

THE UK ELECTRONIC CIGARETTE RESEARCH FORUM

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Electronic Cigarette Research Briefing – January 2020

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.

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

1. [Associations between vaping and relapse to smoking: preliminary findings from a longitudinal survey in the UK](#)

- **Study Aims**

This UK study explored the relationship between vaping and relapse to smoking in adult (18+) participants, who had quit smoking for at least two months in 2016 and were followed up 15 months later (n=374). Among e-cigarette users (n=159), characteristics including frequency, device type and nicotine concentration were assessed against relapse to smoking. Results were adjusted for demographics, current use of other nicotine products and time since quitting smoking.

- **Key Findings**

Compared with participants who had never used e-cigarettes, there was no significant difference between daily use (p=0.8), non-daily use (p=0.098) or past use (p=0.7) of e-cigarettes and relapse to smoking.

Among participants who used e-cigarettes at baseline, non-daily use was associated with an increased odds of relapse (OR=3.88, p=0.035) compared with daily use. Compared with participants using modular devices, those using tank devices were more likely to relapse (OR=3.63, p=0.012). Those using disposable devices were no more likely to relapse compared to those using modular devices (p=0.076).

There was no significant difference in odds ratio of relapse for NRT use compared with no NRT use (p=0.7). Compared with use of 15mg/ml nicotine e-cigarettes, there was also no significant difference in OR for use of 1 to 14 mg/ml (p=0.33) or 0mg/ml/unknown nicotine e-cigarettes (p=0.30).

Participants who had quit smoking for 2 to 12 months at baseline were significantly more likely to relapse than those who had quit for more than 12 months (OR=3.95, p<0.001). Likelihood of relapse decreased per year increase in age (OR=0.98, p=0.002).

- **Limitations**

48.4% of participants were lost to follow-up. Those who remained may not be generalisable to the wider vaping population.

The sample size available among subgroups of e-cigarette users was small which increases the uncertainty of estimates and may not have been able to detect statistical significance due to low power.

The study did not record dependence to cigarettes or self-efficacy to quit. Therefore, the results could not be adjusted for these variables. There are also likely to be other confounding factors which were not adjusted for in the analysis.

All data were self-reported and abstinence from smoking was not biochemically verified. As such, the results may be subject to recall bias.

As the study was based on data collected in 2016-2017, it may not capture more modern e-cigarette devices, for example pods.

Brose LS, Bowen J, McNeil A, Partos TR. (2019). Associations between vaping and relapse to smoking: preliminary findings from a longitudinal survey in the UK. *Harm Reduct J.*; doi: 10.1186/s12954-019-0344-0.

2. Risk of Stroke With E-Cigarette and Combustible Cigarette Use in Young Adults

- **Study Aims**

This cross-sectional US study examined the relationship between smoking, e-cigarette use and dual use with stroke incidence in young adults. Data were collected from 161,529 18-44 year olds who completed the Behavior Risk Factor Surveillance System Survey between 2016 and 2017. Results were adjusted for demographics, BMI, physical activity, binge drinking and diabetes.

- **Key findings**

Compared with non-smokers, current smokers were at an increased risk of stroke (AOR =1.59, 95% CI 1.14-2.22 p<0.01). Current e-cigarette users who used to smoke and dual users were also at an increased risk. (AOR=2.54, 95% CI=1.16-5.56, p<0.05), (AOR=2.91, 95% CI = 1.62 – 5.25,p<0.01). There was no significant difference in stroke risk for current e-cigarette users who had never smoked (p=0.69) compared with non-smokers.

Compared with current exclusive smokers, exclusive e-cigarette users were at a reduced risk of stroke (AOR = 0.43, CI= 0.2-0.93,p<0.05) whereas dual users were at an increased risk (AOR =1.83, CI=1.06-3.17, (p<0.05). There was no significant difference observed for current e-cigarette users who were previously smokers (p=0.27) compared with current exclusive smokers.

Compared with current e-cigarette users who were former smokers, there was no significant difference in risk of stroke for current smokers (p=0.29).

