# E-cigarettes and harm reduction

## An evidence review

Royal College of Physicians

## Acknowledgements

The Tobacco Advisory Group acknowledges the help of Cancer Research UK (CRUK) for supporting some of the original research and literature reviews contained in this report.

## The Royal College of Physicians

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## Citation for this document

Royal College of Physicians. *E-cigarettes and harm reduction: An evidence review*. RCP, 2024.



Report published in April 2024


ISBN 978-1-86016-883-3

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# Declaration of contributors' interests

**John Britton** has acted as an expert witness in a court case in Canada relating to a proposed e-cigarette flavour prohibition. He was not funded, directly or indirectly, by any money from the tobacco industry.

**Jamie Brown** has received unrestricted funding for smoking cessation research from Pfizer and Johnson & Johnson, who manufacture smoking cessation medications.

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**All other contributors** have no interests to declare.

# RCP Tobacco Advisory Group

The Royal College of Physicians' (RCP) Tobacco Advisory Group (TAG) advises the RCP on tobacco control-related policy and activity. Several reports on tobacco and smoking have been produced since the group was established in 1997, providing much of the evidence base for successful campaigns to improve tobacco control in the UK. The most recent reports are:

- *E-cigarettes and harm reduction: An evidence review* (2024)
- *Smoking and health 2021: A coming of age for tobacco control?* (2021)
- *Hiding in plain sight: Treating tobacco dependency in the NHS* (2018)
- *Nicotine without smoke: Tobacco harm reduction* (2016)
- *Smoking and mental health* (2013)
- *Fifty years since smoking and health: Progress, lessons and priorities for a smoke-free UK* (2012)
- *Passive smoking and children* (2010)
- *Harm reduction in nicotine addiction: Helping people who can't quit* (2007)
- *Going smoke-free: The medical case for clean air in the home, at work and in public places* (2005)
- *Nicotine addiction in Britain* (2000)

The current membership of the RCP TAG is:

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# Foreword

Since our foundation in 1518, one of the key priorities for the Royal College of Physicians has been to improve the health and care of our communities not only in the UK, but wherever RCP members and fellows live and work. The major challenges to health over the centuries have typically been infectious diseases, the impact of which have been made worse by poor living conditions, poverty, evolving scientific knowledge or lack of vaccines and effective treatments. The rise of non-communicable diseases such as those related to tobacco, alcohol and poor diet have been a more recent phenomenon but have caused the deaths of countless millions of people, and disproportionately affect the poorest nations and the poorest in our society.

The RCP has been at the forefront of tackling tobacco-related harm for over half a century. With the publication of Smoking and health in 1962 and many subsequent reports relating to tobacco control, it has recognised the need to prevent the uptake of smoking by those who have never smoked but also to consider what more needs to be done for those already addicted to combustible tobacco. For this latter group we have recommended policies in the UK to systematically treat tobacco addiction, to make tobacco products less available and affordable, and to consider alternatives to tobacco that fulfil the craving for nicotine but do not carry the same risk to life as tobacco.

The evolution of alternative nicotine products has been rapid, especially with the advent of e-cigarettes some two decades ago. The large-scale use of e-cigarettes, predominantly in people trying to stop smoking, has been striking and has undoubtedly helped many thousands of people in the UK to avoid the painfully predictable morbidity and mortality from continued smoking. The popularity of these products has also presented undesirable effects, most notably the use of e-cigarettes by children, young people and adults who have never smoked.

There are still, however, 6.4 million regular smokers in the UK in 2023 who are destined for early and avoidable premature morbidity and mortality unless they quit smoking. The potential of e-cigarettes to reduce the burden of ill health as an alternative to smoking warrants a fresh examination as much has changed since the RCP last scrutinised this area with the publication of Nicotine without smoke in 2016.

This report considers how best to maximise the benefits of e-cigarettes for harm reduction while discouraging their use among those who have never smoked, especially children and young people. It concludes that e-cigarettes remain an important tool to alleviate the burden of tobacco use but that much more can and should be done to reduce their appeal, availability and affordability to people who do not smoke and reduce environmental harms. In a country with a mature, highly regulated tobacco control environment, by treading carefully and thoughtfully there remains an opportunity to use e-cigarettes in our ambition to make smoking obsolete.

**Dr Sarah Clarke**
RCP president

# Abbreviations and definitions

| | |
|---|---|
| **ASA** | Advertising Standards Authority |
| **ASH** | Action on Smoking and Health |
| **BMI** | body mass index |
| **BAT** | British American Tobacco |
| **CAP** | Committee on Advertising Practice |
| **CNEMA** | 2-cyanoethyl mercapturic acid |
| **CO** | carbon monoxide |
| **CRP** | C-reactive protein |
| **CRUK** | Cancer Research UK |
| **COPD** | chronic obstructive pulmonary disease |
| **CFTR** | cystic fibrosis transmembrane conductance regulator |
| **CTSI** | Chartered Trading Standards Institute |
| **EU TPD** | European Union Tobacco Products Directive |
| **disposable** | the term disposable has been used throughout this report to describe e-cigarettes that are pre-filled for limited use and are not rechargeable or refillable. Note that single-use is also widely used to describe such devices in the media and literature |
| **e-cigarette/vape** | e-cigarettes and vapes have been used interchangeably in this report |
| **FCLO** | fiscal crime liaison officer |
| **FCTC** | Framework Convention on Tobacco Control |
| **FDA** | Food and Drink Administration (US) |
| **FEV1/FVC** | forced expiratory volume / forced vital capacity of the lungs |
| **FMD** | flow-mediated dilation |
| **HDL** | high-density lipoprotein |
| **HMPPS** | His Majesty's Prison and Probation Service |
| **HMRC** | His Majesty's Revenue and Customs |
| **HRT** | hand rolling tobacco |
| **HTP** | heated tobacco product |
| **IARC** | International Agency for Research on Cancer |
| **ICER** | incremental cost-effectiveness ratio |
| **ITC** | International Tobacco Control |
| **JTI** | Japan Tobacco International |
| **LDL** | low-density lipoprotein |
| **LIN** | Learning and Improvement Network |
| **LMIC** | low- and middle-income countries |
| **MET** | minimum excise tax |
| **MHBMA** | monohydroxybutenylmercapturic acid |
| **MHRA** | Medicines and Healthcare products Regulatory Agency |
| **MPOWER** | Monitor tobacco use and prevention policies, Protect people from tobacco smoke, Offer help to quit tobacco smoking, Warn about dangers of tobacco smoking, Enforce bans on tobacco advertising and sponsorship, Raise taxes on tobacco |
| **mtCN** | mitochondrial DNA copy numbers |
| **nAChRs** | nicotinic acetylcholine receptors |
| **NASEM** | National Academies of Sciences, Engineering and Medicine |
| **NCSCT** | National Centre for Smoking Cessation and Training |
| **NICE** | National Institute for Health and Care Excellence |
| **NNAL** | 4-(methylnitrosamino)-1-(3-pyridyl) -1-butanol |
| **NNK** | 4-(methylnitrosamino)-1-(3-pyridyl) -1-butanone |
| **NNN** | N'-nitrosonornicotine |
| **NRCT** | non-randomised controlled trial |
| **NRT** | nicotine replacement therapy |
| **NVP** | nicotine vaping products |
| **OHID** | Office for Health Improvement and Disparities |
| **ONS** | Office for National Statistics |
| **PAHs** | polycyclic aromatic hydrocarbons |
| **PATH** | Population Assessment of Tobacco and Health |
| **PHE** | Public Health England (now OHID) |
| **PMI** | Philip Morris International |

| | |
|---|---|
| **QALY** | quality-adjusted life year |
| **QoF** | Quality Outcomes Framework |
| **RCP** | Royal College of Physicians |
| **RCT** | randomised controlled trial |
| **SMI** | severe mental illness |
| **SPS** | Scottish Prison Service |
| **STS** | Smoking Toolkit Study |
| **TAG** | Tobacco Advisory Group (of the RCP) |
| **TCS** | Tobacco Control Scale |
| **TGA** | Therapeutic Goods Administration (Australia) |
| **TNE** | total nicotine equivalent |
| **TPD** | Tobacco Products Directive |
| **TRPR** | Tobacco and Related Products Regulation |
| **TSNAs** | tobacco-specific nitrosamines |
| **TTC** | transnational tobacco company |
| **UKVIA** | UK Vaping Industry Association |
| **VAT** | value added tax |
| **VBA** | Very Brief Advice – a clinical intervention designed to be delivered in as little as 30 seconds, which aims to identify and support patients who smoke to quit |
| **VOCs** | volatile organic compounds |
| **WBC** | white blood cell |
| **WEEE** | waste electrical and electronic equipment |
| **WHO** | World Health Organization |
| **WTO** | World Trade Organization |

# Executive summary and recommendations

# 1.Introduction

In 2007 the Royal College of Physicians (RCP) published a report on alternative nicotine products, covering their regulation and role as alternatives to smoking. This was at a time when e-cigarettes were first becoming available in Europe. The report concluded that there is a role for alternative nicotine products to support people to stop smoking tobacco and that regulation for those products should be formalised.

In the years following that publication, use of e-cigarettes rose considerably, primarily among people who typically used them as an aid to stopping smoking. The RCP went on to re-examine emerging data on the role of e-cigarettes and alternative nicotine products in its report *Nicotine without smoke* in 2016, which concluded that e-cigarettes were an effective aid to quitting smoking. That report recommended their promotion as a stop smoking tool but said that data should be reviewed at regular intervals to look for unintended consequences that may require policy adaptation.

Comprehensive evidence reviews on the role of e-cigarettes have been commissioned in the UK at regular intervals by Public Health England (PHE) and subsequently the Office for Health Improvement and Disparities (OHID). The most recent evidence review published in 2022 examined data on the effectiveness of e-cigarettes as a smoking cessation treatment, their health risks and benefits, their use by people who have never smoked including children and young people, and their role in UK tobacco control policy. The review, based on biomarkers of exposure to toxins and biomarkers of organ damage, concluded that vaping, over the short and medium term, poses a small fraction of the risk of smoking; that vaping is not, however, risk-free; and called for further research to increase precision about longer term risks and how these can be reduced or mitigated.

There is marked variation in international approaches to e-cigarettes. This may reflect local trends in tobacco and e-cigarette use, the availability of other nicotine-containing products, commercial opportunities for e-cigarette sales, the regulatory environment and its approach to balancing risk, the maturity of other tobacco control measures, and concern that the tobacco industry might use e-cigarettes to undermine the implementation of other tobacco control measures. The UK has a high level of compliance with the WHO Framework Convention on Tobacco Control (FCTC) and should continue to protect health policy from the vested commercial interests of the tobacco industry. Nevertheless, in endorsing and promoting vaping as part of a comprehensive national tobacco control programme the UK is an international outlier: few other countries have adopted this approach and none so consistently over the past 15 years.

This report looks again at the part e-cigarettes can play in preventing death, disability and inequalities from tobacco use. It examines the role of nicotine and the spectrum of nicotine-containing products, trends in tobacco use and vaping, the effectiveness of e-cigarettes to treat tobacco addiction, and the differences in health effects of vaping in people who smoke, vape or do neither. For those who currently smoke, the report reviews how e-cigarettes can be used to support more people to make quit attempts while discouraging young people and never-smokers from taking up e-cigarette use. The role of the tobacco industry in encouraging 'new entrants' (a term used by the industry to describe never-smokers) to the nicotine market while continuing to sell lethal tobacco products is also examined. Finally, the report considers the ethical dilemmas presented by e-cigarettes, such as managing risk messaging of uncertain long-term safety data, use in never-smokers, balancing the regulatory environment, industry interference, and the environmental impact. We conclude that:

- since the 2016 RCP report the evidence of the effectiveness of e-cigarettes as an aid to quitting has become much stronger
- use of e-cigarettes by young people and non-smokers has increased substantially in recent years
- prompt remedial measures are needed to curb youth vaping without undermining use by adult smokers as an aid to quitting
- the government should commission a series of regular evidence updates on the use and effects of nicotine products to guide policy.

## 2. Nicotine – physiological effects and the characteristics of nicotine-containing products

Switching completely from tobacco smoking to alternative nicotine products such as e-cigarettes has been encouraged in UK health policy to reduce the damage caused by smoking to individuals who smoke and to the people around them exposed to passive smoke (especially children), as well as the broader societal costs of smoking. People who smoke are addicted primarily to the nicotine in tobacco, which drives sustained use of smoked tobacco products and the subsequent devastating harm to health caused primarily by non-nicotine constituents of tobacco smoke, including tar particles and carbon monoxide. Current evidence suggests nicotine itself confers little risk to health, though acute exposure at typical levels from consumer nicotine products can result in addiction, short-term enhanced cognitive effects, elevated heart rate and systolic blood pressure. It will, however, take several decades to accurately quantify any effects of long-term non-tobacco nicotine use.

Nicotine-containing products include combusted tobacco products, non-combusted tobacco products and non-tobacco nicotine products. There is a spectrum of potentially harmful exposures associated with the use of each product – combustible tobacco products generating the greatest toxic exposure and medicinal nicotine products the least. It is likely that e-cigarettes and oral nicotine products fall close to the lower end of this spectrum (see chapter 6, Fig 2.2).

Most of the harmful constituents of e-cigarette vapour are thermodegradation products generated by the vaporisation process. Levels of toxic substances are higher when high power devices are used to vaporise low nicotine concentration liquids, and lower with low power, high nicotine devices.

### Recommendations

- More research should be undertaken to determine the long-term effects of nicotine exposure without confounding from long-term tobacco use.
- Regulations to ensure e-cigarette design minimises the generation of toxic thermodegradation products and exposure to other potentially harmful constituents should be introduced by the UK government.
- Advice should be provided to e-cigarette users on which devices provide lower exposures to thermodegradation products.

## 3. Trends in the use of e-cigarettes and tobacco products

Cigarette smoking among adults has declined steadily, although more slowly in recent years. In 2022, 12.7% of adults in England smoked, while use of vaping products jumped sharply to around 10% of adults in 2023. During the pandemic, rates of vaping rose especially among young adults, growing to over 20% of 18–24-year-olds in 2023. This age group has also shown a continued decline in smoking since 2021.

Smoking among children and young people aged 11–17 years has declined from 6.0% in 2013 to 3.6% in 2023 while vaping has increased to 7.6% in this age group in 2023. Most of the increase in use of vaping products took place after 2021 and coincides with a dramatic rise in use of disposable vapes. This increased use of disposable vaping devices has not displaced use of other types of devices, and so has led to an overall increase in vaping in this age group.

Vaping remains overwhelmingly an activity of smokers and ex-smokers, who represent around 93% of all people who use vaping products. The proportion of adult vapers in the 2023 Action on Smoking and Health (ASH) survey who were never-smokers was 6.7% and has been stable since 2019. The number of people in England using vaping products who have never smoked is uncertain but is likely to be between 320,000 and 840,000.

The rise in e-cigarette use in the UK mirrors that of most countries where data are available, despite the wide range of regulatory environments for e-cigarettes. Apart from New Zealand, which has one of the lowest smoking rates among rich countries, international data demonstrate e-cigarette use among adults remains lower than smoking. Past 30-day use of e-cigarettes among young people is generally higher than among older adults, and in some countries exceeds the prevalence of smoking among youth.

### Recommendations

- Trends in the prevalence of vaping and smoking in time, place and person across the UK should be monitored.
- Longitudinal data should be collected to build on existing cross-sectional survey data and enable better overall understanding of trajectories in use and transitions from smoking to vaping, as well as from vaping to abstinence and use in never-smokers.
- Survey data on vaping in localities and regions, in combination with local sales data for tobacco, should be collected to inform local tobacco control.
- The UK should take part in standardised international comparative studies of smoking and vaping such as The European School Survey Project on Alcohol and Other Drugs (ESPAD) to ensure that we can assess UK vaping trends and tobacco control strategies reliably in an international context.

## 4. Effectiveness of e-cigarettes for smoking cessation

Evidence from randomised controlled trials and from two Cochrane reviews shows e-cigarettes with nicotine are more effective at helping people quit at 6 months or longer than nicotine replacement therapy (NRT), with no clear difference in effectiveness between nicotine e-cigarettes and varenicline or cytisine. Among pregnant women who smoke, the largest randomised trial to date has shown equivalence of quit success for e-cigarettes and NRT and a lower frequency of low birthweight among those randomised to e-cigarettes.

There are signals that e-cigarettes may have a benefit in both stopping smoking and harm reduction in smokers with mental illness, including those who are not motivated to quit and have been unable to quit before. E-cigarettes that are easier to use, such as pod-based devices or disposables, may be more effective in this population. Evidence suggests that e-cigarettes are both acceptable and effective for smoking abstinence and cessation in settings such as prisons and for people experiencing homelessness. The provision of e-cigarette starter kits for smoking cessation has been effective in settings such as emergency departments and social housing. E-cigarette use for smoking cessation and harm reduction in these populations and settings with a high prevalence of smoking and socio-economic deprivation suggests they may have a positive role to play in reducing smoking-related health inequalities.

There is little evidence on vaping for smoking relapse prevention or on the best ways to support people to quit vaping.

Changes in the prevalence of e-cigarette use in England have been positively associated with the success rate of quit attempts. If the association is causal, then the use of e-cigarettes in quit attempts appears to have helped in the region of 30,000 to 50,000 additional smokers to successfully quit each year in England since 2013.

E-cigarettes represent a cost-effective smoking cessation intervention, with an incremental cost-effectiveness ratio of £1,100 per quality-adjusted life year (QALY) gained over the course of 12 months and of £65 per QALY over a lifetime. Implementing e-cigarette interventions could potentially reduce financial burdens on local government stop smoking services and the NHS without imposing additional costs on individuals trying to quit smoking.

### Recommendations

- E-cigarettes should be promoted as an effective means of helping people who smoke to quit smoking tobacco.
- Campaigns recommending e-cigarettes for smoking cessation should include populations who are likely to experience the most benefit, including people with mental disorders, those who experience socio-economic disadvantage and people living in social housing.
- E-cigarettes should be offered as an effective treatment for smoking cessation across all NHS settings alongside established pharmacotherapy.
- Priorities for research include the role of e-cigarettes in smoking relapse prevention, cessation of e-cigarette use, and the effectiveness for smoking cessation of different e-cigarette device types and characteristics, including flavours.

## 5. Health effects of e-cigarettes

The harm of smoking to human health is beyond doubt, accounting for 8 million deaths globally each year and 76,000 deaths annually in the UK. 2 out of 3 people who continue to smoke will die from a smoking-related disease. Using e-cigarettes for harm reduction to reduce morbidity and mortality from combustible tobacco is based on clear evidence that e-cigarettes cause less harm to health than combustible tobacco. It is important to provide users of e-cigarettes with as much accurate data as possible on the relative and absolute health effects of e-cigarettes in comparison to use of combustible tobacco alone, dual use and never smoking.

For this report we have carried out a review of biomarkers of exposure to and harm from e-cigarettes using data published between 2021 and 2023 comparing people who vape, people who smoke, people who do both (dual use), and people who do neither (non-use).

Our overall findings were that:

- blood levels of nicotine and its metabolites in vapers are similar to or lower than those in smokers, and carbon monoxide levels are lower
- levels of tobacco-specific nitrosamines, volatile organic compounds and polycyclic-aromatic hydrocarbons are lower in vapers than in smokers and are higher or similar to non-vapers/non-smokers
- there is inconsistent evidence whether vapers have higher levels of lead, cadmium arsenic or mercury than smokers. Levels of lead and cadmium were higher, and levels of arsenic lower or equal between vapers than non-vapers/non-smokers
- vapers show similar or lower levels of markers of oxidative stress and inflammation to those in smokers and similar levels compared with non-vapers/non-smokers
- findings of research into disease-specific biomarkers has yielded mixed results
- there is some evidence that passive exposure to vaping aerosol results in some nicotine absorption, and in one study, evidence of inflammatory change in those exposed
- evidence on the effects of vaping in pregnancy remains mixed
- vaping nicotine is not associated with a high frequency of adverse health effects.

Research on the health effects of vaping is limited by small sample sizes, a lack of research exploring absolute as well as relative risks, and on the longer-term health risks of vaping when accounting for past smoking history.

### Recommendations

- Agreement needs to be reached on the methods for vaping health risks research, including which biomarkers are the most relevant to study regarding the relative and absolute risks of vaping.
- Large longitudinal cohort studies are needed: firstly, of people who vape and have never smoked, and secondly of former smokers who vape, and which adequately account for their smoking history.

## 6. Regulation of tobacco and nicotine products

E-cigarette policy varies substantially between countries, ranging from promotion to prohibition, with policy variation partly based on the degree to which countries focus policy on combustible tobacco or nicotine use, especially in youth populations. Formulating policy to maximise the public health benefit of vaping should be evidence-based, but predicting the magnitude of intended and unintended consequences of new policy can be difficult as policy decisions typically need to be made well before definitive long-term evidence on outcomes is available.

England is unusual in having actively promoted vaping for smoking cessation since the emergence of e-cigarettes. Canada and New Zealand have moved policy from relative prohibition to relative market freedom while Australia has taken a more and increasingly prohibitionist line, enforcing limited access via medicines regulation. Policies in other countries range from complete prohibition (India), medicines regulation (Japan and Hong Kong) and some restrictions on sales and use (mainland China). Those countries that have banned vapes have left far more harmful combusted tobacco products on general sale.

Nicotine product regulation in the UK has evolved to enable and encourage smokers to quit smoking, either by quitting all nicotine use or by switching to a less harmful nicotine product. Regulation of e-cigarettes should be designed to protect users from avoidable harm and to prevent, as far as possible, children who do not smoke from becoming vapers. It is illegal to purchase nicotine-containing e-cigarettes under the age of 18 and age verification is required by retailers in Scotland, but not in other UK nations.

The main levers for e-cigarette regulation are related to sales; product standards; including nicotine content; flavours; colours; added ingredients; packaging; labelling; advertising; promotion; product registration/notification; authorised use (eg if a prescription is required) and price. Current regulations have been insufficient to prohibit packaging and labelling, including bright colours, cartoon characters and sweet names, which increase the attractiveness of vaping products to children relative to standardised packaging. Compliance with advertising regulations appears to be high for adverts in traditional media, but significantly lower on social media sites. Point-of-sale advertising and display is not covered by the regulations and is not the responsibility of the Advertising Standards Authority.

The Medicines and Healthcare products Regulatory Agency (MHRA) notification of content and emissions is mandatory for all e-cigarettes sold in the UK, but the reporting system lacks standardisation and reports are not independently validated. Although data on safety vigilance and oversight by manufacturers are not readily available, Yellow Card reporting data and hospital admissions episodes suggest that adverse health effects from vaping in the UK are rare. Responsibility for investigating non-compliance and enforcing regulations rests with trading standards departments in local authorities; however, funding for trading standards work has been cut from £213 million in 2009 to £105 million in 2019, limiting their capacity for enforcement. Underage sale to children appears to be common. Since leaving the EU, the UK Parliament lacks legislative powers to amend the UK Tobacco and Related Products Regulations. The government must introduce legislation to take such powers as an urgent priority.

The extent to which illicit vapes (or their health effects) are used in the UK is unknown, although seizure data suggest that availability is growing, possibly because penalties for illicit sale are currently very low and therefore offer little disincentive to sellers. Experience from tackling illicit tobacco suggests that the illicit market is best addressed by targeting supply chains. It is important that research into the illicit market is carried out independently from commercial interests to prevent the generation of disinformation.

Pricing is an important component that can encourage smokers to transition to e-cigarettes to quit smoking. A gradation of taxes at levels that broadly relate to likely harm are imposed on nicotine products in the UK. In the UK, non-tobacco nicotine and e-cigarette products are currently subject to the standard rate of value added tax (VAT) at 20%. Medicinally regulated products that have been formally approved as therapies to help people stop smoking are subject to the reduced rate of VAT at 5%.

The price of e-cigarettes is a critical factor in determining consumption because higher prices are generally associated with lower use. Price regulation is therefore a potential means to reduce consumption of the disposable e-cigarettes that are most commonly used by young people and have the greatest negative environmental impact. However, the elasticity and cross-elasticity of e-cigarette purchasing are not well-defined in the UK, so it is difficult to predict the likely effect of price regulation on vaping in general, and on use of disposable vapes in particular. New price regulation on disposable e-cigarettes would likely have a partial effect on removing access to young people but would be likely to stimulate growth in the illicit market.

Vaping does not generate smoke and is therefore not subject to smoke-free laws. In places where occupants are likely otherwise to smoke, for example in some mental health settings or in prisons, vaping offers smokers a means by which they can adhere to smoke-free laws and enable smoke-free premises. Indoor vaping policies should be formulated in relation to the needs of the people subject to them and consider prohibition of vaping near others on the basis of courtesy, comfort and utility.

Disposable vapes present significant environmental and safety hazards, and recycling of these products has been widely neglected. More effective and accessible recycling schemes for vapes, particularly disposable vapes, are urgently needed. Registering with environment agencies via producer compliance schemes should be a mandatory component of MHRA notification. Creating a separate product category for vapes that falls within waste electrical and electronic equipment (WEEE) regulations to ensure that producers, importers and retailers are properly financing takeback is essential.

## Recommendations

- Since leaving the EU, the UK parliament lacks legislative powers to amend the UK Tobacco and Related Products Regulations. The government must introduce legislation to take such powers as an urgent priority.
- Regulatory restrictions on the promotion, price and availability of all consumer nicotine products should be proportionate to the health risk they represent and designed to discourage uptake among young people and reduce, rather than perpetuate, tobacco smoking.
- The MHRA notification process should be revised to require a standardised system of content and emission reporting, and to require random sampling of products for independent validation of content and emission data.
- Regulations should be revised to enable competent authorities such as the MHRA to raise and use notification fees to carry out systematic validation of notified data, and to fund enforcement activity.
- Trading standards services should be sufficiently resourced to effectively enforce e-cigarette sales legislation and reduce underage sales.
- A register of tobacco and nicotine retailers should be established along with requiring age verification and meaningful sanctions for breaching the law, with the aim of limiting access to young people.
- Regulations on advertising and promotion of e-cigarettes should be introduced to restrict online platforms, content generators and point-of-sale advertising to limit advertising of e-cigarette products to young people.
- A gradation of taxes at levels in broad relation to likely harm should be imposed on nicotine products in the UK.
- E-cigarette price and taxation strategies should target the products that are the cheapest and most commonly used by youth vapers while ensuring that the products most likely to be used by adult smokers/quitters remain affordable.
- Consideration should be given to banning e-cigarette price promotions and discounts; and minimum pricing for e-cigarettes.

