

# THE UK ELECTRONIC CIGARETTE RESEARCH FORUM

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## Electronic Cigarette Research Briefing – February 2018

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.

Past research briefings can be found 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. [Initial ratings of different types of e-cigarettes and relationships between product appeal and nicotine delivery](#)
- **Study aims**

This UK study looked at eight different brands of e-cigarettes and examined the product appeal and nicotine delivery of each one plus the participant's own device. 15 participants tried each product after overnight abstinence and vaped ad libitum for 5 minutes. Blood samples were drawn at baseline and at 2, 4, 6, 8, 10 and 30 minutes after vaping initiation. Participants were asked to rate the device based on characteristics such as: throat hit, craving relief, subjective nicotine delivery and draw resistance. They also then provided an overall ranking of products.

- **Key findings**

All e-cigarettes reduced the urge to smoke at every time point after baseline. There were no significant differences between products and urge to smoke. However, a 2nd generation refillable e-cigarette was perceived as providing the greatest and fastest relief of urges to smoke.

The number of puffs taken was inversely associated with the nicotine delivery, vapour production and throat hit of each product. The refillable products delivered higher nicotine levels than the cig-a-likes (other than one which used the highest concentration liquid), despite being used with fewer puffs. Own brand products were mostly refillable, and provided even higher nicotine levels with lower concentration liquids.

The refillable 2nd and 3rd generation e-cigarettes were perceived as delivering the most nicotine and delivering the strongest throat hit. However, 1<sup>st</sup> generation cig-a-like products were most often selected to be “just right” for these categories, after own brand.

Objective nicotine delivery (blood measures) and perceived nicotine delivery were significantly associated with the rating of throat hit across products. However, perceived nicotine delivery was not associated with objective nicotine delivery.

In the retrospective rankings, mouthpiece comfort, taste, throat hit and perception of nicotine delivery were all significantly associated with overall pleasantness. Mouthpiece comfort, throat hit and ease of draw being “just right” were significantly associated with recommending the product to a friend.

- **Limitations**

The study uses a small sample that was not selected to be representative of the vaping population. The opinions and habits displayed by this sample may not translate to all users.

The small sample size also leaves very limited power to detect significant differences, so perhaps only the strongest trends were clear in this study. Only 9 of the 15 participants completed questions on throat hit and vapour production, as these questions were added later.

The study used a limited range of devices and only tobacco flavour. These will not represent the entire range of products available and did not enable meaningful assessment of different nicotine concentrations or propylene glycol and vegetable glycerol balance.

The participants only used the products on one occasion, and therefore the study couldn't assess how perceptions and usage may adjust over a longertime period.

The overall product ranking occurred at the end of the study, and users may find it hard to remember their earlier experiences after a number of weeks.

One participant had elevated nicotine levels at baseline on two occasions, which may have affected the results.

Hajek, P., Przulj, D., Phillips-Waller, A., Anderson, R., & McRobbie, H. (2018). Initial ratings of different types of e-cigarettes and relationships between product appeal and nicotine delivery. *Psychopharmacology*, 1-10.

## 2. A Qualitative Exploration of the Role of Vape Shop Environments in Supporting Smoking Abstinence.

- **Study aims**

This UK study involved qualitative interviews with 40 people who had used e-cigarettes as part of a quit attempt to explore how vape shops may play a role in this process. The study

also included observational data of six vape shops in different locations. The interviews and observational data were analysed using thematic analysis.

- **Key findings**

The first theme was around making vaping accessible and affordable. The presence of vape shops in everyday environments such as high streets made vaping seem more socially acceptable and low risk to health. Nearly every vaper also mentioned reduced cost compared to smoking as a reason for vaping.

Around a third of vapers in this study intended to stop using their product, but the effect of this on commercial interests was not explored.

The second theme was around creating a shared vaping experience. Many vapers perceived vape shops as offering a friendly personal service and some used the shops as a place to socialise and chat. Five of the six shops had a “café feel” with places to sit and snacks and drinks available. However, not all vapers were keen on this environment, and preferred to buy their product and leave.

