Electronic cigarette research briefing – December 2016 & January 2017

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.

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

1. Second Generation Electronic Nicotine Delivery System Vape Pen Exposure Generalizes as a Smoking Cue.

- **Study aims**
  This US study compared responses of young adult smokers (n=108) to a vaping or smoking cue and a control cue in the lab. Participants were first exposed to someone drinking from a water bottle then the person either using a second-generation vape pen or smoking a cigarette and desire to smoke and use an e-cigarette was rated by participants. Results were also compared to previous results using a cig-a-like e-cigarette cue.

  For a subset of participants (n=26), the study duration was extended and participants were presented with a cigarette, asked to resist smoking and told they would be rewarded the longer they lasted (the smoking latency phase).

- **Key findings**
  Exposure to both the person vaping and smoking increased desire to smoke and vape to a similar extent, and significantly more than the water drinking cue. Results did not differ whether the participants had previously vaped or not. There was no significant difference between increases in desire to smoke and vape in this study with the vape pen and the cig-a-like in the previous study.
In the smoking latency phase, there was no difference in duration to smoking between the cue groups.

- **Limitations**
  There was no cue order randomisation (participants were always exposed to smoking or vaping after the control) – it’s possible that desire to smoke or vape merely increased over time. Increases in desire to smoke or vape were only small; the highest mean increase was +9 on a scale of 0 – 100. It’s not clear how well the lab-based setting replicates real-life exposure and whether the small increase in reported desire to smoke would translate into any changes in behaviour.

  The sample was not representative and people with a range of smoking and e-cigarette experiences were included (though results did not significantly differ when these experiences were compared). No comment can be made on impact in non-smokers as they were not included in this study.

  Different aspects of the cue were not explored, for example whether results were due to the visual aspect or the biochemical exposure to second-hand smoke or vapour in a confined space.


2. **Nicotine levels, withdrawal symptoms, and smoking reduction success in real world use: A comparison of cigarette smokers and dual users of both cigarettes and E-cigarettes.**

- **Study aims**
  This US study aimed to explore smokers and dual users’ responses to instructed 75% and 100% reduction in smoking, separated by ad lib smoking periods. Participants (74 smokers and 74 dual users) not aiming to quit were recruited through point-of-sale displays in convenience stores and social media. Urinary nicotine and CO levels were measured at intervals as well as self-recorded cravings in real-time via a smartphone app.

- **Key findings**
  Overall there was no difference in number of cigarettes smoked (or CO levels) between smokers and dual users in any of the time periods (ad lib, 75% reduction or 100%) however dual users were significantly more likely to be able to abstain from smoking (97% vs. 81%).

  Number of vaping episodes was low in the ad lib periods (mean 1.58 – 1.69 uses/day) and only rose to 5 and 6.21 in the 75% and 100% reduction phases.

  There was no difference in nicotine levels for male smokers and dual users but female dual users had significantly higher levels in the ad lib periods. Female smokers reported larger increases in cravings in the reduction phases than dual users but male dual users reported a greater increase in cravings than male smokers.

  At the end of the study smokers were significantly more motivated to quit but 70% of dual users thought e-cigarettes would help them stop smoking (10% thought they would be less likely to be able to quit.
• **Limitations**

As smokers and dual users were recruited, rather than randomised, the two groups were not representative or directly comparable. It’s not clear whether differences such as quit motivation were a function of the differences between the groups rather than the use or non-use of e-cigarettes. The dual user group did not use e-cigarettes very intensively, most were using disposable e-cigarettes or weren’t sure what sort of device it was and by the nature of the group, e-cigarette users who had successfully stopped smoking will be excluded. Results were not separated by device type or nicotine concentration used (more than 70% of dual users did not know what nicotine concentration they were using).

The study was conducted between March 2013 and May 2014 and used simulated reduction periods so may not be representative of dual users today (who are likely using different devices) or when people are attempting to cut back or quit when they’re ready to do so. The paper does not report dropout rate or adherence to responding to app recording prompts.


