

# THE UK ELECTRONIC CIGARETTE RESEARCH FORUM

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## Electronic Cigarette Research Briefing – December 2019

This research briefing is part of a series of monthly updates aiming to provide an overview of new studies on electronic cigarettes. The briefings are intended for researchers, policy makers, health professionals and others who may not have time to keep up to date with new findings and would like to access a summary that goes beyond the study abstract. The text below provides a critical overview of each of the selected studies then puts the study findings in the context of the wider literature and research gaps.

The studies selected and further reading list do not cover every e-cigarette-related study published each month. Instead, they include high profile studies most relevant to key themes identified by the UK Electronic Cigarette Research Forum; including efficacy and safety, smoking cessation, population level impact and marketing. For an explanation of the search strategy used, please see the end of this briefing.

You can find our previous research briefings at [www.cruk.org/UKECRF](http://www.cruk.org/UKECRF).

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

### 1. [Cardiovascular Effects of Switching from Tobacco Cigarettes to Electronic Cigarettes](#)

#### • **Study Aims**

This UK study randomised 74 adult smokers who were willing to quit to receive either nicotine free (n=37) or nicotine (n=37) e-cigarettes (ECs). An additional 40 participants unwilling to quit made up a smoking control group (n=40). After one month, arterial dilation was compared by measuring flow mediated dilation (FMD). Secondary measures included pulse wave velocity (PWV) (a measure of arterial stiffness), heart rate, blood pressure and biomarkers of inflammation and platelet reactivity. Exhaled carbon monoxide was monitored to determine adherence to smoking abstinence. Results were adjusted for demographic characteristics, blood pressure, CO levels, FMD, vascular stiffness parameters and smoking history.

#### • **Key Findings**

At one month, there was a significant change in FMD across the groups ( $p<0.0001$ ). There was a significant improvement between the tobacco control and both EC groups combined (FMD +1.49%,  $p<0.0001$ ) however there was no difference between the nicotine and nicotine free EC groups ( $p=0.78$ ).

When both EC groups were combined, there was a significant improvement in PWV between the combined EC groups and the TC group (-0.529 m/s, p=0.014).

There was no significant difference across the groups for resting heart rate (p=2.07). For smokers of ≤20 pack years, an increase in resting heart rate was observed (+2.65 beats/min, p=0.03) however for smokers of >20 pack years, a decrease was observed (-2.83 beats/min, p=0.022).

There was no significant difference in systolic (p=0.107) or diastolic (p=0.139) blood pressure across the groups. There was also no difference in biomarkers of inflammation and platelet reactivity such as high sensitivity CRP (p=0.769), oxidised LDL (p=0.612), tissue plasminogen activator (p=0.425) and platelet activation inhibitor (p=0.906).

- **Limitations**

A three-way randomisation could not be performed as it was deemed to be unethical to randomise participants who were willing to quit to continue smoking. Despite adjustment, differences between the groups may remain and therefore results may be subject to confounding.

The study was small (n=114) meaning that the results may not be generalisable to the wider population.

The primary analysis assumed a linear relationship in FMD moving from smoking to nicotine EC to nicotine-free EC groups. This may not reflect the true shape of the relationship between the three groups and may have affected analysis results.

A first-generation e-cigarette was used in the study meaning the findings may not be applicable to newer models.

19 cases of dual use in both the nicotine and nicotine free EC groups were determined by recording exhaled CO. However, full analysis on outcomes of participants who dual used compared to those who only used e-cigarettes was not completed. Therefore, the effects of completely switching from smoking to using e-cigarettes cannot be determined. The cardiovascular effects of dual use also cannot be determined.

The cardiovascular changes in participants who quit smoking without using e-cigarettes was not measured, so comparisons cannot be drawn.

The aim of the study was to determine the short-term effects of switching to e-cigarettes on cardiovascular function and measurements were taken after one month of use. Further studies with a longer follow up are needed to give insight into the long-term effects of switching to e-cigarettes.