- The government should consider a range of policy options to address the challenges of vape recycling from an environmental perspective, including:
  - prohibiting disposable e-cigarettes
  - amending product standards, descriptors and notification to the MHRA to support recycling
  - registration with environment agencies via producer compliance schemes as a mandatory component of MHRA notification
  - amending electrical and battery waste regulations to include disposable vapes
  - ensuring vendors comply with recycling costs for vapes
  - providing accessible drop-off points.

## 7. Encouraging uptake of e-cigarettes for smoking cessation

E-cigarettes are an effective treatment for tobacco dependency, but despite being easily accessible via a wide range of retail settings in the UK, they are under-utilised by people who want to quit or reduce smoking. This represents a large, missed opportunity to reduce morbidity and premature mortality.

Reasons for this under-utilisation include lack of awareness of the efficacy of these products for smoking cessation and harm reduction (chapter 4), and public perceptions of the risks of vaping relative to smoking which do not reflect current evidence (chapter 5). Misinformation in the media is likely to contribute to misperceptions about vaping. Nicotine warnings on e-cigarette packaging may affect harm and addictiveness perceptions and reduce intentions to vape among young people as well as adults who smoke.

Evidence suggests that providing information aimed at increasing accurate relative perceptions of vaping compared with smoking can be successful among adults. Reduced risk messages presented on e-cigarette packs alone (without an addiction message) may increase uptake among smokers but not non-smokers. Access to a variety of device types and flavours can encourage the uptake of e-cigarettes to quit. The price of e-cigarettes is likely to be an important determinant of their consumption; higher prices are generally associated with lower use.

A person's identity in relation to smoking and vaping may play an important role in smoking cessation, with vaping offering an identity that may be attractive to smokers who wish to quit or stay quit. Dual users who are predominantly vapers are more likely to reduce tobacco consumption compared to those who are predominantly smokers. Frequency of e-cigarette use is important in predicting subsequent smoking cessation; daily and frequent use are positively associated with quitting smoking.

Despite national guidelines that clinicians should offer e-cigarettes as a treatment for tobacco dependency to their patients who smoke, a high proportion of health professionals report that they would not advise their patients to use e-cigarettes due to concerns about addiction and uncertainty about long-term harms. Clear information and training on the efficacy and health effects of e-cigarettes may help correct this misapprehension. In addition, many commissioned stop smoking services do not utilise e-cigarettes as part of their treatment interventions. There is an opportunity to proactively support smoking cessation by promoting vaping as a treatment for tobacco dependency in all NHS settings.

### Recommendations

- Measures that encourage e-cigarette use for smoking cessation encompassing policies that address availability, affordability, access to nicotine-containing e-cigarettes together with information and support to use these products should be expanded to improve smoking quit rates in the UK.
- Measures to encourage e-cigarette use by smokers should be used together with measures to discourage uptake of e-cigarettes by people who do not smoke, especially children and young people.
- Interventions to increase accurate perceptions of the risks of vaping, especially relative to smoking, are important, but more research is needed to identify the most effective ways of doing this.
- A range of flavours should be available to facilitate quitting among adults who are using e-cigarettes to quit smoking.
- More research is needed to directly explore the effects of device type, nicotine concentration and other features on smoking cessation.
- Messages on the relative risks of vaping and smoking should be required on cigarette packs and on package inserts, thus reaching smokers but not non-smokers.

- Reduced risk messages should be included on e-cigarette packs.
- More research is needed to explore how to maximise credibility of reduced risk messages; ensure that smokers notice and attend to them; and understand the extent to which message exposure can promote actual use behaviour.
- Detailed research is needed to understand how e-cigarette advertising can increase the uptake of e-cigarettes among people who smoke to support and maintain quit attempts.
- In all healthcare settings, trained specialists should offer support for smoking cessation using e-cigarettes and other evidence-based therapies.
- Smoking cessation interventions should support positive identity change in relation to vaping. Research is needed to identify the most effective ways to do this.
- Smokers who are trying to quit using e-cigarettes should be encouraged and supported to adopt patterns of e-cigarette use most likely to lead to successful smoking cessation.

## 8. Discouraging uptake of e-cigarettes in people who do not smoke

There has been a rise in e-cigarette use among people who do not smoke, particularly among children and young people in the UK. This represents a potential health risk as vaping products are not risk free. Factors that can increase uptake of e-cigarettes among non-smokers include the availability of attractive devices, easy retail access, widespread advertising that includes point of sale advertising and social media visibility, and affordable prices. Many of these factors mimic the conditions that encouraged youth uptake of smoking before tighter regulations were introduced.

While higher nicotine concentrations do not appear to be part of the initial appeal of vaping, higher nicotine content may be associated with continued use and/or more frequent use among young people. Surveys suggest the appeal of flavours is not the main reason why young people who have never smoked start vaping, but the names or 'descriptors' of flavours may be a factor. Modelling suggests that restricting flavours could disproportionately lead to more people continuing to smoke or relapsing to smoking than preventing uptake of vaping or uptake of smoking.

Perceiving vaping as less harmful than smoking predicts subsequent vaping uptake among young people and adults who do and do not smoke, while perceiving vaping as harmful is associated with not starting vaping. Evidence suggests that campaigns aiming to deter youth from trying smoking can increase perceptions of vaping as harmful.

Exposure to vaping prevention messages can increase risk perceptions among non-smokers but effects on use intentions are unclear. Research among young people aged 11–18 in England has found that compared to branded and standardised packaging, youth interest in trying e-cigarettes is lowest when standardised packaging is combined with reduced flavour and brand descriptions.

Evidence suggests that e-cigarettes are widely advertised to young people. There is evidence that in the UK advertising via non-traditional channels such as social media often breaches advertising standards rules and that exposure to advertisements of e-cigarettes on television and in movies may increase uptake of e-cigarettes by 36% in adolescents. There has been a significant increase in awareness of e-cigarette promotion predominantly from local shops and online sources among 11–17-year-olds.

Even though it is prohibited to sell e-cigarettes to people under the age of 18 a significant proportion of young people who vape report that they purchase their e-cigarettes, most commonly from newsagents, corner shops and off-licences. Limiting access could be achieved by using retail licensing schemes which require retailers to be licensed to sell e-cigarettes and e-liquid. Licences can be revoked if they sell to underage customers. Higher e-cigarette prices are likely to reduce youth vaping and could be used to limit their uptake in this age group.

## Recommendations

- Measures should be adopted to discourage people who do not smoke from taking up vaping.
- Policy changes to reduce the uptake of vaping among people who have never smoked needs to be carefully focused to minimise their impact on the uptake of vaping for smoking cessation. The shared goal must be to reduce death, disease and disparities.
- Information should be provided to young people and never smokers on the health risks of vaping, but such information should be carefully designed so as not to misinform people about the relative harms of smoking and vaping, and deter people who smoke from switching to vaping.
- More research is needed on the aspects of product design that a) facilitate smoking cessation in people who smoke and b) reduce appeal among those who do not smoke.
- Standardised plain packaging combined with reduced flavour and brand descriptions together with retail display bans should be introduced to decrease youth interest in trying vaping.
- E-cigarette price and taxation strategies should reduce the affordability of the cheapest products most commonly used by youth vapers (ie disposable e-cigarettes), while ensuring that the products most likely to be used by adults who smoke/quitters (ie rechargeable and refillable products), which are also less damaging to the environment, remain affordable.
- A review of current advertising regulation of e-cigarettes, including social media and retail product placement is required to ensure it adequately protects young people and never smokers.
- Policies and regulations should be introduced to reduce access to e-cigarettes for young people, particularly in retail settings, including retail licensing schemes and age verification at the point of purchase.
- Research is needed to test school-based interventions for preventing e-cigarette uptake.

# 9. Tobacco industry interests, recent conduct and claims around harm reduction

E-cigarettes first emerged in 2003 and in the following years came to represent a significant threat to the major tobacco companies and their uniquely profitable primary product, the cigarette. From 2012, the major tobacco companies responded by rapidly acquiring existing e-cigarette brands and launching their own. From 2013, they also began to launch new heated tobacco products (HTPs) and a variety of new oral tobacco and nicotine-only products.

Although all four transnational tobacco companies (TTCs) now sell e-cigarettes, HTPs and tobacco and nicotine-only pouches for oral consumption, cigarettes remain their primary product. While TTCs dominate the global HTP market, they hold only 26% of the e-cigarette market, which consists largely of other companies. More recently, three TTCs have expanded beyond tobacco and nicotine products to pharmaceutical inhaler, vaccines and cannabis products, which raises ethical issues when they sell medicines used to treat diseases caused by their primary tobacco products.

TTC interests are in profit maximisation and their presentations to investors emphasise that e-cigarettes and HTPs expand rather than substitute lost revenues from cigarette sales and that a significant proportion of growth is being driven by 'new entrants' to the market. Harm reduction involves reducing the health and social risks associated with addictive behaviour at both individual and population level. In the context of tobacco control, this would involve shifting current smokers to lower-risk products (if unable to quit) while not increasing harmful product use among others, notably new users. It is not, therefore, a sustainable business model.

TTCs have been using investments in e-cigarettes and HTPs to claim a commitment to what they label 'harm reduction' via 'transformation' away from cigarettes. Evidence shows that such claims are highly misleading and that, instead, TTCs have strategically co-opted harm reduction and used it against public health. Specifically, they have sought to use 'harm reduction' to:

- rehabilitate their image, increase their policy access and influence
- split and undermine the public health community

- position themselves as the solution to the tobacco epidemic they created
- push against population-level tobacco control measures of proven effectiveness (which reduce their sales) in favour of harm reduction approaches (which increase their product sales), ultimately seeking to amplify their ability to undermine progress in tobacco control.

Simultaneously, TTCs have continued to heavily market and increase the attractiveness of their cigarettes, buy up new cigarette companies and lobby against policies that would reduce smoking.

TTC-funded research accounts for a significant proportion of the science on new products and harm reduction approaches; yet evidence indicates that they may be engaging in many of the problematic scientific practices of the past, raising concerns about the quality and veracity of that research.

While e-cigarettes represent a potential opportunity for tobacco control in countries with strong institutional, regulatory and scientific capacity, this may not be the case in jurisdictions where capacity is more limited.

### Recommendations

- If potential public health benefits from e-cigarettes are to be realised, it is essential to take account of the conduct of TTCs. This requires strong and well-enforced regulation to ensure that companies that profit from the manufacture and sale of tobacco play no role in policy development.
- The impacts of harm reduction approaches will be context specific, varying with regulatory and enforcement capacity such that what works in one jurisdiction may not work elsewhere. Protecting national policy space must therefore be respected.
- The need to de-normalise the tobacco industry and protect public policy from tobacco industry interference in line with Article 5.3 of the Framework Convention on Tobacco Control (FCTC) is more important than ever; the decline in the UK's position in the Global Tobacco Industry Interference Index indicates that this is a key issue in the UK.

## 10. Ethics

As the RCP has consistently argued since 2007, e-cigarettes are not harmless but from an ethical standpoint the significant issue is that they are demonstrably *less* harmful than smoked tobacco to user and bystander alike.

What has changed between 2007 and 2024 is the nature of the market for e-cigarettes. On the supply side, the e-cigarette market has arguably been partly captured by the tobacco industry and on the demand side there is evidence of e-cigarettes being taken up by a currently small but significant number of individuals who have never smoked tobacco.

The RCP's position has been that a risk-based approach to harm reduction is ethically and scientifically more sound than a precautionary approach, especially given the known serious harms of tobacco and the known difficulties in driving tobacco smoking and its associated harms down further without new tools to assist.

However, that precautionary approach may prove to have merit in contexts where e-cigarettes are taken up by individuals who were previously non-smokers.

The ethical arguments for e-cigarettes as a harm reduction tool in the context of a comprehensive tobacco control and smoking cessation strategy are still sound. But the imperative for collection of reliable evidence, including controlled trials, remains.

The need for careful monitoring of the e-cigarette market and industry behaviour in that context continues to be paramount. And the need for caution about the risks and unanticipated harms of interventions, such as e-cigarettes, which may assist in tackling the harms of smoking, is as strong as ever.

# 01

# Introduction

## 1.1 Global tobacco use

Tobacco is currently used by an estimated 1.1 billion people, predominantly from low- and middle-income countries (LMICs), and causes almost 8 million deaths every year.[1] Alongside the health effects of tobacco use, it is well established that tobacco cultivation, production and consumption drive poverty, loss of productivity, and climate and environmental damage that accrues to countries, communities, families and individuals.[2]

Given the success of global efforts to eradicate or attenuate other avoidable major threats to health, such as smallpox, polio and more recently COVID-19, and given that the harms that smoking causes to health have been known to governments and policymakers since the middle of the last century,[3] it is difficult to comprehend why tobacco has been allowed to burden global health so extensively for so long. The major driver behind the ongoing global tobacco epidemic is undoubtedly the tobacco industry, which uses its financial power and influence to shape political environments, regulatory policy and legislation, and to promote its lethal products across international jurisdictions.

Trends in smoking prevalence vary between nations. In recent decades, smoking prevalence has reduced in rich countries, most likely due to the sustained application of tobacco control policies.[4,5] The opposite trend is seen in the majority of LMICs,[1] where the tobacco industry is less constrained.[6]

## 1.2 International approaches to tobacco control

Tackling tobacco consumption requires individual countries to implement and sustain effective tobacco control policies. In 1962, the Royal College of Physicians (RCP) report *Smoking and health* recommended seven measures to control tobacco use, including restrictions to marketing, promotion and advertising, limiting exposure to second-hand smoke, providing education on the harms of tobacco, treating tobacco addiction, altering tobacco products to make them less harmful, and making tobacco products less affordable.[3] These measures were widely adopted as the pillars of tobacco control for several decades before they were codified by the World Health Organization's Framework Convention for Tobacco Control (FCTC) in 2003.[7]

The FCTC recommended several additional measures that countries should adopt, including preventing interference with national policy by the tobacco industry,[8] reducing illicit trade of tobacco products,[9] and consideration of environmental and climate issues.[10] The core policies of the FCTC are described by the MPOWER acronym (see Box 1.1) and provide a set of minimum standards for individual countries to implement and to measure progress against.[4]

**Box 1.1. MPOWER**

**Monitor** tobacco use and prevention policies

**Protect** people from tobacco smoke

**Offer** help to quit tobacco smoking

**Warn** about the dangers of tobacco smoking

**Enforce** bans on tobacco advertising and sponsorship

**Raise** taxes on tobacco

The evolution and implementation of tobacco control policy varies markedly between countries and reflects the complex interaction between the political and regulatory environment, the actions of the tobacco industry, the strength of advocacy from civil society groups, academia, health organisations, public opinion and changing societal norms. Consequently, some countries have struggled to implement the core components of MPOWER, while other (often richer) nations have been able to implement all MPOWER measures and have added further measures to reduce smoking prevalence,[4] such as proposals to create a 'smoke-free generation' by progressively raising the legal age of sale for tobacco products, reducing accessibility through retail licensing schemes, standardised packaging for tobacco products, expanding tobacco dependency treatment services and, in some countries, promoting harm reduction through the use of e-cigarettes or other alternatives to smoked tobacco.[11,12,13,14]

The effectiveness of these newer tobacco control initiatives is in many cases yet to become clear,[12] but experience with more established policy indicates that their individual effects are likely to be modest but complementary, to the effects of a comprehensive package of measures. However, it is also likely that their effectiveness will vary between countries, as a result of differences in resources, regulatory environments and tobacco industry interference.

## 1.3 UK tobacco control policy

The UK has been an international leader in the development and implementation of tobacco control policy.[14] This has been achieved by using evidence-based interventions to reduce smoking initiation, treat tobacco addiction in established smokers, and provide alternatives to using tobacco. Measures to reduce the uptake of smoking in children and young people include the introduction of plain packaging, prohibiting point-of-sale advertising displays and, more recently, an intention to raise the age of sale of tobacco products by 1 year, every year, such that any person born after 2009 will not be able to legally purchase tobacco.[12] Substantial investment in the treatment of tobacco addiction has been provided to locally delivered, nationwide smoking cessation services since 1999,[12,16,17] and more recently the introduction of 'opt-out' treatment services in every hospital and maternity service in England.[18]

The effect of these policies in a UK environment has been a substantial overall reduction in smoking prevalence in adults over the past 40 years (Fig 1.1), while smoking in children and young people is now at the lowest level ever recorded (see chapter 3, Fig 3.8).[18] It is notable that the temporary rise in smoking rates in the 1990s was reversed after the introduction of measures in the *Smoking kills* white paper in 1998[14] and served as a reminder that multiple, funded, sustained tobacco control measures are required to reduce smoking prevalence.

How this reduction in smoking prevalence has been achieved in the UK is likely to be related to the strong foundation of tobacco control over several decades, the regulatory environment that has limited tobacco industry interference, the strong collaboration of health charities, academia, health professional societies, and successive governments that have regularly renewed tobacco control ambitions and planning through a series of national tobacco control plans and announcements.[12,14,15,20]

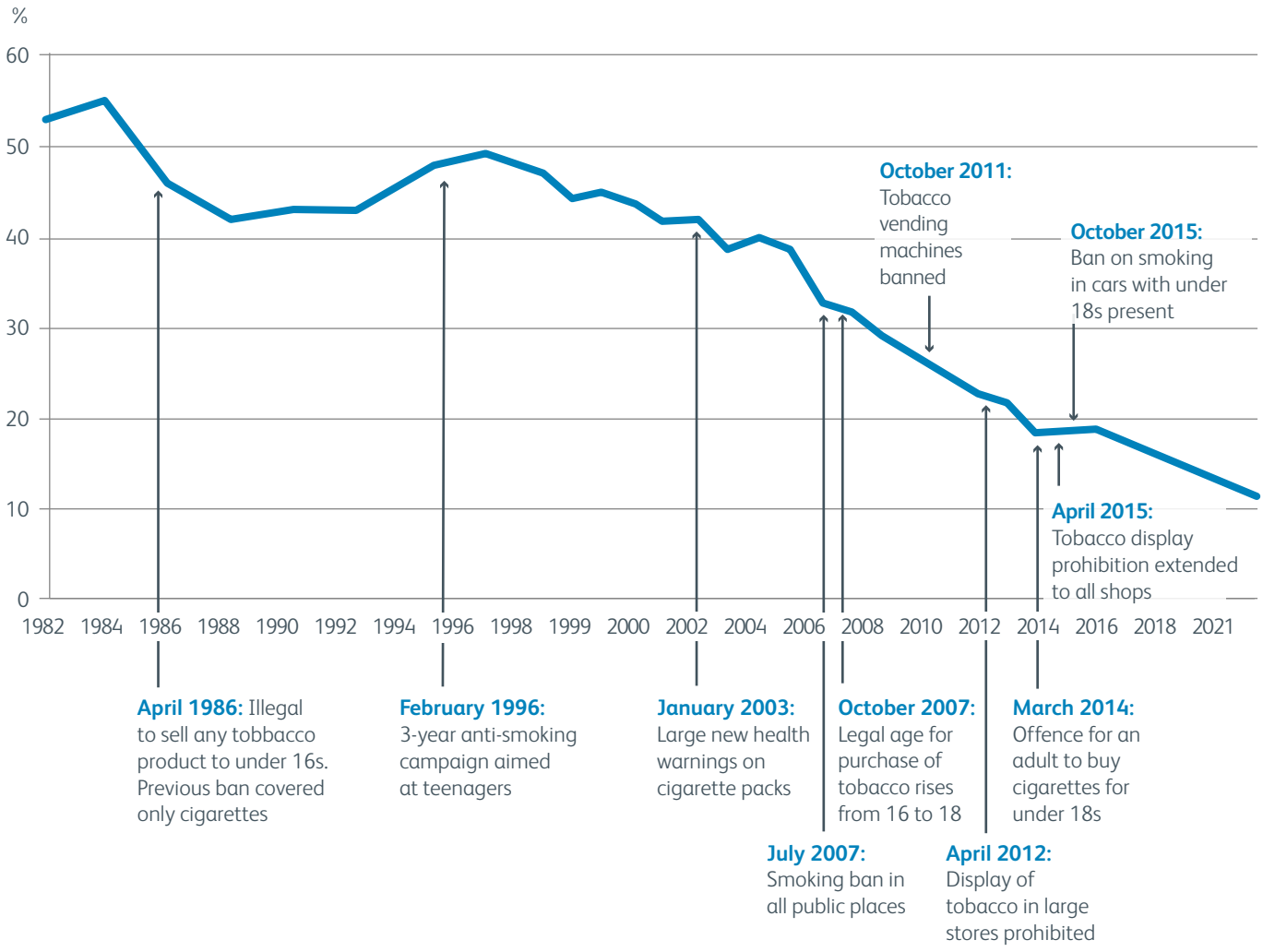



**Fig 1.1. UK Smoking prevalence mapped against key interventions from 1982 to 2021.[12]**

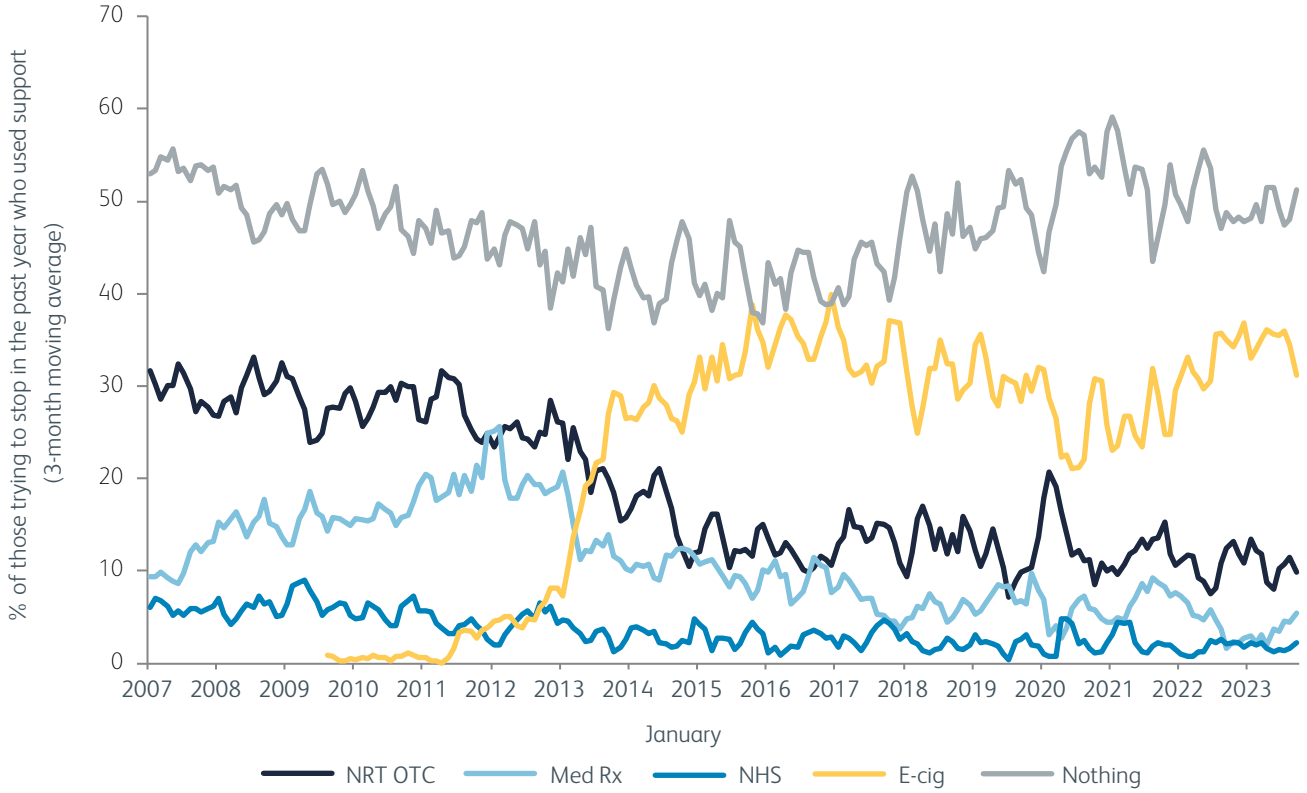
## 1.4 The role of e-cigarettes in UK tobacco control policy

Around 2007, e-cigarettes emerged in the UK as a consumer product intended to be a substitute for cigarettes. As the technology improved, e-cigarettes became increasingly popular with smokers who were trying to cut down or quit smoking, and very quickly became the most popular smoking quit aid (Fig 1.2).[21]

Since 2014, regulation of e-cigarettes in the UK has been directed by the EU Tobacco Products Directive,[22] and after Brexit these regulations were transcribed into UK law without alteration. E-cigarette and e-liquid manufacturers are required to notify their products, including ingredients and toxicology data, to the Medicine and Healthcare products Regulatory Agency (MHRA) (see chapter 6). Successive governments in England have supported the use of e-cigarettes as part of a tobacco control strategy, demonstrated most recently by the 'Swap to stop' scheme, which plans to provide 1 million e-cigarette starter kits to people who are trying to stop smoking.[23] The National Institute for Health and Care Excellence (NICE) has recognised e-cigarettes as an effective treatment for tobacco dependency and recommends their use as one of the interventions that should be offered to people who want to stop smoking.[24,25] The majority of local government stop smoking services now provide e-cigarettes as one of the standard treatments for treating tobacco dependency.[26]

The alignment supporting the use of e-cigarettes for smoking cessation between people who smoke, policymakers, regulators and treatment guidelines in the UK has been echoed by charities, healthcare professional bodies and academics, although this support has not been universal. More recently, as youth vaping prevalence has increased and the environmental impact from disposable e-cigarettes is recognised, the UK government announced a consultation on youth vaping specifically and a separate wider consultation on the regulation vaping products and their promotion.[12]

The government response to these consultations has been published and includes proposals to limit flavours, advertising, packaging, promotion of e-cigarettes and a ban on disposable e-cigarettes;[27] the legislative process is expected to be completed in 2024. Questions pertaining to how best to regulate e-cigarettes to maximise their potential to help smokers quit, while discouraging use among non-smokers, remain to be answered.