It was also felt that most vape shops projected a masculine image and were more appealing to men than women.

The third theme was around ensuring a satisfying and functioning vaping setup. Vape shops are able to provide advice so vapers could navigate the choices available to them. Some vapers did choose to avoid this level of choice and stick to what was available in supermarkets or pharmacies. Advice on devices and nicotine strengths in vape shops was welcomed by many.

The ongoing support from vape shops and staff was recognised by many vapers e.g. offering technical support for devices and troubleshooting if someone had relapsed to smoking.

- **Limitations**

The study used a relatively small sample size and will not represent the views of all people who have used e-cigarettes as part of a quit attempt, or all vape shops frequented by e-cigarette users. Neither can it capture the views of those who may be put off using an e-cigarette as part of a quit attempt and chose other methods.

The short time period for observation of 3 hours may not provide an accurate representation of all interactions within vape shops.

As participants and vape shop workers were aware they were being recorded under observation, this may have influenced the way they acted compared to how they would normally.

This study did not assess the efficacy of support from vape shops for cessation and cannot be compared to specialist support from trained stop smoking advisors.

Ward, E.; Cox, S.; Dawkins, L.; Jakes, S.; Holland, R.; Notley, C. A Qualitative Exploration of the Role of Vape Shop Environments in Supporting Smoking Abstinence. *Int. J. Environ. Res. Public Health* 2018, 15, 297.

### 3. E-Cigarette Marketing and Communication: How E-Cigarette Companies Market E-Cigarettes and the Public Engages with E-cigarette Information.

- **Study aims**

This paper from researchers in the USA reports results from a literature systematic review designed to explore how e-cigarette companies market e-cigarettes and how the public engages with this information. 124 publications were identified that were applicable to e-cigarette marketing and communications, and a narrative synthesis of findings was conducted.

- **Key findings**

21 studies were found that focussed on advertising claims and promotions. E-cigarettes were promoted as healthier, less expensive, more socially acceptable, unhindered by smoke-free policies and more environmentally friendly. They were also marketed as cessation aids, either explicitly or implicitly.

A number of studies focused on e-cigarette advertising as being appealing to youth, and some found that adverts were perhaps being specifically targeted to younger audiences. Discounts, promotions, and loyalty programmes have been used to promote the sale of e-cigarettes, alongside using conventions and expos to present new technologies.

Studies showed that those exposed to e-cigarette marketing had lower harm perceptions and perceived addictiveness of e-cigarettes, and greater intention to use and trial of e-cigarettes. Studies found similar results for children and teenagers exposed to advertising.

There were mixed results from studies looking into the effects of e-cigarette adverts on intentions to smoke and intentions to stop smoking.

Studies found that e-cigarette information is disseminated through television, in-person communication, retail outlets, and the internet. E-cigarette search queries and online content have rapidly increased over recent years.

Communications and discussions about e-cigarettes vary in positivity, with differences shown between countries on aspects including marketing, policy and regulation, and safety.

Studies found that e-cigarette companies are using online communications as an opportunity to market their products via commercial content.

- **Limitations**

The limitations of this study are representative of the limitations of the individual papers included. For example, many of the results are from cross-sectional studies that are not able to conclude causation, and many papers may be subject to recall bias.

This study doesn't provide new analyses of the results of the papers included. There is no quality appraisal and studies aren't weighted, it simply presents a range of findings from previously published research.

The study isn't able to draw new conclusions on how e-cigarette marketing and communications may affect actual e-cigarette or tobacco use.

The search was limited to English-language publications only, so may not include all the available literature on this topic.