George J, Hussain M, Vadiveloo T, Ireland S et al. (2019). Cardiovascular Effects of Switching From Tobacco Cigarettes to Electronic Cigarettes. *J Am Coll Cardiol.*; doi: 10.1016/j.jacc.2019.09.067

2. Effects of e-cigarettes versus nicotine replacement therapy on short-term smoking abstinence when delivered at a community pharmacy

- **Study Aims**

This prospective UK study compared the effectiveness of e-cigarettes (EC) and NRT for smoking cessation at 4-6 weeks when delivered at a community pharmacy in Hertfordshire, England.

Participants chose to receive either an EC (n=37), EC+NRT (n=13) or NRT alone (n=65) and self-reported abstinence at 4-6 weeks. CO validation was conducted where possible. Participants who were lost to follow were assumed to have relapsed.

- **Key Findings**

All three groups reported moderate dependence on cigarettes, with Fagerstrom cigarette dependence scores of 4.45, 4.37, 4.85 in the NRT group, EC group and EC + NRT group respectively.

62.2% of participants who used ECs alone reported abstinence from smoking at 4-6 weeks, compared to 61.5% of those who used ECs+NRT and 34.8% of those who used NRT alone.

Participants who attempted to quit with an EC and an EC+NRT were 3.23 and 3.14 times more likely to be successful at 4-6 weeks than those who used NRT alone.

- **Limitations**

The study was not randomised and there was no adjustment for confounding variables. Therefore, other factors may have influenced the quit rates observed in each group. Participants chose the aid they wanted to use in their quit attempt which could have introduced bias.

The article states that participants were offered behavioural support alongside an EC or NRT, but not whether this was taken up in all cases or whether this offering was standardised across the groups.

Statistical significance between the EC/EC + NRT group and the NRT control group was not calculated. Therefore, it cannot be confirmed that the difference between the two groups was significant.

The study was very small (n=115) and participants were recruited from one pharmacy in the UK meaning that the results may not be applicable to the wider population.

Participants were only followed up for 4-6 weeks so it is not possible to determine whether e-cigarettes could be effective in long term smoking cessation from this study.

Only one brand of e-cigarette was used meaning the results may not be generalisable to other devices.

Cox S, Dawkins L, Doshi J, Cameron J. (2019). Effects of e-cigarettes versus nicotine replacement therapy on short-term smoking abstinence when delivered at a community pharmacy. *Addict Behav rep.*; doi: 10.1016/j.abrep.2019.100202

### 3. [Social Influence in the Uptake and Use of Electronic Cigarettes: A Systematic Review](#)

- **Study Aims**

This systematic review assessed the influence of social factors on e-cigarette initiation and use. The review included 43 studies that examined the effects of e-cigarette advertisement, peers, friends, family, social media interactions and social norms. The risk of bias of randomised control trials (RCTs) was accessed using the Cochrane risk of bias tool.

- **Key findings**

Seven out of nine experimental studies found that exposure to e-cigarette advertising resulted in a higher intention to use e-cigarettes. Three out of five longitudinal studies found associations between e-cigarette advertising and initiation of e-cigarettes at follow up.

27 studies examined the role of family, peers and friends on e-cigarette use. Three out of six longitudinal studies found a positive association between participant's peers and friends e-cigarette use and their initiation or continuation of e-cigarette use. In several qualitative studies, participants reported first using e-cigarettes with friends and being influenced by family or friends to try them.

The role of social norms was examined in 13 studies and was considered an important factor for the initiation and continuation of e-cigarette use by several participants. In one study, social stigma around e-cigarettes was claimed to be a disadvantage of using e-cigarettes.

In two experimental studies, social media advert exposure lead to a greater intention to use e-cigarettes and one longitudinal study determined that recent social media advert exposure at baseline predicted initiation of e-cigarettes at follow up. Five qualitative studies also found that social media platforms were used by participants for information and decision-making regarding e-cigarette use.

- **Limitations**

This review is vulnerable to any limitations of the individual studies included. There was no indication of how well studies adjusted for confounding factors. Therefore, this review cannot establish causal relationships.

Although the risk of bias was assessed in randomised control trials, 81% of the studies were not RCTs. A quality validation tool was not used to assess the quality of all studies meaning the quality was not weighted in the analysis.