**NRT OTC** = nicotine replacement therapy bought over the counter; **Med Rx** = prescription medication; **NHS** = NHS Stop Smoking Service; **E-cig** = e-cigarette

**Fig 1.2. Support used in quit attempts.[21]**

## 1.5 Objectives of this report

As the nations of the UK strive to make smoking obsolete and accelerate the decline in smoking prevalence, a critical analysis of the evidence in the complex area relating to e-cigarettes has been undertaken by the RCP Tobacco Advisory Group.

This report focuses on key areas of policy debate that include examining the role of nicotine, trends in the use of nicotine products, the effectiveness of e-cigarettes for smoking cessation and consequent health harm or benefits. We consider how best to discourage e-cigarette uptake in never-smokers, while encouraging their use among people who want to stop smoking, and providing a regulatory framework that supports these dual objectives. The behaviour of the tobacco industry with tobacco and alternative nicotine products is examined, as well as the important ethical considerations of policy approaches.

The RCP recognises that the focus of this report is on UK policy and the role that e-cigarettes can play as part of the extensive tobacco control policy measures already in place. The RCP also understands that that the UK approach of embracing harm reduction as a complement to more conventional policy has been controversial and has attracted criticism, and does not seek to advocate that other countries should necessarily follow the UK in this approach. The RCP remains of the view that harm reduction approaches have significant potential to reduce the premature death and disability that smoking causes in the UK. This report aims to provide guidance on how that potential can best be realised.

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# 02

# Nicotine – physiological effects and the characteristics of nicotine-containing products

## Key points

- The physiological effects of nicotine are determined by the amount of nicotine taken in, individual metabolism, the route of entry into the body and the delivery mechanism.
- Acute exposure to the levels of nicotine typically delivered by nicotine products can lead to psychoactive effects that can result in elevated heart rate and systolic blood pressure, short-term enhanced cognitive effects and addiction.
- There is little evidence of a long-term harmful physiological effect of nicotine that is not confounded by those of other constituents of tobacco smoke.
- It will take several decades and data from several types of experimental and epidemiologic sources to establish the effects of long-term non-tobacco nicotine use.
- There are many nicotine-containing products, and these include combusted tobacco products, non-combusted tobacco products and non-tobacco nicotine products.
- Nicotine-containing e-cigarettes are a form of non-tobacco nicotine product that has evolved rapidly over the past 15 years.
- Cigarettes and other combustible tobacco products generate thousands of potentially toxic chemicals, and most of the harm from smoking is caused by these products of combustion.
- Smokeless tobacco products do not expose the user to inhaled toxicants but do expose the user to a variety of carcinogenic chemicals.
- When smoking a cigarette, a person typically takes 8–10 puffs over 8 or 9 minutes, resulting in a peak in blood nicotine levels of around 10–20 ng/ml.
- E-cigarette users typically inhale in groups of puffs that are smaller than those of cigarette smokers, and peak nicotine levels are usually lower than those of smokers. However, on average, daily intake of nicotine is similar for smokers and e-cigarette users.
- In recent years nicotine in e-liquids is present in combination with an organic acid (forming nicotine salts). This protonated form of nicotine makes nicotine inhalation less aversive to users, facilitating addiction.
- The aerosol of e-cigarettes contains many fewer chemicals than that of combusted tobacco.
- The extent of generation of toxic thermodegradation products from e-cigarettes depends on the heating temperature. Levels are higher with high power mod devices used with low nicotine concentration liquids, and lower with low power, high nicotine pod devices.
- In the absence of evidence of long-term effects of e-cigarette use, it remains vital to minimise the potential risks.

## Recommendations

- More research should be undertaken to determine the long-term effects of nicotine exposure without confounding from long-term tobacco use.
- Regulations to ensure e-cigarette design minimises the generation of toxic thermodegradation products and exposure to other potentially harmful constituents should be introduced by the UK government.
- Advice should be provided to e-cigarette users on which devices provide lower exposures to thermodegradation products.

# 2.1 Introduction

Human use of nicotine derived from tobacco leaf dates back thousands of years[1] and spans numerous cultures and use in every continent.[2] The market for tobacco-derived nicotine products has grown into a multi-billion pound industry, with new products entering the market each year.[3] The large product range, and differing definitions of tobacco products across jurisdictions can lead to confusion and conflation between tobacco and non-tobacco containing nicotine products. In this chapter we will review the physiological effects of nicotine, the range of nicotine-containing products, how they are used and their constituents with a focus on electronic nicotine delivery devices. Data on the health effects of e-cigarettes are reviewed in detail in chapter 5.

# 2.2 Nicotine

Nicotine is the major active component of tobacco. It is an addictive substance that acts as a stimulant in concentrations typically delivered by consumer nicotine products. If inhaled into the lungs, nicotine is rapidly absorbed into the bloodstream and reaches the brain within 10–20 seconds.[4] In comparison, nicotine is absorbed much more slowly via other routes of administration, such as the skin or oral/nasal mucosa.[4] The amount of nicotine that reaches the brain is dependent on the amount of nicotine intake, the route and rate of absorption, and the rate of metabolism of the individual. Nicotine is primarily, although not exclusively, metabolised in the liver by the CYP2A6 enzyme.[5] After the same dose of nicotine, less nicotine will reach the brain of an individual with a faster nicotine metabolism compared with an individual with a slower metabolism, particularly if the route of nicotine delivery is likely to pass through the liver before the brain. Therefore, the same nicotine dose may have differing physiological effects depending on the individual, the delivery mechanism, and the route of entry into the body.

## 2.2.1 Known physiological effects of nicotine

Before e-cigarettes became available, the most common nicotine delivery mechanism was via cigarettes.[6] Consequently, much of the evidence of long-term nicotine use is confounded by exposure to the many harmful components of cigarette smoke. Data on the Swedish oral tobacco product snus and its health effects provide insight into nicotine effects, separated from the effects of cigarette smoking.[7] Our knowledge of the physiological effects of nicotine primarily relates to the effects of acute nicotine exposure on the brain and cardiovascular system.

Nicotine acts upon nicotinic acetylcholine receptors (nAChRs) in the central and peripheral nervous system.[8] When nicotine stimulates nAChRs, it triggers the release of neurotransmitters such as dopamine in the brain, producing rewarding psychoactive effects that can lead to addiction.[5] Aside from addiction, acute nicotine exposure can result in short-term cognitive enhancing effects, including beneficial effects on attention, fine motor skills, working memory and episodic memory.[9] Animal studies also indicate that acute nicotine exposure may have specific short-term effects on adolescents that include increased rewarding effects, and long-term effects on the maturation of the prefrontal cortex that could impair cognition.[10,11]

Increases in heart rate have been observed among people who smoke following acute exposure to nicotine replacement therapies (for example, nicotine patches), cigarettes and nicotine-containing e-cigarettes.[12,13] However, some evidence suggests that increases in heart rate are far greater when exposed to cigarettes compared with e-cigarettes in studies of acute exposure to nicotine.[14] This effect is also seen in circadian studies of heart rate during ad lib vaping and smoking, which found people experienced both a higher heart rate and higher nicotine levels while smoking.[15] Acute nicotine exposure also has an impact on blood pressure, whereby nicotine increases systolic blood pressure[12,16,17] and diastolic blood pressure (diastolic blood pressure increases to a lesser extent than systolic blood pressure).[7,15] Compared with placebo, nicotine replacement therapy (NRT) has also been shown to lead to palpitations and arrhythmia during 3–24 weeks of use,[18] while arterial and aortic stiffness have been found to occur after acute exposure to cigarette smoke and e-cigarette aerosol, in some, but not all, studies.[16,19,20,21]

### 2.2.2 Unknown physiological effects of nicotine

Given the lack of experimental evidence and observational evidence free from confounding, the specific effects of long-term nicotine use are less well-known. For example, multiple studies comparing short-term use of NRT with placebo show no increased risk of cardiovascular events,[22,23] but while there is clear evidence that long-term smoking causes cardiovascular events, this is not the case for long-term e-cigarette use.[24,25] This contrasting evidence could reflect an effect of other constituents of tobacco smoke or e-cigarette aerosols rather than nicotine or could reflect an impact of dose or delivery mechanism.

Additionally, it is not clear exactly how long-term nicotine use impacts cognitive function or mental health. Evidence suggests acute and sustained nicotine exposure could have long-term effects on cognitive functioning, which could persist into adulthood as smokers are more likely to experience psychiatric disorders and attention deficits.[11] However, the relationship is complex, confounded by other constituents of tobacco smoke, socio-economic status, parental smoking[26] and potentially due to reverse causation whereby people with psychiatric disorders and attention deficits may self-medicate using nicotine,[27,28] however, a Cochrane review suggests stopping smoking is associated with improvements in mental health.[29]

There are also complex relationships between smoking and body mass index (BMI). People who regularly smoke tend to have a lower BMI, and acute exposure to nicotine (via nicotine versus placebo gum/nasal spray among smokers and non-smokers) appears to reduce appetite.[30,31] Nicotine increases metabolic rate and blunts the normal increase in appetite that occurs when metabolic rate increases.[32] However, the evidence of acute nicotine exposure reducing appetite is inconsistent,[33] and increased BMI increases the likelihood of someone initiating smoking and the number of cigarettes they smoke.[34] Stopping smoking can lead to weight gain, which NRT partially prevents.[35]

People who smoke are more likely to develop impaired lung function in relation to the number of years of smoke exposure,[36] but it is difficult to ascertain the role of nicotine in the development of lung problems. When switching to NRT, these issues can sometimes improve and declines in function may slow,[37] but evidence from e-cigarette studies is mixed. Healthy e-cigarette users may experience an increase in oxidative stress, nitric oxide deficiency, endothelial/vascular dysfunction, coughing and throat irritation after acute aerosol exposure, which could be due to nicotine or non-nicotine components of the aerosol.[38]Although this evidence suggests that nicotine exposure is not the sole cause of impaired lung function in people who smoke, it is not sufficient to determine that nicotine plays no role in the development of impaired lung function, particularly when used for decades.

### 2.2.3 Closing knowledge gaps

It could take another decade before we are able to more precisely assess the health impact of long-term nicotine use via non-tobacco mechanisms like e-cigarettes, both in ex-smokers and never smokers and potentially another four or five decades to understand the total impact. In the meantime, we rely on evidence assessing biomarkers[39,40,41] and genetically informed methodologies like Mendelian randomisation.[42] By triangulating these methods together with emerging evidence and existing evidence from smoking studies, we can better predict the effects of long-term non-tobacco nicotine use.

## 2.3 Current product range of nicotine-containing products

Cigarettes are the most commonly consumed nicotine-containing products, but many different nicotine-containing products are marketed. Nicotine-containing products can be classified as those containing tobacco leaf and those containing nicotine without tobacco leaf.[43] Tobacco-leaf products can be considered in categories of combusted tobacco products, heated tobacco products and non-combusted tobacco products. Combusted tobacco products include cigarettes, cigars, pipe tobacco, waterpipe and bidis. Cigars, which consist of tobacco wrapped in tobacco leaf, vary from small cigars and cigarillos that resemble cigarettes in size, to large premium cigars. Tobacco combined with cannabis products include spliffs and blunts. Heated tobacco products, marketed by major tobacco companies in recent years, include brands such as IQOS (Philip Morris International), Glo (British American Tobacco) and Ploom Tech (Japan Tobacco International).

Non-combusted tobacco products, generally termed smokeless tobacco, include chewing tobacco (which may be loose-leaf, plugs or twist), loose moist oral snuff (marketed both as loose tobacco and in portioned pouches), dry snuff (which can be taken orally or nasally).[44] Swedish snus, a subject of much of the currently available health epidemiology data regarding smokeless tobacco, is a government-regulated moist snuff pouch product that is used by 20% of men in Sweden. Smokeless tobacco has also been marketed in compressed tablets and lozenges in the USA. Many regional varieties of smokeless tobacco are marketed in different countries around the world. Examples include Gutkha in India (containing areca, betel nuts and lime), Chimo in Venezuela (containing spices and sugars), Toombak in Sudan, and Iq'mik among Alaskan Natives in the USA (containing punk ash).

Products that contain nicotine without tobacco include NRT medications to aid quitting smoking (nicotine gum, lozenges, patches, nasal spray and oral spray), tobacco industry-marketed oral nicotine products, and electronic nicotine delivery systems (electronic cigarettes). Many oral nicotine products are marketed, with common brands including Zyn (Swedish Match), Velo and Lyft (British American Tobacco) and On! (Altria).[45]

Numerous types of e-cigarette devices and liquids are also available. These devices comprise a battery that heats a coil within a vaporising chamber that generates an aerosol, usually containing nicotine, that is inhaled. E-cigarette devices have evolved over time from low power, cigarette-like cartridge devices (first generation), to larger pen and tank style refillable devices (second generation), to adjustable and often high power devices known as 'mods' or 'advanced personalised vaporisers' (third generation), to devices using replaceable pods often containing nicotine salts (fourth generation), and most recently, disposable devices with strong flavours.[46] Importantly, the health risks of e-cigarette devices are likely to vary considerably based on the power and coil temperature generated and the types of flavouring chemicals in the liquid. The higher the power, the more aerosol and greater the generation of toxic thermodegradation products.

Table 2.1 below describes the main characteristics of the three main e-cigarette types (cartridge devices, tank devices and pod devices), sub-types of these and terminology used. Devices are classified according to the nature of the e-liquid reservoir as this is the only distinct, non-overlapping feature between products.

**Table 2.1. Characteristics of the three main types of e-cigarettes**

| Characteristics | E-cigarette device type | | | | | |
|---|---|---|---|---|---|---|
| | Cartridge | | Tank | | Pod | |
| **Sub-type (see Fig 2.1)** | **Cig-a-likes** | **Newer disposables** | **Vape pen*** | **Mods** | **Pre-filled** | **Refillable** |
| Other terminology / examples | First generation, cartomiser, cigarette-like | Vape bars, puff bars, single-use vapes, Elf Bar | Second generation, all-in-one, pen-like, eGo | Third generation, box kits, box mods, mechanical mods, regulated mods | Fourth generation, pod vapes, Juul | Pod mods |
| Battery life and power | Short, low | Short, low | Medium, medium | Long, high | Short, low | Short, low but can be longer, higher with pod mods |
| Rechargeable battery? | Can be either | No | Yes | Yes | Yes | Yes |
| Refillable with e-liquid? | No | No | Yes | Yes | No | Yes |
| Reusable or single use? | Can be either, cartridges can be replaced on some | Single use | Reusable | Reusable | Reusable | Reusable |
| Replaceable components | None, or cartridge | None | Tank, atomiser, mouthpiece | Tank, atomiser, coil, mouthpiece, battery | Pods | Pods<br>In pod mods, coils can be replaced |
| Adjustable components | None | None | Varies from none to some of all: airflow, voltage, wattage, atomiser resistance, temperature control | Usually airflow, voltage, wattage, atomiser resistance, temperature control screen display | Usually none | Typically none but for newer pod mods airflow, wattage, temperature control |
| Draw activated or button press? | Can be either | Draw activated | Can be either | Usually button-press | Can be either | Can be either |
| Size | Small | Small to medium | Small to medium | Medium to large | Small | Small to medium |
| Vapour production | Low | Low | Moderate | High | Low | Low to moderate |
| Typical# e-liquid formulation | Either | Salt | Either | Freebase | Salt | Salt<br>Pod mod can be either |
| Typical# nicotine strength used | High | High | Any | Low | High | High<br>Pod mod – any |

**Note:** while the above descriptions are broadly accurate, there is still overlap between devices, features and terminology. For example, some 'cig-a-likes' can have small tanks rather than cartridges, some newer pods now have 'mod' features,* any cartridge, tank or pod device that is straight in shape can be classed as a 'vape pen'.

# Any nicotine formulation and/or strength can be used with any refillable device type but depends on the atomiser coil resistance, device power and the user. Some e-liquids also use a hybrid blend combining nicotine salt and freebase.


**Fig 2.1. Types of e-cigarette.**

## 2.4 Constituents of combustible tobacco, heated tobacco and other nicotine products

To contextualise the process of nicotine consumption and its byproducts by inhalation or oral use, in comparison to e-cigarettes, it is necessary to first consider tobacco and other nicotine-containing products. The smoking of cigarettes and other combustible tobacco products generates thousands of potentially toxic chemicals. Most of the harm from smoking is caused by products of combustion, which include oxidising chemicals (such as free radicals and nitrogen oxides), volatile organic chemicals (such as acrolein, acetaldehyde, formaldehyde and benzene), carbon monoxide and potent carcinogens (such as nitrosamines and polycyclic aromatic hydrocarbons).[47] These chemicals cause disease by a number of mechanisms, including oxidative stress, inflammation, endothelial dysfunction, thrombogenic effects and carcinogenesis. The pH of most cigarette smoke is in the range of 5.5–6, such that nicotine is primarily in the non-protonated form and is easily inhaled.[48] Cigars and pipe tobacco generate similar smoke to cigarettes, although the quantitative composition of various toxicants varies according to the tobacco blend and the curing and manufacturing process.[49] The pH of the smoke of large cigars is higher than those of smaller cigars and cigarettes, which may result in less inhalation of the smoke and lower health risks. Waterpipe/hookah tobacco is a mixture of dried fruit, molasses and conventional tobacco. The waterpipe heats the tobacco via charcoal, following which the smoke passes through a water-filled chamber. Waterpipe smoke differs from cigarette smoke with higher levels of carbon monoxide and benzene, a different profile of polycyclic hydrocarbons,[50] related to the fact that the combustion source is charcoal.

Heated tobacco products heat a disposable tobacco stick. The stick, which resembles a short cigarette, is inserted into a holder and heated to around 350°C, a much lower temperature than that at which a cigarette burns (around 800°C). Heated tobacco can deliver nicotine in levels similar to smoking a cigarette. However, the lower heating temperature results in much less generation of most tobacco combustion chemicals compared with a cigarette.[51] However, as presented in Philip Morris International's application to the US Food and Drug Administration for modified-risk tobacco product authorisation, concentrations of 56 constituents were higher in IQOS emissions and 22% of these were twice or more as high compared with that found in cigarette smoke.[52] The impact of these chemicals on adverse health effects of heated tobacco products is unknown. Smokeless tobacco products do not expose the user to inhaled toxicants but can deliver as much nicotine as does cigarette smoking. The rate of nicotine absorption depends on the pH of the products, with more rapid absorption at high pH and slower absorption at low pH.[53] Smokeless tobacco use does expose the user to a variety of carcinogenic chemicals. These include benzo[a]pyrene, N'-nitrosonornicotine (NNN) and 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK).[54] Swedish smokeless tobacco (snus), is regulated according to the GOTHIATEK standard, which sets maximal limits on the content of these carcinogens, and Northern European snus products have lower nitrosamine levels than US snus products.[55] The risks of various smokeless tobacco products around the world varies widely depending on the content of carcinogens and other toxicants.

While e-cigarettes deliver nicotine by inhalation, the pattern of nicotine self-administration by vaping is different than for cigarette smoking.[46] When smoking a cigarette, typically 8–10 puffs are taken over 8 or 9 minutes, resulting in a peak in blood nicotine levels of around 10–20 ng/ml.[56,57] E-cigarette users typically inhale in groups of puffs that are smaller than those of cigarette smokers, so peak levels with ad lib use are usually lower than that of smokers. However, on average, daily intake of nicotine is similar for smokers and e-cigarette users. This is the case even comparing users of e-liquids with substantially different concentrations of nicotine, presumably reflecting the need to maintain particular levels of nicotine in the body to achieve desired pharmacologic effects.[59]

Nicotine in different e-liquids is present in various degrees of protonation.[48] The earliest generations of e-cigarettes contained nicotine mostly in free-base (unprotonated form), with pH levels of 7–8. The presence of free-base nicotine results in an irritating vapour, which may have limited initial use by nicotine-naïve individuals. In recent years, nicotine in e-liquids is present in combination with an organic acid (such as lactic, benzoic, levulinic, salicylic, malic and tartaric acids).[58] In combination with these acids, the pH of the e-liquid is much lower (for example 5.5 for Juul) and most of the nicotine is protonated, which makes inhalation easier, and means users potentially inhale more nicotine and become dependent more easily.

Aside from nicotine, the aerosol of e-cigarettes contains many fewer chemicals than that of combusted tobacco. The aerosol contains propylene glycol, vegetable glycerin and flavouring chemicals.[46] The heating of propylene glycol and vegetable glycerin can generate toxic thermodegradation products such as acrolein, formaldehyde and acetaldehyde (carbonyl compounds), as well as oxidising chemicals.[59] The extent of generation depends on the heating temperature, puff duration and flavour types. Levels of carbonyl compounds are higher with high power mod devices used with low nicotine concentration liquids, and lower with low power, high nicotine pod devices.[60,61] Numerous flavouring chemicals are found in e-liquids. Some like diacetyl, cinnamaldehyde and acetals of vanillin and other flavour chemicals may be toxic.[62] Trace metals have been detected in some e-cigarette aerosols, including chromium, nickel, copper, lead and tin. There is wide variation in metal presence and concentration depending on the materials used to construct the device and the coils.[63,64] The carbonaceous particles of cigarette smoke are believed to contribute to oxidative stress and other harmful effects of smoking. The particles in e-cigarette aerosols are different liquid particles that dissipate quickly and with unknown toxicity.

Non-medicinal oral nicotine products are marketed as buccal pouches, tablets and lozenges. The nicotine may be natural (tobacco-derived) or synthetic. Synthetic nicotine may be nearly pure (S) nicotine or racemic (mixture of (S) and (R) nicotine). Oral nicotine products are marketed with different nicotine concentrations and in many flavours, including menthol, fruit, dessert and tobacco. Nicotine pouches typically contain between 2 and 8 mg of nicotine. The nicotine is in powdered form and combined with fillers and stabilisers, pH adjusters and sweeteners. The absorption profile for non-medicinal oral nicotine products is similar to that of medicinal nicotine gum or smokeless tobacco products, with dose-dependent increases in peak nicotine blood levels.[65] Most oral nicotine pouch products are buffered to an alkaline pH (7–10), such that most of the nicotine is in free-base form and is readily absorbed through the buccal mucosa.[66]

## 2.5 Potential for harm of nicotine products

The wide range of rapidly evolving nicotine products, their properties and risk profile outlined above, are complex[67] and provides regulators significant challenge (see chapter 6). Fig 2.2 provides an illustration of the nicotine product range and the likelihood of associated risk, although detailed additional data on the risks of newer nicotine products is required before firm conclusions can be drawn.[26]

However, it also has to be acknowledged that quantifying any harm caused by e-cigarettes, and indeed of heated tobacco requires long-term data from people who have never smoked but have vaped or used other novel non-combustible products for decades. Given, however, the extremely high risk of continuing to smoke or taking up smoking, decisions by society on public policy on vaping, and decisions by individuals on switching from smoking to vaping, should be based on the best currently available evidence.

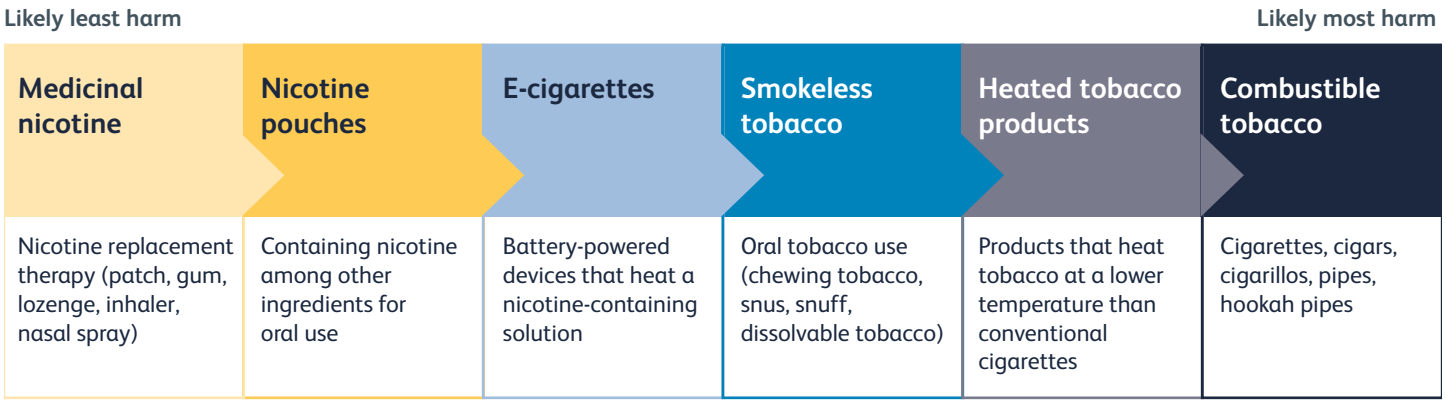


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**Fig 2.2. Nicotine products and the likelihood of risk.**

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# 03

# Trends in the use of e-cigarettes and tobacco products

## Key points

- The prevalence of vaping in adults in the UK was stable at about 5% from 2013 to 2020, but increased sharply from 2020 to around 10% in 2023.
- The increase in use of vaping products since 2020 has been greatest in young people.
- There has been a striking increase in use of disposable vaping devices from 2021, especially in users under 18 years and which has not displaced use of other types of device. This has led to an overall increase in vaping prevalence in this age group.
- During the pandemic vaping prevalence rose, especially in younger adults aged 18–24 years, of whom over 20% vaped in 2023.
- The prevalence of vaping among children and young people aged 11–17 increased over several years to 7.6% in 2023. Most of this increase occurred after 2021 (when prevalence was 3.2%) and coincides with a dramatic rise in use of disposable vapes, particularly among young people.
- Vaping is still overwhelmingly an activity of smokers and ex-smokers. The proportion of adult vapers in the ASH survey who are never-smokers in 2023 was 6.7% and has been stable since 2019. The number of people in England using vaping products who have never smoked is uncertain, but is likely to lie between 320,000 and 840,000.
- Smoking has declined in prevalence in all age groups over recent years. Although the decline in smoking among adults may have slowed since 2021, smoking among children and young people aged 11–17 years declined from 6.0% in 2013 to 3.6% in 2023.