- **Limitations**

The study was cross sectional and the order of events was not recorded. Therefore, reverse causality (having a stroke before commencing e-cigarette use) cannot be ruled out. In addition, full health details of participants before commencing e-cigarette use was not recorded. Therefore, they may have been prompted to switch due to poor health.

The absolute number of stroke cases was not reported. This was extremely low in the exclusive e-cigarette groups (<14 cases).

They did not adjust for all stroke risk factors, for example family history and blood pressure. Therefore, the results may be subject to confounding. The study did not adjust for pack years smoked or dependency in cigarette users. Therefore, the results may have been confounded by level of tobacco use.

All data was self-reported meaning results may be subject to recall bias.

The results stated that compared with non-smokers, greater intensity of e-cigarette use (someday use vs everyday use) among current smokers resulted in an increased AOR of stroke (AOR someday use = 2.87, 95% CI=1.43-5.77), (AOR everyday use = 2.96, CI=1.53-5.73). However, no statistical test was performed so it's not clear whether there was any significant difference.

Parekh T, Pemmasani S, Desai R. (2019). Risk of stroke with e-cigarette and combustible cigarette use in Young Adults. *Am J Prev Med.*; doi: 10.1016/j.amepre.2019.10.008

3. [Electronic cigarette vapour increases virulence and inflammatory potential of respiratory pathogens.](#)

- **Study Aims**

This UK *in vitro* study examined the effect of growing common lung bacteria (*H.influenzae*, *S.aureus*, *S.pneumoniae* and *P.aeruginosa*) in culture medium exposed to different concentrations (25, 50, 75 or 100%) of cigarette smoke extract (CSE) or e-cigarette vapour extract (ECVE) on growth and biofilm formation. Virulence was compared by observing survival

of *G. Mellonella* (a species of moth) after CSE/ECVE cultured bacterial infection and the immune response of human airway epithelial cells was determined by measuring cytokine production.

- **Key Findings**

CSE or ECVE of any concentration had no effect on the growth of any strain of bacteria. Biofilm production was significantly greater only for *S. pneumoniae* ($p=0.0047$) and *P. aeruginosa* ($p=0.0043$) grown in CSE exposed medium and *S. aureus* ($p<0.001$) grown in ECVE exposed medium.

There was a significant decrease in survival of *G. mellonella* infected with all strains of bacteria grown in CSE or ECVE exposed medium (all p values <0.024). The decrease was greater following exposure to CSE than ECVE for *S. pneumoniae* ($p=0.00007$), *S. aureus* ($p=0.0001$) and *P. aeruginosa* ($p=0.006$), but not *H. influenzae*.

Cytokine production by epithelial cells significantly increased when infected with *H. influenzae* ($p=0.0002$), *S. aureus* ($p=0.0372$) and *P. aeruginosa* ($p=0.0022$) grown in 100% CSE exposed medium compared with non-exposed medium. Cytokine production also significantly increased when infected with all bacteria grown in 100% ECVE exposed medium (*H. influenzae* ($p=0.0002$), *S. aureus* ($p=0.0372$), *S. pneumoniae* ($p=0.0343$), *P. aeruginosa* ($p=0.0019$) compared with non-exposed medium.

- **Limitations**

The CSE/ECVE exposed medium was prepared by passing cigarette smoke or e-cigarette vapour through it every 15s for five minutes. This is unlikely to be representative of bacterial exposure to CSE/ECVE in humans.

This study examined the virulence of lung bacteria implicated in the development of respiratory diseases such as COPD and asthma after exposure to CSE/ ECVE. However, the mechanism of how these bacteria are implicated in disease pathogenesis of chronic lung disease and real-world response to CSE/ECVE is unconfirmed. As such, this study can only provide a basis for potential mechanism of harm.

The study looked at survival of *G. mellonella*, a species of moth, after infection with CSE/ECVE exposed bacteria. As such, the findings may not be equivalent in mammalian models of lung infection.

There were some uncertainties in the methods used. It is unclear how many repeats were completed and what exposure concentration of CSE/ECVE was used in some experiments.

