Electronic Cigarette Research Briefing – August/September 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. **Association Between Youth Smoking, Electronic Cigarette Use, and Coronavirus Disease 2019**

   **Study Aims**

   This cross-sectional US study assessed the association between smoking, exclusive use and dual use of e-cigarettes and COVID-19-related symptoms, testing, and diagnosis. Participants (n=4,351) were adolescents and young adults (aged 13-24 years) and data was self-reported. Results were weighted by population data and adjusted for sociodemographic characteristics, body mass index, compliance with social distancing regulations and state percentage of COVID-19 cases.

   **Key Findings**

   There was no association between ever and past 30-day smoking and reporting COVID-19 symptoms or testing positive. Ever, but not past 30-day smokers, were more likely to be tested (OR=3.94, 95%CI=1.43-10.86).
There was no association between ever exclusive use of e-cigarettes and reporting COVID-19 symptoms. However ever exclusive users were more likely to have been tested (OR=3.25, 95%CI=1.77-5.94) and to test positive (OR=5.05, 95%CI=1.82-13.96).

There was no association between past 30-day exclusive e-cigarette use and reporting COVID-19 relating symptoms or testing positive. However, past 30-day exclusive e-cigarette users were more likely to be tested (OR=6.84, 95%CI=2.4-19.55).

Past 30-day dual use of e-cigarettes and cigarettes was associated with an increased risk of reporting COVID-19 symptoms (OR=4.69, 95% CI=3.07-7.16, p<0.05). No significant association was observed for ever dual use.

Both ever and past 30 day dual users were more likely be tested for COVID-19 (OR=3.58, 95% CI=1.96-6.54, p<0.05 and OR=9.16, 95% CI=5.43-15.47, p<0.05) and receive a positive result (OR=6.97, 95%CI=1.98-24.55 and OR=6.84, 95%CI=2.40-19.55, p<0.05).

**Limitations**

Data was cross sectional meaning it cannot establish causality. It was also self-reported meaning that it may be subject to recall bias and error.

Results were not adjusted for all potential confounders which may affect COVID-19 infection. For example, results were adjusted for state cases which does not account for differences between areas within states.

E-cigarette and cigarette use were defined as “ever” or “past 30-day use” rather than “regular use”. As such, there is a limited ability to distinguish regular users from experimenters.

The study examined incidence rather than hospitalisation or severity of COVID-19. Therefore, it cannot draw conclusions around patient outcomes.


2. **Youth vaping and smoking and parental vaping: a panel survey**

**Study Aims**

This UK study reviewed data from 3291 young people (aged 10-15) in the Understanding Society survey between 2015-2017. The effects of youth vaping on smoking (ever, current and past year initiation), and parental vaping on youth smoking and vaping were investigated. Results were adjusted for sociodemographic characteristics and parental smoking. Propensity weighting was used to compare effects of vaping in all respondents (Average Treatment Effect (ATE)) and in respondents who vaped/had parents who vaped (Average Treatment Effect among the Treated (ATT)).
• **Key Findings**

In both the ATE and ATT estimates, youth vaping was associated with both ever smoking (ATE OR=12.03, 95%CI=5.16-28.04. ATT OR=10.54, 95%CI=5.99-18.53) and current smoking (ATE OR=22.71, 95%CI=8.99-57.40. ATT OR=10.49, 95%CI=5.04-21.82).

In the ATE estimate, youth vaping was associated with smoking initiation in the past year (OR=32.46, 95%CI=9.84-107.08). This association did not remain significant in the ATT estimate.

For all youth, the ATE and ATT estimate showed parental vaping was associated with ever smoking (ATE OR=2.43, 95% CI=1.05-5.63. ATT OR=1.68, 95%CI=1.03-2.72), but not current smoking or vaping. Parental vaping was associated with past-year smoking initiation in the ATT (OR=1.27, 95%CI=1.27-11.19) but not the ATE estimate.

For youth with ex-smoking parents, the ATE and ATT estimates showed parental vaping was associated with past year smoking initiation (ATE OR=11.28, 95% CI=2.74-46.44. ATT=6.81, 95%CI=1.78-25.96), but not ever smoking or vaping. Parental vaping was associated with current smoking in the ATE (OR=1.13,95% CI=1.13-7.06) but not ATT estimate.

For youth with parents who currently smoke, there was no association between parental vaping and ever smoking, current smoking, past year smoking initiation or vaping.

• **Limitations**

The estimates assume a directional relationship from vaping to smoking, however estimates could be explained by reverse causality.