Due to heterogeneity in the data, a meta-analysis was not performed. Therefore, common effects of the studies cannot be statistically verified.

Due to heterogeneity in the way which intention to use e-cigarettes was measured, the ability to draw conclusions on the effect of social factors on this outcome is limited.

As few studies limited recruitment to smokers or non-smokers and the majority of participants across the studies (81%) were non-smokers, the ability to compare the effects of social factors on e-cigarette use between these groups is limited.

This review included studies from a range of countries, but the majority (77%) were US-based. It's therefore unclear how applicable these are to countries such as the UK.

Amin S, Dunn AG, Larenjo L. (2019). Social Influence in the Uptake and Use of Electronic Cigarettes: A Systematic Review. *Am J Prev Med*; doi: 10.1016/j.amepre.2019.08.023

## Overview

This month we've selected just three articles to get the bulletin out to you before the holiday season, but we also include a list of all the articles we've included this year. This can be found at the end of the bulletin and we've organised the articles by theme so you can see the breadth of what has been covered.

Our first article focuses on the cardiovascular effects of e-cigarettes. Conducted by clinical researchers at the University of Dundee, it was funded by the British Heart Foundation. There has been limited research with human participants on how vaping affects cardiovascular health, particularly in comparison with smoking. The researchers recruited 114 smokers who completed both baseline and follow up visits. Among this group, those motivated to stop smoking were randomised to either an e-cigarette with 16mg nicotine or 0mg nicotine, to be used over four weeks. The control group (who were unwilling to quit at the time) continued smoking. The primary outcome for the study was a change in arterial function (blood flow from the heart to other tissues and organs) as measured by [flow-mediated dilation \(FMD\)](#).

At one month follow up, the researchers found a significant improvement in FMD among participants who vaped (the nicotine and nicotine free groups combined) compared to those who continued to smoke. Whether the participants vaped with or without nicotine did not make a significant difference to the change in FMD. Improvements were particularly marked among women and those who had the lowest levels of exhaled carbon monoxide at follow up (indicating complete or almost complete switching from smoking to vaping). The authors point out that [previous research](#) has found that relative risks of cardiovascular events is 13% lower for every 1% improvement in FMD, and in this study FMD improved by just over 1% in both e-cigarette arms. Longer term studies are needed to determine if vaping for smoking cessation leads to sustained improvements in cardiovascular health.

This month's second study is a brief article reporting findings from a small observational study. Conducted by researchers at London South Bank University in partnership with pharmacists, it examined whether smokers accessing support to quit in a pharmacy setting were more successful when they chose e-cigarettes compared to NRT. 115 smokers took part, with 37 choosing an e-cigarette, 13 e-cigarette plus NRT and 65 using NRT alone. Behavioural support was offered to all groups by pharmacy staff (although the extent to which this was delivered/taken up isn't reported). The primary outcome was self-reported abstinence from smoking at four weeks.

Smokers who chose an e-cigarette either alone or with NRT were more likely to have stopped smoking at four weeks – with just under two thirds quitting in these groups (62% and 61% respectively) compared to just over a third (35%) who chose NRT. In the UK, many smokers who [access stop smoking services](#) do so [via a pharmacy](#), but to date trials or observational studies of vaping for smoking cessation have not been conducted in this setting. Therefore, although this study was small, the fact that participants selected which product rather than being randomised, and that validated (CO) quit rates were not available or reported for all participants, it still contains useful information that could inform future studies.

Our final paper this month is a systematic review conducted by researchers in Australia. They were interested in examining the influence of social factors on e-cigarette intentions and use. Social factors were defined as advertising, social media interactions, the influence of peers, family and friends and social norms. The systematic review inclusion criteria were broad, with no limit on the year of publication and included experimental, longitudinal, qualitative and mixed method study designs.

