to provide an overview of new studies on electronic cigarettes (e-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.

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

Jamie Hartmann-Boyce and Nicola Lindson discuss emerging evidence in e-cigarette research. In the latest episode, Jamie Hartmann-Boyce and Nicola Lindson discuss e-cigarette packaging, flavours and brand names with Eve Taylor, King's College London. 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 Cancer Research UK (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 January 2024 and includes 10 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.

As part of a Cancer Research UK funded project grant, researchers are looking to get feedback on a set of recommendations for future research exploring the relationship between e-cigarette use and subsequent smoking in young people. The survey is anonymous and on average takes 10-15 minutes – any researchers or policymakers with an interest in this topic are encouraged to complete it, and share it with their networks: https://forms.office.com/e/2zm3HmuqTn

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.

Summary

We start this quarter's bulletin with an update to the Cochrane Living Systematic Review of E-cigarettes for Smoking Cessation. A further 10 trials have been added, confirming existing conclusions showing that e-cigarettes with nicotine lead to higher quit rates than nicotine replacement therapy, non-nicotine e-cigarettes, or matched levels of behavioural support. Randomised controlled trials are considered the best way to establish causality, but can be limited in their degree of generalisability. Fortunately, large, well-conducted cohort studies can be used to triangulate this trial data. Jackson *et al* is a great example of this, using data from the English Smoking and Alcohol Toolkit Study up to 2022. They found a statistically significant association between the increase in e-cigarette use and the success of quit attempts, and conclude that if this association is causal, the use of e-cigarettes in quit attempts has helped approximately 30,000 to 50,000 additional people who smoke in England to successfully quit smoking each year since e-cigarettes became popular in 2013, over and above those who quit before e-cigarettes were available.

Our other three studies this month also use observational data, in different forms. Ammar et al use data from a US pregnancy cohort and report that exclusive e-cigarette use in pregnancy was associated with preterm birth and lower birth weight, though the latter association was not statistically significant after adjusting for age. Risks were reduced in those who quit vaping during pregnancy compared to those who continued vaping during pregnancy. Risk was highest in those using combustible cigarettes (with or without concurrent vaping), as opposed to not smoking or vaping, or vaping only. These data are somewhat limited due to small sample sizes for vaping analyses and a limited number of confounders available for analyses, but provide important avenues for further investigation.

Etter followed 375 people who vaped continuously over eight years – this is a small sample size for this type of study, but still very useful given the scarcity of data available on people who have vaped for longer periods of time. In this cohort of continuous vapers, smoking rates went down over time, as did self-reported levels of nicotine dependence, use of tobacco flavours, and nicotine content.

Finally, Borowiecki and colleagues used US Sales data to examine device types and flavours purchased before and after FDA's prioritised enforcement policy on flavoured e-cigarettes. This policy restricted sale of all unauthorised flavoured cartridge based e-cigarettes (other than tobacco and menthol). Sales of these appeared to decline accordingly, but this was accompanied by a steep rise in sales of disposable e-cigarettes, which were largely driven through sales of fruit flavoured products. The authors conclude that this highlights the weaknesses of selective regulation, and suggests the need for more comprehensive approaches to flavour regulations. Further analyses of US approaches and unintended consequences may help inform actions proposed in the UK regarding new vaping legislation.

Lindson et al: **Electronic cigarettes for smoking cessation**

Study aims

This is the latest update of the Cochrane Living Systematic Review of trials comparing nicotine e-cigarettes with non-nicotine e-cigarettes, other smoking cessation treatments and no treatment. Outcomes investigated are smoking abstinence of at least six months, adverse events and serious adverse events. This update includes 88 studies, of which 47 were randomised controlled trials, and 27, 235 participants.

