Electronic Cigarette Research Briefing – July and August 2021

This research briefing is part of a series of 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. 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.

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

July 2021

Jamie Hartmann-Boyce and Nicola Lindson discuss emerging evidence in e-cigarette research. Dr Katie Myers Smith discusses findings from her recent study looking at e-cigarettes versus nicotine replacement therapy (NRT) as a harm reduction intervention for people who smoke and who find quitting difficult.

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This podcast series is funded by CRUK.

1. From gateways to multilinear connections: A qualitative longitudinal investigation of the relationships between vaping and smoking among adolescent users

- **Study Aims**

  This qualitative UK study investigated trajectories of e-cigarette and cigarette use in a socio-economically diverse sample of adolescents (aged 14-18). Participants (n=36) were a mixture of regular, frequent or sporadic e-cigarette users and were interviewed twice, with an interval of 6 to 12 months between interviews. Analyses explored understandings, uses, experiences of e-cigarettes, tobacco and other substances or behaviours.

- **Key Findings**

  Participants highlighted categorical differences between vaping and smoking, with some expressing cultural stigmatisation and denormalisation of smoking. The connections and contrasts between smoking and vaping often involved complex interactions of ethnicity, gender, status and social class.

  Some participants positioned vaping in an age/phase bound manner. For example, one participant described e-cigarettes as a phase, comparing them to loom bands. Others described vaping as one of a collection of behaviours linked to growing up and trying new experiences.

  26 participants had tried both smoking and vaping by the second phase of interviews. All but four of these participants had tried smoking first. When participants drew connections between e-cigarette use and smoking, these associations were complex and included factors involved in adolescent development, transitioning between friendship groups and navigation of the social landscape.

  Participants demonstrated an understanding of the risks associated with vaping (for example addictiveness, potential to lead to smoking and potential long-term harms), however described aspects of their own use that contradicted these ideas.

- **Limitations**

  Incentives were used to boost recruitment which may have resulted in participant self-selection.

  Most participants smoked before using e-cigarettes meaning there were limited accounts exhibiting the gateway effect.

  The sample size was small, so findings cannot be generalised to the broader population.

  The study included a fairly broad age range of participants, so it's unclear how findings differ between older/younger adolescents.

Hughes J, Sykes G, Hughes K, O'Reilly M et al. (2021). From gateways to multilinear connections: A qualitative longitudinal investigation of the relationships between vaping and smoking among adolescent users. *Int J Drug Policy*. doi: 10.1016/j.drugpo.2021.103341.

2. Trends in use of e-cigarette device types and heated tobacco products from 2016 to 2020 in England

- **Study Aims**

  This English study reviewed data collected from 3786 adults (aged 16+) who reported currently using e-cigarettes or heated tobacco products (HTPs) between 2016-2020. Changes in device types and nicotine concentrations used over this time period were assessed. Differences in e-cigarette device type or nicotine concentration used by smoking status was also assessed.

- **Key Findings**

  Among e-cigarette users, 53.7% (52.0-55.1%) used tank devices, 23.7% (22.4-25.1%) used modular devices (mods), 17.3% (16.1-18.4%) used pods and 5.4% (4.7-6.2%) used disposables.

  Generally, use of e-cigarette device types remained stable over time. Modular devices were the second most commonly used device until 2020 when pods overtook them.

  Compared to non-daily e-cigarette users, daily users were more likely to use tank devices (RR=1.18, 95%CI=1.09-1.25), equally likely to use mods, but less likely to use disposables (RR=0.70, 95%CI=0.48–0.92) or pods (RR= 0.67, 95%CI=0.57–0.78).

  E-cigarette/HTP users who had never smoked were more likely to use JUUL (RR=6.32, 95%CI=3.89–8.82) and less likely to use pods (RR=0.72, 95%CI=0.50-0.97) than current smokers.

  41% (39.4-42.4%) of e-cigarette users used a concentration of ≤6 mg/ml nicotine, 23.4% (21.8-24.9%) used 12-19 mg/ml, 13.4%(12.0-14.6%) used 7-11mg/ml, 14.2% (13.2-15.1%) used no nicotine, 4.1% (3.4-4.9%) used ≥ 20mg/ml and 3.2% (2.6-3.8%) did not know. Use of different concentrations remained relatively stable over time.