Forty three studies were identified that met the inclusion criteria. Four of these were RCTs plus five using other forms of experimental design. Longitudinal and mixed method research was also identified but the largest group of studies were qualitative. Half of the studies were with adolescents and school pupils and for all but one, the reported outcome was intention to vape or trying (initiation) of e-cigarette use rather than regular or continued use. All the experimental studies that

were included looked at advertising and found that viewing e-cigarette ads increased intentions to try vaping. This was also the case when social media was used as an advertising platform and in qualitative studies where social media was used to find information about e-cigarettes. Social connections played a role, with several studies finding an association between peer or friend's e-cigarette use and intention to try vaping or vaping initiation. Social norms could increase the acceptability of vaping, although one study discussed social stigma as a perceived disadvantage of e-cigarette use. The authors found that few studies in the review adequately reported the smoking status of their participants. In addition, the identified research rarely reported how social factors might influence vaping intentions or behaviour in different ways depending on smoking status.

### **Other studies from November that you might find of interest**

#### **Patterns of Use**

[Electronic cigarette use among heart failure patients: Findings from the Population Assessment of Tobacco and Health study \(Wave 1: 2013-2014\).](#)

[Investigating E-cigarette Particle Emissions and Human Airway Depositions under Various E-cigarette Use Conditions.](#)

[The Prevalence of Tobacco and E-Cigarette Use in Poland: A 2019 Nationwide Cross-Sectional Survey.](#)

[Adult use of and transitions from nicotine and non-nicotine containing e-cigarettes: Data from the Population Assessment of Tobacco and Health \(PATH\) Study, 2013-2016.](#)

[E-Liquid Flavor Preferences and Individual Factors Related to Vaping: A Survey among Dutch Never-Users, Smokers, Dual Users, and Exclusive Vapers.](#)

[Socioeconomic Inequalities in e-Cigarette Use in Korea: Comparison with Inequalities in Conventional Cigarette Use Using Two National Surveys.](#)

[Smokers with pain are more likely to report use of e-cigarettes and other nicotine products.](#)

[Use of Electronic Cigarettes with Conventional Tobacco Is Associated with Decreased Sleep Quality in Women.](#)

#### **Perceptions**

[Social norms towards smoking and vaping and associations with product use among youth in England, Canada, and the US.](#)

[Rural-urban differences e-cigarette ever use, the perception of harm, and e-cigarette information seeking behaviors among U.S. adults in a nationally representative study.](#)

[Social Influence in the Uptake and Use of Electronic Cigarettes: A Systematic Review.](#)

[Adults' favorability toward prohibiting flavors in all tobacco products in the United States.](#)

[Baseline assessment of noticing e-cigarette health warnings among youth and young adults in the United States, Canada and England, and associations with harm perceptions, nicotine awareness and warning recall.](#)

[Mental health professionals' perceptions, judgements and decision-making practices regarding the use of electronic cigarettes as a tobacco harm reduction intervention in mental healthcare: A qualitative focus group study.](#)

### **Cessation**

[Real-world effectiveness of smoking cessation strategies for young and older adults: Findings from a nationally representative cohort.](#)

[E-cigarettes and Smoking Cessation in Smokers With Chronic Conditions.](#)

[Effects of e-cigarettes versus nicotine replacement therapy on short-term smoking abstinence when delivered at a community pharmacy.](#)

### **Youth Use**

[Determinants of e-cigarette use among a sample of high school students in Jakarta, Indonesia.](#)

[Patterns and trends of dual use of e-cigarettes and cigarettes among U.S. adults, 2015-2018.](#)

[JUUL in school: JUUL electronic cigarette use patterns, reasons for use, and social normative perceptions among college student ever users.](#)

[The role of flavors in vaping initiation and satisfaction among U.S. adults.](#)

[A qualitative study of e-cigarette emergence and the potential for renormalisation of smoking in UK youth.](#)

[Prevalence of tobacco smoking and electronic cigarette use among adolescents in Italy: Global Youth Tobacco Surveys \(GYTS\), 2010, 2014, 2018.](#)

### **Harms and Harm Reduction**

[Microbial Toxins in Nicotine Vaping Liquids.](#)

[E-cigarette vapor exposure alters \*Streptococcus pneumoniae\* transcriptome in a nicotine-dependent manner without affecting pneumococcal virulence.](#)

[Evaluation of Second-Hand Exposure to Electronic Cigarette Vaping under a Real Scenario: Measurements of Ultrafine Particle Number Concentration and Size Distribution and Comparison with Traditional Tobacco Smoke.](#)