## Recommendations

- Trends in the prevalence of vaping and smoking in time, place and person across the UK should be monitored.
- Longitudinal data should be collected to build on existing cross-sectional survey data and enable better overall understanding of trajectories in use and transitions from smoking to vaping, as well as from vaping to abstinence and use in never-smokers.
- Survey data on vaping in localities and regions, in combination with local sales data for tobacco, should be collected to inform local tobacco control.
- The UK should take part in standardised international comparative studies of smoking and vaping such as the European School Survey Project on Alcohol and Other Drugs (ESPAD) to ensure that we can assess UK vaping trends and tobacco control strategies reliably in an international context.

## 3.1 Introduction

The use of e-cigarettes and other nicotine-containing vaping products is a relatively recent phenomenon, having started around 2007. Since then, the vaping industry has evolved rapidly to meet demand, promote their products and respond to regulatory constraints,[1] users have formed online communities and vaping is discussed extensively on social media,[2] and users have customised some commercial products themselves.[3] All of these developments are likely to continue to have an influence on the risks and benefits of vaping, and emphasise the need for vigilance in this fast-moving field.

Fortunately, good-quality representative surveys were set up more than a decade ago, with sufficient coverage and statistical power to provide valuable insight into patterns of use, particularly in England.[4–7] There have been substantial changes in use since then, although vaping prevalence in adults was relatively stable for some years before the global coronavirus pandemic in 2020.[8] Recent data suggest, however, an increase in the prevalence of use in children and young people and in non-smokers. This is thought to reflect the increased availability of disposable and perhaps also illicit vapes, but may also represent a more diffuse impact of the coronavirus pandemic and its control measures on smoking and vaping behaviours.[9]

Previous RCP reports[10] and reports commissioned by Public Health England[11] and its successor, the Office for Health Improvement and Disparities (OHID), have extensively reviewed sources of information on use in adults, and in children and young people in England. The latest review commissioned by the OHID was published in September 2022 and included a detailed analysis of recent trends in use of vaping products in England.[12] It reported data from the Smoking Toolkit Study (STS)[4] up to September 2021 and included some data from the Action on Smoking and Health (ASH) surveys[5,13] up to March 2022. In this chapter, we update that work by reporting results from the STS up to and including March 2023, and from the ASH surveys up to March 2023[14] and surveys that cover other countries of the UK. We consider international trends on the use of vaping products and the additional data required to better approach this complex public health intervention.

## 3.2 Data sources

Sources of data on smoking and use of e-cigarettes in adults across the UK have recently been reviewed and summarised.[6] The two main dedicated longitudinal sources of data on use of e-cigarettes and other vaping products in adults in the UK are the STS and ASH surveys, which are described in more detail below. Data on e-cigarette use are also available for Great Britain from large-scale general government surveys such as the Opinions and Lifestyle Survey, and these also demonstrate trends in e-cigarette use broadly similar to those described in the ASH and STS surveys.[15]

Sources of data on vaping for adults and children in Scotland have been compiled and reported recently by the Population Health Directorate of the Scottish government.[16]

Several surveys on use of e-cigarettes and vaping products in children and young people across the UK are available, including the ASH Youth survey reported below.[17] In Wales, data on e-cigarette use by school students are available up until January 2022 from the School Health Research Network Student Health and Wellbeing Survey.[18]

### 3.2.1 Smoking toolkit study

The STS is a monthly cross-sectional survey of adults aged 16 and over in England. The methods are described in full elsewhere.[4,6] Briefly, England is split into approximately 170,000 output areas of around 300 households each, which are stratified by region and demographic characteristics before being randomly selected for inclusion on an interview list. Interviews are conducted in these selected areas until quotas tailored to the area and based on working status, age and gender are met. Comparisons with national random probability surveys and sales data indicate that sociodemographic characteristics, smoking prevalence and cigarette consumption are nationally representative.[4,19]

Data were collected with face-to-face computer-assisted interviews up to February 2020. However, social distancing restrictions under the COVID-19 pandemic meant that no data were collected in March 2020, while data from April 2020 onwards were collected via telephone, and the lower age bound for participation was temporarily increased from 16 to 18 years until December 2021. The telephone-based data collection relied upon the same combination of random location and quota sampling and weighting approach as the face-to-face interviews; the two data collection modalities show good comparability.[20–22]

From October 2020, the STS has been expanded to cover Scotland and Wales and will do so until at least 2024. A sample of approximately 1,700 adults in England, 450 adults in Scotland and 300 adults in Wales complete the survey each month (total n=29,400 per year).[6] Results for Scotland are reported regularly by the Scottish government.[23]

### 3.2.2 ASH surveys

The ASH Smokefree GB and Smokefree Youth surveys are annual surveys conducted by YouGov on behalf of ASH to determine use of and attitudes to smoking and e-cigarettes in the Great Britain (GB) population. The adult survey began in 2008 and the youth survey in 2013 and they are carried out once a year in spring. They were updated with questions on e-cigarettes addressed to all respondents from 2012 onwards. All figures have been weighted and are representative of GB adults (aged 18+) and youth (aged 11–18). Although the youth data capture 18-year-olds, these are excluded from the analysis so as not to duplicate them in the adult survey. Not all questions are asked every year, especially where answers have proven stable in the past, and a few new questions are also introduced each year. The surveys are conducted using an online interview administered to members of the YouGov Plc UK panel of 800,000+ individuals who have agreed to take part in surveys. An email is sent to panellists selected at random from the base sample according to the sample definition, inviting them to take part in the survey and providing a link to the survey. YouGov Plc normally achieves a response rate of between 35% and 50% to surveys; however, this does vary dependent upon the subject matter, complexity and length of the questionnaire. The responding sample is weighted to the profile of the sample definition to provide a representative reporting sample. The profile is normally derived from census data or, if not available from the census, from industry-accepted data. All results are based on a sample and are therefore subject to statistical errors normally associated with sample-based information. Sample sizes were approximately 12,000 for the Adult Smokefree GB survey and 2,000 for the Smokefree Youth survey reported below.

## 3.3 Summary of STS and ASH data

These sections summarise the latest available data, mainly from the STS and ASH surveys, on the use of e-cigarettes, heated tobacco products and pouches among adults and children in the UK. The STS collects data on adults aged 16 and over, whereas the ASH adult survey covers adults aged 18 and over.

The focus is on non-tobacco nicotine products, but equivalent data on cigarette smoking are reported where a comparison of trends between e-cigarettes and smoking is illustrative. These sections report prevalence overall for each product, stratified by age group and by smoking status separately.

### 3.3.1 Prevalence of e-cigarette use

Data from the STS show that the use of e-cigarettes by adults (aged 16 and over) in England started to become popular in 2011 before remaining relatively stable at around 5% between 2013 and 2020 (Fig 3.1). Since 2020 use has increased again, approximately doubling to around 10%. This upward trend has occurred across the UK, for example the latest Health Survey for Northern Ireland reported that in 2021/22 7% of adults were using e-cigarettes or vaping devices, compared with 5% in 2020/21 and 6% in 2019/20.[24]

The rate of decline in adult smoking prevalence stagnated during and since the COVID-19 pandemic.[9,25] The proportion of the population who either smoked or used e-cigarettes remained relatively stable until 2021, with a declining proportion smoking, but has increased somewhat since 2021 due to recent marked increases in vaping prevalence.

It is estimated that, since 2013, use of e-cigarettes to quit smoking in England has led to an additional 30,000–50,000 people stopping smoking each year (see chapter 4, section 4.3),[26,27] contributing to the decline in the prevalence of cigarette smoking in England since 2010.

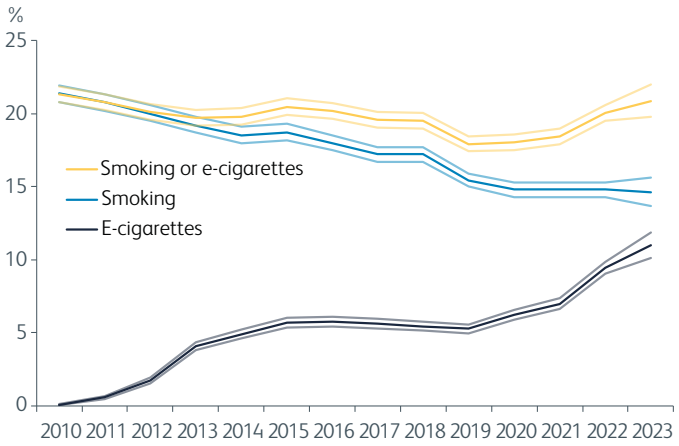



**Fig 3.1. Prevalence (and 95% CIs) of cigarette smoking, e-cigarettes and smoking, or e-cigarettes among adults (aged 16 and over) in England between 2010 and 2023 (up to and including March). n=225,928.[28]**

The ASH Smokefree GB survey shows that adult smoking prevalence declined between 2013 and 2021 as vaping prevalence increased but remained stable between 2021 and 2023, while vaping rates have continued to increase (see Fig 3.2). The ASH Smokefree GB adult survey reports somewhat lower vaping prevalence than in the STS and may relate to different sampling approaches and wording of the survey questions.

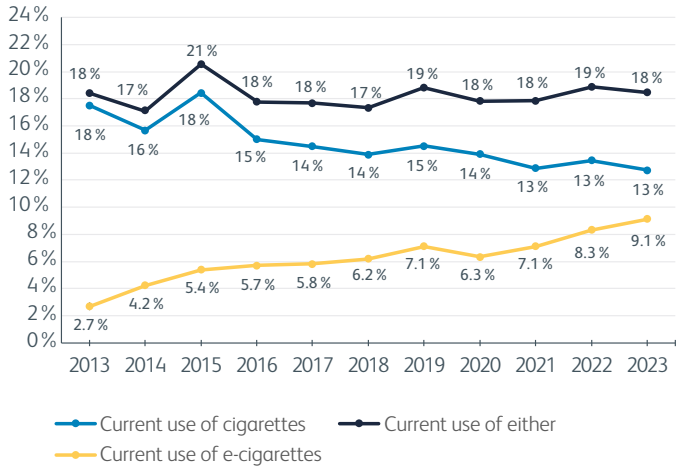



**Fig 3.2. Prevalence of cigarette smoking, e-cigarettes and smoking, or e-cigarettes among adults (aged 18 and over) in Great Britain between 2013 and 2023.[29]**

## 3.3.2 E-cigarette device types

The use of different device types has been measured since 2016 in the STS. Disposable devices (pre-filled for limited use, non-rechargeable and non-refillable) were the least popular until 2021, before increasing sharply in popularity[30] and becoming the most popular by 2023 (Fig 3.3). The increase does not appear to have substantially reduced the use of other devices but has, instead, contributed to a rise in the overall prevalence of the use of e-cigarettes. Tank models (rechargeable devices with tanks that can be refilled) were the most popular type between 2016 and 2021.[31] Cartridge models (rechargeable devices with cartridges that can be replaced) and modular devices (where users combine device parts) have consistently been less popular device types, at approximately 1%.

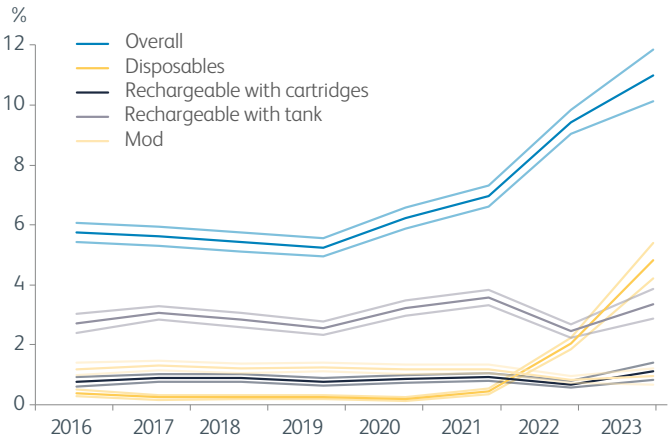



**Fig 3.3. Prevalence (and 95% CIs) of e-cigarettes by device type among adults in England between 2016 and 2023 (up to and including March). n=135,453.[28]**

The ASH Smokefree GB survey has also tracked vapers' main type of device since 2014 (Fig 3.4). Disposable products were used by very few adult vapers before 2022. In 2022 they were as popular as refillable pod devices, and in 2023 they became the second most popular device after tanks. The use of tanks, however, fell between 2022 and 2023. The increased use of disposable vapes has been associated with a growth in the overall numbers of adults vaping. Differences between the findings of the STS and ASH surveys, for example use of disposables, is lower in the ASH adult survey than in the STS survey and may relate to different sampling approaches and wording of the survey questions.

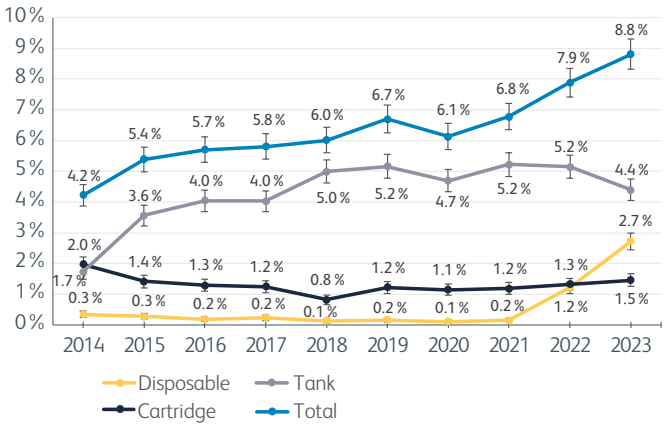



**Fig 3.4. Prevalence (and 95% CIs) of e-cigarettes by main device type among adults in Great Britain between 2014 and 2023.[29]**

## 3.4 Heated tobacco

The use of heated tobacco products has been measured since 2016 in the STS. The use of heated tobacco has remained extremely rare, at consistently less than 0.5 % of adults (Fig 3.5).[31] Very similar results are found in the ASH Smokefree GB surveys.[29]

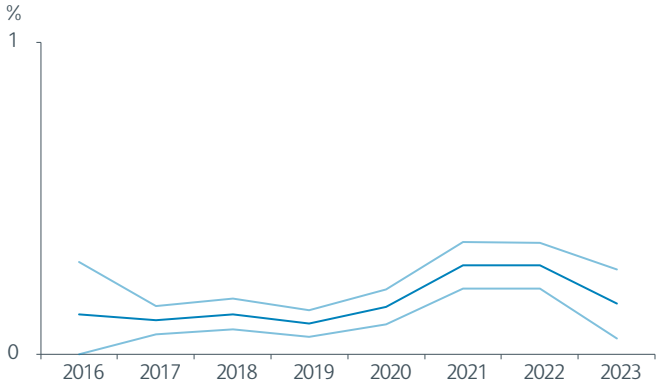



**Fig 3.5. Prevalence (and 95% CIs) of heated tobacco among adults in England between 2016 and 2023 (up to and including March 2023). n=126,999.[28]**

## 3.5 Nicotine pouches

The use of nicotine pouches has also been measured since 2020 in the STS. The use of pouches has also remained extremely rare, at consistently less than 0.5 % of adults (Fig 3.6).[32] Very similar results are found in the ASH Smokefree GB surveys.[28]

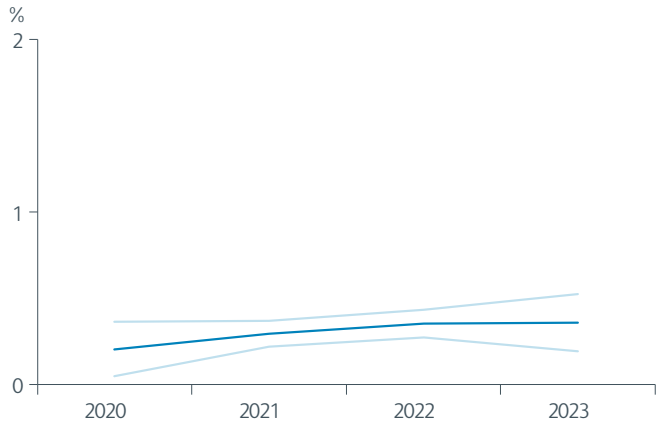



**Fig 3.6. Prevalence (and 95% CIs) of nicotine pouches among adults in England between 2020 and 2023 (up to and including March 2023). n=48,255.[28]**

## 3.6 Trends by age

### 3.6.1 E-cigarette use

Data from the STS show that until 2020, e-cigarette use was more prevalent among younger and middle-aged adults aged 25–54 (see Fig 3.7). From 2020, e-cigarette use has become most prevalent in the younger age groups, with more than 20 % of 16–24-year-olds using them. E-cigarette use has been consistently less prevalent among those aged 65 and over.

Young adults appear to have been excluded from the stagnation in the rate of decline in smoking prevalence during the COVID-19 pandemic (Fig 3.7). However, the prevalence of smoking or using e-cigarettes also appears to have increased in that same period, to the extent that approximately one-third of 16–24-year-olds reported smoking cigarettes or using e-cigarettes in 2023 (Fig 3.7).

Looking at 18–24-year-olds in the ASH Smokefree GB survey, prevalence of smoking fell between 2013 (17 %) and 2020 (15 %), but has not fallen since (Fig 3.8). Current vaping prevalence was flat in this age group between 2013 and 2021 and grew significantly between 2021 and 2022, up to 11 %. Neither smoking nor vaping prevalence grew significantly between 2022 and 2023.

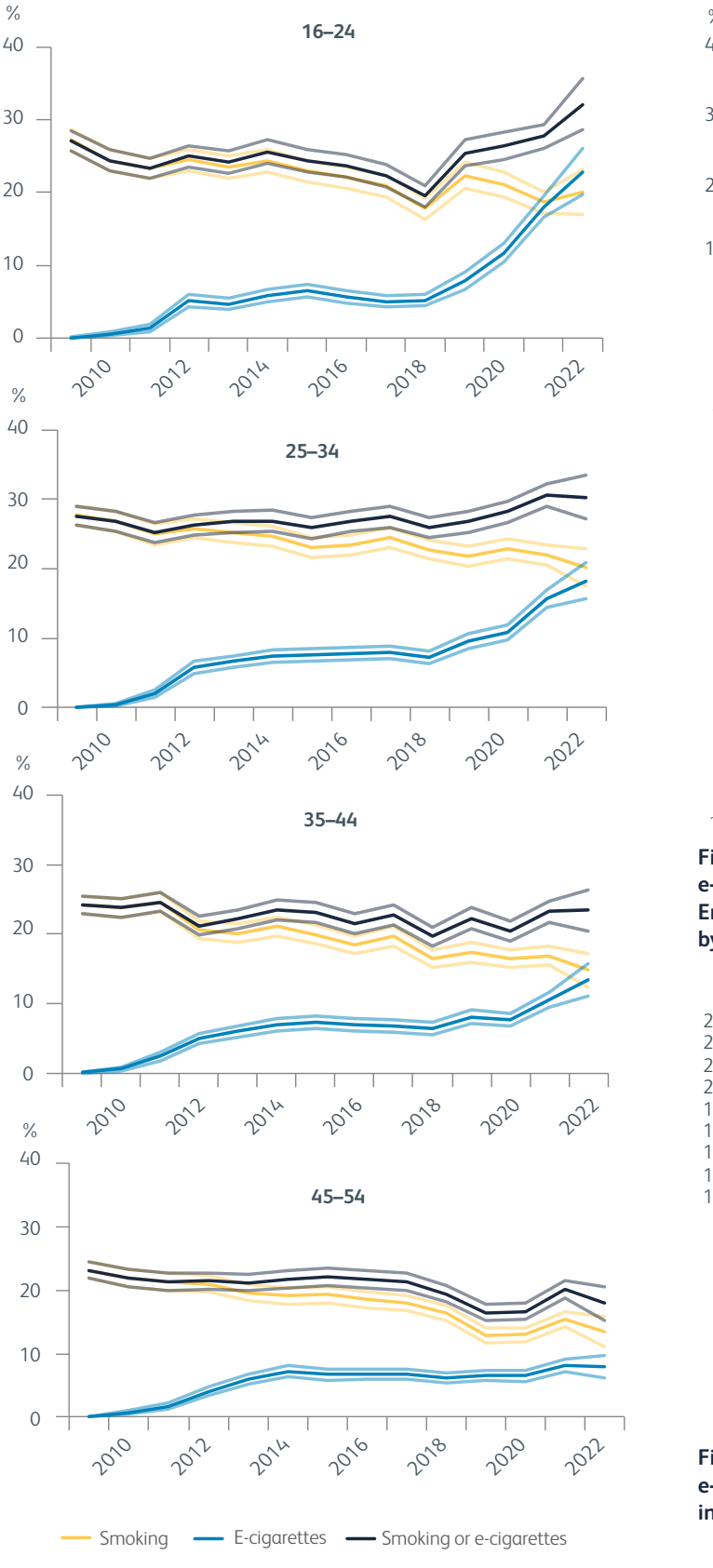



**Fig 3.7. Prevalence (and 95% CIs) of cigarette smoking, e-cigarette use and smoking, or e-cigarette use among adults in England between 2010 and 2023 (up to and including March) by age groups. n=225,928.[28]**

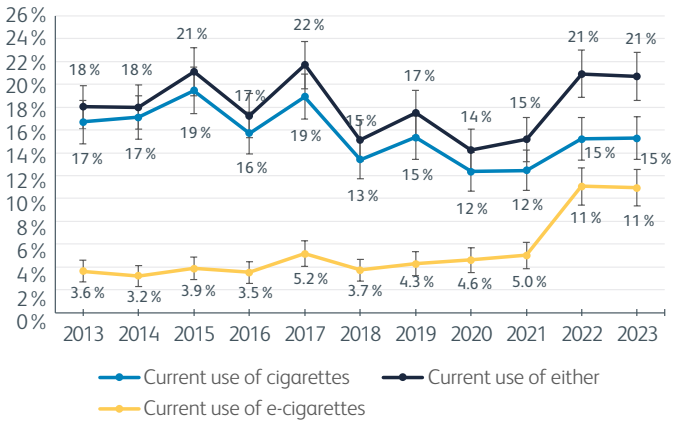



**Fig 3.8. Prevalence (and 95% CIs) of cigarette smoking, e-cigarettes and smoking, or e-cigarettes among 18–24-year-olds in Great Britain between 2013 and 2023.[29]**

Among 11–17-year-olds in the ASH Smokefree Youth survey, smoking prevalence has been low throughout the period of the survey and was lower in 2023 (3.6%) than it was in 2013 (6.0%) (Fig 3.9). Vaping prevalence was also low but growing over the same period.

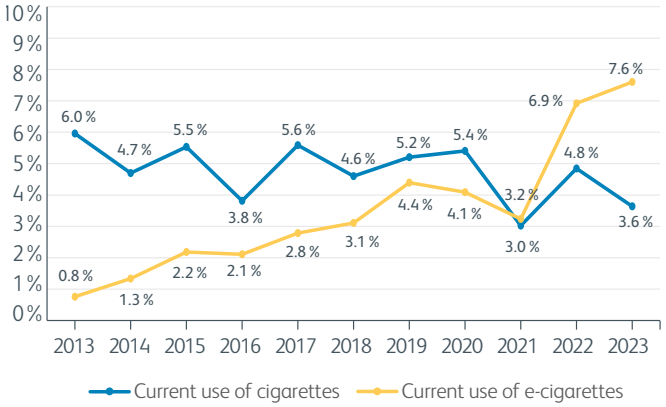



**Fig 3.9. Prevalence of cigarette smoking and e-cigarettes among 11–17-year-olds in Great Britain between 2013 and 2023.[33]**

ASH surveys have shown a significant growth in experimentation with e-cigarettes among children (Fig 3.10). The proportion of 11–17-year-olds ever having tried an e-cigarette has doubled between 2021 and 2023, from 10.4% in 2021 to 19.2% in 2023. Vaping in the past month grew between 2021 and 2022, but growth was not significant between 2022 and 2023. The majority of vapers who have only tried vaping once or twice have never smoked (62%), while the majority of current vapers have tried smoking (70%).