Key findings

- High-certainty evidence was found that quit rates among people randomised to nicotine e-cigarettes were higher than those randomised to nicotine replacement therapy ('NRT') (RR 1.59, 95% CI 1.29 to 1.93).
- Moderate-certainty evidence was found that quit rates among people randomised to nicotine e-cigarettes were higher than those randomised to non-nicotine e-cigarettes (RR 1.46,95% CI 1.09 to 1.96).
- Low-certainty evidence was found that quit rates among people randomised to e-cigarettes were higher than those randomised to behavioural support only or no support (R 1.88, 95% CI 1.56 to 2.25).
- Moderate-certainty evidence was found that rates of adverse events were similar between participants randomised to nicotine e-cigarettes and those randomised to NRT (RR 1.03, 95% CI 0.91 to 1.17) and that there was no difference in rates of adverse events between participants who used nicotine and non-nicotine e-cigarettes (RR 1.01, 95% CI 0.91 to 1.11).
- There was insufficient evidence to determine whether rates of serious adverse events differed between those randomised to nicotine e-cigarettes and other groups.

Limitations

- The small number of randomised controlled trials reporting adverse and serious adverse events leads to imprecision.
- None of the included studies tested disposable e-cigarettes, so the Review is unable to investigate their effects when used for smoking cessation.
- Studies included in the Review only include data on safety for up to two years, so the Review is unable to explore longer-term effects.

Lindson N, Butler AR, McRobbie H, Bullen C, Hajek P, Begh R, Theodoulou A, Notley C, Rigotti NA, Turner T, Livingstone-Banks J, Morris T, Hartmann-Boyce J. Electronic cigarettes for smoking cessation. Cochrane Database Syst Rev. 2024 Jan 8;1(1):CD010216. doi: 10.1002/14651858.CD010216.pub8. PMID: 38189560; PMCID: PMC10772980.

Jackson *et al.* Associations of prevalence of e-cigarette use with quit attempts, quit success, use of smoking cessation medication, and the overall quit rate among smokers in England: a time-series analysis of population trends 2007-2022

Study aims

This time-series analysis uses data from the Smoking Toolkit Study from January 2007 to December 2022 to investigate any association between prevalence of e-cigarette use in England, smoking cessation attempts and success and use of licenced smoking cessation treatments. Respondents who reported currently smoking every day or some days or having stopped smoking within the past year (n = 67,548) were asked about use of nicotine products, including e-cigarettes and quit attempts. Respondents who reported making one or more quit attempts in the past year were asked about any cessation aids used in their most recent attempt. Analyses were adjusted for government spending on national tobacco control mass media campaigns, tobacco control policies, and onset of the Covid-19 pandemic.

Key findings

- No association was found between prevalence of e-cigarette use among participants who currently smoked and the number of quit attempts or overall quit rates (defined as the number who reported they were still not smoking following a quit attempt divided by the number of participants who reported smoking in the past year).
- In adjusted analyses, prevalence of e-cigarette use during a quit attempt was positively associated with the quit success rate, with every 1% rise in use associated with a 0.040% increase in the quit success rate (95% CI 0.019-0.062, p<0.001).
- No association was found between prevalence of e-cigarette use during a quit attempt and use of licenced smoking cessation treatments.

Limitations

- Some data are missing and were estimated. For example, the Smoking Toolkit Study did not collect data on e-cigarette use until 2009, and between 2009 and 2011 only use of e-cigarettes in a recent quit attempt was recorded rather than use prevalence.
- The time period covered includes the Covid-19 pandemic, during which the data collection method changed from face-to-face to telephone.
- The analysis did not adjust for frequency or intensity of smoking.

Jackson SE, Brown J, Beard E. Associations of prevalence of e-cigarette use with quit attempts, quit success, use of smoking cessation medication, and the overall quit rate among smokers in England: a time-series analysis of population trends 2007-2022. Nicotine Tob Res. 2024 Jan 12:ntae007. doi: 10.1093/ntr/ntae007. Epub ahead of print. PMID: 38214664.