Vaping status was determined by asking “do you ever use e-cigarettes”, meaning that participants who had used them once or infrequently may have been included. This also does not account for motivations or patterns of vaping.

The overall prevalence of smoking and vaping in participants was very low. As such, confidence intervals were wide which may have affected the accuracy of estimates.

The study focused on young teenagers (aged 10-15), meaning the associations may not be relevant to older youth who are more likely to adopt smoking or vaping.

Differences in ATT and ATE estimates indicate that unmeasured confounding may have impacted the results. However, the extent of the effect of confounding is unclear.

3. **QuitNic: A Pilot Randomized Controlled Trial Comparing Nicotine Vaping Products With Nicotine Replacement Therapy for Smoking Cessation Following Residential Detoxification**

- **Study Aims**

This Australian pilot study randomised 100 adult smokers discharged from a residential substance use disorder treatment centre, to either a 12-week supply of nicotine replacement therapy (NRT) or an e-cigarette with a 12-week supply of e-liquid. Both groups received telephone behavioural support. Acceptability, continuous and 7-day abstinence, cigarettes smoked per day, craving frequency, withdrawal symptoms and psychological distress were compared across the two groups at 6 and 12 weeks.

- **Key Findings**

In the e-cigarette group, 64% and 48% of participants reported adherence to the treatment at 6 and 12-week follow up. In the NRT group, 40% and 34% reported adherence to the treatment at 6 and 12-week follow up.

There were no significant differences in 7 day and continuous abstinence between the e-cigarette and NRT groups at 6 (p=0.479, p=0.212) or 12-weeks follow-up (p=0.696, p=0.876).

There were no significant differences in nicotine withdrawal symptoms between the e-cigarette and NRT groups at 6 (p=0.580) and 12-weeks (p=0.570) follow-up.

There was no significant difference between the e-cigarette and NRT groups in the number of cigarettes smoked at baseline compared with 6 (p=0.142) and 12-weeks follow-up (p=0.368).

At 12-weeks follow up, 91.7% of participants in the e-cigarette group agreed that their product was effective at reducing their cravings. In the NRT group, agreement varied from 61.5% to 93.3% depending on the product used.

- **Limitations**

The sample size was small, and attrition was high (50%) which increases the uncertainty of estimates. This may have affected the accuracy of estimates and statistical power.

There was no adjustment for confounding variables. Therefore, other factors may have influenced the outcomes in each group.

Data was self-reported and smoking abstinence was not biochemically verified. Participants may have misreported their smoking status which could have biased the results.

The study only followed up participants at 6 and 12 weeks. Future trials should collect outcomes at longer term follow-up points.

Withdrawal symptoms reported at the start of the trial may have been from drugs other than nicotine. This could have biased the results.

4. **Exclusive E-Cigarette Users Report Lower Levels of Respiratory Symptoms Relative to Dual E-Cigarette and Cigarette Users**

**Study Aims**

This cross-sectional US study assessed respiratory symptoms (according to the American Thoracic Society Questionnaire (ATSQ)) of exclusive users of e-cigarettes (n=59) and dual users of e-cigarettes and cigarettes (n=54). Differences between total and individual ATSQ scores in dual and exclusive e-cigarette users were compared. Hierarchical regression was used to compare the extent to which smoking status, vaping topography, nicotine concentration and e-cigarette dependence predicted ATSQ score severity.

**Key Findings**

The mean ATSQ score for exclusive e-cigarette users was 13.4 (SD=5.3) whereas the mean score for dual users was 19.0 (SD=6.7). This difference was statistically significant (p<0.001).

Dual e-cigarette users were more likely than exclusive users to report a cough first thing in the morning (p<0.001), a cough frequently throughout the day (p=0.001), wheezing (p=0.003), shortness of breath when walking (p=0.004), shortness of breath during exercise (p<0.001), phlegm or mucous when coughing (p<0.001), pain or tightness in the chest (p=0.05) and getting very tired in a short time (p=0.05).

After adjusting for age, sex, race, cotinine level, vaping topography and e-cigarette dependence, use of combustible cigarettes significantly predicted ATSQ score severity (p<0.01). Vaping topography variables and e-cigarette use variables did not predict ATSQ score severity.

**Limitations**

In the comparison of ATSQ scores, results were not adjusted for other variables. Therefore, they may be subject to confounding. Odds ratios were also not calculated meaning the increased risk of reporting severe ATSQ symptoms in dual vs exclusive users cannot be determined.