3. **Tobacco Consumption and Toxicant Exposure of Cigarette Smokers Using Electronic Cigarettes**

• **Study aims**

This US study aims to assess changes in tobacco consumption and levels of exposure to different chemicals in smokers switching to a second-generation e-cigarette.

The study recruited 40 cigarette smokers and gave them an e-cigarette with a choice of eight flavours in 12 or 24mg nicotine dosage. Disease-associated biomarkers and a panel of common volatile organic compounds (VOCs) were monitored for 4 weeks.

• **Key findings**

All participants with follow-up data (92.5%) reported using the e-cigarette, but the frequency of e-cigarette use per day decreased over the duration of the study.

When compared to the 30 days prior to the study, there was a significant decrease in cigarette consumption. But, during the four week study period the results suggest there was a gradual increase in the daily number of cigarettes consumed after the initial decrease. 40% of participants reported no cigarette consumption at Week 2 and this reduced to 15% by Week 4.

There was no significant change in nicotine intake over the 4 weeks. Toxicants such as carbon monoxide, NNAL, and metabolites of benzene and acrylonitrile were significantly decreased in the study sample. Some metabolites (HEMA and AAMA) were significantly reduced in participants who switched exclusively to e-cigarettes for at least half of the study period.

Smoking dependence significantly decreased from baseline to Week 4, and self-efficacy to resist smoking cigarettes significantly increased. Carrying of cigarettes (always or most of the time) when leaving the house also decreased throughout the study, while carrying an e-cigarette increased to the baseline level for cigarettes.
• **Limitations**
  Each participant used the same device, so it’s not possible to extrapolate to different devices (e.g. toxicity, e-liquid consumed). There’s also no breakdown of results for the different flavours and nicotine concentrations of fluids used, or for different sub-groups.

  Vaping sessions were defined as any discrete time in which a participant took out their e-cigarette and used it for any number of puffs. There was no puffing regimen, so the effects of each session can’t be compared.

  This study used participants who may or may not have wanted to stop smoking, and can’t give useful information as to whether e-cigarettes will be an effective cessation tool for those who are looking to stop. The study also includes non-daily and light smokers, who may find it more feasible to switch to e-cigarettes than heavier smokers.

  A study period of 4 weeks is insufficient to understand the full extent of change in chemical exposure, for example NNAL, or explore any health impact.

  This was a small study, and it’s possible that there could be confounders such as differences in eating, drinking, product use and exposure to passive smoke or vapour that were not accounted for.


4. [E-cigarettes and equity: a systematic review of differences in awareness and use between sociodemographic groups](#).

• **Study aims**
  This UK systematic review summarised variations in e-cigarette awareness, ever use or current use by different sociodemographic groups. 58 studies were included from 35 developed nations, both longitudinal and cross-sectional or repeat cross-sectional.

• **Key findings**
  Awareness, ever use and current use of e-cigarettes were found to be more prevalent among older adolescents and younger adults, males and people of white ethnicity.

  Some higher quality papers showed awareness and use (particularly ever-use) were positively associated with higher levels of education, better self-reported health status and, in the EU, higher use in urban areas.

  For other characteristics, including socioeconomic status, disability, health status, place of residence, occupation and sexual orientation, the findings were too inconsistent to identify patterns.

• **Limitations**
  Significant heterogeneity between studies meant this review was qualitative and could not be a quantitative meta-analysis.
This paper defined current use as once during the past 30 days rather than a more rigorous frequency of use measure, owing to this being the predominant definition in original studies.

All studies used self-reported outcome measures that were of unknown validity or reliability due to the lack of research to date on such matters.

Only general population studies were included, so larger studies on specific clinical populations may have been left out.

The study does not include comparisons to cigarette smoking, and cannot answer questions related to potential gateway effect, smoking cessation, dual use and health outcomes. There are also no details on types of e-cigarettes being used and whether they contain nicotine or not.

The tool for quality assessment was tailored to requirements for this review and not validated.


5. E-Cigarette Awareness, Use, and Harm Perception among Adults: A Meta-Analysis of Observational Studies

- **Study aims**
  
  This Chinese study reviewed and synthesised the published literature on the previous and current use, and harm perceptions of e-cigarettes. 28 articles were included, with survey times from 2009 to 2014.