Lauren Collins, Allison MGlasser, Haneen Abudayyeh, Jennifer L Pearson, Andrea C Villanti; E-Cigarette Marketing and Communication: How E-Cigarette Companies Market E-Cigarettes and the

**4. E-cigarette smoke damages DNA and reduces repair activity in mouse lung, heart, and bladder as well as in human lung and bladder cells.**

- **Study aims**

This US study assessed the effects of e-cigarette vapour on DNA and repair activity in organs of exposed mice and in human cell cultures. The mice were exposed to e-cigarette vapour, whereas the human cells were treated with nicotine and nitrosamine ketone (NNK). The researchers directly assessed the effects of mutagenic  $O^6$ -methyldeoxyguanosines ( $O^6$ -medG) and  $\gamma$ -hydroxy-1,  $N^2$ -propano-deoxyguanosines ( $\gamma$ -OH-PdG), by measuring DNA adducts. They also measured levels of DNA repair activity and the XPC and OGG1/2 proteins crucial for this activity.

- **Key findings**

Exposure to e-cigarette vapour led to significant increases in  $O^6$ -medG and  $\gamma$ -OH-PdG adducts in lung, bladder and heart tissue in mice compared to exposure to filtered air. There were no significant differences in liver tissue when exposed to vapour.

The levels of adducts were higher in lung tissue than in the bladder and heart. And the levels of  $\gamma$ -OH-PdG adducts were 25 to 60-fold higher than the level of  $O^6$ -medG adducts.

DNA repair by nucleotide excision repair (NER) and base excision repair (BER) was significantly lower in the lung tissue of mice exposed to e-cigarette vapour than filtered air. Similarly, the XPC and OGG1/2 repair proteins were significantly lower in mouse lung tissue compared to controls.

Treating human cells with increasing concentrations of nicotine and NNK was found to induce  $\gamma$ -OH-PdG and  $O^6$ -medG adducts, and reduce DNA repair activity and levels of DNA repair proteins XPC and hOGG1/2.

These treatments were found to enhance spontaneous, UV and  $H_2O_2$  induced mutation frequency by two to four-fold. Soft-agar anchorage-independent growth of lung and bladder cells was also induced by this treatment.

- **Limitations**

Studies in mice and human cells aren't able to assess real-world exposure to e-cigarette vapour and actual harms, but can only provide a basis for potential mechanisms of harm. Conclusions about e-cigarette vapour being carcinogenic are unfounded.

The concentrations and volume of vapour that mice were exposed to (10 mg/ml, 3 hours per day, 5 days per week for 12 weeks) are not easily comparable to real-world consumption of e-cigarette vapour, and may not represent actual use. Only one type of e-cigarette vapour was tested, and no comparisons to tobacco smoke.

Filtered air is not a suitable background exposure control, as this does not represent regular exposure to unfiltered air.

The studies on human cells did not use e-cigarette vapour, but nicotine and NNK treatments, which are not representative of real-world use. There were no control results presented, and no comparisons made to tobacco, which is known to lead to significantly higher levels of NNK than e-cigarette vapour.

The study consistently refers to e-cigarette vapour as “e-cigarette smoke” which does not accurately reflect its composition, as it’s not formed by combustion.

Lee, H. W., Park, S. H., Weng, M. W., Wang, H. T., Huang, W. C., Lepor, H., Tang, M. S. (2018). E-cigarette smoke damages DNA and reduces repair activity in mouse lung, heart, and bladder as well as in human lung and bladder cells. *Proceedings of the National Academy of Sciences*, 115(7), E1560-E1569.

## Overview

This month we include two papers from the UK and two from the USA. They explore a diverse range of topics including: product appeal and nicotine delivery; qualitative research in vape shops; e-cigarette marketing; and the effects of e-cigarette vapour on the lungs, bladder and hearts of mice and on human cells.

The first paper aimed to examine the features of e-cigarettes which might play a role in smokers switching to vaping. This involved a small group (n=15) of experienced vapers testing eight e-cigarette brands (along with their usual brand), providing blood samples to test for nicotine delivery, and rating the brands in relation to key characteristics. Most of the participants were dual users, while four had stopped smoking and were vaping. Participants travelled to the lab on several occasions and were asked to abstain from smoking and vaping the night before each visit.