Gilpin DF, McGown KA, Gallagher K, Bengoechea J, Dumigan A, Einarsson G, Elborn JS, Tunney MM. (2019). Electronic cigarette vapour increases virulence and inflammatory potential of respiratory pathogens. *Respir Res.*;doi:10.1186/s12931-019-1206-8

4. [A Randomised Clinical Trial Examining the Effects of Instructions for Electronic Cigarette Use on Smoking-Related Behaviours and Biomarkers of Exposure](#)

- **Study Aims**

This US study randomised 264 adult daily smokers uninterested in quitting to 8 weeks of different instructions relating to e-cigarette use: (1) ad libitum use of e-cigarettes (AD-E), (2) complete substitution of cigarettes with e-cigarettes (CS-E), (3) complete substitution of cigarettes with nicotine gum (CS-NRT), (4) Continued use of usual brand cigarettes (UB). The number of cigarettes smoked per day and biomarkers of tobacco exposure were recorded at 1, 2, 4, 6- and 8-weeks follow-up. Participants in the complete substitution groups received brief counselling on smoking abstinence. Intervention compliance was incentivised through payment.

- **Key Findings**

Compared to baseline, at week 8, there was an 27% ($p<0.001$), 75% ($p<0.001$) and 71% ($p<0.001$) reduction in cigarettes smoked per day for the AD-E, CS-E and CS-NRT groups, respectively. The median change in CPD at week 8 from baseline was -2.7, -12.7, -9.6 and -0.7 (p values <0.001) for the AD-E, CS-E, CS-NRT and UB groups respectively.

Compared to baseline, at both 4 and 8 weeks, there was a significantly greater reduction in CPD for CS-E compared with AD-E ($p<0.001$) and AD-E compared with UB ($p<0.001$).

At each intervention week, there was a significant reduction in exhaled CO in the AD-E, CS-E and CS- groups compared with baseline ($p=0.002$ to $p<0.001$). There was a significant reduction of other biomarkers including NNAL at 8 weeks in the AD-E ($OR=0.75$, $p<0.01$), CS-E ($OR=0.47$, $p<0.001$) and CS-NRT ($OR=0.48$, $p<0.001$) groups compared to baseline. There was no significant difference observed for any biomarkers in the UB group over the 8 weeks, with the exception of CO at week six ($AOR=0.79$, $p<0.5$).

At week 8, significant differences in the magnitude of the decrease in CO ($p<0.001$), PheT ($p=0.008$), CEMA ($p=0.001$) and HMPMA ($p=0.006$) levels were observed between the CS-E and AD-E groups. There was no significant difference in magnitude of the decrease in total NNAL and 3-HPMA.

- **Limitations**

Participants were given a bonus voucher of \$30 at week one and \$10 increments each subsequent visit if study requirements were met. Therefore, this study may not accurately represent real world use of e-cigarettes and NRT for smoking cessation.

Participants in the UB group were not encouraged to quit smoking until after the trial. Because some other groups were attempting to quit, this may not have been an appropriate comparison. There was a significant difference in dropout rates between groups ($p=0.041$) so it's not clear how this may have impacted results.

The study size was relatively small meaning that the results may not be generalisable to the wider population.

The follow up period for the study was only 8 weeks. Therefore, it does not provide information on the relationship between the interventions and long-term abstinence from smoking.

Adherence to the intervention was also not analysed so a full picture of the effect of e-cigarette use on changes in smoking behaviour and biomarker exposure cannot be gathered.

Hatsukami D, Meier E, Lindgren BR, Anderson A, Resinger S. (2019). A Randomized Clinical Trial Examining the Effects of Instructions for Electronic Cigarette Use on Smoking-Related Behaviors, and Biomarkers of Exposure. *Nicotine Tob Res.*; doi: 10.1093/ntr/ntz233

Overview

This month we include papers authored by researchers based in England, Northern Ireland and the USA. They cover a range of topics including smoking relapse, stroke, respiratory pathogens and smoker's responses to different instructions for cutting down and stopping smoking.

