# The UK Electronic Cigarette Research Forum

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## Electronic Cigarette Research Briefing – May 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 interview Dr Ian Pope, an emergency medicine physician and honorary associate professor at Norwich Medical School, about his new trial, the COSTED trial, the Cessation of Smoking Trial in the Emergency Department (also covered in this briefing). 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. A further update is currently underway.

**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**

This quarter we bring you a diverse group of studies.

March saw the publication of the COSTED trial by **Pope *et al***. This trial, conducted in UK adults who smoked and were attending emergency departments, compared e-cigarette advice, an e-cigarette starter kit and referral to stop smoking services with a control group who received a leaflet. At six months, abstinence was significantly higher in the intervention than control group. No serious adverse events were reported related to the intervention. This new trial adds to a strong body of evidence showing that nicotine e-cigarettes can increase quit rates and do not appear to cause serious adverse events in trial settings. It's encouraging to see this translated into a new environment, namely, emergency departments.

The remaining four studies in this briefing have young people as a unifying theme. Two used large surveys. **Gomes *et al*** investigated nicotine dependence via a multi-national survey of people aged 16 to 19. Amongst young people who vaped, the authors found that dependence increased from 2017-2022. In 2017, indicators of vaping dependence were substantially lower for vaping than smoking, whereas by 2022 this shifted, including prevalence of vaping compared to smoking within 30 minutes of waking. The authors call for further research to examine factors underlying dependence among young people who vape, including nicotine profile and design of e-cigarettes.

**Jackson *et al*** used data from the Smoking Toolkit Study to investigate changes in prevalence of disposable e-cigarette use in adults between Jan 2021 and August 2023. Use of disposables increased across most populations during this time, with increases most pronounced in young people, people who currently smoked, and people who had recently stopped smoking. The authors conclude that a ban on disposable e-cigarettes (which is in the process of being introduced across the UK) would affect 1 in 20 adults in Great Britain, and that this would most affect young people, including both those who had never smoked and those who currently smoke or previously smoked.

Of course, device type is not the only e-cigarette characteristic that might affect use patterns. In their online study of young people in the UK aged 11-17 who had never regularly smoked or vaped, **Dyer *et al*** compared responses to different flavouring descriptions. They found that young people responded more positively to the flavoured than unflavoured descriptions, and participants rated sweet/candy flavour packs as more child-oriented than fruit packs. The authors note that although packaging responses were more positive for flavoured than unflavoured products, overall adolescents who did not smoke or vape had low appraisal and receptivity for e-liquids regardless of flavour.

Finally, **Matheson *et al*** was a small study comparing 21 people who reported regular e-cigarette use with 21 demographically matched participants who reported non-use, aged 21-31. Of the 21 people who used e-cigarettes regularly, 20 reported having never smoked. The authors found that participants who vaped were more likely to have premature microvascular (small blood vessel) dysfunction. Macrovascular (large blood vessel) dysfunction was found in those reporting using e-cigarettes for longer than three years. The authors state that together, these findings associate regular e-cigarette use with premature vascular dysfunctions, which may lead to adverse cardiovascular outcomes. Larger studies with cardiovascular endpoints would be needed to confirm this.

## Pope *et al:* Cessation of Smoking Trial in the Emergency Department (COSTED): a multicentre randomised controlled trial

**Study Aims**

This randomised controlled trial investigated the effectiveness of offering an opportunistic smoking cessation intervention using e-cigarettes in the emergency department to adult patients (18+) who smoke. Between January and August 2022, adults attending emergency departments at six UK hospitals were randomised to an intervention group (n = 484) who received brief advice, an e-cigarette starter kit and referral to stop smoking services, or a control group (n = 488) who received a leaflet with information on stop smoking services. Participants were followed up at one, three and six months to ask their current smoking status, and those who reported abstinence at 6 months were invited to undergo carbon monoxide test. The primary outcome was continuous biochemically-verified abstinence at six months (defined as having smoked fewer than six times in the past six months). Secondary outcomes included self-reported 7-day point prevalence smoking status at one, three and six months and self-reported serious adverse events (resulting in hospitalisation) and adverse events (dry cough and throat/mouth irritation).