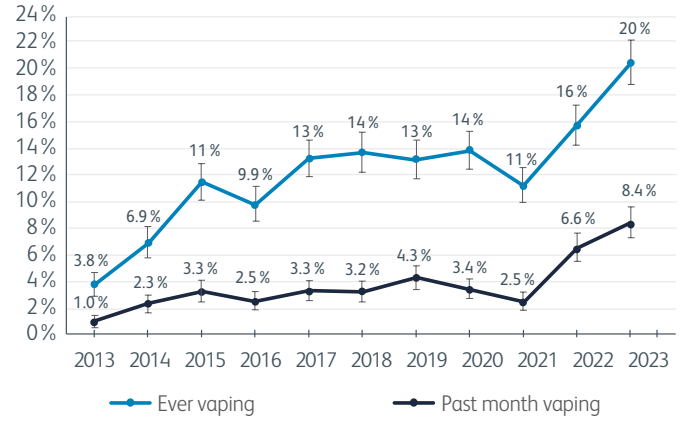


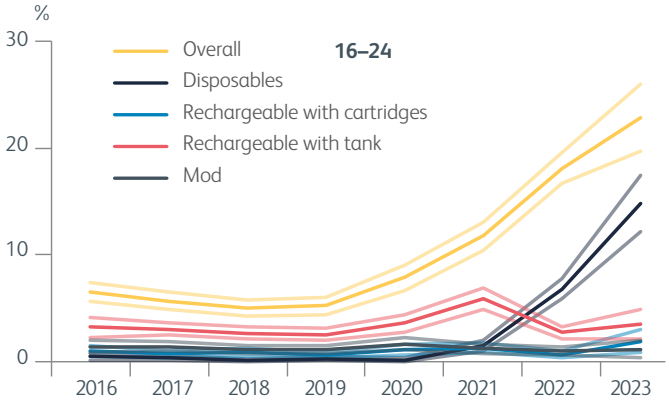

**Fig 3.10. Prevalence (and 95% CIs) of ever vaping and past month vaping among 11–17-year-olds in Great Britain between 2013 and 2023.[33]**

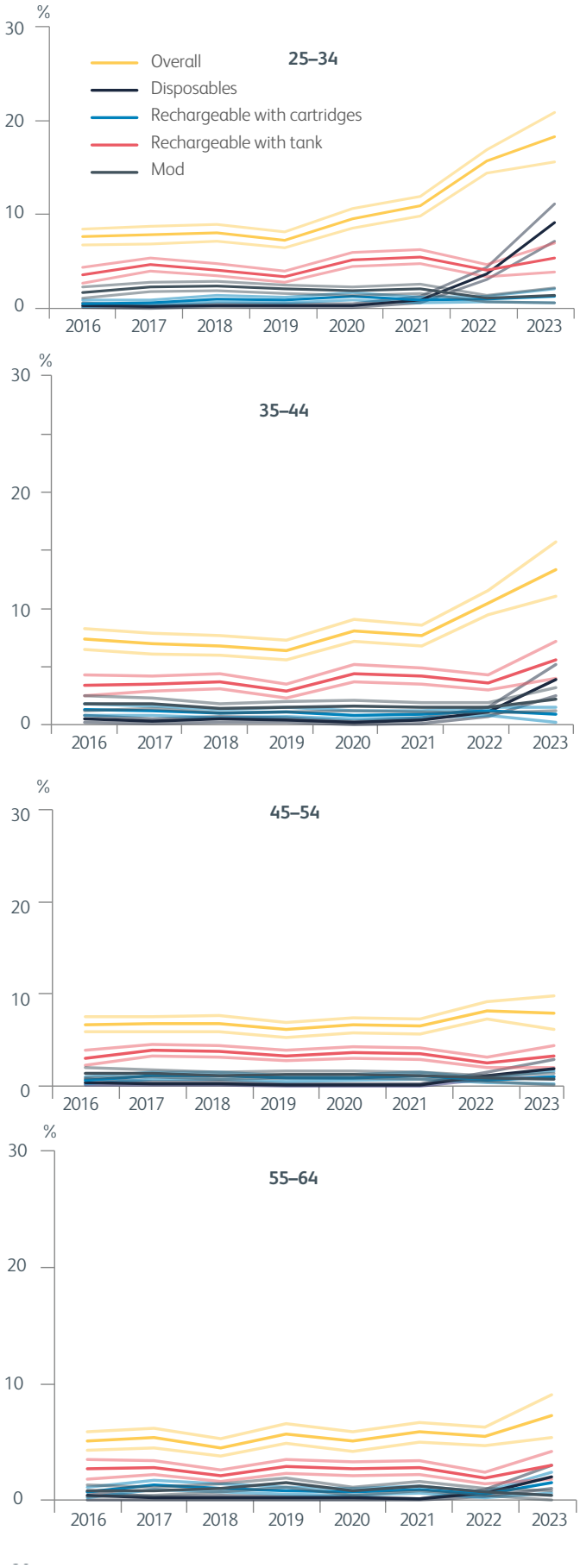
The latest national survey of secondary school pupils (aged 11–15 years) in England found reductions in smoking and an increase in use of vaping.[34] In 2021, 12% of pupils had ever smoked, down from 16% in 2018; 3% were current smokers compared with 5% in 2018; and only 1% were regular smokers (at least one cigarette per week), down from 2% in 2018. Current e-cigarette use was 9%, up from 6% in 2018; regular use (at least once per week) also increased, and was 4% for boys and 5% for girls.

In Wales, the School Health Research Network survey for 2021/22 found that 20% of 11–16-year-old school students reported ever having tried an e-cigarette.[18] Overall, 5% of young people reported current (at least weekly) use of e-cigarettes. Fewer boys (4%) reported current use of e-cigarettes than girls (7%) and compared with young people who identified as neither a boy nor a girl (8%).

## 3.6.2 E-cigarette device types by age

The STS data show that the recent overall increase in disposable devices is driven by especially rapid increases among the youngest age groups (Fig 3.11). In all age groups 35 years old and over, the use of disposables has also increased to be the second most popular category, but tank models remain the most popular. Cartridge models and modular devices have consistently been less popular device types across all age groups. In all age groups, there is little evidence of the increased use of disposables replacing the use of other devices.





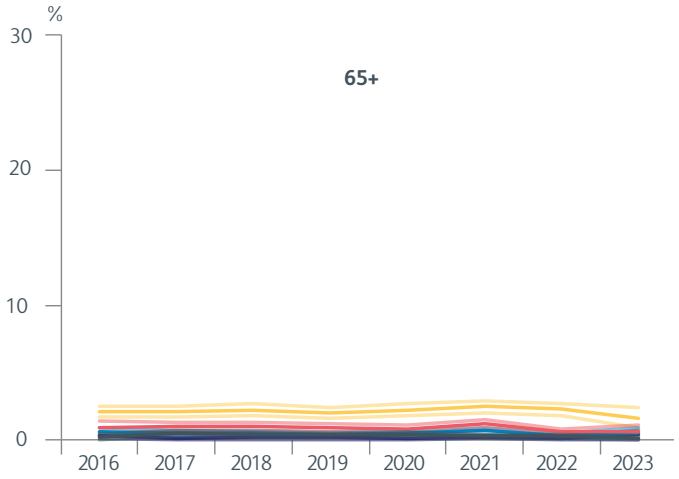




**Fig 3.11. The prevalence (and 95% CIs) of e-cigarette use by device type among adults in England between 2016 and 2023 (up to and including March) by age groups. n=135,453.[28]**

Among 11–17-year-olds in the ASH Smokefree Youth survey, the use of disposable vapes increased 18-fold between 2021 and 2022 from 0.2% to 3.6%, with lower growth between 2022 and 2023 (Fig 3.12). This coincides with the growth in children vaping between 2021 and 2022.

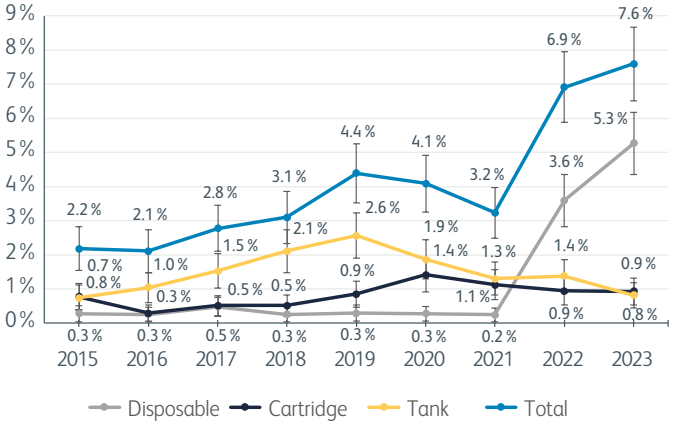



**Fig 3.12. Prevalence (and 95% CIs) of e-cigarettes by device type among 11–17-year-olds in Great Britain between 2015 and 2023.[33]**

## 3.6.3 Heated tobacco and pouches use by age

The STS survey shows that use of heated tobacco and pouches has remained rare among all age groups. Use of both products has been more popular among younger than older people since 2020, although still very low at approximately 0.5% to 1%.[28] ASH data show that ever having tried nicotine pouches is twice as common among 18–24-year-olds than among all adults (8.3% versus 4.1%), although current use remains low even in this age group, at 1.6%.[35]

## 3.7 Trends in e-cigarette use by smoking status

Data from the STS show that, when e-cigarettes first became popular, they were used almost exclusively by current smokers and recent (≤1 year) ex-smokers, and have always been most popular in these groups (Fig 3.13). After the initial rapid increase, use by current smokers plateaued between 2013 and 2020, but has grown since. Use by recent ex-smokers increased to a peak in 2016 before declining through to 2020, and then growing again recently. Use by long-term (>1 year) ex-smokers did not start to increase until 2013, but has steadily increased since – presumably as earlier cohorts of people who had quit smoking with the support of e-cigarettes accumulated years of abstinence and have continued to represent a greater proportion of long-term ex-smokers.

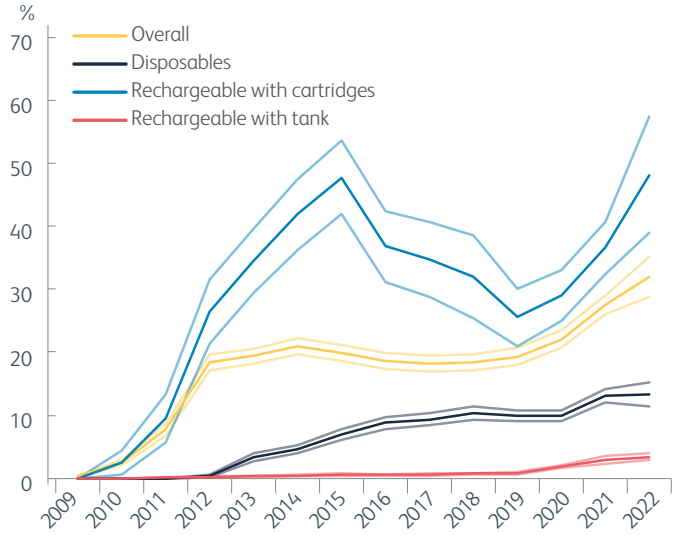



**Fig 3.13. Prevalence (and 95% CIs) of e-cigarette use among adults in England between 2010 and 2023 (up to and including March) by smoking status. n=225,928.[28]**

### 3.7.1 Prevalence of vaping in never-smokers

E-cigarette use by never-smokers in the STS was consistently rare at <0.5% until 2020, but has since increased to between 2% and 3% in 2023.[28] Although the rate of use in never-smokers is very low compared with smokers and ex-smokers, it must be remembered that adults who have never smoked regularly are much more numerous, with some 28 million never-smoking adults in England. Thus, even a rate of vaping of 3% in this group would imply some 840,000 adult users nationally who had never smoked regularly. The ASH Smokefree GB survey provides a lower estimate of the use of e-cigarettes or other vaping products in never-smokers of 1.1% (Fig 3.14).[35] This estimate is based on the result that 6.7% of those who vape are defined as having never smoked. The ASH estimate suggests that the total number of adult non-smokers who vape is some 320,000 across Great Britain.

The difference in these estimates is likely due to their different definitions of a 'never-smoker'. ASH Smokefree GB surveys define a never-smoker as someone who agrees with the statement 'I have never smoked', while in the STS a never-smoker is someone who agrees with the statement, 'I have never been a smoker (ie smoked for a year or more)'. It is likely that a number of ex-smokers who did not smoke for more than a year are included in the STS category of 'never-smokers', while the ASH category of 'ex-smokers' likely includes a number of people who have only ever experimented a few times with cigarettes.

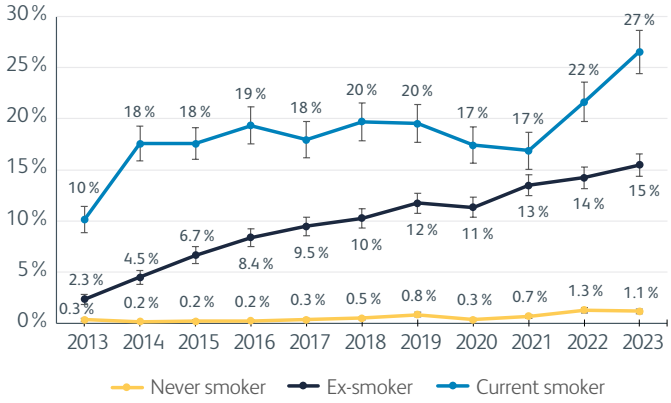



**Fig 3.14. Prevalence (and 95% CIs) of vaping by smoking status among adults aged 18+ in Great Britain between 2013 and 2023.[29]**

Among 11–17-year-olds in the ASH Youth survey, current vaping grew among those who have ever smoked between 2013 and 2019 (Fig 3.15).[33] It then declined slightly between 2019 and 2021 during the COVID pandemic, increased significantly between 2021 (20%) and 2022 (38%) and did not grow between 2022 and 2023. Vaping among never-smokers was below 1% prior to 2021. It has increased since then and, at the time of writing, 2.3% of 11–17-year-olds who have never smoked currently vape.

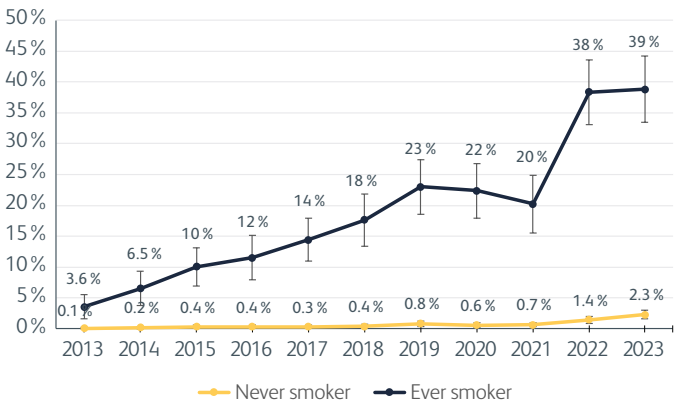



**Fig 3.15. Prevalence (and 95% CIs) of current vaping by ever having smoked among 11–17-year-olds in Great Britain between 2013 and 2023.[33]**

## 3.7.2 Use of e-cigarette device type by smoking status

STS data show that, with the exception of long-term ex-smokers, disposables quickly became the most popular device type among all smoking status groups since 2020, with the category representing approximately half of the overall prevalence in each group (Fig 3.16). Among long-term ex-smokers there was no growth until 2022, but it has since become the second most popular device type to tank models in 2023. This lagging suggests that long-term ex-smokers may not be taking up disposables, with the later change instead reflecting cohorts of people who previously quit smoking with disposable devices gradually accumulating years of abstinence.

## 3.7.3 Use of heated tobacco products and pouches by smoking status

The use of heated tobacco and pouches is extremely rare in never-smokers at <0.2%. Use of both products is more popular among ever-smokers, especially current smokers and recent ex-smokers, although still low at approximately 1%.[28]

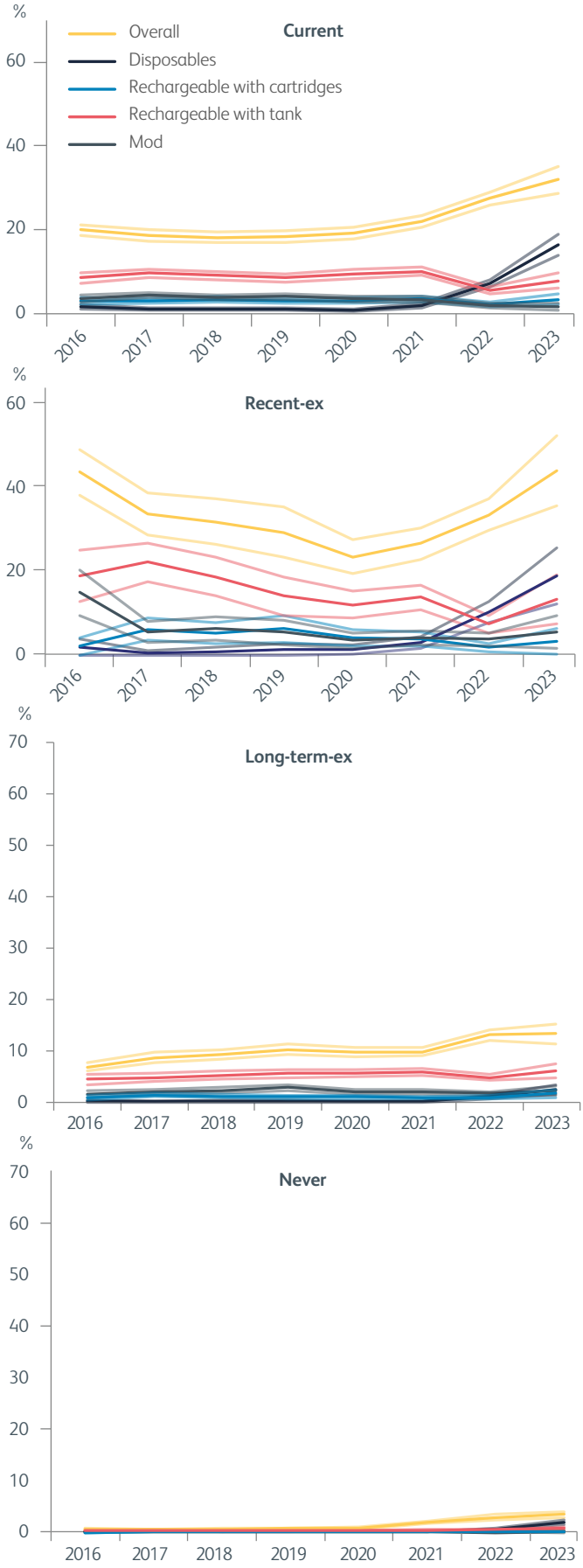



**Fig 3.16. Prevalence (and 95% CIs) of e-cigarette use by device type among adults in England between 2016 and 2023 (up to and including March 2023) by smoking status. n=135,453.[28]**

# 3.8 E-cigarette use by socio-economic position

## 3.8.1 Prevalence of e-cigarette use by occupation and smoking status

Data from the STS show that, between 2014 and 2022, the prevalence of e-cigarette use in all adults was socio-economically patterned, with greater use among those of less advantaged social grade. Between 2014 and 2019, e-cigarette use among those with professional and managerial (4–5%) and routine and manual (6–7%) occupations remained relatively stable. From 2019, e-cigarette use increased consistently across all social grades such that, by 2022, it was estimated to be 11.5% in less advantaged compared with 7.5% in more advantaged groups (Fig 3.17).

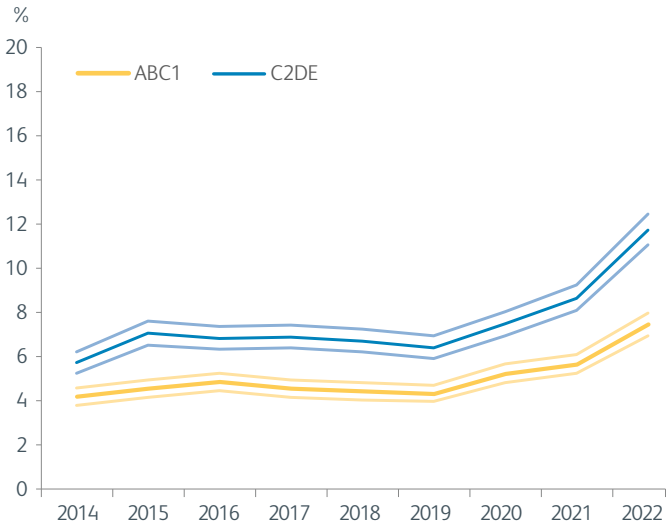



**Fig 3.17. E-cigarette use in all adults by occupational groups.[28]**

AB: Higher and intermediate managerial, administrative and professional occupations

C1: Supervisory, clerical, and junior managerial, administrative and professional occupations

C2: Skilled manual occupations

DE: Semi-skilled and unskilled manual occupations; unemployed and lowest grade occupations

Source: Office for National Statistics Census 2021 approximated social grade data

The overall socio-economic patterning in the use of e-cigarettes among adults reflects the substantially higher rates of smoking among less advantaged social grades, and the higher prevalence of e-cigarette use among people who smoked in the past year. Among only those who smoked in the past year, e-cigarette use was conversely higher in more advantaged social grades between 2014 and 2016, but this difference attenuated over time and by 2017 was no longer present (Fig 3.18).

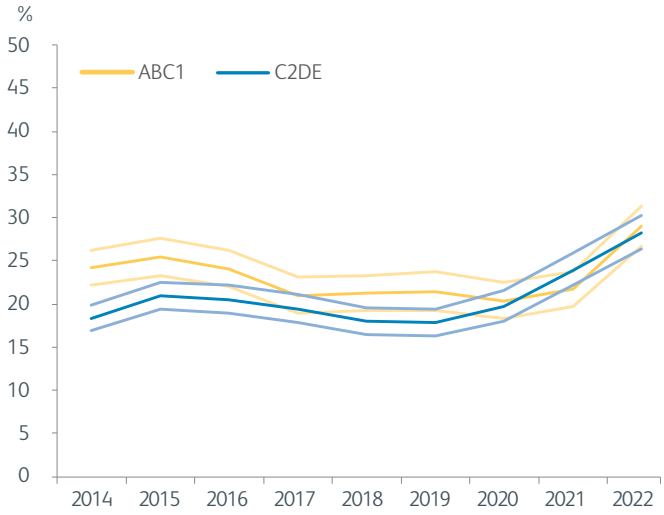



**Fig 3.18. E-cigarette use in people who smoked in the past year by occupational group.[28]**

## 3.8.2 E-cigarette use in quit attempts by occupation and smoking status

Between 2014 and 2022, approximately one-third of people who attempted to quit smoking used an e-cigarette during an attempt to quit, and there were no socio-economic differences or clear time trend according to occupational social grade (Fig 3.19). Socio-economic differences in use during an attempt to quit smoking are relevant because previous analyses have shown e-cigarette use to be positively associated with success rates.[36]

E-cigarette use among people who used to smoke but have not smoked for a year or more has increased overall between 2014 and 2022 (Fig 3.20). E-cigarettes are the most commonly used nicotine product used by former smokers for 1 year or more[37] and their use has remained generally higher among those in less advantaged social grades throughout this time period. Should e-cigarettes protect against relapse to smoking, then this may have a beneficial impact in reducing existing inequalities in

smoking rates (see chapter 4, section 4.4.) If the opposite is true, then the use of e-cigarettes in the longer term after cessation may undermine progress in reducing smoking-related inequalities. Previously published analyses using data from the STS have shown that initiation of e-cigarette use among people who quit smoking before e-cigarettes existed has increased very marginally over time, but this did not differ according to socio-economic position.[38]

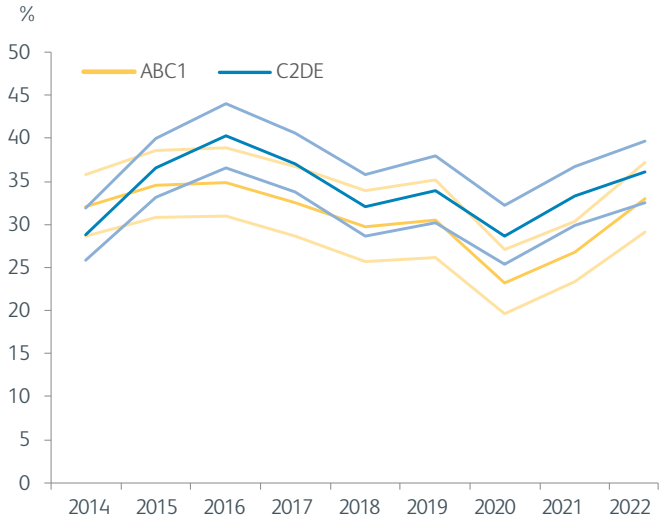



**Fig 3.19. E-cigarette use in a quit attempt by occupational group.[28]**

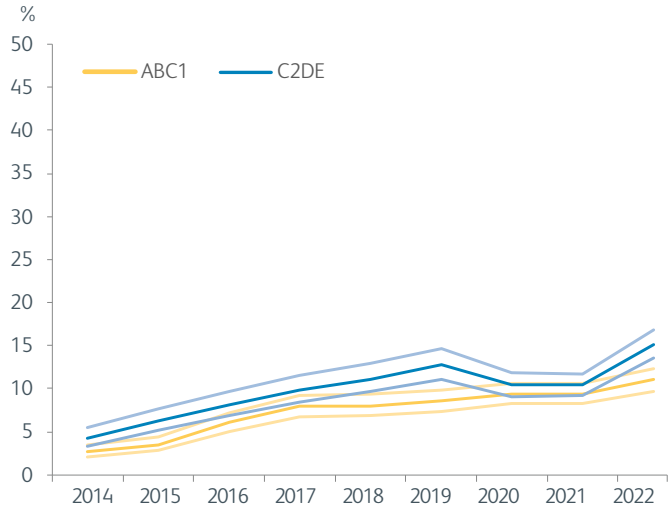



**Fig 3.20. E-cigarette use in long-term former smokers by occupational group.[28]**

E-cigarette use among people who have never smoked remained rare between 2014 and 2021, with no apparent differences according to socio-economic position (Fig 3.21). An increase occurred in 2022, when rates appeared to be higher among never-smokers in routine and manual (2.3%, 95% CI 1.9%, 2.8%) compared with professional and managerial (1.5%, 95% CI 1.2%, 1.8%) occupations. This has occurred during a time in which the use of disposable e-cigarettes grew rapidly, particularly among younger adults, and the mental health of young adults has deteriorated.[30,39]

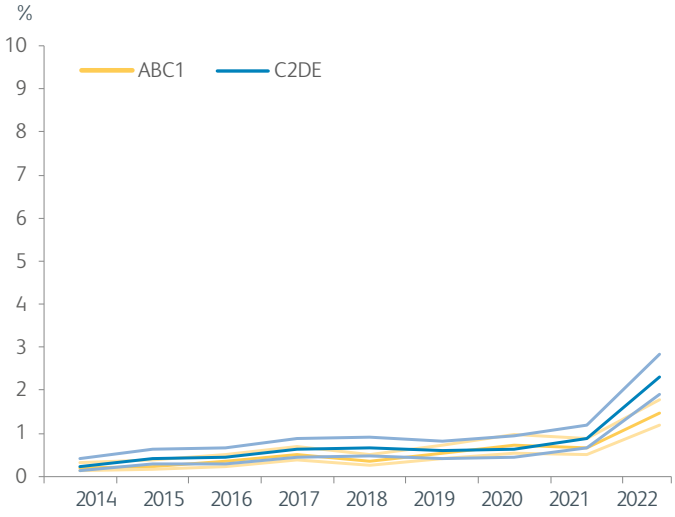



**Fig 3.21. E-cigarette use in people who have never smoked.[28]**

## 3.9 International trends of smoking prevalence and e-cigarette use

Globally, the use of non-tobacco nicotine products has increased, particularly the use of e-cigarettes (see chapter 9, Fig 9.6). Data on e-cigarette use are now routinely collected in many national surveys that measure tobacco smoking status; however, some countries still have relatively little data on their use. Other products, such as oral nicotine pouches, are only now being included in some national surveys. In this section, we will review trends in smoking and e-cigarette use in countries and continents with relatively diverse approaches to the use of e-cigarettes in tobacco control policy.