Our first paper aimed to examine whether vaping increases or decreases relapse to smoking by analysing responses from a longitudinal web-based survey funded by Cancer Research UK. This survey had five waves of data collection from 2012 to 2017 and the current paper focused on the fourth and fifth wave. Analysis was restricted to participants successfully followed up between these two waves who reported being non-smokers for at least two consecutive months at wave four.

Follow up took place on average 15 months after wave four data collection. By that point, four in ten participants had relapsed to smoking. This may appear high, but [smoking relapse is common](#), and even studies of intensive interventions for smoking cessation show [significant rates of relapse at one year](#). There were no significant differences in relapse to smoking between participants who had used e-cigarettes (ever, non-daily or daily) compared to those who had never vaped. When analysis was restricted to just the vaping group, however, there were higher odds of relapse among those who vaped less frequently (non-daily use compared with daily use). Participants were also asked about device type and nicotine strength. There were no significant differences in relapse rates on the basis of reported nicotine content (no nicotine, 1-14mg and above 15mg). Device type did seem to make a difference - those using devices that were not modular (tanks, disposables) appeared to be more likely to go back to smoking. Overall the sample for the study was relatively small (374) and only half of those who participated in wave four were successfully followed up. This limits the conclusions we can draw from the findings, but the study does point to the importance of considering different elements of vaping when examining longer term outcomes like relapse to smoking.

In our second study, researchers were interested in examining any links between vaping and the risk of stroke, in the context of recent rises in stroke incidence linked to smoking in young adults. They examined cross-sectional data from a telephone survey conducted in 2016-17 with a large, representative sample of 18-44 year olds in the USA. The survey included questions on smoking and vaping and also whether participant had ever had a stroke. They didn't find any evidence that vaping alone (without smoking) increased the risk of a stroke compared with not smoking. But they did find that dual users were at statistically significant higher risk of stroke compared to both non-smokers and smokers who did not vape. Their results received considerable [coverage in the media](#) suggesting that younger adults who dual use could be putting themselves at even greater risk of stroke than smoking alone. Earlier in this bulletin, we've highlighted in some of the limitations of this type of cross-sectional survey research in terms of determining causality. Further comments from nicotine and tobacco researchers on the study can be found in the [expert reaction section](#) of the Science Media Centre's website.

This month's third study involved lab-based research using human lung cells and also moths. It received [press coverage](#) suggesting that vaping may cause lung infections in a similar way to smoking. The researchers were interested in studying bacteria (pathogens) in cells that have previously been shown to be markers of respiratory diseases such as COPD. They exposed lung cells to tobacco smoke (in four concentrations) and to e-cigarette vapour, and then examined the growth of four types of common bacteria (including one linked to influenza and another pneumonia). They didn't find any differences in bacterial growth when the cells were exposed to different concentrations of tobacco smoke or to the e-cigarette vapour. They also examined the extent to which lung cells infected with bacteria produced cytokines, which are markers of inflammation linked to respiratory diseases. Cytokine production increased in both the cells exposed to smoke and those exposed to e-cigarette vapour, compared to cells not exposed to either.

Studies of this kind are valuable in that they identify biological changes in cells used in experiments outside of the human body that can be further explored in humans. However, the extent to which the findings point to vaping causing respiratory disease depends on a number of factors that couldn't be explored in the current study. There are limits to cell line studies in terms of their implications for human health, particularly when the exposures (in this case e-cigarette vapour extract) may be at concentrations that can't necessarily mirror human use. It's also not fully understood how the bacteria used in the study contribute to lung disease. A recent trial of e-cigarettes for smoking cessation [found reported improvements in respiratory symptoms](#) (cough and phlegm production) when smokers switch to vaping, and a small longitudinal study found [improvements in asthma outcomes](#) among asthmatic patients who switched to vaping.