**Key Findings**

- Biochemically-verified self-reported continuous abstinence at 6 months was significantly higher in the intervention group (7.2%) than in the control group (4.1%) (RR 1.76, 95% CI 1.03 to 3.01, p = 0.038).
- Self-reported 7-day point prevalence abstinence was significantly higher in the intervention group than the control group at 1 (RR 1.92, 95% CI 1.39 to 2.64, p < 0.0001), 3 (1.97, 95% CI 1.47 to 2.63, p < 0.0001) and 6 (RR 1.80, 95% CI 1.36 to 2.38, p < 0.0001). No serious adverse events were reported that were related to the intervention.

**Limitations**

- In order to obtain follow-up data, it was necessary for participants allocated to the control group to receive not only the leaflet but interaction with the research team (for example, carbon monoxide testing, questions about smoking history and follow-up contact to ask about smoking behaviour), which could have increased quit rates in this group.
- There was difficulty in encouraging participants to undergo biochemical validation, so of those who reported continuous abstinence at 6 months a minority underwent biochemical validation (35/122 (28.7%) in the intervention group and 20/64 (31.3%) in the control group) and more participants in the intervention group underwent validation than in the control group.

Pope I, Clark LV, Clark A, Ward E, Belderson P, Stirling S, Parrott S, Li J, Coats T, Bauld L, Holland R, Gentry S, Agrawal S, Bloom BM, Boyle AA, Gray AJ, Morris MG, Livingstone-Banks J, Notley C. Cessation of Smoking Trial in the Emergency Department (COSTED): a multicentre randomised controlled trial. Emerg Med J. 2024 Mar 26:emermed-2023-213824. doi: 10.1136/emermed-2023-213824. Epub ahead of print. PMID: 38531658.

## Gomes *et al*: Comparison of indicators of dependence for vaping and smoking: Trends between 2017 and 2022 among youth in Canada, England and the United States

**Study aims**

This cross-sectional study used data from the International Tobacco Control Policy Evaluation Project (ITC) Youth Tobacco and Vaping Study. It examined trends in measures of nicotine dependence between 2017 and 2022 among young people aged 16-19 who reported smoking and/or vaping in the past 30 days (n = 23,145) in Canada, England and the US. Respondents completed four measures of dependence for both smoking and vaping: perceived addiction, frequent strong urges, time to use after waking and days used in the past month. Two measures were used for vaping only: use events per day and E-cigarette Dependence Scale.

**Key findings**

In England:

- All six indicators of dependence increased significantly among participants who reported vaping in the past 30 days.
- Most measures also increased significantly among participants who reported smoking in the past 30 days.

Among all respondents:

- Perceived addiction to vaping was higher among those who dual used than those who exclusively vaped (AOR 2.19, 95% CI 2.02 to 2.38), but this difference narrowed over time (F=3.23, p=0.002). A similar pattern was found for strong urges to vape 'at least most days' (AOR 1.95, 95% CI 1.80 to 2.11; F=4.01, p=0.0002).
- The difference in the proportion of respondents who smoked within 30 minutes of waking between those who exclusively smoked and those who dual used widened over time. In 2022 respondents who dual used reported smoking their first cigarette later than those who exclusively smoked (AOR 0.53, 95% 0.40 to 0.70).

**Limitations**

- The ITC survey relies on self-reported data and is not biochemically verified, so results are open to bias.
- Participants were selected based on past-30-day smoking and vaping and any previous smoking or vaping history was not included.
- Categories of use were wide (for example, whether the first vaping episode/cigarette smoked occurred within 30 minutes or longer than 30 minutes of waking), so more detailed categories could not be reflected in the results.
- Some subsample sizes were relatively small (for example, the largest subsample among English participants by smoking/vaping status was 599 respondents who exclusively vaped in 2022).
- The study sample may not be representative of the wider UK population.

- Figures for individual countries are presented for all respondents reporting smoking/vaping in the past 30 days and not separated into those who exclusively smoked/vaped and those who dual used, so country-level differences between these groups are not available.

Gomes MN, Reid JL, Rynard VL, East KA, Goniewicz ML, Piper ME, Hammond D. Comparison of indicators of dependence for vaping and smoking: Trends between 2017 and 2022 among youth in Canada, England and the United States. Nicotine Tob Res. 2024 Mar 26:ntae060. doi: 10.1093/ntr/ntae060. Epub ahead of print. PMID: 38531767.