Ammar *et al.* Electronic cigarette use during pregnancy and the risk of adverse birth outcomes: A cross-sectional surveillance study of the US Pregnancy Risk Assessment Monitoring System (PRAMS) population

Study aims

This cross-sectional secondary analysis of data from the US Pregnancy Risk Assessment Monitoring System (PRAMS) aimed to investigate any associations between use of e-cigarettes during pregnancy and risk of preterm birth, low birth weight, and small-for-gestational-age (SGA) among 190,707 survey participants who had singleton live births between 2016 and 2020. Potential confounders adjusted for included maternal age at delivery, maternal ethnicity, maternal education, marital status, household income and pre-pregnancy body mass index (BMI).

Key findings

- Compared with non-use, e-cigarette only use was associated with a significantly increased risk of low birth weight (aRR: 1.38, 95% CI: 1.09, 1.75).
- Use of combustible cigarettes only and dual use of combustible cigarettes and e-cigarettes were both associated with significantly increased risks of preterm birth, low birth weight, and SGA.
- When additionally adjusted for gestational age, the association between e-cigarette only use and low birth weight became non-significant but remained significant for combustible cigarette only (aRR: 1.54, 95%CI: 1.45, 1.64) and dual (aRR: 1.71, 95%CI: 1.42, 2.06) use.

- Among women who did not use combustible cigarettes either before or during pregnancy and quit using e-cigarettes during pregnancy the risk of preterm birth (aRR: 0.68, 95%CI: 0.48, 0.98) and low birth weight (aRR: 0.60, 95%CI: 0.42, 0.84) were significantly lower than those who did not quit vaping.

Limitations

- The survey relies on self-reported use in the last 3 months of pregnancy, which was not biochemically verified and so the data are subject to potential inaccuracy and bias.
- Some subsample sizes are small (for example, 977 women were included in the analysis of those who used e-cigarettes during the last 3 months of pregnancy), so the study may be underpowered to detect effects.
- As a cross-sectional study, it is unable to establish causality.
- There may be additional unidentified confounders not accounted for in the analysis.
- Only women who had live births are included in the study, so it is unable to investigate any association between use of e-cigarettes on foetal survival.
- Smoking and vaping intensity were not adjusted for in the analysis of product use and adverse birth outcomes.

Ammar L, Tindle HA, Miller AM, Adgent MA, Nian H, Ryckman KK, Mogos M, Piano MR, Xie E, Snyder BM, Ramesh A, Yu C, Hartert TV, Wu P. Electronic cigarette use during pregnancy and the risk of adverse birth outcomes: A cross-sectional surveillance study of the US Pregnancy Risk Assessment Monitoring System (PRAMS) population. PLoS One. 2023 Oct 24;18(10):e0287348. doi: 10.1371/journal.pone.0287348. PMID: 37874824; PMCID: PMC10597477.

Etter. An 8-year longitudinal study of long-term, continuous users of electronic cigarettes

Study aims

This longitudinal study surveyed adults who currently or formerly used e-cigarettes recruited via a smoking cessation website and e-cigarette websites in 2012-16. In 2021, 375 participants were resurveyed who were still vaping daily or occasionally and had been vaping continuously for at least 5 years. Its aim was to identify any changes in use behaviour, attitudes and dependence over time.

Key findings

- Compared with the original survey, respondents were significantly less likely to report smoking in the past 31 days ($T = 6.5$, $p<0.001$).
- Compared with the original survey, respondents were significantly less likely to report vaping in order to quit smoking or avoid relapse ($Z = 4.6$, $p<0.001$) or deal with tobacco cravings ($Z = 6.1$, $p<0.001$) or withdrawal symptoms ($Z = 7.9$, $p<0.001$).
- Compared with the original survey, respondents reported significantly lower perceived addiction to e-cigarettes ($Z = 3.8$, $p<0.001$), strong or extremely strong urges to vape ($Z = 4.9$, $p<0.001$) and frequency of urges to vape ($Z = 5.4$, $p<0.001$).