The eight brands tested included six 1<sup>st</sup> generation cig-a-like products with different nicotine concentrations, a 2<sup>nd</sup> generation refillable tank product and a 3<sup>rd</sup> generation tank product with a variable power setting.

All the products reduced the urge to smoke, which can be important for smoking cessation. Participants puffed more frequently on devices that contained less nicotine. However, more frequent puffing did not result in higher nicotine delivery in most cases, suggesting that the products in this study (and possibly others on the market, as suggested by [previous research](#)) don’t allow users to titrate nicotine delivery in the same way as smoking. When comparing the 1<sup>st</sup> and later generation devices, the 2<sup>nd</sup> and 3<sup>rd</sup> generation models delivered more nicotine and were more highly rated in terms of key characteristics (urge relief, throat hit, vapour volume) than 1<sup>st</sup> generation products with one exception, a single 1<sup>st</sup> generation product that rated particularly well on mouthpiece comfort and also taste. The findings on ‘draw resistance’ (which varies depending on the aperture of the mouthpiece) and the feel of the mouthpiece in general slightly surprised the researchers as these turned out to be important elements of product appeal. These additional features may well be worth including in future studies on product characteristics, particularly in relation to vaping for smoking cessation.

The second study, funded by Cancer Research UK, aimed to explore what happens in the retail environment where e-cigarettes are purchased. It focused on vape shops, which are the [most common place of purchase for e-cigarettes](#) in the UK. Data were drawn from semi-structured interviews with 40 people who had used e-cigarettes as part of a quit attempt and were taking part in a larger study, with the current paper focusing on the extent to which the vape shop environment might assist in maintaining smoking cessation. Interview data were supplemented with observations (of around three hours) in six vape shops in London and East Anglia. Notes taken during the observation period focused on the nature of the retail environment, interactions between shop staff and clients and conversations between the researcher and staff.

Previous studies have reported on the [growth of vaping retail outlets](#), their [attributes](#) and [retailer attitudes and behaviours](#). Most of this research has been conducted in the USA so the current study provides recent insights from the UK.

It identified a number of themes relating to how specialist shops may support customers to maintain abstinence from smoking. Observations and interviews suggested that shop assistants gave advice to customers about products and tried to tailor that advice to customer needs and preferences and their smoking history. Retail staff also served as an ongoing point of contact and were there to offer advice and practical assistance about how to use and maintain the products, particularly given that the technology involved can be challenging for some. Although not formally trained in smoking cessation, interviews and observation identified examples of staff using their knowledge and experience to deliver informal behavioural support which may help clients who are aiming to maintain abstinence from smoking. This was not universal - examples were also provided of retailers or shop staff who delivered poor service or advice. For some customers, aspects of the retail environment reinforced vaping identity, but others found this off-putting. The authors suggested that health professionals who have smoking cessation as part of their role could engage with vape shops, and the study identified some examples of this. There may also be opportunities for vape shop staff to receive more [formal training in smoking cessation](#). Future studies could examine the viability, and any relevant outcomes, from these approaches.

This month's third study is from a team of researchers in the USA who have conducted [a series of systematic literature reviews](#) on different topics relevant to e-cigarettes and tobacco harm reduction. This latest article aimed to understand how e-cigarette companies market their products and how the public engages with this information. This article follows a [recent rapid literature review](#) on e-cigarette marketing conducted for Cancer Research UK that focused on the UK context.

Searches were conducted up to June 2017 and aimed to identify empirical research on e-cigarette marketing. 124 articles met the inclusion criteria. The range of studies identified was very broad and included many different research designs. Given these diverse designs the authors could only provide a narrative synthesis. This was divided into two broad categories - marketing and communication. Studies exploring marketing provided findings related to six themes: advertising claims and promotions; exposure and receptivity to e-cigarette marketing; marketing and its association with perceptions and use; impact of marketing on cigarette smoking; e-cigarette warning labels; and tobacco and e-cigarette prevention messages. Studies with findings on communication related to: engagement with e-cigarette information; and portrayal of e-cigarettes in the media.