Participants who reported any smoking in the past 30-days were classified as dual users and previous smoking history was not recorded. As such, adjustment for smoking status does not consider smoking history, intensity or patterns.

The study is cross-sectional meaning any improvements in respiratory symptoms gained from switching from dual use to exclusive vaping cannot be determined.

The study did not examine exclusive smokers meaning that differences in respiratory symptoms cannot be compared to this group.

The sample size was relatively small (n=113). This may have affected the accuracy of estimates.
Overview

This month’s papers include two from the USA, one from the UK and one from Australia, focusing on: youth smoking, vaping and Covid-19; parental smoking and youth smoking and vaping; vaping for smoking cessation following discharge from a substance use treatment centre; and respiratory symptoms among exclusive vapers and dual users.

Our first study aimed to examine any relationship between vaping and Covid-19 in young people (aged 13-24) in the USA. Participants were recruited from existing online panels and completed a brief survey in May 2020. Quota sampling was used to obtain a sample of just over 4,000 - roughly half of whom were ever users of e-cigarettes and the other half non users. They were asked a series of questions about their smoking and vaping behaviour and self-reported symptoms, testing and whether they’d had a positive diagnosis for Covid-19.

The study found that receiving a positive diagnosis for Covid-19 was significantly more likely among those who had ever or recently (past 30 days) used e-cigarettes, and ever dual users. Self-reported symptoms of Covid-19 were more likely among past 30 day dual users. Vapers were also more likely to have been tested for the presence of the virus (SARS-CoV-2) and this included both past 30 day e-cigarette only users and dual users. Among smokers, ever (but not recent) smokers were more likely to be tested but not to report symptoms or test positive.

There is almost no existing research on vaping and Covid-19 which may explain why this study received media attention with headlines such as ‘Vaping teens and young adults up to seven times more likely to contract Covid-19’. This is in contrast to smoking and Covid-19, where there are a number of studies to date. These are the focus of a rapid living review that is regularly updated and published as a pre-print in Qeios. As the critical overview above describes, caution is needed before assuming that the findings of the current study provide any evidence of a causal association between vaping and Covid-19. In fact if you examine the data more closely, a roughly equal proportion of participants in the study who had never vaped tested positive (14%) as those who had ever used an e-cigarette (13%). But vapers were more likely to have been tested, which is important context for understanding the results. There is a need for more research on vaping and Covid-19, including among young people who make up an increasing proportion of those testing positive for the virus in many countries around the world.

This month’s second study is the latest from ongoing analysis of the UK’s large ‘Understanding Society’ survey. In the current paper, the authors examined panel data from just over 3,291 10-15 year olds in Wave 7 of the survey to estimate any effects of youth vaping on smoking, and parental vaping on youth smoking and vaping. Given the age of the participants, the numbers vaping or smoking were very low (110 vaping, 242 ever tried smoking and 74 currently smoking). The authors used a statistical modelling technique - propensity weighting - to adjust for factors that might explain the relationships found.
Overall the study did find some evidence that youth who vaped were more likely to go on to try smoking in the past year, but this effect was attenuated considerably after adjusting for confounders such as socio-economic status, gender, age, family structure and parental smoking and, as the authors point out, would also likely be weakened by confounders not measured in the study such as beliefs, values, personality, or sibling/friends smoking. For parental vaping, this was associated with smoking initiation, but not ever smoking or vaping, particularly among young people whose parents were ex-smokers rather than dual users. But again the authors point out that factors not measured in the study could explain these effects and that the findings didn’t support concerns that parents using e-cigarettes to quit smoking could directly contribute to children taking up smoking or vaping.

The third study aimed to assess the feasibility of providing a vaping product compared to nicotine replacement therapy to smokers who were discharged from a residential drug and alcohol treatment centre in Australia. Smoking rates are high among people dependent on drugs and/or alcohol and tobacco causes more deaths in this group than substance use. In this study, 100 clients were recruited and randomised to either receive twelve weeks supply of NRT (combination therapy - patch plus oral forms) or a vaping product starter kit with four weeks supply of e-liquid. Both groups received behavioural support via telephone from trained advisors.

Follow up was at six weeks and three months. At the final follow up, self-reported quit rates (seven day point prevalence) were 12% for the NRT group and 18% of the vaping group. Two thirds of the NRT group reported using the products at follow up as did almost all of the vaping group. Among those still smoking, cigarettes per day significantly reduced in both groups as did craving and withdrawal symptoms. Whilst this study was small pilot with several limitations outlined in the summary above, the findings indicate that e-cigarette use for smoking cessation in this group should be explored further. This has led to a larger study (the NEAT trial) being funded by the Australian National Health and Medical Research Council.