[Carbon monoxide concentration in mainstream E-cigarette emissions measured with diode laser spectroscopy.](#)

[Analysis of Toxic Metals in Liquid from Electronic Cigarettes.](#)

[Nicotine e-cigarette vapor inhalation effects on nicotine & cotinine plasma levels and somatic withdrawal signs in adult male Wistar rats.](#)

[Quantification of selected aroma compounds in e-cigarette products and toxicity evaluation in HUVEC/Tert2 cells.](#)

[Short halt in vaping modifies cardio-respiratory parameters and urine metabolome: a randomized trial.](#)

[Short-term e-cigarette vapour exposure causes vascular oxidative stress and dysfunction: evidence for a close connection to brain damage and a key role of the phagocytic NADPH oxidase \(NOX-2\).](#)

[Chronic E-Cigarette Use Increases Neutrophil Elastase and Matrix Metalloprotease Levels in the Lung.](#)

## **Marketing**

[An analysis of e-cigarette marketing in New Zealand tobacco retail outlets prior to legislative change.](#)

## **Misc**

[Association Between e-Cigarette Use and Depression in the Behavioral Risk Factor Surveillance System, 2016-2017.](#)

[Characterization of Nicotine Salts in 23 Electronic Cigarette Refill Liquids.](#)

[Vitamin E acetate is not present in licit e-cigarette products available on the UK market.](#)

[Single- and cross-commodity delay discounting of money and e-cigarette liquid in experienced e-cigarette users.](#)

[Impact of Vaping Regimens on Electronic Cigarette Efficiency.](#)

[Effect of e-cigarette flavors on nicotine delivery and puffing topography: results from a randomized clinical trial of daily smokers.](#)

[Comparison of monoamine oxidase inhibition by cigarettes and modified risk tobacco products.](#)

[Policy Debates Regarding Nicotine Vaping Products in Australia: A Qualitative Analysis of Submissions to a Government Inquiry from Health and Medical Organisations.](#)

[Topic Clustering of E-Cigarette Submissions Among Reddit Communities: A Network Perspective.](#)

[Combining Crowd-Sourcing and Automated Content Methods to Improve Estimates of Overall Media Coverage: Theme Mentions in E-cigarette and Other Tobacco Coverage.](#)

[E-liquid-related posts to Twitter in 2018: Thematic analysis.](#)

## **Overview of 2019**

In the research briefing this year we have covered 12 papers on the patterns of use of e-cigarettes, 12 papers on cessation, eight papers on youth use, three papers on attitudes and perceptions, six papers on harms and harms reduction and two papers on marketing.

### **Patterns of use**

[January](#)

- [Predicting vaping uptake, vaping frequency and ongoing vaping among daily smokers using longitudinal data from the International Tobacco Control \(ITC\) Four Country Surveys](#)
- [IQOSTM vs. e-cigarette vs tobacco cigarette: a direct comparison of short-term effects after overnight-abstinence](#)

#### March

- [Parental smoking and e-cigarette use in homes and cars](#)

#### April

- [How Does Smoking and Nicotine Dependence Change after Onset of Vaping? A Retrospective Analysis of Dual Users](#)

#### May

- [Changes in Use Patterns Over One Year Among Smokers and Dual Users of Combustible and electronic cigarettes](#)

#### June

- [Mental Health Problems and Initiation of E-cigarette and Combustible Cigarette Use](#)

#### July

- [Patterns and predictors of e-cigarette, cigarette and dual use uptake in UK adolescents: Evidence from a 24-month Prospective Study](#)
- [Associations of Cigarettes Smoked Per Day with Biomarkers of Exposure Among US Adult Cigarette Smokers in the Population Assessment of Tobacco and Health \(PATH\) Study Wave 1 \(2013-2014\)](#)

#### August

- [Changes in E-Cigarette Use Behaviors and Dependence in Long-term E-Cigarette Users](#)
- [JUUL electronic cigarettes: Nicotine exposure and the user experience](#)