The articles included were from a wide range of countries but dominated by studies from the USA. Few restrictions on e-cigarette marketing are in place in the USA, unlike in Europe where all broadcast marketing is prohibited and where some member states including the UK have extended this ban to include other forms of promotion. With that caveat in mind, the literature suggests that similar strategies have been employed for both tobacco and e-cigarette marketing including using price promotions, themes that appeal to young people, and advertisements across the full range of retail and media channels. Some marketing promotes e-cigarettes as healthier alternatives to cigarettes and as smoking cessation aids. Studies with young people suggest that exposure to e-cigarette advertising may be associated with young people trying e-cigarettes. There was no evidence, however, that e-cigarette marketing exposure affects tobacco use.

The authors identified a number of gaps in the literature. One of these was in relation to communication around e-cigarettes including media coverage. The authors did not find any studies examining how misleading or inaccurate information on e-cigarettes in marketing or

communications affects e-cigarette or tobacco use, which could be a relevant topic for future research.

The final study this month is from environmental medicine and urology researchers in the USA. They aimed to determine whether e-cigarette vapour can induce DNA damage in the internal organs (lung, bladder and heart) of mice and whether e-cigarette vapour can affect DNA-repair activity. They also aimed to explore the effect of e-cigarette vapour metabolites on the susceptibility to mutations and transformation of cultured human cells, which are changes which can lead to cancer developing in these cells.

Live mice were exposed to vapourised e-liquid that contained 1% nicotine for three hours a day, five hours a week for twelve weeks in order to model the equivalent of light vaping by humans over 10 years. Other mice acted as a control group and were not exposed to e-cigarette vapour but instead filtered air. Experiments were then carried out on cells from the same mouse organs. In the exposed group, the researchers found that two compounds that can cause mutations developed in the heart, lungs and bladder of mice. In the experiment involving cells from mouse organs, the researchers found that that DNA repair activity was affected and specific repair proteins were reduced in mouse lung cells. Human cells from the lining of the lungs and bladder were treated with a nicotine solution. More DNA mutations and less DNA repair activity was found in cells treated with stronger (higher nicotine concentration) solution. These types of changes in both the mice and human cells have been found in other studies to be early markers of cancer developing.

These types of studies with rodents and human cells can be valuable as they can help researchers understand the cellular or biological mechanisms that may cause harm and need to be considered in research with humans. However, some specific aspects of this study are worth noting which go beyond any caveats that normally apply to rodent and cell line studies. First, the study focused in particular on nicotine which when separated from the many other chemicals in cigarette smoke is not recognised as cancer-causing in humans. It also did not compare e-cigarette vapour exposure with tobacco smoke exposure to either the mice or cells in the study, and this is an important comparison if we are to draw conclusions about any relative risks of vaping vs smoking. Also, the mice were exposed to substantial amounts of e-cigarette vapour over an extended period and the article does not provide any information about how the researchers reached the conclusion that this amount or duration of exposure would mimic use in humans. Finally, some of the author's conclusions are based on a statement that human e-cigarette users have higher levels of NNAL (a carcinogen) than non-users and to support this they cite a CRUK funded [study](#), which did not in fact find this.

The results in the article has been discussed elsewhere including in a [CRUK blog](#) and on the [NHS Choices](#) website.

**Public Health England** published an updated independent evidence review on e-cigarettes which also included some material on heat not burn tobacco products. The report can be found [here](#).