  Never smokers were more likely than current smokers to use nicotine concentrations ≥ 20mg/ml (RR=1.88, 95%CI=1.04-2.87) and no nicotine (RR=1.62, 95%CI=1.17-2.02). Ex-smokers were less likely than current smokers to use no nicotine (RR=0.82, 95%CI=0.68-0.96) and 7-11mg/ml (RR=0.72, 95%CI=0.58-0.83), but were more likely to use ≤6 mg/ml (RR=1.08, 95%CI=1.01-1.18) and 12-19mg/ml (OR=1.35, 95%CI=1.19-1.51).

- **Limitations**

  There were less data for 2016 and 2020 compared with other years. There were also very low numbers of participants in certain subgroups. This may reduce the certainty of estimates.

Participants who used combinations of e-cigarette/HTPs were not asked about the nicotine concentration and device type for each product separately, so they had to be excluded from some analyses.

The data was cross sectional so cannot establish causality.

The high prevalence of JUUL use among never smoking e-cigarette/HTP users was primarily driven by data from a single month in a specific local authority area. Therefore, it may not be representative of general trends.

The study did not examine participant's reasons for using e-cigarettes. Therefore, associations between motivations for use and device type/nicotine concentration cannot be examined.

Tattan-Birch H, Brown J, Shahab L, Jackson SE. (2021). Trends in use of e-cigarette device types and heated tobacco products from 2016 to 2020 in England. *Sci Rep*. doi: 10.1038/s41598-021-92617-x.

3. E-cigarettes versus nicotine replacement treatment as harm reduction interventions for smokers who find quitting difficult: randomized controlled trial

- **Study Aims**

This English study randomised 135 adults (18+) who were previously unable to stop smoking, to either an e-cigarette starter pack and instructions to purchase further supplies, or nicotine replacement therapy (NRT) products of their choice. Participants received two behavioural support sessions. Biochemically validated smoke reduction of at least 50% and sustained abstinence was measured at four weeks and six months follow-up.

- **Key Findings**

At six-months, the rate of reduction in smoke intake of at least 50% (including cessation) was 26.5% of participants in the e-cigarette group and 6% in the NRT group (RR=4.4, 95%CI=1.6-12.4, p=0.005).

At six months, the rate of sustained validated abstinence was 19.1% in the e-cigarette group and 3% in the NRT group (RR=6.4, 95%CI=1.5-27.3, p=0.01).

In participants who reported nicotine concentrations of e-liquids used, the strength was significantly reduced at 6-months follow-up.

Use of e-cigarettes and NRT was similar in the two groups at week 1 and 4. At 6-months, product use was 47% in the EC arm versus 10% in the NRT arm (p<0.001).

At week 4, e-cigarettes received higher ratings than NRT for helpfulness and taste, but the products continued to receive similar ratings for satisfaction.

- **Limitations**

The sample size was relatively small meaning there may be imprecision in the effect sizes observed.

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 may be the most effective method of smoking cessation.

The participants were recruited from one Stop Smoking Service in London, so may not be representative of the wider smoking population.

Participants may have had a preference for either treatment which could have biased their engagement with the study.

Myers Smith K, Phillips-Waller A, Pesola F, McRobbie H, Przulj D, Orzol M, Hajek P. (2021). E-cigarettes versus nicotine replacement treatment as harm reduction interventions for smokers who find quitting difficult: randomized controlled trial. *Addiction*. doi: 10.1111/add.15628.

4. Has increased youth e-cigarette use in the USA, between 2014 and 2020, changed conventional smoking behaviours, future intentions to smoke and perceived smoking harms?

- **Study Aims**

  This study analysed data from two cross sectional, national US youth surveys between 2014-2020. Changes in smoking prevalence, intention to smoke in the future and perceived harms were assessed by e-cigarette use status in participants of the National Youth Tobacco Survey (NYTS) (n=98,454-132,003, aged 11-18) and Monitoring the Future (MTF) (n=17,870-30,981, aged 17-18).