### 3.9.1 USA

Between 2017 and 2022, use of e-cigarettes by adults aged 18 and over in the USA increased by 3.2 percentage points from 2.8% to 6.0% for any current use, with the increase largely from 2017 to 2019 and again between 2021 and 2022 (Figs 3.22–3.24).[40–46] Adult smoking prevalence fell from 14% to 11.6% between 2019 and 2022.[46] In 2022, the prevalence of smoking still greatly exceeded the use of e-cigarettes among adults.

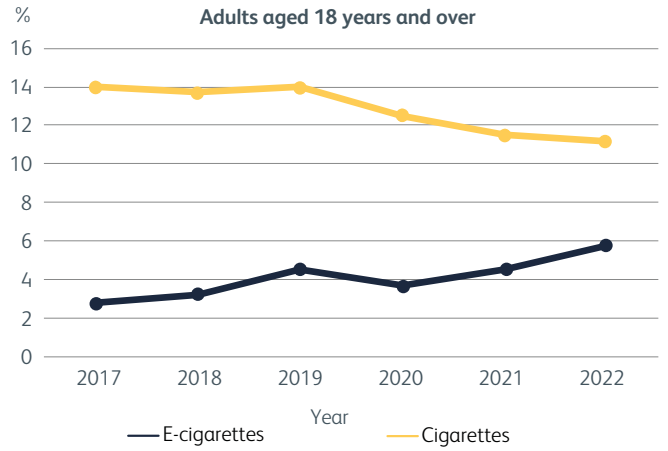



**Fig 3.22. Tobacco and e-cigarette use among adults in the USA, 2017–22.[46,47]**

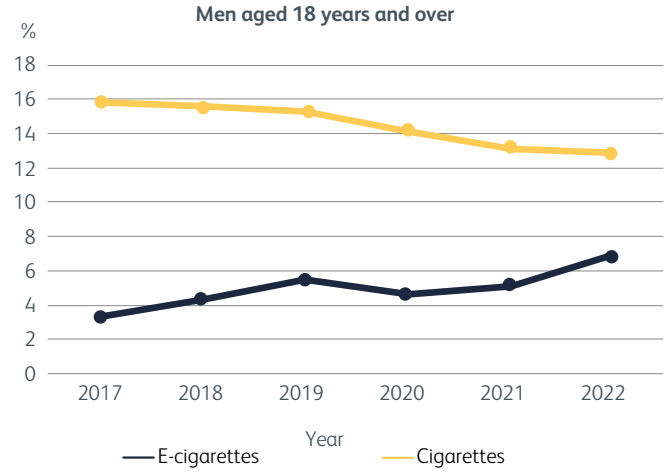



**Fig 3.23. Tobacco and e-cigarette use among men in the USA, 2017–22.[46,47]**

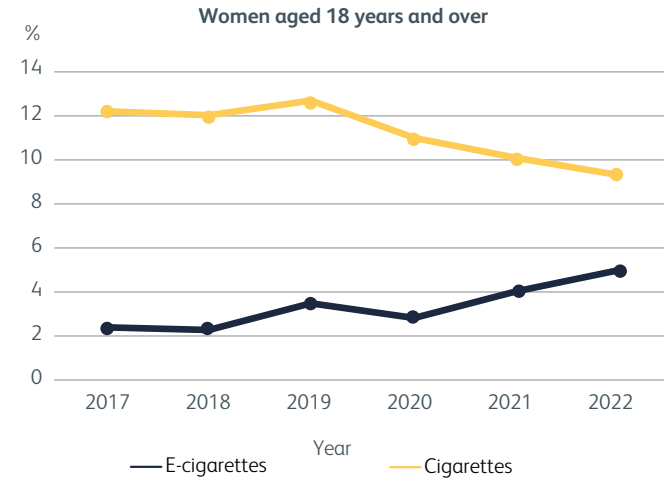
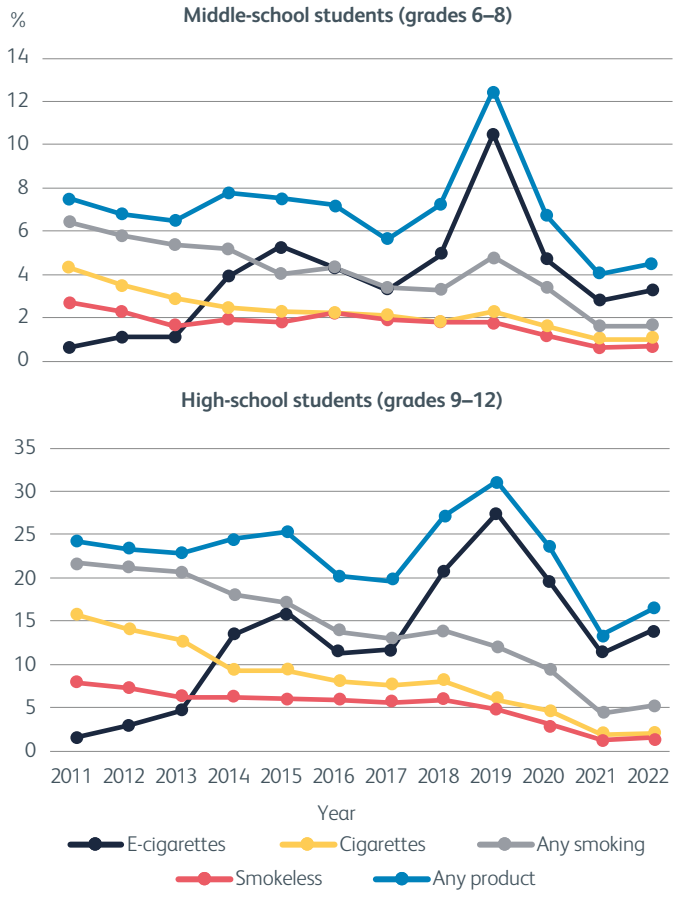


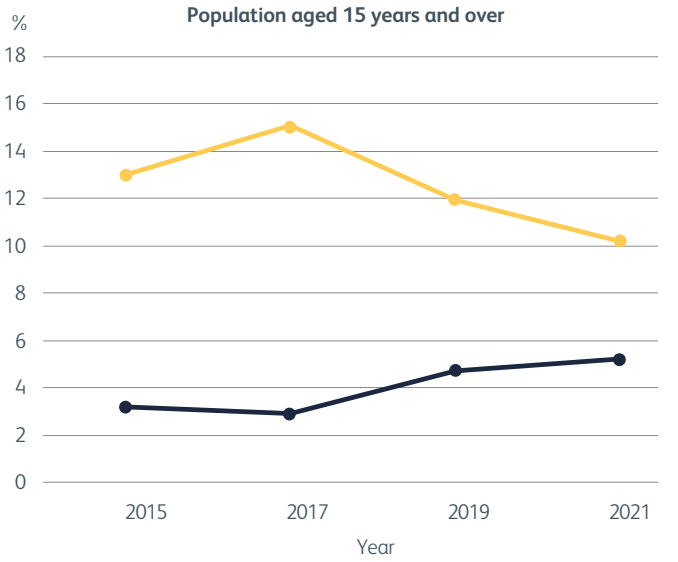

**Fig 3.24. Tobacco and e-cigarette use among women in the USA, 2017–22.[46,47]**

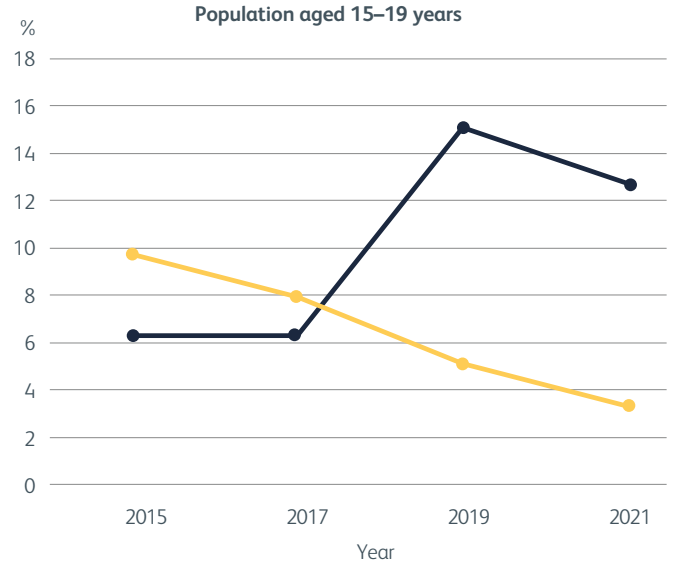
Over the period of 2011–22, past 30-day e-cigarette use increased from 0.6% to 3.3% for middle-school students (grades 6–8 / age 11–13 years) in the USA and from 1.5% to 14.1% for high-school students (grades 9–12 / age 14–17 years) (Fig 3.25).[48–55] Hence, prevalence of past month e-cigarette use by high-school students greatly exceeds prevalence of current use by adults. The steepest increases in e-cigarette use among middle- and high-school students occurred between 2013 and 2014 and from 2018 to 2019. Use peaked in 2019 and declined thereafter. The change in use from 2011 to 2019 represented a change of 9.9 percentage points for middle-school students and a 26-percentage point increase for high-school students, with a decline from 2019 to 2022 of 7.2 percentage points for middle-school students and 13.4 percentage points for high-school students. Between 2019 and 2020, the use of disposable e-cigarettes increased. In 2021, disposables overtook refillable pod/cartridge devices as the most common type of e-cigarette device used by youth (2021 53.7%; 2022 55.3%; 2023 16.1%), followed by refillable pods or cartridges (2021 28.7%; 2022 25.2%).[55,56] The most popular e-cigarette brands in 2022 among US youth were Puff Bar (14.5%), Vuse (12.5%), Hyde (5.5%) and SMOK (4%). In 2023, the most popular brands were Elf Bar (31.1%), Vuse (8.7%), Esco Bars (6.0%), Juul (3.4%).[55]

Tobacco smoking declined in both middle- and high-school students from 2011 to 2022, dropping from 6.4% to 1.6% for middle-school students for any smoking (cigarettes, cigars, cigarillos, waterpipe) and from 4.3% to 1.0% for cigarette smoking. Among high-school students, any smoking declined from 21.8% in 2011 to 5.2% in 2022, and from 15.8% to 2.0%. for cigarette smoking. The largest drops in cigarette smoking among high-school students occurred between 2013 and 2014, and between 2018 and 2019, corresponding to the steepest increases in e-cigarette use among school students. E-cigarette use has surpassed smoking since 2018 among high-school students and since 2015 among middle-school students.

Smokeless tobacco use declined by 2 percentage points from 2011 to 2022 among middle-school students (2.7% to 0.7%) and by 6.3 percentage points among high-school students (7.9% to 1.6%). Use of oral nicotine pouches increased from 0.3% to 0.5% among middle-school students and from 1.1% to 1.4% among high-school students from 2021–22.



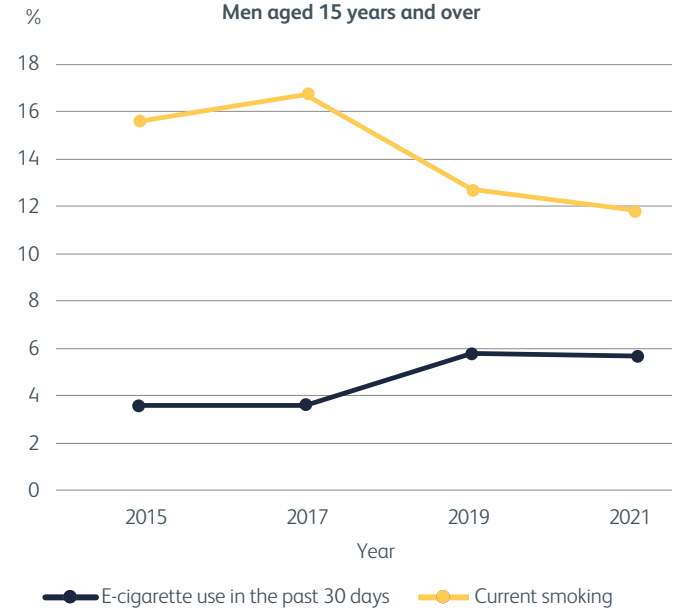




**Fig 3.25. Tobacco product and e-cigarette use among middle- and high-school students in the USA from 2011 to 2022.[40]**

## 3.9.2 Canada

Past 30-day e-cigarette use in Canada among the population aged 15 years and over increased from around 2% in 2013 to 5.2% in 2021, with use slightly higher among men than women (Fig 3.26).[57–63] Prevalence was relatively steady between 2019 and 2021 among adults. Among young people aged 15–19 years, e-cigarette use approximately doubled between 2013 and 2015 (3.0% to 6.3%), and then more than doubled between 2017 and 2019, when it peaked at 15.1% before starting to trend downwards. Smoking has been steadily decreasing among the population aged 15 years and older, and among young people aged 15–19 years. In 2021, more Canadians aged 15 years and older smoked than used e-cigarettes. However, since 2019, e-cigarette use has greatly overtaken smoking among Canadians aged 15–19 years.

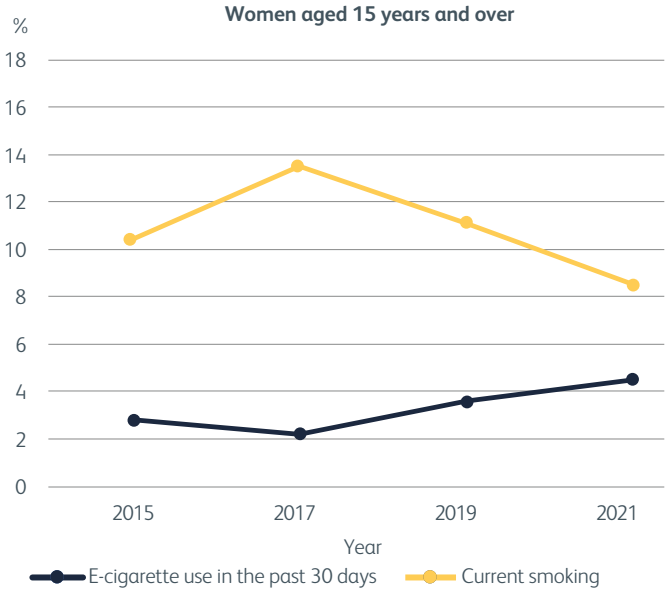



**Fig 3.26. Current smoking, e-cigarette use and use of any tobacco or nicotine product in the past 30 days in Canada, 2015–21.[59,62,63]**

## 3.9.3 Australia

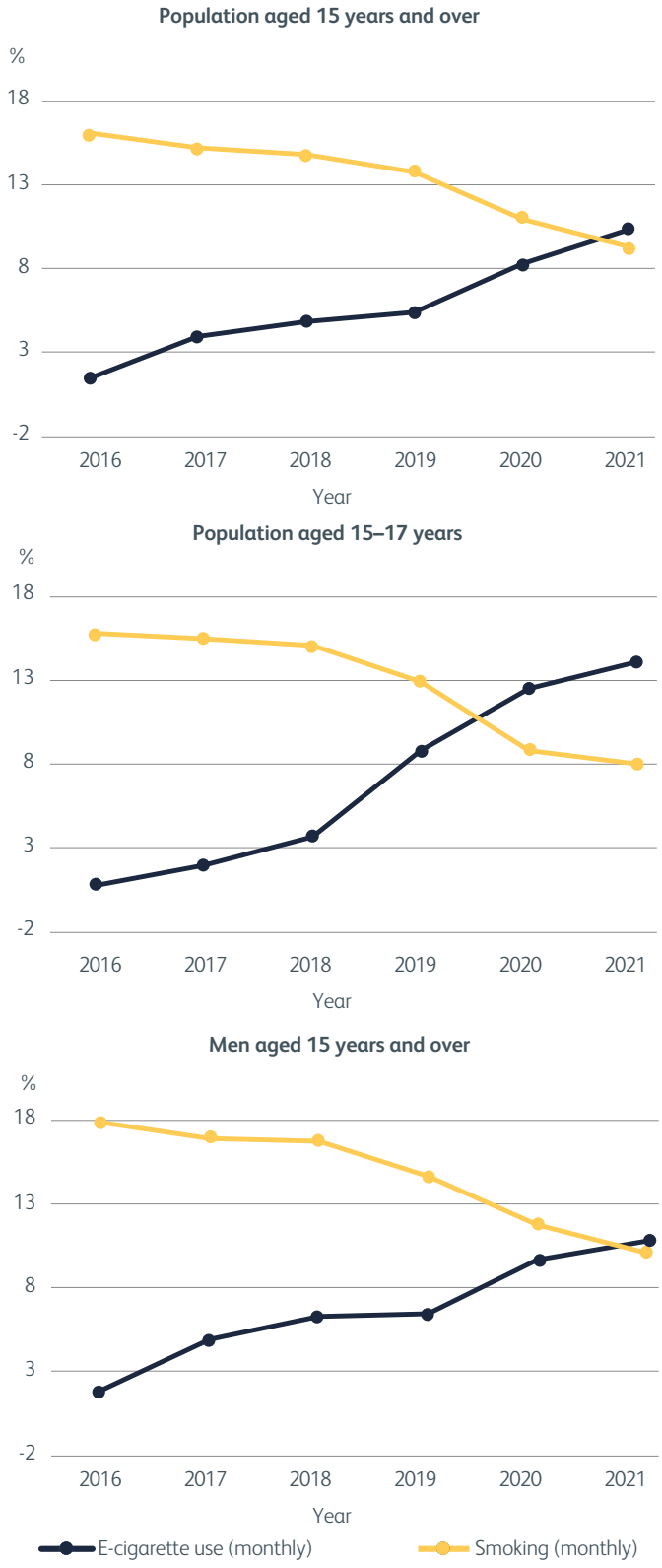
E-cigarette use in Australia has only been measured in official national surveys among the whole population since 2016.[64] Current use among adults aged 18 and over increased from 1.2% in 2016 to 2.6% in 2019. The corresponding figures for current smoking were 14.9% (2016) and 14.0% (2019). Lifetime use of e-cigarettes among young people aged 14–17 years in that survey was estimated to be 9.2% in 2016 and 9.6% in 2019, and current use increased from 0.9% to 1.8%. Another national survey in 2020/2021 estimated current e-cigarette use to be 2.2% among adults aged 18 years and over, with current smoking estimated to be 11.8%.[65] Among people aged 15–17 years, current e-cigarette use was estimated to be 1.1% (with caution needed in interpretation due to high margin of error), and current smoking prevalence was 2.1%. The Australian Secondary Schools Survey of Alcohol and Other Drugs estimated that past month e-cigarette use increased from 3.4% in 2014 to 5.5% in 2017 among year 9 students (14–15 years old).[66]

Other data collected by convenience or other non-representative sampling methods have reported higher prevalence of e-cigarette use in more recent years among both adults and youth. An analysis of commercial market research panel data suggested that the prevalence of current vaping steadily increased every year from 1.4% in 2018 among people aged 14 and over to 8.9% in 2023.[67] The prevalence of smoking remained relatively stable, ranging from 12.3% in 2018 to 11.8% in 2023. Current e-cigarette use among 14–17-year-olds increased from 0.8% in 2018 to 14.5% in 2023, with a steep rise between 2021 and 2023. However, the estimates from the aggregated monthly data were highly erratic during the period of rapid rise, which coincided with a change in methodology from April 2020 onwards due to COVID-19 impacts on data collection.[67] Smoking prevalence in this age group also showed a similar pattern in the dataset of increasing from 2.1% in 2018 to 12.8% in 2023, with the increase commencing in 2020, and the majority of this rise being dual use of both vaping and smoking.

## 3.9.4 New Zealand

E-cigarette use has steadily increased year on year in New Zealand among adults aged 15 years and over, from 1.4% in 2016/17 to 10.3% in 2021/22, with the steepest increase (2.9 percentage points) occurring between 2019/20 and 2020/21 (Fig 3.27).[68] The same pattern was seen among men and women, but with slightly lower prevalence of use among women than men. As of 2021/22, the prevalence of e-cigarette use exceeds that of smoking in New Zealand. Among teens aged 15–17 years, e-cigarette use increased from 0.6% in 2016/17 to 13.9% in 2021/22. A steep rise in e-cigarette use among 15–17-year-olds occurred between 2018/19 and 2019/20, when it rose from 3.5% to 8.6%. The prevalence of e-cigarette use among 15–17-year-olds has exceeded that of smoking in that age group since 2020/21.

The decline in smoking prevalence in New Zealand has generally mirrored the increase in e-cigarette use among the whole population aged 15 years and older, and among youth aged 15–17 years. Among adults aged 15 years and over, smoking prevalence decreased from 16.0% in 2016/17 to 9.2% in 2021/22, and among 15–17-year-olds, it declined from 15.6% to 7.8% over the same period, with most of this decrease occurring since 2018/19 (7.1 percentage point drop).



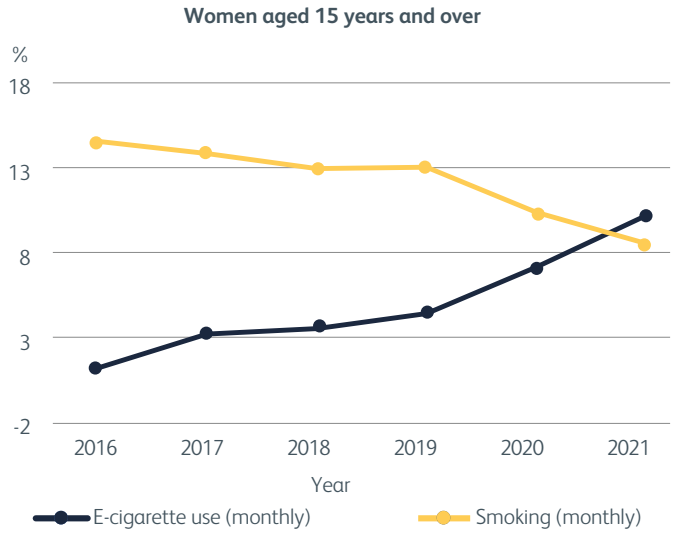




**Fig 3.27. Current smoking and e-cigarette use prevalence in New Zealand, 2016–21.[68]**

## 3.9.5 European countries

Across EU countries and the UK, the prevalence of current e-cigarette use is provided by the Eurobarometer survey and ranged from 0.1% to 4.0% in 2014, from 0.2% to 5.1% in 2017 and from 0.1% to 6.7% in 2020, while the median prevalence increased from 1.1% to 1.7% from 2014 to 2020 (Table 3.2).[69–71] The average prevalence of e-cigarette use increased from 1.8% to 2.5% between 2014 and 2020, while smoking (cigarettes, cigars, cigarillos and pipe tobacco) decreased from 26.2% to 23.2%. This pattern of increasing e-cigarette use and declining smoking was seen in 12 countries (Belgium, Denmark, Germany, Estonia, Republic of Ireland, Spain, France, Cyprus, Austria, Slovenia, Sweden and the UK). However, eight countries saw an increase in both e-cigarette use and smoking (Bulgaria, Czech Republic, Greece, Italy, Latvia, Lithuania, Luxembourg and Slovakia), and both vaping and smoking declined in five countries (Hungary, the Netherlands, Poland, Portugal and Finland). In 2020, the prevalence of e-cigarette use was <1% in five countries (Croatia, Hungary, Malta, Portugal and Finland) and 3% or higher in nine countries (Belgium, Czech Republic, Denmark, Republic of Ireland, France, Lithuania, Luxembourg, Austria and the UK).