Our final study this month focuses on the type of advice that could be given to smokers regarding vaping for smoking cessation. In the USA (where the researchers are based) [most vapers are dual users](#) and it may be that providing specific instructions on complete switching to vaping could be beneficial. The researchers tested this by recruiting a sample of 264 smokers who were not interested in immediately stopping smoking and randomised them to four groups. One group received information on using e-cigarettes in whatever form/frequency they preferred; the second group advice on complete switching; the third advice on switching to NRT products; and the fourth continued smoking. Incentives were provided for compliance (vaping and NRT arms) and for attending follow up sessions (weekly and then bi - weekly visits up to eight weeks).

At the final follow up point of eight weeks the three intervention groups had all cut down their smoking with the biggest reduction in the e-cigarette arm. The study team also assessed a range of biomarkers of smoking. Exhaled carbon monoxide readings were lower (compared to baseline) in all three intervention groups at each intervention week and final follow up. There was also a significant reduction in some other biomarkers at final follow up. All these outcomes point to reduced smoking in the groups given information on freely using e-cigarettes, complete switching to e-cigarettes and complete switching to NRT. Smoking cessation at the end of the study was assessed using [point prevalence](#) (having stopped smoking for at least the past week). Quit rates were highest in the group provided with instructions on complete switching to e-cigarettes. The study also collected a variety of other interesting data on a range of topics (flavour preferences, puffs per day, number of smokefree days etc) that can be found in the paper. Although involving a relatively small sample, the study provides encouraging evidence of both cessation and reductions in exposure to tobacco toxicants in the intervention groups, particularly the group given instructions on completely switching to vaping.

Finally, just to highlight a [UK study](#) not included in this bulletin's review that may be of interest to readers. This is a paper evaluating the impact of a pilot that Cancer Research UK conducted of an

outdoor health marketing campaign about the relative risks of vaping compared to smoking in one region of England.

Tattan – Birch H, Jackson SE, Ide C, Bauld L, Shahab L. (2019). *Nicotine Tob Res.* Evaluation of the impact of a regional educational advertising campaign on harm perceptions of e-cigarettes, prevalence of e-cigarette use, and quit attempts among smokers.;doi: 10.1093/ntr/ntz236.

Other studies from January that you might find of interest

Patterns of Use

[Who Uses E-cigarettes and Why? E-cigarette Use among Older Adolescents and Young Adults in Japan: JASTIS Study.](#)

[Trends and sociodemographic factors of e-cigarette use among adult daily smokers in South Korea.](#)

[Physical Activity and Use of Cigarettes and E-Cigarettes Among Young Adults.](#)

[Use of E-Cigarettes for Nicotine, Marijuana, and Just Flavoring Among U.S. Youth.](#)

[Lifestyle characteristics of parental electronic cigarette and marijuana users: healthy or not?](#)

[Sensory attributes of e-cigarette flavours and nicotine as mediators of interproduct differences in appeal among young adults.](#)

[Sex and Polytobacco Use among Spanish and Turkish University Students.](#)

[E-Cigarette, Cigarette, and Dual Use in Korean Adolescents: A Test of Problem Behavior Theory.](#)

[Net Effect of Young Adult Dual Combusted Cigarette and E-Cigarette Users' Anticipated Responses to Hypothetical E-Cigarette Marketing Restrictions.](#)

Perception

[Mapping Public Concerns of Electronic Cigarettes in China.](#)

[Examining the vulnerability of ambivalent young adults to e-cigarette messages.](#)

[Effects of a Nicotine Fact Sheet on Perceived Risk of Nicotine and E-Cigarettes and Intentions to Seek Information About and Use E-Cigarettes.](#)

[Evaluation of the impact of a regional educational advertising campaign on harm perceptions of e-cigarettes, prevalence of e-cigarette use, and quit attempts among smokers.](#)

[JUUL on Twitter: Analyzing Tweets About Use of a New Nicotine Delivery System.](#)

[Pain severity and e-cigarette health literacy: the moderating role of sex.](#)

[Socioeconomic and Demographic Status and Perceived Health Risks of E-Cigarette Product Contents Among Youth: Results From a National Survey.](#)

Cessation

[Associations between vaping and relapse to smoking: preliminary findings from a longitudinal survey in the UK.](#)