- **Key Findings**

  Overall, both surveys showed a significant decrease in the prevalence of regular smoking (≥20 occasions in the past month in the NYTS/≥1-5 cigarettes per day in MTF) and an increase in regular e-cigarette use (≥20 occasions in the past month).

  Between 2014 to 2020, the NYTS showed the probability of regular smoking declined from 27.8% to 6.7% in those who regularly used e-cigarettes (Absolute Change (AC) = -21.1, 99.7%CI=-32.3,-9.9, $p<0.001$), from 9.6% to 2.5% in those who occasionally used e-cigarettes (1-19 days in past month) (AC=-7.3, 99.7%CI=-10.9,3.4,$p < 0.001$), and from 0.8% to 0.1% in those who abstained from using e-cigarette (AC=-0.7, 99.7%CI=-1.1,-0.3, $p < 0.001$). Similar trends were observed for the MTF data.

  There was no significant change in intentions to smoke in the next year among regular e-cigarette users in the NYTS (ps>0.190) and intentions to smoke in the next five years in those who abstained from e-cigarette use in MTF. Intentions to smoke significantly declined in all other categories in both surveys (ps<0.001).

  The prevalence of youth who perceived cigarette smoking as harmless did not significantly change from 2014-2020.

- **Limitations**

Results were not adjusted for sociodemographic characteristics, so this may have influenced the trends observed.

The two datasets were not directly comparable due to differences in variable definitions.

Other factor influencing cigarette use such as taxation or anti-tobacco advertising were not considered in the analysis so may have influenced outcomes.

Differences in the decline in smoking probability between different e-cigarette use groups were not statistically tested so the significance of differences is unclear.

The data was cross-sectional so cannot prove causality.

Sun T, Lim CCW, Stjepanović D, Leung J et al. (2021). Has increased youth e-cigarette use in the USA, between 2014 and 2020, changed conventional smoking behaviors, future intentions to smoke and perceived smoking harms? *Addict Behav*. doi: 10.1016/j.addbeh.2021.107073.

Overview

This July and August 2021 bulletin includes four articles from research teams in England and Australia examining vaping among young people, trends in the use of different products and vaping for smoking cessation.

Our first article is an in-depth qualitative study involving 14 to 18 year olds in Leicester who were interviewed twice, with the second interview occurring six to twelve months after the first (between February 2018 and August 2019). 36 young people were involved at baseline and 30 of these also completed a second interview. The researchers were interested in exploring the relationship between smoking and vaping.

The team recruited young people with experience of vaping and at recruitment, seventeen were vaping at least once a week, twelve more than once a day and the remainder were more occasional users including three who described themselves as recent ex users at the time of interview. Most had some experience of smoking, with twenty-five having tried smoking before vaping and four trying vaping first. The researchers acknowledge that they approached the study specifically intending to examine the relationship between the two which somewhat pre-supposed that there was a direct relationship. Many of the young people saw the two behaviours as quite distinct. Vaping was located within a much wider context of risk-taking behaviour and substance use in general. They also found that views and experiences were influenced by gender, socio-economic status and ethnicity among a diverse sample. As with all qualitative research it is difficult to do it justice in a short summary and I would recommend reading the full article, which has some fascinating quotes and illustrates the diversity of experiences and views the young people had.

This month's second article examines trends in device types and also the use of heated tobacco products (HTPs) from 2016 to 2020. Data were from the Smoking Toolkit study that we have featured many times in this bulletin before, a repeat cross sectional study of a representative sample of adults in England. This is a very useful form of surveillance not available via national annual surveys.

The toolkit study found that a very small proportion (one in 200) were using e-cigarettes or HTPs over this six year period, with the vast majority using e-cigarettes. Among vapers, just over half were using tank devices, one in four mods, one in six pods but this increased over time. Heated tobacco products were introduced to the market later but have not caught on in England, being used by 3% of adults in 2016 to 4% in 2020. Most vapers were using lower strength nicotine products, and this did not change much over time. The study suggests that refillable tank devices remain the most popular despite product innovation during the period of the study.