#### November

- [The Relationship Between Electronic Cigarette Use and Conventional Cigarette Smoking Is Largely Attributable to Shared Risk Factors](#)
- [A Combination of Factors Related to Smoking Behaviour, Attractive Product Characteristics, and Socio-Cognitive Factors are Important to Distinguish a Dual User from an Exclusive ECigarette User](#)

### **Cessation**

#### January

- [Attitudes to E-Cigarettes and Cessation Support for Pregnant Women from English Stop Smoking Services: A Mixed Methods Study](#)
- [E-Cigarettes May Support Smokers With High Smoking Risk Awareness to Stop Smoking in the Short Run: Preliminary Results by Randomized Controlled Trial](#)

#### February

- [A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy](#)

#### March

- [Cohort study of electronic cigarette use: safety and effectiveness after 4 years of follow up](#)
- [Are long-term vapers interested in vaping cessation support?](#)

#### April

- [Association of electronic cigarette vaping and subsequent smoking relapse among former smokers](#)

#### June

- [Moderators of real-world effectiveness of smoking cessation aids: a population study](#)

#### October

- [Association between electronic cigarette use and smoking reduction in France](#)
- [Nicotine patches used in combination with e-cigarettes \(with and without nicotine\) for smoking cessation: a pragmatic, randomised trial](#)
- [Association of prevalence of electronic cigarette use with smoking cessation and cigarette consumption in England: a time series analysis between 2006 and 2017](#)

#### November

- [Prevalence and correlates of long-term e-cigarette and nicotine replacement therapy use: a prospective study in England](#)

#### December

- [Effects of e-cigarettes versus nicotine replacement therapy on short-term smoking abstinence when delivered at a community pharmacy](#)

### **Youth Use**

#### February

- [Association of Electronic Cigarette Use With Subsequent Initiation of Tobacco Cigarettes in US Youths](#)
- [Transcriptomic response of primary human airway epithelial cells to flavouring chemicals in electronic cigarettes](#)

#### April

- [Have e-cigarettes re-normalised or displaced youth smoking? Results of a segmented regression analysis of repeated cross sectional survey data in England, Scotland and Wales.](#)

#### May

- [Measuring e-cigarette addiction among adolescents](#)

#### June

- [Impact of e-cigarette and cigarette prices on youth and young adult e-cigarette and cigarette behaviour: evidence from a national longitudinal cohort](#)
- [Adolescents' E-Cigarette Use: Increases in Frequency, Dependence, and Nicotine Exposure Over 12 Months.](#)

#### July

- [E-Cigarettes are More Addictive than Traditional Cigarettes-A Study in Highly Educated Young People](#)

#### November

- [Impact of non-menthol flavours in tobacco products on perceptions and use among youth, young adults and adults: an updated systematic review](#)

### **Attitudes and Perceptions**

#### May

- [Perceptions, Knowledge, and Use of Electronic Cigarettes: A Survey of Mental Health Patients](#)

#### July

- [Perceived Relative Harm of Using E-Cigarettes Predicts Future Product Switching among U.S. Adult Cigarette and E-Cigarette Dual Users](#)

#### August

- [Age differences in electronic nicotine delivery systems \(ENDS\) usage motivations and behaviors, perceived health benefit, and intention to quit.](#)

### **Harms and harm reduction**

#### February

- [E-Cigarette use and respiratory disorder in an adult sample](#)

#### March

- [Cardiovascular effects of electronic cigarettes: A systematic review and meta-analysis](#)

#### May

- [The Health Risks of Electronic Cigarette Use to Bystanders](#)

#### August

- [Safety of Electronic Cigarette Use During Breastfeeding: Qualitative Study Using Online Forum Discussions](#)

#### October

- [Electronic-cigarette smoke induces adenocarcinoma and bladder urothelial hyperplasia in mice](#)

December

- [Cardiovascular Effects of Switching from Tobacco Cigarettes to Electronic Cigarettes](#)

## **Marketing**

October

- [Youth self-reported exposure to and perceptions of vaping advertisements. Findings from the 2017 International Tobacco Control Youth Tobacco and Vaping Survey](#)

December

- [Social Influence in the Uptake and Use of Electronic Cigarettes: A Systematic Review](#)

## **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 UK ECRF 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 and Sophia Lowes 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.*