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

- [Carbonyl Emissions in E-cigarette Aerosol: A Systematic Review and Methodological Considerations.](#)
- [Patient Perspectives on Discussions of Electronic Cigarettes in Primary Care.](#)
- [Educational gradients in the use of electronic cigarettes and heat-not-burn tobacco products in Japan.](#)

- [Comparison of Bladder Carcinogens in the Urine of E-cigarette Users Versus Non E-cigarette Using Controls.](#)
- [Brief Report: Lead Levels in Selected Electronic Cigarettes from Canada and the United States.](#)
- [What Factors are Associated with Electronic Cigarette, Shisha-Tobacco and Conventional Cigarette Use? Findings from a Cross-Sectional Survey of Australian Adolescents?](#)
- [Host-agent-vector-environment measures for electronic cigarette research used in NIH grants.](#)
- [Awareness, use and perceptions about E-cigarettes among adult smokers in Karachi, Pakistan.](#)
- [Impact of an Outdoor Smoking Ban at Secondary Schools on Cigarettes, E-Cigarettes and Water Pipe Use among Adolescents: An 18-Month Follow-Up.](#)
- [Urinary Metabolite Levels of Flame Retardants in Electronic Cigarette Users: A Study Using the Data from NHANES 2013-2014.](#)
- [Vape and Aviate: Electronic-Cigarette Use and Misuse in Naval Aviation.](#)
- [Speaking up about Lighting up in Public: Examining Psychosocial Correlates of Smoking and Vaping Assertive Communication Intentions among U.S. Adults.](#)
- [Documentation of e-cigarette use and associations with smoking from 2012 to 2015 in an integrated healthcare delivery system.](#)
- [Effects of six weeks of electronic cigarette use on smoking rate, CO, cigarette dependence, and motivation to quit smoking: A pilot study.](#)
- [Bidirectional associations of e-cigarette, conventional cigarette and waterpipe experimentation among adolescents: A cross-lagged model.](#)
- [Addictive behaviors, social and psychosocial factors, and electronic cigarette use among adolescents: a population-based study.](#)
- [E-Cigarette Use Among Adolescents Not Susceptible to Using Cigarettes.](#)
- [Chronic Inhalation of E-Cigarette Vapor Containing Nicotine Disrupts Airway Barrier Function and Induces Systemic Inflammation and Multi-Organ Fibrosis in Mice.](#)
- [An Online Survey of New Zealand Vapers.](#)
- [Inflammatory and Oxidative Responses Induced by Exposure to Commonly Used e-Cigarette Flavoring Chemicals and Flavored e-Liquids without Nicotine.](#)
- [Preferring more e-cigarette flavors is associated with e-cigarette use frequency among adolescents but not adults.](#)
- [Substitutability of nicotine alone and an electronic cigarette liquid using a concurrent choice assay in rats: A behavioral economic analysis.](#)

- [Dual Use of E-Cigarettes and Traditional Cigarettes Among Adolescents in Taiwan, 2014-2016.](#)
- [A Longitudinal Study of Predictors for Adolescent Electronic Cigarette Experimentation and Comparison with Conventional Smoking.](#)
- [Dual use of electronic nicotine delivery systems \(ENDS\) and smoked tobacco: a qualitative analysis.](#)
- [Sociodemographic disparities in e-cigarette retail environment: Vape stores and census tract characteristics in Orange County, CA.](#)
- [E-cigarette use and quantity of cigarette smoking among adolescent cigarette smokers: A finite mixture model analysis.](#)
- [Effects of nicotine-containing and "nicotine-free" e-cigarette refill liquids on intracranial self-stimulation in rats.](#)
- [Motives and perceptions regarding electronic nicotine delivery systems \(ENDS\) use among adults with mental health conditions.](#)
- [Prevalence of Use and Perceptions of Electronic Smoking Devices in a US Army Infantry Division.](#)
- [E-Cigarette Airflow Rate Modulates Toxicant Profiles and Can Lead to Concerning Levels of Solvent Consumption.](#)
- [The Effect of Electronic Cigarettes on Hand Microcirculation.](#)

### **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 UKERCRC 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 Carl Alexander from Cancer Research UK with assistance from Professor Linda Bauld at the University of Stirling 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.*