Our final study this month examined respiratory symptoms in vapers and dual users. Participants were volunteer vapers in the USA who were originally recruited to take part in behavioural economics study whose main results are reported elsewhere. They were all using a tank style refillable e-cigarette, and to be eligible to take part had to be between age 18-60 and vaping at least three times a week for the past month. In the current research, a roughly equal sample of exclusive vapers (n=59) and dual users who were smoking cigarettes as well as vaping (n=54) were involved. They attended a single laboratory session where they provided a saliva sample (to assess nicotine exposure), were asked to vape their own device for an hour and completed a number of questionnaires including one that included a validated measure to assess self-reported respiratory symptoms, the American Thoracic Society Questionnaire (ATSQ). The researchers were primarily interested in examining differences in respiratory symptoms between the exclusive vapers and the dual users.

The study found a significant difference in ATSQ scores, with higher scores among the dual users. The researchers then conducted statistical modelling to explore further the extent to which smoking status predicted ATSQ scores after controlling for socio-demographic variables, cotinine level, vaping topography (how participants used their device), e-cigarette dependence and other factors. In the
final results, only smoking status and not other factors (for example, vaping frequency, nicotine concentration of e-liquid etc) predicted higher ATSQ scores and therefore greater respiratory symptom severity. The study provides just a snapshot (it was cross-sectional) so we don’t know if respiratory symptoms would improve if the dual users in the study switched completely to vaping. However, other studies with follow up have found this type of improvement. The current research adds to evidence about the importance of stopping smoking completely, including when the chosen cessation aid is a vaping product.

Other studies from August/September you might find of interest

Patterns of use

Trends in youth e-cigarette and cigarette use between 2013 and 2019: insights from repeat cross-sectional data from the COMPASS study

Prevalence of Flavored e-Cigarette Use Among Subpopulations of Adults in the United States

Electronic Cigarettes Prevalence and Awareness Among Jordanian Individuals

E-cigarette use and cigarette smoking initiation among Australian women who have never smoked

Home smoking and vaping policies among US adults: results from the Population Assessment of Tobacco and Health (PATH) study, wave 3

Marijuana Vaping in U.S. Adults: Evidence From the Behavioral Risk Factor Surveillance System

E-Cigarette Use and Transition in Adult Smoking Frequency: A Longitudinal Study

Defining adult e-cigarette prevalence: comparing a categorical definition with days of use

Associations Between Nicotine Metabolite Ratio and Gender With Transitions in Cigarette Smoking Status and E-Cigarette Use: Findings Across Waves 1 and 2 of the Population Assessment of Tobacco and Health (PATH) Study

Perception

Descriptive and Injunctive Norms Related to E-Cigarettes

"Don't do vape, bro!" A qualitative study of youth's and parents' reactions to e-cigarette prevention advertisements

Knowledge and Beliefs of Jordanian Community Toward E-cigarettes: A National Survey

The Dilemma of Correcting Nicotine Misperceptions: Nicotine Replacement Therapy versus Electronic Cigarettes

Knowledge, Attitudes, and Perceptions of Young Adults About Electronic Nicotine Delivery Systems in the United States: An Integrative Review

Vape shop owners/managers' opinions about FDA regulation of e-cigarettes

Comparison of a General and Conditional Measure of E-Cigarette Harm Perceptions

Where there's smoke, there's fire: what current and future providers do and do not know about electronic cigarettes

Cessation
QuitNic: A pilot randomised controlled trial comparing nicotine vaping products with nicotine replacement therapy for smoking cessation following residential detoxification

E-Cigarette Use to Aid Long-Term Smoking Cessation in the US: Prospective Evidence from the PATH Cohort Study

Youth

Association of E-cigarettes with adolescent alcohol use and binge drinking-drunkenness: a systematic review and meta-analysis

E-cigarette environmental and fire/life safety risks in schools reported by secondary school teachers

School Use and Normative Perceptions of Electronic Nicotine Product Use Among Middle and High School Students - November 2018

Tobacco Product Promotions Remain Ubiquitous and are Associated with Use and Susceptibility to Use among Adolescents

Up in Smoke: Exploring the Relationship between Bullying Victimization and E-Cigarette Use in Sexual Minority Youths

Youth vaping and smoking and parental vaping: a panel survey

Factors associated with electronic cigarette use among adolescents asthma in the Republic Of Korea

Exploring Associations between Susceptibility to the Use of Electronic Nicotine Delivery Systems and E-Cigarette Use among School-Going Adolescents in Rural Appalachia