**Table 3.2. Eurobarometer surveys on current use of e-cigarettes and tobacco smoking among adults in EU countries and the UK, 2014, 2017 and 2020**

| Country | Currently use e-cigarettes (%) | | | Currently smoke tobacco (%) | | |
|---|---|---|---|---|---|---|
| | 2014 | 2017 | 2020 | 2014 | 2017 | 2020 |
| EU27+UK | 1.8 | 2.0 | 2.5 | 26.2 | 26.1 | 23.2 |
| Austria | 1.3 | 2.7 | 3.7 | 25.6 | 28.3 | 25.4 |
| Belgium | 0.6 | 3.5 | 3.2 | 25.4 | 19.2 | 20.7 |
| Bulgaria | 1.1 | 0.2 | 1.1 | 34.8 | 36.0 | 38.1 |
| Croatia | 1.2 | 0.4 | 0.9 | 33.2 | 35.1 | 36.0 |
| Cyprus | 1.8 | 2.8 | 2.4 | 30.8 | 27.5 | 27.5 |
| Czech Republic | 1.1 | 1.2 | 3.0 | 24.4 | 28.9 | 30.2 |
| Denmark | 2.1 | 2.1 | 3.2 | 23.0 | 18.6 | 15.6 |
| Estonia | 0.9 | 1.5 | 2.2 | 22.1 | 23.3 | 18.3 |
| Finland | 1.3 | 1.3 | 0.8 | 18.7 | 20.2 | 14.9 |
| France | 4.0 | 4.5 | 5.6 | 31.8 | 36.0 | 28.0 |
| Germany | 1.3 | 1.8 | 2.1 | 27.0 | 25.4 | 22.9 |
| Greece | 0.9 | 2.7 | 2.1 | 38.0 | 36.5 | 41.5 |
| Hungary | 0.5 | 0.6 | 0.4 | 30.2 | 26.6 | 28.1 |
| Ireland | 2.7 | 2.1 | 6.7 | 21.5 | 19.4 | 18.3 |
| Italy | 0.4 | 0.2 | 1.4 | 20.9 | 24.7 | 23.2 |
| Latvia | 0.8 | 0.9 | 2.0 | 29.9 | 32.2 | 31.6 |
| Lithuania | 0.4 | 0.8 | 3.2 | 25.9 | 29.1 | 27.9 |
| Luxembourg | 1.4 | 1.6 | 3.1 | 21.2 | 21.0 | 23.5 |
| Malta | 0.2 | 2.0 | 0.8 | 20.1 | 24.0 | 20.1 |
| Netherlands | 1.9 | 1.7 | 1.0 | 22.6 | 19.4 | 11.9 |
| Poland | 1.9 | 1.1 | 1.1 | 28.5 | 29.7 | 26.0 |
| Portugal | 1.6 | 0.9 | 0.1 | 25.5 | 25.6 | 21.3 |
| Romania | 0.5 | 0.5 | 1.0 | 27.5 | 28.0 | 30.2 |
| Slovakia | 0.5 | 0.3 | 1.3 | 20.8 | 26.3 | 24.8 |
| Slovenia | 0.1 | 0.6 | 1.5 | 30.5 | 27.9 | 26.7 |
| Spain | 0.5 | 0.5 | 1.3 | 29.5 | 27.4 | 24.5 |
| Sweden | 0.3 | 0.3 | 1.1 | 11.5 | 7.1 | 6.6 |
| UK | 4.0 | 5.1 | 4.4 | 21.6 | 17.4 | 12.4 |

The European School Survey Project on Alcohol and Other Drugs (ESPAD) report uses data collected from 15–16-year-olds in 35 European countries, although the UK has not participated in this study since 2015. The study found that average prevalence of past 30-day e-cigarette use was 14% in 2019, ranging from 5.4% in Serbia to 41% in Monaco.[72] Prevalence was <10% in 11 countries (Faroes, Finland, Georgia, Malta, Montenegro, Netherlands, North Macedonia, Portugal, Serbia, Spain and Sweden), between 10% and 15% in 14 countries (Austria, Bulgaria, Croatia, Cyprus, Denmark, Estonia, Greece, Ireland, Italy, Kosovo, Norway, Romania, Slovenia and Ukraine), and >15% in 10 countries (Czech Republic, France, Germany, Hungary, Iceland, Latvia, Lithuania, Monaco, Poland and Slovakia). The average prevalence of current cigarette smoking declined from 33% in 1995 to 20% in 2019, and ranged from 5.1% in Iceland (the only country with <10% smoking prevalence) to 32% in Italy and Bulgaria. Smoking was between 10% and 15% in 10 countries (Cyprus, Georgia, Greece, Ireland, Kosovo, Malta, Netherlands, Norway, Portugal and Sweden), between 16% and 20% in nine countries (Estonia, Faroes, Finland, Germany, Monaco, Montenegro, North Macedonia, Serbia and Slovenia), and >20% in 15 countries (Austria, Bulgaria, Croatia, Czech Republic, Denmark, France, Hungary, Italy, Latvia, Lithuania, Poland, Romania, Slovakia, Spain and Ukraine).

An analysis of WHO's Global Youth Tobacco Survey data from 17 European countries (which did not include the UK) indicated that six countries had a prevalence of <10% past 30-day e-cigarette use among students aged 11–17 years (Kyrgyzstan, North Macedonia, Albania, Serbia, Romania and Slovakia); six had a prevalence between 10% and 15% (Bulgaria, Croatia, Czech Republic, Bosnia and Herzegovina, Georgia and Republic of Moldova), and four had a prevalence greater than 15% (Ukraine, Italy, Latvia and Poland).[73] Prevalence was lowest in Kyrgyzstan and highest in Poland. Analysis of five countries that measured e-cigarette use in two different years found that prevalence has increased over time in Georgia (6.1% in 2014 and 12.4% in 2017), Latvia (10.3% in 2014 and 18.5% in 2019) and Italy (9.1% in 2014 and 18.3% in 2018), whereas the difference in prevalence was not statistically different between years for Romania and San Marino.

### 3.9.6 WHO Global Adult Tobacco Surveys

Data from the Global Adult Tobacco Surveys (GATS) (Table 3.3) indicate that, between 2011 and 2016, current e-cigarette use prevalence among adults (aged 15 and over) was <1% in Indonesia, Malaysia, Qatar, Mexico, Philippines, Senegal, Vietnam and Ethiopia; between 1% and 1.9% in Greece, Kazakhstan, Costa Rica and Turkey; and between 3% and 3.9% in Russia.[74] In countries participating in GATS before 2017 that reported both smoking and vaping prevalence, the ratio of smoking to vaping ranged from 7:1 in Costa Rica to 116:1 in Indonesia. Between 2017 and 2021, e-cigarette use prevalence was <1% in India, Bangladesh, Uruguay, China and Saudi Arabia; between 1% and 1.9% in Ukraine and Kazakhstan; between 2% and 2.9% in Philippines and South Africa; and between 3% and 3.9% in Romania and Indonesia. Estimates for two different years were only available for three countries (Indonesia, Philippines and Kazakhstan); e-cigarette prevalence increased from 0.3% in 2011 to 3.0% in 2021 in Indonesia, and from 0.8% in 2015 to 2.1% in 2021 in Philippines, but decreased from 1.7% in 2014 to 1.3% in 2018 in Kazakhstan. The ratio of smoking to vaping ranged from 9:1 in Romania and the Philippines to 535:1 in India in 2017–21.

**Table 3.3. Current vaping, smoking and smokeless tobacco use among population aged 15 and over reported in WHO Global Tobacco Surveys from 2011–21**[69–71]

| Country | Year | Current e-cigarette use (%) | | | Current smoking (%) | | | Current smokeless tobacco use (%) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Overall | Men | Women | Overall | Men | Women | Overall | Men | Women |
| Indonesia | 2011 | **0.3** | 0.5 | 0 | **34.8** | 67.0 | 2.7 | **1.7** | 1.5 | 2.0 |
| Malaysia | 2011 | **0.8** | 1.6 | 0 | **23.1** | 43.9 | 1.0 | **0.7** | 0.9 | 0.6 |
| Greece | 2013 | **1.9** | 1.7 | 2.1 | **38.2** | 51.2 | 25.7 | **0.2** | 0.2 | 0.2 |
| Qatar | 2013 | **0.9** | 1.6 | 0.2 | **12.1** | 20.2 | 3.1 | **0.7** | 1.3 | 0 |
| Kazakhstan | 2014 | **1.7** | 2.5 | 0.9 | **22.4** | 42.4 | 4.5 | **1.3** | 2.8 | 0 |
| Costa Rica | 2015 | **1.3** | 1.6 | 0.9 | **8.9** | 13.4 | 4.4 | **0.1** | 0.1 | 0 |
| Mexico | 2015 | **0.6** | 1.1 | 0.2 | **16.4** | 25.2 | 8.2 | **0.2** | 0.4 | 0 |
| Philippines | 2015 | **0.8** | 1.3 | 0.2 | **22.7** | 40.3 | 5.1 | **1.7** | 2.7 | 0.7 |
| Senegal | 2015 | **0.1** | 0.1 | 0.04 | **5.4** | 10.7 | 0.4 | **0.7** | 0.3 | 1.0 |
| Vietnam | 2015 | **0.2** | 0.4 | 0.1 | **22.5** | 45.3 | 1.1 | **–** | – | – |
| Ethiopia | 2016 | **0.1** | 0.1 | 0.02 | **3.7** | 6.2 | 1.2 | **1.7** | 2.6 | 0.8 |
| Russian Federation | 2016 | **3.5** | 5.4 | 1.9 | **30.3** | 49.5 | 14.4 | **0.4** | 0.8 | 0.1 |
| Turkey | 2016 | **1.3** | 2.1 | 0.6 | **27.1** | 41.5 | 13.1 | **–** | – | – |
| India | 2016-17 | **0.02** | 0.03 | 0.01 | **10.7** | 19 | 2.0 | **21.4** | 29.6 | 12.8 |
| Bangladesh | 2017 | **0.2** | 0.5 | 0 | **18.0** | 36.2 | 0.8 | **20.6** | 16.2 | 24.8 |
| Ukraine | 2017 | **1.7** | 2.5 | 1.0 | **22.8** | 39.7 | 8.8 | **0.2** | 0.4 | 0 |
| Uruguay | 2017 | **0.2** | 0.2 | 0.2 | **21.6** | 25.6 | 18 | **0.1** | 0.3 | 0 |
| China | 2018 | **0.9** | 1.6 | 0.1 | **26.6** | 50.5 | 2.1 | **0.9** | 1.6 | 0.1 |
| Romania | 2018 | **3.4** | 5.0 | 1.8 | **30.2** | 39.8 | 21.2 | **1.1** | 1.8 | 0.4 |
| Kazakhstan | 2019 | **1.3** | 2.0 | 0.6 | **21.5** | 38.3 | 6.4 | **1.4** | 2.7 | 0.1 |
| Saudi Arabia | 2019 | **0.8** | 1.1 | 0.4 | **17.9** | 27.5 | 3.7 | **2.7** | 3.7 | 0.5 |
| Indonesia | 2021 | **3.0** | 5.8 | 0.3 | **34.5** | 65.5 | 3.3 | **1.0** | 0.9 | 1.1 |
| Philippines | 2021 | **2.1** | 3.6 | 0.5 | **18.5** | 33.3 | 3.7 | **1.5** | 2.3 | 0.7 |
| South Africa | 2021 | **2.2** | 3.8 | 0.7 | **29.4** | 41.7 | 17.9 | **4.3** | 1.1 | 7.2 |

### 3.9.7 Global estimates of youth e-cigarette use

An analysis of data from the WHO Global Youth Tobacco Surveys (GYTS) collected in 67 countries between 2012 and 2019 and the 2019 National Youth Tobacco Survey in the USA estimated the prevalence of current use (use in the past 30 days) among young people aged 12–16 years to be 9.2%.[75] Most use was infrequent, with only 1.4% reporting having used an e-cigarette on 10 days or more in the past 30 days. Use was higher among boys (11.7%) than girls (6.6%), and among those aged 15–16 (11.2%) than those aged 12–14 years (8.0%). By WHO region, past 30-day prevalence was lowest in South-East Asia (3.3%) and highest in Western Pacific (10.8%) and Eastern Mediterranean (10.6%). Regional prevalence was 7.8% for the Americas, 9.3% for Europe and 9.9% for Africa. By individual country, use was lowest in Kazakhstan (1.9%) and highest in Guam (33.2%).

### 3.9.8 International trends – conclusions

E-cigarette use has increased in most countries where data are available for more than one time point. Apart from New Zealand, e-cigarette use among adults remains lower than smoking. Past 30-day use of e-cigarettes among young people is generally higher than among adults, and in some countries exceeds the prevalence of smoking among youth. Population-level data on use of nicotine oral pouches is very limited, but there is early evidence of an increase in use of these products among school students in the USA.

## 3.10 Improving datasets

The UK benefits from excellent surveys of smoking and e-cigarette use. However, these are almost entirely based on cross-sectional designs such that different individuals are sampled on each occasion. To improve understanding of trajectories of smoking and use of vaping products over time, it would be helpful to collect more longitudinal data from the same individuals at different time points. There are high-quality surveys in the UK on smoking and vaping, but it is also important to participate in international surveys to make meaningful comparisons with other countries. This is essential to assess the relative success or otherwise of tobacco control policies internationally. The European School Survey Project on Alcohol and Other Drugs (ESPAD) is a cross-sectional survey carried out every 4 years since 1995, which in 2019 collected data from almost 100,000 16-year-old children in 35 European countries.[76] The UK stopped participating in 2015, which was the first year that the survey asked about use of e-cigarettes. To enable comparisons with other countries it would benefit the UK to rejoin ESPAD, which could be secured from 2027.[77]

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# 04

# Effectiveness of e-cigarettes for smoking cessation

## Key points

- Evidence from randomised controlled trials and from two Cochrane reviews shows that e-cigarettes with nicotine are more effective at helping people quit for 6 months or longer than nicotine replacement therapy, with no clear difference in effectiveness between e-cigarettes with nicotine and varenicline, or cytisine.
- People who smoke in pregnancy may use e-cigarettes as part of a quit attempt, but the number of studies that have assessed the safety and effectiveness of this approach is limited. The largest randomised controlled trial to date suggested that e-cigarettes may be more effective than NRT and better at reducing the incidence of low birthweight.
- The available evidence signals the potential of e-cigarettes for both smoking cessation and harm reduction in smokers with mental illness, including those who are not motivated to quit and have been unable to quit before, but overall this is still limited. E-cigarettes that are easier to use, such as pod-based devices or disposables, may be more effective.
- Early data highlight the potential of e-cigarettes as a tool for smoking cessation among individuals experiencing socio-economic disadvantage, including in people experiencing homelessness.
- No randomised controlled trials have investigated the use of e-cigarettes for smoking cessation specifically among LGBTQ+ smokers, a community in which there is a higher prevalence of smoking than the general population. The wider literature suggests there are several simple actions that can be taken to make health services and vape shops more visibly LGBTQ+ friendly to break down perceived barriers.
- Smoke-free policies introduced into the prison system have led to widespread uptake of e-cigarettes to replace combustible tobacco, but there are limited data on the impact of e-cigarettes on smoking behaviours on release from prison.
- Trial evidence suggests that there is an opportunity to proactively support smoking cessation by promoting vaping in primary and emergency care settings.
- Estimates from modelling suggest that providing targeted quitting support, including an offer of a free e-cigarette starter kit to people who smoke and live in social housing across England, would result in approximately 298,000 additional long-term ex-smokers between 2022 and 2030.
- Changes in the prevalence of e-cigarette use in England up until 2022 have been positively associated with the success rate of quit attempts. If the association is causal, then the use of e-cigarettes in quit attempts appears to have helped in the region of 30,000–50,000 additional smokers to quit successfully each year in England since 2013.
- The evidence on e-cigarettes and smoking relapse is limited, suggesting no clear effect of post-cessation vaping on relapse rates, but more data are needed to clarify the issue.
- There is little evidence on the best ways to support people to quit vaping.
- E-cigarettes represent a cost-effective smoking cessation intervention, with an incremental cost-effectiveness ratio of £1,100 per quality-adjusted life year (QALY) gained over a 12-month time horizon, and of £65 per QALY over a lifetime.
- Implementing e-cigarette interventions could potentially reduce financial burdens on local government stop smoking services and the NHS without imposing additional costs on individuals attempting to quit smoking.

## Recommendations

- E-cigarettes should be promoted as an effective means of helping people who smoke to quit smoking tobacco.
- Campaigns recommending e-cigarettes for smoking cessation should include populations who are likely to experience the most benefit, including people with mental disorders, those who experience socio-economic disadvantage and people living in social housing.
- E-cigarettes should be offered as an effective treatment for smoking cessation across all NHS settings alongside established pharmacotherapy.
- Priorities for research include the role of e-cigarettes in smoking relapse prevention, cessation of e-cigarette use, and the effectiveness for smoking cessation of different e-cigarette device types and characteristics, including flavours.

## 4.1 Introduction

The evidence base examining the effectiveness of e-cigarettes for smoking cessation has expanded considerably since the Royal College of Physicians report examining the role of e-cigarettes and smoking cessation in detail was published in 2016.[1] In this section, we examine the most recent evidence on the effectiveness of e-cigarettes for smoking cessation in research settings, in specific population segments and settings, and provide an updated report of the associations of e-cigarette use and quit rates among people who smoke in the general population. In addition, we review the role of e-cigarettes in preventing relapse to smoking, interventions to support cessation of e-cigarette use, and a cost-effectiveness analysis of e-cigarette use as a smoking cessation intervention.

## 4.2 Clinical trial evidence

The 2024 update of the Cochrane review of e-cigarettes for smoking cessation found high-certainty evidence from seven randomised controlled trials (n=2,544 participants) that e-cigarettes with nicotine can help more people quit smoking than traditional nicotine replacement therapies (NRT) (risk ratio (RR) 1.59, 95% confidence interval (CI) 1.29, 1.93).[2] Evidence also showed that e-cigarettes with nicotine can help more people quit smoking than e-cigarettes without nicotine, with no support or behavioural support only, but more data are needed to increase certainty in those findings, due to imprecision in current estimates (RR 1.46, 95% CI: 1.09, 1.96, six studies, n=1,613 participants and RR 1.88, 95% CI: 1.56, 2.25, nine studies, 5,024 participants, respectively). Pooled data did not suggest that e-cigarettes increase rates of serious adverse events (SAEs), but data were sparse on this outcome and the longest study was up to 2 years in duration. The adverse effects reported most often with nicotine e-cigarettes were throat or mouth irritation, headache, cough and feeling sick. These effects reduced over time as people continued using nicotine e-cigarettes, and were similar in nature to those reported in trials of traditional NRT.

In 2023, a new Cochrane review used component network meta-analysis to investigate the comparative benefits and harms of different smoking cessation pharmacotherapies and e-cigarettes, when used to help people stop smoking tobacco.[3] This type of analysis uses data from indirect and direct comparisons to estimate treatment effects. In total, 319 studies, representing 157,179 participants, contributed data. The review found high-certainty evidence that e-cigarettes with nicotine can help more people quit smoking at 6 months or longer than placebo interventions or no pharmacotherapy (odds ratio (OR) 2.37, 95% credibility interval (CrI) 1.73, 3.24). This was a comparable effect to varenicline (OR 2.33, 95% CrI 2.02, 2.68) and cytisine (OR 2.21, 95% CrI 1.66, 2.97). In the absence of head-to-head comparisons between e-cigarettes and varenicline/cytisine, this means the best available evidence suggests that nicotine e-cigarettes, varenicline and cytisine are similarly effective (Fig 4.1). The analyses suggested that e-cigarettes with nicotine were more effective for smoking cessation at 6 months or longer than NRT (both combination and single forms) and bupropion (see Fig 4.1 for ORs). Low-certainty evidence did not show a clear difference in the number of people reporting SAEs for nicotine e-cigarettes, varenicline, cytisine or NRT when compared with no pharmacotherapy/e-cigarettes or placebo. However, people who received bupropion experienced a slightly higher rate of SAEs.

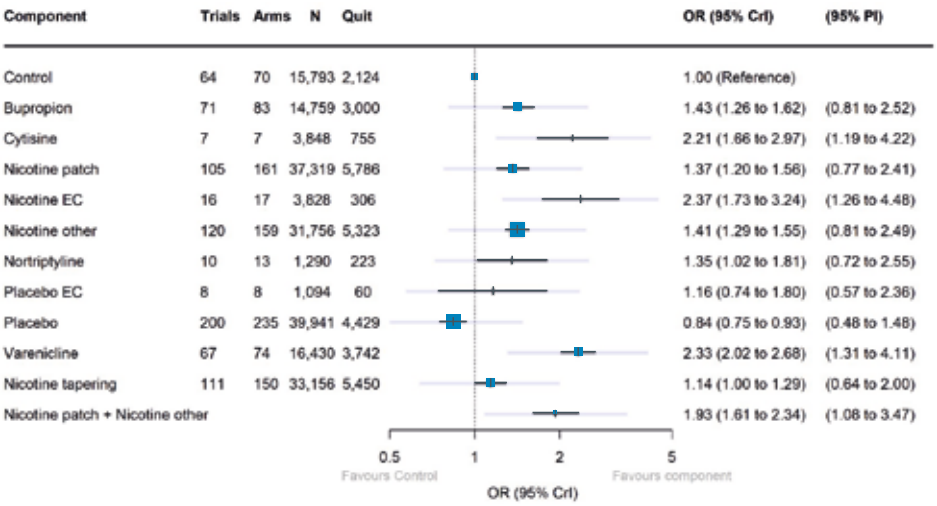


**Fig 4.1. Forest plot illustrating final model for abstinence (efficacy) outcome from Cochrane network meta-analysis.[3]**
Note: darker intervals represent CrI and lighter intervals represent PI. Control: no pharmacological or EC intervention. Abbreviations: CrI = credibility interval; EC = e-cigarette; n = number of participants; OR = odds ratio; PI = prediction interval

## 4.3 Specific populations and settings

Of the 88 studies included in the Cochrane review of e-cigarettes for smoking cessation, the majority (58 studies) were conducted in general populations of adult smokers.[2] We know that smoking is not evenly distributed across populations and settings, so in this section we focus on available evidence on the use of e-cigarettes in specific populations (4.3.1 pregnancy, 4.3.2 mental health disorders, 4.3.3 socio-economic position, 4.3.4 LGBTQ+) and settings (4.3.5 emergency and primary care, 4.3.6 prisons, 4.3.7 social housing).

### 4.3.1 Pregnancy

Rates of smoking in pregnancy in the UK have declined in recent years to 8.6% of mothers at the time of delivery in England.[4] However, this masks considerable inequalities between geographical areas and fell short of the national ambition to reach 6% prevalence or less by 2022, and still represents, on average, over 50,000 births every year in England and Wales.[5,6] People who smoke in pregnancy may use e-cigarettes as part of a quit attempt, but the number of studies that assess the effectiveness and safety of this approach is limited.

A systematic review of e-cigarettes in pregnancy was published in early 2021 and included studies up to February 2020.[7] A total of 23 studies reporting prevalence, patterns and reasons for vaping, cessation or health effects of vaping in pregnancy were included; animal and *in vitro* studies were excluded. Most studies were surveys, along with several qualitative and cohort studies and two secondary analyses of randomised controlled trials. The identified literature was limited to research conducted in the USA, UK and one study from Ireland. Prevalence was examined in four population surveys from the USA. Between 3.6–7% of all pregnant women in the surveys reported any use of e-cigarettes at any stage of pregnancy. Although there were some studies on patterns of use, the findings were inconsistent. Reasons for use were, unsurprisingly, focused on reducing or stopping smoking. The six studies that evaluated e-cigarettes and smoking cessation had mixed findings, precluding any conclusions being drawn. There were three studies that had health-related outcomes; two of these were underpowered, but one good-quality study from Ireland found that babies born to women who vaped rather than smoked during pregnancy had higher birthweight than babies born to smokers, and similar birthweight to babies born to non-smokers.

Since the systematic review was conducted, a clearer picture of the prevalence of vaping in pregnancy in the UK is now available, based on a longitudinal study that was published in 2021.[8] It recruited women in England and Scotland in early pregnancy (weeks 8–24), who were either recent ex-smokers, current smokers and/or vapers, and followed them up in late pregnancy as well as at 3 months postpartum. 867 were surveyed at baseline and a proportion of these (n=392) completed all three surveys. The study found that between 16–23% of pregnant smokers and ex-smokers had vaped during pregnancy or postpartum (16% in early pregnancy, 18% late pregnancy and 23% postpartum). Among all people reporting vaping, most also continued to smoke (dual use). Among those who were only vaping (3.5% in early pregnancy, 5.2% in late pregnancy), people reported vaping at fairly stable levels throughout pregnancy, and just one relapsed to smoking postpartum (became a dual user). In contrast, among those who were both smoking and using e-cigarettes in early pregnancy, around a third returned to exclusive smoking postpartum, and the remainder continued to dual use.

The evidence on vaping for smoking cessation in pregnancy has also grown. A multi-centre randomised controlled trial was conducted between 2018–2020.[9] A total of 1,140 pregnant women who smoked in early pregnancy were recruited from 23 hospital sites in England and one smoking cessation service in Scotland. They were randomised to either e-cigarettes or NRT patches, both combined with the offer of stop smoking service behavioural support. For the primary outcome of prolonged abstinence from smoking at the end of pregnancy, no statistically significant differences were observed (6.8% had quit in the vaping arm vs 4.4% in the NRT arm). However, some women randomised to NRT, and who were validated as not smoking at the end of pregnancy, reported vaping during the study. Once this group was removed, the analysis found that the vaping group were statistically significantly more likely to have quit smoking (6.8% vs 3.6%). The trial also examined some aspects of safety, including adverse events and birthweight. There was no significant difference in safety between the vaping and NRT groups. Low birthweight was less frequent in the babies of mothers in the vaping group.

It is unclear whether the findings from this trial or future research currently influence practice in the UK. Although information on vaping in pregnancy has been provided to stop smoking services, midwives and others since 2015, via the Smoking in Pregnancy Challenge Group (a multi-agency group established in 2012 to support efforts to reduce smoking in pregnancy),[10] health professionals

remain cautious about vaping in the context of pregnancy. A survey of stop smoking services and NHS trusts in England conducted in late 2020 found that 11% of cessation services and 7% of trusts reported providing e-cigarettes to pregnant women trying to quit.[11] A qualitative study involving midwives, health visitors, GPs and stop smoking staff across the UK identified a number of barriers to discussing vaping as a tool to quit smoking in pregnancy. These included: lack of knowledge regarding the evidence on vaping in pregnancy; lack of training to raise the issue with smokers; organisational barriers; negative social influences (sensationalist media, stigma); and concerns about litigation if adverse effects of vaping in pregnancy arose in future.[12] Formal guidance for health professionals on vaping in pregnancy has only recently been provided via the National Institute for Health and Care Excellence (NICE) in 2021, but e-cigarettes for smoking cessation in pregnancy are still not mentioned in other relevant documents, including the NHS Long Term Plan in England.[13] Some ambiguity therefore remains regarding what midwives and others should say to pregnant women who smoke, for whom vaping may be a harm reduction option. It is likely that further research is needed before clearer recommendations can be provided across all parts of the UK and indeed in other countries.