  Analyses were conducted for each smoking sub-group (current smokers, former/ever smokers, never smokers, current and ever smokers, smokers and non-smokers, users of cigarettes, and those aware of e-cigarettes). A cumulative meta-analysis was also performed to summarise any changes over time by adding each survey in chronological order.

- **Key findings**
  
  There was a high degree of heterogeneity in all prevalence values. The overall e-cigarette awareness estimate was 61.2% (95% CI: 51.5%-70.8%), with the highest awareness among current smokers and lowest among non-smokers. The cumulative meta-analysis showed a gradual increase in awareness since mid-2010.

  The overall previous use estimate was 16.8% (95% CI: 14.0%-19.6%), with current smokers more likely to try e-cigarettes than former and non-smokers 27.2% vs. 15.7% vs. 2.5% respectively. The overall current use estimate was 11.1% (95% CI: 9.2%-13.1%). 18.2% of former smokers were current users, 16.8% of current smokers and 1.2% of non-smokers. The cumulative meta-analysis showed that the current and previous use trends remained stable after an initial increase and then a decrease.
Overall 52.6% (95% CI: 42.5%-62.6%) of those surveyed thought e-cigarettes were healthier than cigarettes. A lower proportion of e-cigarette users (37.9%) believed e-cigarettes were healthier than tobacco, compared to current, former and non-smokers. The level of people believing e-cigarettes are healthier than smoking has been relatively stable at 40% to 60% in the last few years.

There was no quality assessment of the studies included in the meta-analysis.

- **Limitations**
  Heterogeneity in prevalence estimates resulted in notable changes when undertaking the sensitivity analysis and large confidence intervals. This is likely due to studies taking place at different times, locations and with different methodologies, surveys and populations.

  Most of the data was from self-reported online surveys, and many studies had a high non-response rate.

  Current use of an e-cigarette is predominantly defined in studies as once during the last 30 days, so may include people that have only recently tried an e-cigarette.

  The paper only includes English-language studies up to February 2015, and therefore likely misses some more recent data, and possibly studies in other languages.

  There were limited prospective studies in the analysis, so this study cannot assess the gateway effect, dual use or smoking cessation trends over time.

  This study didn’t look at the level of understanding of e-cigarettes, only whether people had heard of e-cigarettes, and whether they thought they were healthier than smoking.


6. **E-cigarettes, a safer alternative for teenagers? A UK focus group study of teenagers’ views**

- **Study aims**
  This UK study used focus groups to qualitatively explore how teenagers from diverse backgrounds in the UK currently perceive e-cigarettes and how and why they do or do not use them.

  16 focus groups (11 in Scotland and 5 in England) were conducted between November 2014 and February 2015, with 83 teenagers aged 14-17. Participants completed a brief questionnaire about their use of e-cigarettes and cigarettes.

- **Key findings**
  In 13 groups the general consensus was that the primary beneficiaries of e-cigarettes were long-term smokers of an older generation looking to quit or reduce cigarette use.

  Most conversations focused on the potential harms of e-cigarettes to users or bystanders. But teenagers typically viewed e-cigarettes as substantially less harmful than cigarettes.
E-cigarettes were considered appealing to participants, due to the variety of flavours and colours and tricks that could be performed. Sources such as Facebook, Twitter and YouTube were specifically mentioned as ones that influenced their opinions, alongside the internet and stories from families and friends.

Those that used e-cigarettes either purchased them online or were given them by other teenagers.

A number of participants expressed how e-cigarettes can be used to maintain a nicotine addiction through covert use. Most discussions about a gateway effect from vaping to smoking were speculative. Only one participant mentioned people he knew moving from experimenting with e-cigarettes to traditional cigarettes.

- **Limitations**
  
  This is not a representative sample, and is skewed towards opinions from deprived areas.

  The sample size did not allow for detailed analyses based on differences in opinions split by smoking status, e-cigarette use and socioeconomic status. The qualitative nature of the study means any speculative comments cannot provide reliable evidence of behaviour.