Our third article reports results from a small randomised controlled trial of e-cigarettes compared with nicotine replacement therapy for cutting down smoking. The researchers recruited 135 smokers in London who had a history of unsuccessful quit attempts with stop smoking medications and were not currently vaping or using such medications. They randomised them into two groups. The first received an up to eight week supply of an NRT product of their choice (or a combination of products) from a local pharmacy on prescription. The second were shown different refillable e-cigarettes and then given a £40 voucher to purchase one device and an accompanying supply of e-liquid. After two clinic visits participants were followed up at one and four weeks and six months. The primary outcome for the trial was a self-reported reduction in smoking of at least 50% at six months validated by CO breath test.

The trial found that vaping was more successful for cutting down smoking than NRT, with just over one in four (26.5%) of those in the vaping arm reducing their cigarette consumption by half compared to just over one in twenty (6%) in the NRT arm. Some of the participants stopped smoking completely by six months - 19% in the vaping arm compared with 3% in the NRT group. These results are in some ways similar to the large previous trial of vaping for smoking cessation members of the same team at Queen Mary University of London published in 2019 which found higher quit rates in smokers randomised to vaping for smoking cessation vs NRT, although the previous trial combined this with stop smoking service support. As with that study, the current research found more people continued vaping at the last point of follow up than persisted with NRT use. 47% of people in the trial were still vaping at 6 months compared with just 10% still using NRT.

This month's final study was conducted by researchers in Australia but using data from the USA. They were interested in the relationship between vaping and smoking in young people over time, between 2014 and 2020. The study involved secondary analysis of data from two large repeat cross-sectional national surveys of secondary school aged young people. It examined trends in smoking behaviour, intention to smoke and perceptions of harm from smoking among young people who did and did not use vaping products, with the definition of vaping being use within the last thirty days. Young people who had vaped during that period were divided into three groups - abstainers (no vaping), occasional (1 to 19 days) and regular (20-30 days within the last month).

Over the study period, both surveys found that the prevalence of regular smoking decreased and vaping increased. In one survey, for example, regular smoking declined from 27.8% in 2014 to 6.7% in 2020 among young people who regularly vaped and from 9.6% to 2.5% among those who occasionally vaped. There was just a small decline in regular smoking from a very low base among (0.8% to 0.1%) among those who hadn't vaped in the past month. Intention to smoke in the future also declined in both surveys although the results differed between the two, with one survey finding declines in abstainers and occasional vapers but not in regular vapers, and the other declines in all vaping groups but not abstainers. There was little change over the period in either survey in relation to perceiving smoking as harmless. Overall, the authors concluded that their results suggest vaping may be displacing smoking among young people at the population level in the USA, but that further

efforts may be needed to discourage vaping uptake among young people given that the health effects are not yet fully understood.

Other studies from May/June you might find of interest:

Patterns of Use

Disposable E-Cigarette Use Prevalence, Correlates, and Associations with Previous Tobacco Product Use in Young Adults.

State-specific prevalence of current e-cigarette use by disability status and disability type-United States, BRFSS 2016-2018.

The Effect of Cigarette Use and Dual-Use on Depression and Sleep Quality.

Electronic Cigarette Cessation among Adolescents and Young Adults.

Shared Environmental Influences on Electronic Cigarette Use Among Adolescent and Young Adult Females.

A qualitative examination of e-cigarette use among California young adults during the EVALI outbreak.

Stealth vaping among college students on four geographically distinct tobacco-free college campuses: prevalence and practices.

Impact of flavours, device, nicotine levels and price on adult e-cigarette users' tobacco and nicotine product choices.

Electronic nicotine delivery systems (ENDS) cue reactivity in dual users: A combined analysis.

Patterns of Tobacco Smoking and Nicotine Vaping among University Students in the United Arab Emirates: A Cross-Sectional Study.

Examining Adult E-cigarette Use in Kentucky and Its Appalachian Region Using the Behavioral Risk Factor Surveillance System, 2016-2017.