Characterizing Social Media Messages Related to Underage JUUL E-Cigarette Buying and Selling: Cross-Sectional Analysis of Reddit Subreddits

The Road to Vaping: E-cigarette Susceptibility and Curiosity Among U.S. Adolescents Susceptible and Nonsusceptible to Cigarette Smoking

Harms and harm reduction

Exclusive e-cigarette users report lower levels of respiratory symptoms relative to dual e-cigarette and cigarette users

Association Between Youth Smoking, Electronic Cigarette Use, and Coronavirus Disease 2019

Vaped Humectants in E-cigarette are a Source of Phenols

Pod-based menthol and tobacco flavored e-cigarettes cause mitochondrial dysfunction in lung epithelial cells

In utero Exposure to Nicotine Containing Electronic Cigarettes Increases the Risk of Allergic Asthma in Female Offspring

Cell invasion, RAGE expression, and inflammation in oral squamous cell carcinoma (OSCC) cells exposed to e-cigarette flavoring

In vivo assessment of the toxicity of electronic cigarettes to zebrafish (Danio rerio) embryos, following gestational exposure, in terms of mortality, developmental toxicity, and hair cell damage: Toxicity of E-cigs to zebrafish embryos

The Impact of Device Settings, Use Patterns, and Flavorings on Carbonyl Emissions from Electronic Cigarettes

Electronic cigarette extract induced toxic effect in iPS-derived cardiomyocytes

Tobacco, but Not Nicotine and Flavor-Less Electronic Cigarettes, Induces ACE2 and Immune Dysregulation

Replacing smoking with vaping during pregnancy: impacts on metabolic health in mice
Glyoxal and Methylglyoxal as E-cigarette Vapor Ingredients-Induced Pro-Inflammatory Cytokine and Mucins Expression in Human Nasal Epithelial Cells

Electronic Cigarette (e-cigarette) Use and Frequency of Asthma Symptoms in Adult Asthmatics in California

Differential effects of tobacco cigarettes and electronic cigarettes on endothelial function in healthy young people

Urinary Biomarkers of Exposure to Volatile Organic Compounds from the Population Assessment of Tobacco and Health Study Wave 1 (2013-2014)

Electronic cigarette liquid substances propylene glycol and vegetable glycerin induce an inflammatory response in gingival epithelial cells

Analysis of potential associations of JUUL flavours with health symptoms based on user-generated data from Reddit

The JUUL E-Cigarette Elevates the Risk of Thrombosis and Potentiates Platelet Activation

Potential effects of E-cigarettes and vaping in pediatric asthma

Burn injuries related to E-cigarettes reported to poison control centers in the United States, 2010-2019

Electronic cigarette vapor increases Streptococcus mutans growth, adhesion, biofilm formation, and expression of the biofilm-associated genes

Metabolites of Tobacco- and E-Cigarette-Related Nitrosamines Can Drive Cu 2+-Mediated DNA Oxidation

Toxic Metal-Containing Particles in Aerosols from Pod-Type Electronic Cigarettes

Electronic nicotine delivery system-induced alterations in oral health via saliva assessment

Hot Wires and Film Boiling: Another Look at Carbonyl Formation in Electronic Cigarettes

Chemical and Toxicological Characterization of Vaping Emission Products from Commonly Used Vape Juice Diluents

Marketing

Content Analysis of Instagram Posts From 2019 With Cartoon-Based Marketing of e-Cigarette-Associated Products

Misc

Are in silico approaches applicable as a first step for the prediction of e-liquid toxicity in e-cigarettes?

E-Cigarette Demand: Impact of Commodity Definitions and Test-Retest Reliability

Green Apple e-Cigarette Flavorant Farnesene Triggers Reward-Related Behavior by Promoting High-Sensitivity nAChRs in the Ventral Tegmental Area

E-cigarette Tobacco Retail Licensing Laws: Variance Across US States as of January 1, 2020

Search strategy

The Pubmed database is searched in the middle of each month, for the previous month using the following search terms: e-cigarette*[title/abstract] OR electronic cigarette*[title/abstract] OR
ecig[title/abstract] OR (nicotine AND (vaporizer OR vaping OR vapourizer OR vaporiser OR vapouriser))

Based on the titles and abstracts new studies on e-cigarettes that may be relevant to health, the UK and the UKECRF key questions are identified. Only peer-reviewed primary studies and systematic reviews are included – commentaries will not be included. Please note studies funded by the tobacco industry will be excluded.

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