**Jackson *et al:* Who would be affected by a ban on disposable vapes? A population study in Great Britain**

**Study aims**

This study used monthly cross-sectional data from respondents (n = 69,973) to the Smoking Toolkit Study in Great Britain. It investigated changes in the prevalence of disposable e-cigarette use among adults (18+) between January 2021 and August 2023 (n = 67,977). Modelling was used to estimate changes in disposable use stratified by sociodemographic characteristics including age and smoking status. The sociodemographic characteristics and smoking status of respondents (16+, n = 19,134) using disposable devices in 2023 were compared with those using refillable and pod devices.

**Key findings**

- Use of disposable e-cigarettes increased significantly across most adult population subgroups between 2021 and 2023. Larger modelled increases were seen among younger people than among older age groups. For example, an increase of 15.59 percentage points (95% CI 11.73-18.17) among 18-year-olds compared to 2.26 pp among 55-year-olds (95% CI 1.69-2.73) and no significant change among 65-year-olds. Particularly large increases in modelled prevalence were also found among people who currently smoked (15.90 percentage points, 95% CI 13.01-17.60, an estimated 1.2 million people in 2023) and had stopped smoking less than a year previously (17.88, 95% CI 10.86-23.19, an estimated 242,000 people in 2023). The increase in modelled prevalence of use of disposable e-cigarettes between January 2021 and June 2023 was about three times higher among people who had a history of mental illness (9.24, 95% CI 7.05-9.89) than among those who did not (3.00, 95% CI 2.23-3.37).

- There was no significant increase in use of disposable e-cigarettes among adults who had never smoked. Exploratory analysis of the modelled data found that the largest rise in prevalence of disposable vaping among respondents who had never smoked was in the 18-24 age group, of whom 7.1% used disposable devices in August 2023 (estimated at around 316,000 people).

- People who had never smoked regularly were approximately twice as likely to use disposable e-cigarettes (19.0%, 95% CI 16.0-22.4) than either refillable (10.2%, 95% CI 8.1-12.8) or pod (9.2%, 95% CI 5.6-14.6).

**Limitations**

- The definition of 'never-smoking' was never having smoked for a year or more, so the results may overestimate use prevalence among those who have never smoked.

- Participants aged 16 and 17 were not surveyed in 2021, so it was not possible to include this age group in the trend analysis.

- Participants were asked which device type they mainly used, so the data would not reflect any secondary devices used.

- Some subsample sizes were relatively small, for example 245 participants who had never smoked, of whom 134 used disposable e-cigarettes, and some confidence intervals are wide.

Jackson SE, Tattan-Birch H, Shahab L, Oldham M, Kale D, Brose L, Brown J. Who would be affected by a ban on disposable vapes? A population study in Great Britain. Public Health. 2024 Feb;227:291-298. doi: 10.1016/j.puhe.2023.12.024. Epub 2024 Jan 24. PMID: 38267284.

**Dyer *et al*: Do Flavour Descriptions Influence Subjective Ratings of Flavoured and Unflavoured E-liquids Among Non-smoking and Non-vaping UK Adolescents?**

**Study aims**

This online observational study aimed to investigate any association between flavoured and unflavoured descriptions on e-liquid packaging and young people's perceptions of them. 120 young people from the UK aged 11-17 who had never smoked nor vaped regularly (defined as not having tried smoking or vaping on more than 10 occasions) viewed images of e-liquid packaging with flavoured and unflavoured descriptions (with other characteristics kept consistent) and completed a survey. Primary outcomes were packaging appraisal, packaging receptivity, perceived harm, and perceived audience. Secondary analysis compared the same outcomes between sweet and fruit flavoured descriptions.

**Key findings**

- Packaging appraisal (comprising how attractive, eye-catching, cool and boring/fun respondents rated the pack) was significantly higher (more positive) for the flavoured descriptions than the unflavoured (mean difference 5.9, 95% CI: 4.2 to 7.6, $p < .001$).

- Packaging receptivity (comprising how 'meant for someone like me' the pack was, to what extent it tempted respondents to smoke, how much respondents liked and would like to have the pack and to what extent it tempted respondents to vape) was significantly higher for the flavoured descriptions than for the unflavoured descriptions (mean difference 4.2, 95% CI: 2.8 to 5.6, $p < .001$).