Smoking and vaping patterns during pregnancy and the postpartum: A longitudinal UK cohort survey.

Patterns of E-Cigarette Use Among Primary Care Patients at an Urban Community Center.

Electronic Nicotine Vapor Exposure Produces Differential Changes in Central Amygdala Neuronal Activity, Thermoregulation and Locomotor Behavior in Male Mice.

Prospective association between use of electronic cigarettes and use of conventional cigarettes: a systematic review and meta-analysis.

Community- and individual-level risk factors of past month e-cigarette use among adolescents in France.

Subjective experiences at e-cigarette initiation: Implications for e-cigarette and dual/poly tobacco use among youth.

Rising vape pod popularity disrupted declining use of electronic nicotine delivery systems among young adults in Texas, USA from 2014 to 2019.

Adverse Childhood Experiences and Past 30-Day Cigarette and E-Cigarette Use Among Sexual and Gender Minority College Students.

Perception

#FlavorsSaveLives: An Analysis of Twitter Posts Opposing Flavored E-cigarette Bans.

Developing and validating measures of absolute and relative e-cigarette product risk perceptions: Single items can be surprisingly comprehensive.

Associations between absolute and relative electronic cigarette harm perceptions and information-seeking behaviours among US adult current, former and never smokers.

Reactions to sales restrictions on flavored vape products or all vape products among young adults in the US.

Leading Topics in Twitter Discourse on JUUL and Puff Bar Products: Content Analysis.

An investigation of factors encouraging and deterring EC use: a thematic analysis of accounts from UK adults.

Trends in use of e-cigarette device types and heated tobacco products from 2016 to 2020 in England.

Electronic cigarettes and public health awareness: a cross-sectional analysis of Google search inquiries.

Use and perceptions of electronic nicotine delivery systems among patients attending lung cancer screening who smoke.

Examining e-cigarette perspectives before and after the EVALI peak in cases.

Cessation

The role of electronic cigarette use for quitting or reducing combustible cigarette use in the 30s: Longitudinal changes and moderated relationships.

Examining intention to quit using Juul among emerging adults.

Youth, family and society: Examining the dynamics of e-cigarette use in Latino college students.

Predictors of smoking reduction among African American and Latinx smokers in a randomized controlled trial of JUUL e-cigarettes.

Targeted smoking cessation for dual users of combustible and electronic cigarettes: a randomised controlled trial.

Effectiveness of a Vaping Cessation Text Message Program Among Young Adult e-Cigarette Users: A Randomized Clinical Trial.

E-cigarettes versus nicotine replacement treatment as harm reduction interventions for smokers who find quitting difficult: randomized controlled trial.

Participant Experiences of a Quit Smoking Attempt Through
Either Nicotine Replacement Therapy (NRT) Methods or the Use of an E-cigarette.

Variations in Electronic Nicotine Delivery System (ENDS) device types and association with cigarette quit attempts.

Correlates of e-cigarette use for smoking cessation among clients in residential substance use disorder treatment.

Youth

An examination of how e-cigarette/cigarette use during adolescence is associated with future use during the third trimester of pregnancy.

Adolescent E-cigarette Users at Highest Risk of Cigarette Smoking Intention.

Has increased youth e-cigarette use in the USA, between 2014 and 2020, changed conventional smoking behaviors, future intentions to smoke and perceived smoking harms?

Adolescent electronic cigarette use and tobacco smoking in the Millennium Cohort Study.

Exploring the gateway hypothesis of e-cigarettes and tobacco: a prospective replication study among adolescents in the Netherlands and Flanders.

From gateways to multilinear connections: A qualitative longitudinal investigation of the relationships between vaping and smoking among adolescent users.

Use of E-Cigarettes and Associated Factors among Youth in Thailand.

Differences in electronic cigarette use among adolescents in Korea: A nationwide analysis.
Tobacco Use Status and Temptation to Try E-Cigarettes among a Sample of Appalachian Youth.
Identifying message themes to prevent e-cigarette use among youth and young adults.