  It’s possible that using friendship groups may have caused people to conform to the consensus of stronger characters in the group, based on prior relationships. However, participants regularly questioned, challenged and amended each other’s statements, suggesting high levels of involvement.


**Overview**

The first article this month looks at whether seeing someone use a second generation e-cigarette increases urge and desire to smoke among young adult smokers aged 18-35. This was a study conducted in a lab in the USA and two experiments were carried out. Experiment 1 involved 108 people who were randomised to seeing another person drinking water (followed by a break) and then smoking a cigarette, or drinking water (followed by a break) and then vaping. Both seeing smoking and vaping increased the urge to smoke and desire for a cigarette amongst participants. It also increase desire for an e-cigarette. In contrast, after seeing another person drinking water, smoking urge and desire for a cigarette or e-cigarette were not present. These results were not significantly affected by whether the smokers in the study had ever used e-cigarettes (83% had).

Experiment 2, with a sample of 26 daily smokers, repeated the main elements of the first but looked and whether people could resist smoking a cigarette when exposed to the same cues (a cigarette was available on a tray with a lighter). A small incentive of 20 cents was provided for each 5 minutes that passed when they did not smoke. No significant difference was found in the duration of time participants could resist smoking a cigarettes between the two cues (seeing someone smoking or seeing someone vaping), and this result didn’t differ when controlling for the amount participants smoked or whether they’d tried an e-cigarette.
This study of smoking cues and smoking latency is interesting and suggests that smokers perceive vaping in a similar way to smoking. The behaviour is similar so this is perhaps not particularly surprising. However, just seeing the act of vaping only increased smoking (or vaping) urge by a very small extent and the experiment couldn’t assess how this might affect behaviour outside of the lab setting. We know visual cues are important for consumption (similar experiments have been conducted with alcohol and junk food, for example) particularly for people who already regularly consume the product in question. However, this study didn’t include any ex-smokers, so it is not known how they might respond, which could be more interesting in terms of any concerns about cues and relapse to tobacco smoking.

The second study examined dual use. Two groups of adults were involved, some who smoked regularly, and some who smoked and also vaped. Both groups were asked to reduce their cigarette consumption, by 75% in the first week, followed by a week of smoking as much as they chose, and then asked to reduce by 100% for three days. Participants were asked to report how much they smoked or vaped and biochemical validation (carbon monoxide -CO- and cotinine) was also conducted. The study didn’t find a significant difference between the number of cigarettes smoked or CO readings in any of the study periods. What it did find was that dual users were more likely to be able to not smoke at all during the 100% reduction period and had fewer withdrawal symptoms when not smoking. There were some gender differences which might merit further research - but the most interesting finding in the study was that e-cigarette use did appear to help dual users to avoid smoking all together. This may have implications not just for cessation research but also in terms of e-cigarettes as a tool for temporary abstinence (building on NRT studies for temporary abstinence) and could be explored in further studies. It’s also worth noting that the similarities in CO levels between smokers and dual users are at odds with some previous research. This may be explained by the fact that, on average, the dual users were vaping at very low levels (less often than twice a day) during the ‘smoke as much you choose’ (ad lib) periods which is unlikely to serve as an adequate replacement for cigarettes.

Switching was the focus of this month’s third study which looked at changes in tobacco consumption and exposure to toxicants among 40 smokers interested in using e-cigarettes. All were provided with a second generation device and choice of e-liquid flavours with 24mg/ml nicotine (or 12mg for those who reported 24 was too high for them). Participants were provided with advice and action planning to make the switch and were followed up two weeks and then four weeks later. Everyone in the study used the e-cigarette provided but success in making a complete switch was greater in the initial period and tapered off slightly at one month. 40% of participants were no longer smoking at two weeks but this had dropped to 15% by four weeks. Nicotine intake remained largely the same, but toxicant exposure (including CO) declined for all participants, particularly those who switched entirely to e-cigarettes. This was a study with regular smokers provided with information but not additional support and it is perhaps not surprising that not everyone stopped smoking. However, smoking dependence declined in the sample and psychological and behavioural measures (self-efficacy, carrying cigarettes when leaving the house) of resisting tobacco increased, suggesting increased confidence amongst participants. This is promising for smoking cessation and longer term follow up in a study of this kind would be worth conducting.