- Perceived audience (comprising how childish/grown-up respondents rated the pack) was significantly lower for the flavoured descriptions than the unflavoured (mean difference -4.9, 95% CI -7.3 to -3.1, $p<.001$), indicating that participants rated the flavoured packs as more childish than the unflavoured ones.

- Perceived audience was also significantly lower for the fruit than the dessert-flavoured packs (mean difference −3.0, 95% CI: −4.7 to −1.2, $p = .001$), indicating that participants rated the sweet-flavour packs as more childish than the fruit-flavoured packs.

**Limitations**

- The question to respondents was "…can you tell me the number that best describes the packaging?" so there may have been some variation in how the question about harmfulness was interpreted to mean the product or the packaging it was in.

- Unflavoured e-liquid availability in the UK is limited, so the packaging used in the study was not necessarily representative of the UK market.

- The secondary analyses were underpowered and so may not have detected effects.

- Only five examples of flavour descriptions were used for each category, so the findings may not generalise to other products on the market, including disposable e-cigarettes, which are more popular with this age group.

- There was high attrition (29%) and 26% of respondents took longer than predicted to complete the survey, which could introduce bias if they were taking breaks. The length of the survey may have been onerous for adolescents.

Dyer ML, Suddell SF, Khouja JN, Havill MA, Blackwell AKM, Maynard OM, Munafò MR, Attwood AS. Do Flavour Descriptions Influence Subjective Ratings of Flavoured and Unflavoured E-Liquids among Non-Smoking and Non-Vaping UK Adolescents? Nicotine Tob Res. 2024 Mar 12:ntae054. doi: 10.1093/ntr/ntae054. Epub ahead of print. PMID: 38468465.

**Matheson *et al:* Evidence of premature vascular dysfunction in young adults who regularly use e-cigarettes and the impact of usage length**

**Study aims**

This study compared measures of micro- and macrovascular function in young people who vaped regularly with those who did not vape. Participants were adults aged 21-31 (n = 42), of whom 21 had used e-cigarettes at least three times a week for at least three months and 21 participants did not use them and were demographically matched in age, sex and body mass index. 20 members of the e-cigarette use group reported never smoking tobacco. Exclusion criteria included use of any tobacco product within the past 60 days and diagnosis of any cardiovascular disease. Participants underwent reactivity tests to investigate micro- and macrovascular function, which are often markers of cardiovascular and other diseases. Measures of micro- and macrovascular function were compared between the e-cigarette and non-e-cigarette groups and between those who reported vaping for three years or less and those who had vaped for more than three years.

**Key findings**

- Several measures of microvascular function were significantly lower in the e-cigarette group than the non-use group. For example, a significantly lower overall hyperaemic response in the post-occlusive hyperaemia test (red blood flux p = 0.003).

- No differences in measures of macrovascular function were found between the e-cigarette and non-use groups.

- Two measures of microvascular (red blood flux p = 0.044 and cutaneous vascular conductance p = 0.036 in the post-occlusive hyperaemia test) and one of macrovascular function (flow-mediated dilation, p = 0.002) were found to be significantly reduced among participants who had used e-cigarettes for more than three years compared to those who had used them for up to three years.

**Limitations**

- The sample size was very small and details of other demographic aspects such as ethnicity and deprivation are not provided, so the results may not generalise to the UK population. There may also be additional potential confounding factors.

- The study was carried out in the US, which has a different regulatory climate, so the devices and liquids used may not be comparable to those available in the UK.

- Comparisons were made between use/non-use and duration of use. It was therefore not possible to investigate any effects of patterns/intensity of use or different device/e-liquid types.

- Smoking and vaping status and history were assessed through self-report and not biochemically verified.

- Participants were only excluded if they had used tobacco products within the preceding 60 days, so any less recent smoking history would not be captured. While participants in the non-use group did not currently vape, it is unclear whether they had vaped previously.

- Recruitment methods are not clear, so there may be a risk of sampling bias.

Matheson C, Simovic T, Heefner A, Colon M, Tunon E, Cobb K, Thode C, Breland A, Cobb CO, Nana-Sinkam P, Garten R, Rodriguez-Miguelez P. Evidence of premature vascular dysfunction in young adults who regularly use e-cigarettes and the impact of usage length. Angiogenesis. 2024 Feb 12. doi: 10.1007/s10456-023-09903-7. Epub ahead of print. PMID: 38345700.

**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.