Marketing

E-cigarette advertising exposure among South African adults in 2017: findings from a nationally representative cross-sectional survey.
Electronic Cigarette Product Placement and Imagery in Popular Music Videos.

Changes in Recall to E-Cigarette Advertisement Exposure among Florida Youth, 2016-2019.

Early evidence of the associations between an anti-e-cigarette mass media campaign and e-cigarette knowledge and attitudes: results from a cross-sectional study of youth and young adults.

The Association between E-Cigarette Price and TV Advertising and the Sales of Smokeless Tobacco Products in the USA.

A content analysis of the tweets of e-cigarette proponents in Australia.

Harms and harm reduction

Use of electronic cigarettes as a predictor of cannabis experimentation: A longitudinal study among German youth.

Association of 1 Vaping Session With Cellular Oxidative Stress in Otherwise Healthy Young People With No History of Smoking or Vaping: A Randomized Clinical Crossover Trial.

Association of 1 Vaping Session With Cellular Oxidative Stress in Otherwise Healthy Young People With No History of Smoking or Vaping: A Randomized Clinical Crossover Trial.

The effect of electronic cigarettes exposure on learning and memory functions: behavioral and molecular analysis.

Impact of e-cigarettes on colonic mucosa and the role of recovery: involvement of oxidative and inflammatory pathway.

Biomarkers of Inflammation and Oxidative Stress Among Adult Former Smoker, Current E-Cigarette Users Results from Wave 1 PATH Study.

Preliminary assessment of the subjective effects of electronic-cigarettes in young-adult low-dose electronic-cigarette users: Effects of nicotine dose and e-liquid flavor.

Cannabis use and electronic cigarette use: The role of dual use on use frequency and related problems.

Firsthand and Secondhand Exposure Levels of Maltol-Flavored Electronic Nicotine Delivery System Vapors Disrupt Amino Acid Metabolism.

Respiratory Symptom Incidence among People Using Electronic Cigarettes, Combustible Tobacco, or Both.

Association between dual use of e-cigarette and cigarette and chronic obstructive pulmonary disease: an analysis of a nationwide representative sample from 2013 to 2018.

Metal exposure and biomarker levels among e-cigarette users in Spain.

Estimation of the dose of electronic cigarette chemicals deposited in human airways through passive vaping.

Exposure to nicotine vapor produced by an electronic nicotine delivery system causes short-term increases in impulsive choice in adult male rats.

Adverse Birth Outcomes Associated With Prepregnancy and Prenatal Electronic Cigarette Use.

Patterns of combustible and electronic cigarette use during pregnancy and associated pregnancy outcomes.

Long-term cerebrovascular dysfunction in the offspring from maternal electronic cigarette use during pregnancy.

Misc

Adolescents and Young Adults Have Difficulty Understanding Nicotine Concentration Labels on Vaping Products Presented as mg/mL and Percent Nicotine.

Characterization of Electronic Cigarette Warning Statements Portrayed in YouTube Videos.

"Don't Know" Responses for Nicotine Vaping Product Features among Adult Vapers: Findings from the 2018 and 2020 ITC Four Country Smoking and Vaping Surveys.

Vaping on TikTok: a systematic thematic analysis.

Anxiety Sensitivity and Emotion Dysregulation in Dual and Exclusive E-Cigarette Users.

Tracing the movement of electronic cigarette flavor chemicals and nicotine from refill fluids to aerosol, lungs, exhale, and the environment.

Exploratory Analysis of Electronic Cigarette-Related Videos on YouTube: Observational Study.

Are e-cigarette use and vaping associated with increased respiratory symptoms and poorer lung function in a population exposed to smoke from a coal mine fire?

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.

This briefing is produced by Alice Davies from Cancer Research UK with assistance from Professor Linda Bauld at the University of Edinburgh and the UK Centre for Tobacco and Alcohol Studies, primarily for the benefit of attendees of the CRUK & PHE UK E-Cigarette Research Forum. If you wish to circulate to external parties, do not make any alterations to the contents and provide a full acknowledgement. Kindly note Cancer Research UK cannot be responsible for the contents once externally circulated.