Limitations

- Characteristics of both the original survey population and the subsample resurveyed in 2021 are unlikely to be representative of the general population or to generalise to people in the

UK who vape. For example, the original 2012-16 sample was recruited via smoking cessation and e-cigarette websites and people who had been vaping long term and were satisfied with vaping were oversampled. Respondents in 2021 differed significantly in several respects from those in 2021-16.

- The study relied on self-reported use behaviour and tobacco and e-cigarette use were not biochemically verified.
- The sample size in the 2021 survey was relatively small at 375, as were subsamples within it, and as such the study may be underpowered to detect effects.

Etter JF. An 8-year longitudinal study of long-term, continuous users of electronic cigarettes. Addict Behav. 2024 Feb;149:107891. doi: 10.1016/j.addbeh.2023.107891. Epub 2023 Oct 15. PMID: 37866230.

Borowiecki *et al.* A Patchy Prohibition: Product and Flavor Substitution After the Food and Drug Administration's Prioritized Enforcement Policy on Flavored E-cigarettes

Study aims

This US study used e-cigarette sales data to examine device types and flavours purchased before and after the FDA's enforcement policy. This was introduced in February 2020 and restricted the sale of all unauthorised flavoured cartridge-based e-cigarettes (also known as pod systems) other than tobacco and menthol flavour. Data obtained from The Nielsen Company are analysed from March 2017 to December 2021 and include sales of pod systems and disposable devices in convenience stores, grocery stores, pharmacies, mass merchandisers, club stores, discount stores, and military commissaries but not online or in specialty stores such as tobacco and vape shops. The average percentage change in sales per 4-week period ('AMPC') is calculated.

Key findings

- Overall e-cigarette sales declined significantly between July 2019 and March 2020 (AMPC −2.58, 95% CI −3.17, −1.99, p<.001), which includes the 'EVALI' lung disease outbreak in the US from August 2019 caused by contaminated illicit vapes. Sales growth resumed between March and May 2020 (AMPC 9.6, 95% CI 4.83, 14.58, p<.001) and slowed between May 2020 and December 2021 (AMPC 0.53, 95% CI 0.41, 0.64, p<.001)
- Sales of prefilled pod e-cigarettes also declined between July 2019 and March 2020 (AMPC −3.60 (95% CI −4.23, −2.97, p<0.001)), followed by no significant change between March and May 2020 then a slower increase (AMPC 0.5, 95% CI 0.37, 0.64, p< 0.001) between May 2020 and December 2021.
- Sales of disposable e-cigarettes increased rapidly between December 2019 and March 2020 (AMPC 48.75, 95% CI 37.46, 60.96, p<.001), followed by slower increases until August 2020. They then declined significantly between August 2020 and February 2021 (AMPC −2.77, 95% CI −3.57, −1.97, p<.001), increased again between February and May 2021 (AMPC 5.02, 95% CI 1.21, 8.97, p=.011).
- The rapid rise in sales of disposable e-cigarettes seen in 2020 was largely driven by fruit-flavoured products, mainly 'mentholated fruit' flavours such as 'Banana Chill.'

Limitations

- The study does not include online sales, specialist vape or tobacco shops or products other than pod and disposable e-cigarettes and so does not reflect the whole market for vaping products.
- Factors such as the 'EVALI' outbreak, the Covid-19 pandemic and withdrawal by JUUL of certain flavours are potential confounders, as they are likely to have influenced purchasing behaviour in addition to the FDA enforcement decision.

Borowiecki M, Kim Y, Emery S. A Patchy Prohibition: Product and flavor substitution after the FDA's prioritized enforcement policy on flavored e-cigarettes. Nicotine Tob Res. 2023 Nov 8:ntad212. doi: 10.1093/ntr/ntad212. Epub ahead of print. PMID: 37948576.

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 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.