[Smoking Cessation and Vaping Cessation Attempts among Cigarette Smokers and E-Cigarette Users in Central and Eastern Europe.](#)

[A Randomized Clinical Trial Examining the Effects of Instructions for Electronic Cigarette Use on Smoking-Related Behaviors, and Biomarkers of Exposure.](#)

Youth

[Breadth of Media Scanning Leads to Vaping among Youth and Young Adults: Evidence of Direct and Indirect Pathways from a National Longitudinal Survey.](#)

[Sex Differences in Becoming a Current Electronic Cigarette User, Current Smoker and Current Dual User of Both Products: A Longitudinal Study among Mexican Adolescents.](#)

[Adolescent E-cigarette use trajectories and subsequent alcohol and marijuana use.](#)

[Trends in E-Cigarette, Cigarette, Cigar, and Smokeless Tobacco Use Among US Adolescent Cohorts, 2014-2018.](#)

Harms and Harm Reduction

[Electronic cigarettes and insulin resistance in animals and humans: Results of a controlled animal study and the National Health and Nutrition Examination Survey \(NHANES 2013-2016\).](#)

[Systemic biomarkers in electronic cigarette users: implications for noninvasive assessment of vaping-associated pulmonary injuries.](#)

[Systems toxicology assessment of a representative e-liquid formulation using human primary bronchial epithelial cells.](#)

[Prenatal Electronic Cigarette Exposure Decreases Brain Glucose Utilization & Worsens Outcome in Offspring Hypoxic-ischemic Brain Injury.](#)

[Daily Cigarette Consumption and Urine Cotinine Level between Dual Users of Electronic and Conventional Cigarettes, and Cigarette-Only Users.](#)

[Cinnamon-flavored electronic cigarette liquids and aerosols induce oxidative stress in human osteoblast-like MG-63 cells.](#)

[Association of E-Cigarette Use With Respiratory Disease Among Adults: A Longitudinal Analysis.](#)

[Biomarkers of Exposure and Effect in the Lungs of Smokers, Nonsmokers, and Electronic Cigarette Users.](#)

[Electronic cigarette vapour increases virulence and inflammatory potential of respiratory pathogens.](#)

[Twenty-four Hour Subjective and Pharmacological Effects of Ad Libitum Electronic and Combustible Cigarette Use among Dual Users.](#)

[E-cigarette flavored pods induce inflammation, epithelial barrier dysfunction, and DNA damage in lung epithelial cells and monocytes.](#)

[Are E-Cigarette Flavors Associated with Exposure to Nicotine and Toxicants? Findings from Wave 2 of the Population Assessment of Tobacco and Health \(PATH\) Study.](#)

[Use of electronic cigarettes and self-reported COPD diagnosis in adults.](#)

[Risk of Stroke With E-Cigarette and Combustible Cigarette Use in Young Adults.](#)

[Electronic Cigarette Use and Chronic Respiratory Symptoms Among United States Adults.](#)

[Effects of Electronic Cigarettes on Indoor Air Quality and Health.](#)

[Association Between E-Cigarette Use and Chronic Obstructive Pulmonary Disease by Smoking Status: Behavioral Risk Factor Surveillance System 2016 and 2017.](#)

Marketing

[Effects of Social Media on Adolescents' Willingness and Intention to Use E-Cigarettes: An Experimental Investigation.](#)

Misc

[Health Effects Associated With Electronic Cigarette Use: Automated Mining of Online Forums.](#)

[Assurances of Voluntary Compliance: A Regulatory Mechanism to Reduce Youth Access to E-Cigarettes and Limit Retail Tobacco Marketing.](#)

[Effects of electronic cigarette heating coil resistance and liquid nicotine concentration on user nicotine delivery, heart rate, subjective effects, puff topography, and liquid consumption.](#)

[Pod-Mod vs. Conventional E-cigarettes: Nicotine Chemistry, pH and Health Effects.](#)

[Nicotine in tobacco product aerosols: 'It's déjà vu all over again'.](#)

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 UKERCRF 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.