Our fourth study this month is from UK colleagues at LSHTM and the University of Bath. They conducted a systematic review of published and grey literature on socio-demographic differences in
awareness of e-cigarettes and ever and current use. This is a useful paper given the relative paucity of e-cigarette research that takes into account issues that may be relevant for inequalities in health. A reasonable number of sources were identified (58 studies) that met their inclusion criteria. Almost all were cross-sectional surveys plus six longitudinal studies, and data from 35 countries were included. They found that awareness of e-cigarettes as well as current and ever use varied between groups. People with higher levels of education were more likely to know about these devices and have tried them (‘ever use’) and all three measures of interest were more common amongst people of white ethnicity, males, older teenagers and younger adults. The authors point out that this pattern is fairly consistent with how new technologies tend to be used initially in populations. To some extent the patterns identified are consistent with findings from the CRUK funded smoking toolkit survey in England, where we still see a present gradient in e-cigarette use among more affluent compared with less affluent smokers, although in England use is distributed fairly evenly across the age range and slightly more women than men use e-cigarettes. The authors of the review provide a useful section on implications for research, policy and practice which merits further reading, emphasising the importance of gathering data on socio-economic status in relevant studies as well as reporting outcomes (i.e. smoking cessation) for different social groups.

The fifth study is another systematic review that also looked at awareness and use but also harm perceptions. This review covered the period 2003 to February 2015 and focused on cross-sectional or cohort studies with sample sizes of over 200 participants. The authors conducted a meta-analysis using 28 studies from a range of countries. They found that awareness of e-cigarettes was high at 61.2% overall, despite some studies being included from the ‘early days’ of e-cigarettes. Unsurprisingly, smokers were more likely to be aware of the products. As we’ve reported before in the bulletin, awareness grew over time as product use became more prevalent. Just over one in four smokers across studies had tried e-cigarettes, with use amongst non-smokers (note: this was not ‘never’ smokers so might include some long term ex-smokers or users of tobacco products other than cigarettes) very low at 2.5%. Unsurprisingly current use was lower, but higher amongst ex-smokers (which will include some recent quitters) than current smokers, and negligible (1.2%) amongst non-smokers. The article also includes data on harm perceptions, highlighting as we have previously in this bulletin, that a significant proportion of people don’t see e-cigarettes as less harmful (with the term ‘healthier’ used here) than smoking. The authors describe a number of limitations to the review but it is worth pointing out that meta-analysis is usually used in reviews of randomised controlled trials and can be fairly problematic when it is applied to observational data. A key weakness being that the populations surveyed are likely to vary a lot, and the questions asked in the surveys are likely to have been highly variable even if the same general issues (awareness, use, harm perceptions) are explored. This and other factors may explain some slightly strange findings in parts of the review. This includes the finding that current users of e-cigarettes were least likely of all groups to think e-cigarettes were healthier than smoking, which seems counter-intuitive. The authors do make the point that standard measures are needed for surveys that ask about e-cigarette use to improve scope for comparisons.

The final article in this month’s bulletin is from the team at the MRC CSO Social and Public Health Sciences Unit at Glasgow University. They conducted 16 focus groups with 83 teenagers in England and Scotland to examine perceptions of e-cigarettes and reasons for use or not using them. The study was set up at a relatively early period for research on e-cigarettes and young people in the UK, with the fieldwork being conducted over two years ago. Overall the participants viewed e-cigarettes
as products for smokers. There was confusion about safety and risks, including relative to smoking, but most correctly viewed them as less harmful than smoking. Some evidence of appeal, including amongst never smokers, was reported, as was awareness of some marketing (at a time when current marketing restrictions were not yet in place). Experimentation could be prompted by novelty, viewing advertising or even flavourings -although it is worth emphasising that the only teenagers in the study who had ever tried these devices were smokers. There is some attention in the abstract and discussion to ‘covert’ use of e-cigarettes (i.e. not smelling like smoke so less detectable) and whether this could reinforce nicotine dependence, but the source of this is a quote from a single participant. The study was conducted at a time before the UK’s current policy framework, including age of sale laws were introduced, and this may limit how applicable the findings are in today’s context.

Other studies from the last month that you may find of interest:

- Using e-cigarettes in the home to reduce smoking and secondhand smoke: disadvantaged parents’ accounts.
- Blood Pressure Control in Smokers with Arterial Hypertension Who Switched to Electronic Cigarettes.
- Nicotine delivery to users from cigarettes and from different types of e-cigarettes.
- Youth-Targeted E-cigarette Marketing in the US.
- Perceptions of E-Cigarettes among Black Youth in California.
- Prevalence and Perceptions of Electronic Cigarette Use during Pregnancy.
- E-cigarettes and Urologic Health: A Collaborative Review of Toxicology, Epidemiology, and Potential Risks.
- Criterion validity of measures of perceived relative harm of e-cigarettes and smokeless tobacco compared to cigarettes.
- Do Emotions Spark Interest in Alternative Tobacco Products?
- Comparison of cellular and transcriptomic effects between electronic cigarette vapor and cigarette smoke in human bronchial epithelial cells.
- Experimentation with e-cigarettes as a smoking cessation aid: a cross-sectional study in 28 European Union member states.
- How hearing about harmful chemicals affects smokers' interest in dual use of cigarettes and e-cigarettes.
- Trends in E-Cigarette Awareness and Perceived Harmfulness in the U.S.
- Electronic cigarette use and uptake of cigarette smoking: A longitudinal examination of U.S. college students.
- E-cigarette susceptibility as a predictor of youth initiation of e-cigarettes.
- Prevalence of and beliefs about electronic cigarettes and hookah among high school students with asthma.
- Vaping to lose weight: Predictors of adult e-cigarette use for weight loss or control.
- Global approaches to regulating electronic cigarettes.
- Smoking Cessation and Electronic Cigarettes in Community Mental Health Centers: Patient and Provider Perspectives.
- Frequency of E-cigarette Use, Health Status, and Risk and Protective Health Behaviors in Adolescents.
- Flavored e-cigarette use: Characterizing youth, young adult, and adult users.
- E-cigarette Nicotine Delivery: Data and Learnings from Pharmacokinetic Studies.
- A pilot study of the gingival response when smokers switch from smoking to vaping.
- Evidence for harm reduction in COPD smokers who switch to electronic cigarettes.
- E-Cigarette Social Media Messages: A Text Mining Analysis of Marketing and Consumer Conversations on Twitter.
- Nicotine Replacement, Topography, and Smoking Phenotypes of E-cigarettes.
- Association of e-Cigarette Vaping and Progression to Heavier Patterns of Cigarette Smoking.
- Recent Findings on the Prevalence of E-Cigarette Use Among Adults in the U.S.
- Perceptions of e-Cigarettes and Noncigarette Tobacco Products Among US Youth.
- Flavored Electronic Cigarette Use and Smoking Among Youth.
- Characteristics of Electronic Cigarette Use Among Middle and High School Students - United States, 2015.
- Motivations and Limitations Associated with Vaping among People with Mental Illness: A Qualitative Analysis of Reddit Discussions.
- Frequency of youth e-cigarette and tobacco use patterns in the U.S.: Measurement precision is critical to inform public health.
- The Associations Between E-Cigarettes and Binge Drinking, Marijuana Use, and Energy Drinks Mixed With Alcohol.
- Racial/ethnic differences in electronic cigarette knowledge, social norms, and risk perceptions among current and former smokers.
- The Readability of Electronic Cigarette Health Information and Advice: A Quantitative Analysis of Web-Based Information.
- Electronic cigarette retailers use Pokémon Go to market products.

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 e-cig*[title/abstract] OR (nicotine AND (vaporizer 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 Nikki Smith and Carl Alexander from Cancer Research UK with assistance from Professor Linda Bauld and Kathryn Angus at the University of Stirling and the UK Centre for Tobacco and Alcohol Studies, primarily for the benefit of members 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.