## 4.3.2 Mental health disorders

The importance of addressing tobacco smoking among people with mental illness has been identified as a national health priority for England.[14–16] Tobacco smoking remains approximately twice as common in people with mental illness compared with the general population, but can reach figures of around 70% in certain subgroups, such as people with psychosis.[17] High smoking prevalence among people with mental illness is commonly matched by high levels of nicotine dependence,[18] making smoking the single largest contributor to health inequalities for people with mental illness.[19] Smokers with mental illness are similarly motivated[18] and able[20] to stop smoking as smokers in the general population. High levels of dependence determined by complex links between smoking and some neurobiological, psychosocial and genetic aspects of mental illness[21] can, however, make successful, lasting smoking cessation particularly challenging.[17] The importance of ensuring the development and provision of effective interventions that meet the needs of smokers in this population has been emphasised.[16] E-cigarettes are considered to have substantial potential for smoking cessation and harm reduction among people with mental illness,[15] due to their high general appeal in this population,[22] ability to deliver nicotine effectively to smokers with high dependence levels, and ability to enable cigarette-like 'hand-to-mouth action'[23] as an important behavioural component. National policy,[14] clinical guidelines,[13] and the Royal College of Psychiatrists[24] explicitly recommend the inclusion of e-cigarettes in treatment offers for people with mental illness.

While evidence relating to the safety, effectiveness and cost-effectiveness of e-cigarettes for smoking cessation and harm reduction is steadily increasing for the general population, the number of published e-cigarette studies focused on smokers with mental illness remains small. Smokers from this group, particularly those with severe mental illness (SMI), such as schizophrenia, are commonly excluded from research studies in the general population, limiting the generalisability of findings. A secondary data analysis of a large smoking cessation trial involving e-cigarettes (n=657) included data for a subset of 86 participants who had reported the use of antidepressant (69%), antipsychotic (29%), hypnosedative (9%) or anxioloytic (6%) drugs, and drugs for addictive disorders (1%) in the trial.[25] E-cigarettes appeared equally effective, safe and acceptable for this subset of study participants and were associated with greater smoking reduction than NRT. However, the self-reported use of medications is not a reliable indicator of a current clinical mental health diagnosis and well-designed intervention studies focused on this population and potential specific needs are required.[13]

To our knowledge, seven intervention studies designed to investigate the impact of e-cigarette use in smokers with mental illness, including two randomised controlled trials and five prospective, non-randomised, pre-post pilot studies have been published to date.[23,26–29] Core study characteristics and findings are summarised below and in Table 4.1.

Two studies focused on smokers with schizophrenia,[23,26] three on SMI (including, but not limited to, schizophrenia),[27,28,30] and two included patients with both common mental disorders (eg depression, anxiety, PTSD) and SMI.[29,31] In all cases, participants were community-dwelling and clinically stable at the time of study. Apart from one study, which specified that participants needed to be 'willing to address their smoking' (eg by reducing consumption or quitting),[31] all other studies were explicitly aimed at smokers with mental illness who did not intend to quit. All studies included the provision of e-cigarette devices (pod- or tank-based) and nicotine-containing pods or cartridges in different flavours sufficient to cover use for up to 12 weeks (see Table 4.1). Behavioural support related to harm reduction or smoking cessation was provided briefly in two studies[26,31] and not at all in the others. All studies included concise advice on the technicalities of using e-cigarettes.

Six of the studies were pilot or feasibility studies, focused on establishing acceptability and early indications of benefits of e-cigarette provision for smokers with mental illness.[23,26–29,31] All found that the e-cigarette intervention provided was appealing to participants, resulting, for example, in daily use and substitution of combustible cigarettes,[23,26–28,30] even in participants who had unsuccessfully tried to quit before and had no intention to try again.[30] No SAEs judged likely to be related to the studies were reported and adverse effects were generally mild, with typical symptoms such as throat irritation, dry cough and nausea reported. The UK-based randomised controlled feasibility study reported acceptability of the intervention, but highlighted the need for enhanced support of smokers with aspects of using tank-based devices, concluding, like others,[30] that less complicated to use, pod-based devices may be particularly suited to this group.[31] It also highlighted practical challenges encountered with attempting to incorporate the e-cigarette intervention as an adjunct into NHS usual care, emphasising that further work is needed to ensure the devices can become part of standard smoking cessation support for smokers with mental illness as stipulated by the NHS Long Term Plan.[14]

With one exception,[31] the smoking-related outcome of interest in the studies was a reduction in cigarette consumption of at least 50%. All studies found that providing e-cigarettes resulted in varying proportions of reported (and mostly biochemically validated) reduction of consumption at follow-up points (see Table 4.1), thus confirming the potential of e-cigarettes for harm reduction in this vulnerable group. Although the authors describe it as 'the first fully powered RCT' in this field, no details of the power calculation were provided for the Pratt *et al* trial.[30] It is unclear whether the study was adequately powered to detect statistically significant group difference at appropriate levels for the primary outcome.

Although focused on harm reduction and enrolling smokers who were explicitly not motivated to quit, all study findings included self-reported and mostly biochemically validated smoking cessation in varying proportions of their study participants, ranging from 2%–40% (see Table 4.1). None of the studies were adequately powered to detect statistically significant group differences in this outcome. In the two e-cigarette RCTs that, by design, included control groups (usual care and 'assessment only'), quit rates were higher in the intervention groups.[30,31]

Together, the available evidence signals potential of e-cigarettes for both smoking cessation and harm reduction in smokers with mental illness, including those who are not motivated to quit and have been unable to quit before, but remains preliminary. Further research related to the effectiveness and cost-effectiveness of e-cigarette interventions that can be successfully delivered as part of standard care and consider potential particular needs of this vulnerable group of smokers, for example in terms of supporting long-term harm reduction or abstinence,[22] remains a priority.

**Table 4.1. E-cigarettes for harm reduction and cessation in smokers with mental illness; key study characteristics and findings**

| Author/ year | Country | Study design | Participants | Intervention/ type of e-cigarette | Control group | Reduction in consumption (at longest follow-up) | Smoking cessation (at longest follow-up) |
|---|---|---|---|---|---|---|---|
| Caponnetto *et al* 2013 | Italy | Pre-post pilot | n=14 (schizophrenia) | 'Categoria' e-cigarette (tank). A 4-week supply of nicotine cartridges was supplied and participants were trained how to load them onto the e-cigarette's atomiser. | N/A | Sustained 50% reduction in cigarettes per day at week 52 was shown in 7/14 (50%) of participants. | 14.3% of participants had stopped smoking, confirmed by exhaled CO (52 weeks). |
| Caponnetto *et al* 2021 | Italy | Pre-post pilot | n=40 (schizophrenia) | JUUL device with 5% nicotine pods. Participants were provided with instructions on how to use the e-cigarette. A 4-week supply of pods equivalent to current smoking behaviour was supplied. Brief behavioural support was provided. | N/A | Sustained 50% reduction in smoking or smoking abstinence in 37/40 (92.5%) of participants (24 weeks). | 35% of participants had stopped smoking, confirmed by exhaled CO (24 weeks). |
| Hickling *et al* 2019 | UK | Pre-post pilot | n=50 (schizophrenia, bipolar disorder, delusional disorder, unspecified psychosis) | Tobacco-flavoured NJOY traditional bold disposable e-cigarette, containing 4.5% nicotine. Participants were instructed in the use of the e-cigarette. | N/A | Reduction in cigarettes per day from baseline (17.94) remained significant at week 24 (12.8), and there was a significant reduction in CO levels (24 weeks). | One participant (2%) had stopped smoking at 24 weeks. |
| Kale *et al* * 2024 (manuscript submitted) | UK | Pilot RCT | n=43 (common mental disorders and severe mental illness) | ASPIRE Pockex device (tank) with a 4-week supply of nicotine-containing cartridges (three flavours in three different strengths). Brief behavioural support was provided. | Usual care | 13.6% of the participants in the control condition and 61.9% in the experimental condition (difference 48.3%) reported at least 50% reduction of consumption (4 weeks). | 4.6% of participants in the control condition and 28.6% in the experimental condition (difference 24%) reported cessation, confirmed by exhaled CO (4 weeks). |
| Pratt *et al* 2016 | USA | Pre-post pilot | n=19 (schizophrenia, bipolar disorder) | 2nd-generation e-cigarettes (NJOY brand) based on participant's level of use of combustible tobacco. Members of the research team instructed participants on proper use of e-cigarettes. | N/A | Mean self-reported tobacco use declined from 192 to 67 cigarettes/ week, confirmed by reduction in exhaled CO (4 weeks). | N/A |
| Pratt *et al* 2022 | USA | RCT | n=240 (schizophrenia, bipolar disorder) | Disposable NJOY Daily e-cigarette (up to 300 puffs), with brief information provided by study coordinator. Participants provided with additional 2-week supplies at 2, 4 and 6 weeks. | 'Assessment only' | Mean self-reported cigarettes per day reduced in intervention group (14.4) and remained significantly lower than the control group (18.7) (24 weeks). | 10.7% of participants self-reported smoking no cigarettes vs 5.7% in control group (24 weeks). |
| Valentine *et al* 2018 | USA | Pre-post pilot | n=43 (schizophrenia, bipolar disorder, PTSD, depression, anxiety, ADHD) | eVic Supreme (tank system). Participants were taught how to use the e-cigarette and provided with two e-liquid bottles for the first week. Additional bottles were dispensed as required. | N/A | Significant reductions in exhaled CO and mean cigarettes per day (from 16.6 to 5.7) were observed across the study period (4 weeks). | 10% of participants who completed follow-up assessment had stopped smoking, confirmed by exhaled CO (4 weeks). |

### 4.3.3 Socio-economic position, including people experiencing homelessness

Socio-economic position is a broad, multidimensional measure which refers to the social and economic position that individuals occupy in society relative to one another.[32] It is typically measured by income, wealth, education and occupation, and more recently other social issues such as access to and quality of housing and health facilities. Individuals on low incomes, with fewer years of education, working in routine and manual occupations or who are unemployed, have traditionally had higher rates of smoking and dependence compared with those of more advantaged socio-economic position. For instance, although the prevalence of smoking has declined in the past decade in all groups, in 2021 25.7% of those who were unemployed were smoking, compared with 13.3% in employment.[33] The rate of e-cigarette use among adults is also highest in less advantaged socio-economic groups, which reflects the fact that most e-cigarette users are current or former smokers (chapter 3, section 3.8).[34] This socio-economic patterning is not currently apparent in younger age groups. In the 2022 ASH youth survey, the prevalence of e-cigarette use in 11–18-year-olds was similar between more and less advantaged social grades.[35]

E-cigarettes may represent a viable option to replace cigarette smoking among less socio-economically advantaged individuals who struggle to maintain quit attempts using other means. As discussed in chapter 3, population-level data in England suggest that there are currently no apparent socio-economic differences in the use of e-cigarettes during an attempt to quit smoking. Although there are currently few e-cigarette interventions that are specifically designed for or targeted at disadvantaged socio-economic groups, evidence that exists is promising. One pilot intervention in a deprived area of Salford, Greater Manchester provided e-cigarette starter kits, e-liquid and support on device use to smokers. Of the 1,022 participants who engaged with the pilot, 614 were still engaged at 4 weeks, of whom 62% had quit (see section 4.3.7 below for more information on this study).[36] Qualitative data from other studies provide some insight into this potential adoption of e-cigarettes as a smoking cessation aid. An ethnography of smokers in working class areas of northern England argued that by representing both a rewarding activity and a smoking cessation tool, e-cigarette use is compatible with both recreational enjoyment and family responsibility.[37,38] In the context of a pragmatic RCT taking place in smoking cessation services, interviewed smokers from routine and manual occupations stated that e-cigarettes were cheaper than tobacco cigarettes, could replace the habit of smoking and suppress cigarette cravings. Despite these reflections, concerns remained that the devices were 'replacing one addiction with another'.[39] Together, these early data highlight the potential of e-cigarettes as a tool for smoking cessation among individuals experiencing some level of socio-economic disadvantage.

E-cigarettes may also be beneficial for priority subgroups who experience acute levels of poverty, lack or have infrequent access to basic resources, and have high smoking rates. People who are experiencing homelessness (eg rough sleeping, insecure/inadequate shelter or sofa surfing) suffer multiple adverse health outcomes, to which smoking is a significant contributor.[40–42] Data from the UK on smoking and homelessness are scarce and not routinely collected. Longitudinal data from this priority group in the USA show that smoking is a leading cause of death in those aged 45 and over, and the second leading cause of death in adults under this age.[41] The *Unhealthy state of homelessness 2022* report, which presents findings from 2,776 individuals in England, showed that 76% of people surveyed smoked and 50% reported wanting to quit.[43] Receipt of smoking cessation support varies across the homeless sector and most people who want to quit do not receive advice or support.[43,44]

A range of interventions for helping this specific population to quit smoking have been tested in the USA and Australia, including motivational interviewing, cognitive behavioural therapy, quit lines, NRT, and other pharmacotherapies.[45,46] However, the Cochrane systematic review of smoking cessation interventions in people experiencing homelessness found insufficient evidence to determine the effects of any intervention in this population.[46] The only e-cigarette intervention study included in the review – a cluster feasibility study providing e-cigarettes to people who smoked and were experiencing homelessness (described in more detail below) – concluded that the devices showed promise for boosting smoking cessation in this population.[47] Promise was also shown in a small study in Ireland that explored the efficacy and feasibility of offering e-cigarettes to support smoking cessation in those accessing a homeless service.[48]

Qualitative work has highlighted several key barriers to why people who are homeless fail to quit successfully despite trying. Barriers include social and environmental factors; for example, having a high percentage of people smoking around them and frequent transgressions to no smoking policies,[44,49,50] along with high rates of mental health conditions and stress.[49] Negative views of, and a lack of interest in using, established cessation approaches

such as NRT and a preference to engage in self-defined, alternative tobacco harm reduction interventions such as e-cigarettes are also highlighted in the literature.[49,51] One survey of 283 smokers accessing homeless services across Great Britain found that more people wanted to quit with an e-cigarette than any other product, but only 34% reported that they were willing or able to afford a starter kit.[51]

One study has explored the feasibility of offering e-cigarettes to adult smokers accessing homeless services in the UK.[50,52] In this four-centre trial, two clusters were assigned to offer participants usual care, which consisted of the standard offer of referral to the local stop smoking service and two clusters offered participants a free e-cigarette starter pack, which consisted of one refillable e-cigarette device and e-liquid provided once per week for 4 weeks. The results showed that the intervention was acceptable to both staff and participants. Reports of unintended consequences (including adverse effects of use, trading the device) were very low. The 24-week sustained biochemically validated abstinence rates were 6.25% e-cigarette vs 0% usual care. This work is now being developed into a larger trial, and is expected to report in 2025.[53] 'Everyone In', a UK government initiative during the COVID-19 pandemic that provided accommodation for insecurely housed people in hotels and hostels, saw many e-cigarettes given out to help people quit smoking while having to isolate and or social distance but, to date, the effects of this have not been evaluated.

## 4.3.4 LGBTQ+

Surveys in the USA suggest that e-cigarette use is more common among lesbian, gay, bisexual, transgender and queer (LGBTQ+) people than heterosexual and cisgender people.[54–61] Evidence from the UK is more limited. The best available data are from the Smoking Toolkit Study, a nationally representative survey of adults in England. Among >112,000 adults surveyed between 2013–19, the prevalence of e-cigarette use was 8.8% among bisexual men and women; around 1.5–1.8 times higher than in heterosexual men (5.9%) and women (4.9%) (Fig 4.2A–B).[62] There was also uncertain evidence of higher prevalence of e-cigarette use among gay men (7.1%) compared with heterosexual men (Fig 4.2A), but rates were similar between lesbians (4.5%) and heterosexual women (Fig 4.2B). It was not possible to estimate prevalence of use among trans people due to very low numbers in the sample. There were no differences in e-cigarette use by sexual orientation among current smokers (Fig 4.2C–D).[62] This is consistent with e-cigarette use being more common among smokers, and smoking being more common among members of the LGBTQ+ community.[62,63] By implication, higher rates of e-cigarette use among LGBTQ+ individuals appear to be driven primarily by higher cigarette smoking rates among sexual minorities.

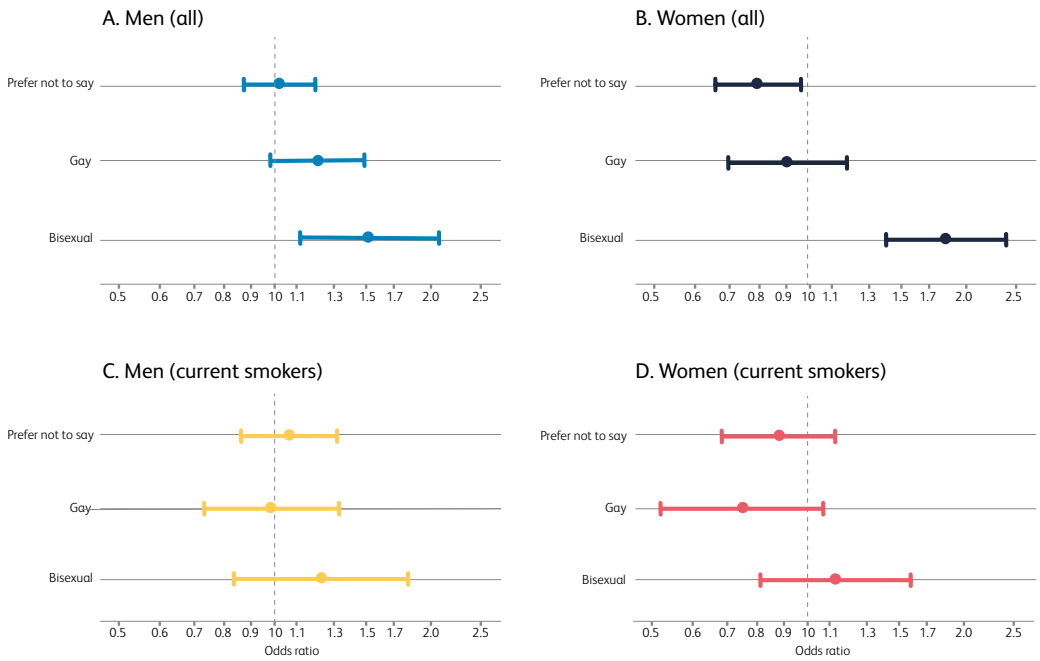


**Fig 4.2. Odds ratios represent the unadjusted odds of e-cigarette use among minority sexual orientation groups (gay/lesbian, bisexual, and prefer not to say) compared with those who identified as heterosexual (reference group).[62]**

Factors driving higher smoking prevalence among the LGBTQ+ community have been described in detail elsewhere.[64] Briefly, they include LGBTQ+ people being more likely than heterosexual and cis-gender people to: (i) experience discrimination and 'minority stress', (ii) face strong smoking norms within their social networks, (iii) be targeted by the tobacco industry, and (iv) have other risk factors for smoking (eg mental health problems, socio-economic disadvantage). Given the strong links between rates of smoking and e-cigarette use, these factors likely also indirectly promote e-cigarette use among the LGBTQ+ community. However, there may also be direct influences; for example, LGBTQ+ people report greater exposure to e-cigarette marketing (in addition to tobacco marketing) than their non-LGBTQ+ peers, which could encourage vaping uptake independent of smoking status.[65,66]

No randomised controlled trials have investigated the use of e-cigarettes for smoking cessation among LGBTQ+ smokers specifically.[2] However, there are learnings from the wider literature on smoking cessation and the LGBTQ+ community that can be applied to e-cigarettes. Many LGBTQ+ people face problems accessing health services and delay seeking help due to fears of insensitivity, misgendering (being referred to as the incorrect gender) and discrimination.[67,68] Such fears may also discourage them from seeking advice and support for e-cigarette use from specialist vape shops.[69,70] There are a number of simple actions that can be taken to make health services and vape shops more visibly LGBTQ+ friendly and help to break down perceived barriers. These include displaying the rainbow flag or other LGBTQ+ symbols; healthcare professionals wearing rainbow lanyards; including LGBTQ+ people in campaign communications; and giving people the chance to share their preferred pronouns (she/her, he/him, they/them) alongside their name.[71] In addition to ensuring that services and retail outlets are LGBTQ+ friendly, outreach activities can proactively target LGBTQ+ smokers and provide advice and support for using e-cigarettes for smoking cessation. For example, this may include working with local LGBTQ+ organisations to reach the local LGBTQ+ community (eg co-designing targeted activity), working with the local LGBTQ+ community to provide information on vaping at events and festivals (eg pride events), promoting vaping as an alternative at smoke-free events, and recruiting LGBTQ+ people to stop smoking services.[72]

## 4.3.5 Emergency and primary care

Current national guidance recommends promoting smoking cessation at every point of contact with the NHS.[13,14] Primary and emergency care settings offer the greatest opportunity to engage with large numbers of people who smoke who may not otherwise be seeking cessation support.[73] In England, general practice provides over 300 million patient consultations each year, and emergency departments provide an additional 23 million.[74] Primary care clinicians will be familiar with patients who smoke tobacco and are financially incentivised to make referrals for cessation support as part of the GP contract.[75] There is a positive association with GP incentives and referrals for smoking cessation support, as recording of referral to stop smoking services increased by 38.8% (95% CI: 15.2, 62.4) in the year after the introduction of the GP incentives.[76] Smoking status is covered by a routinely asked question in primary care health checks and is meant to be recorded in patient notes on screening and admission to hospital if presenting at an emergency department.[77] A 2021 hospital tobacco audit found that smoking ascertainment rates were consistently around 80% upon admission to hospital.[78] Recent investigative work in three UK hospital emergency departments found that approximately 24% of patients were active current tobacco smokers,[79] compared with population-level smoking prevalence of <14%,[80] suggesting that these settings are an ideal opportunistic location to engage people who smoke who may not otherwise be seeking support. The offer of an e-cigarette may be particularly helpful in this context as a 'no-pressure' opportunity to switch away from using harmful tobacco without having to stop using nicotine, at least in the short term.

GPs and physicians working in hospital emergency departments are seen as credible sources of information and advice, and can be influential in prompting and supporting positive health behaviour change.[81] Intervening to address cigarette smoking in primary or emergency care settings may be particularly beneficial, as people are engaged with at a 'teachable moment' when they are experiencing poor health requiring intervention, some of which may be directly linked to tobacco smoking.[82] The Cochrane living review of e-cigarettes for smoking cessation includes four trials recruiting from primary care clinics or GP practices.[2] Three of these are from the USA. The included UK trial[83] recruited 325 current tobacco smokers from 39 GP practices. Participants were identified by GPs as having one or more chronic condition(s) and not being currently motivated to quit smoking (ie not actively seeking cessation support). The intervention included brief advice and support delivered in a non-judgemental way and the offer of an e-cigarette starter kit. The focus was on switching rather than quitting. Assessing smoking abstinence at 8 months post-consultation, the trial more than doubled the number of quits in the e-cigarette arm compared with the

NRT arm (RR 2.29, 95% CI: 0.60, 8.70), though quit rates were low overall and the difference was not statistically significant. However, the effect is consistent with that from the Cochrane review, showing that e-cigarettes are more effective than behavioural support / no support for smoking cessation.[2]

A recent review concluded that hospital emergency departments are suitable environments to effectively engage the hard-to-reach population who smoke, but did not include trials of e-cigarette interventions.[84] The COSTED trial (Cessation of smoking trial in the hospital emergency department)[79] recruited 972 patients attending UK hospital emergency departments and randomised them to a switching intervention including brief advice, the offer of a pod-based e-cigarette starter kit, and referral to specialist stop smoking service support. The 6-month biochemically verified abstinence rate was 7.2% in the intervention group and 4.1% in the control group (relative risk, 1.76; 95% CI: 1.03, 3.01; p=0.038). Self-reported 7-day abstinence at 6 months was 23.3% in the intervention group and 12.9% in the control group (relative risk, 1.80; 95% CI: 1.36, 2.38; p<0.001). No serious adverse events related to taking part in the trial were reported. The trial successfully recruited ahead of target, demonstrating that, with sufficient staff time and capacity dedicated to offering this support in a high-pressure and fast-moving clinical environment, recruitment and intervention are achievable. [85]

## 4.3.6 Prisons

Prisoners experience substantially poorer health than the general population, in part because of the high prevalence of tobacco smoking.[86,87] Smoking prevalence among prisoner populations in the UK is estimated to be around 70%,[88–90] over five times the national average.[80] Complete smoke-free policies (indoor and outdoor) have been increasingly introduced to protect prison staff and prisoners from exposure to high levels of second-hand smoke. Between 2015–2018, Her Majesty's Prison and Probation Service (HMPPS) in England and Wales introduced a complete smoke-free policy in its 103 closed prisons (categories A–C) and a partial policy (permitting tobacco smoking on the prison sites within designated shelters) in the 15 open prisons (category D).[91] The Scottish Prison Service (SPS) soon followed, taking all of its 11 prisons (categories A–D) completely smoke-free in November 2018.[92] Across the three nations, nearly 92,000 people are currently held in smoke-free prison.[93,94] The Northern Ireland Prison Service (NIPS) was set to roll out a complete smoke-free policy in 2020; however, this was delayed due to the pandemic; no new implementation date has yet been set.[95]

To support smokers with their nicotine dependence, smoke-free prison sites across the UK either offer access to a smoking cessation course or provide prisoners with the opportunity to purchase NRT or an e-cigarette.[96,97] In England, the free-to-access smoking cessation support is offered by the prison's healthcare provider and offers prisoners up to 8 weeks of behavioural and pharmacological support (such as NRT patches or lozenges).[96] Interviews carried out with healthcare providers across three establishments per year, after English prisons moved to smoke-free, outline how there was little to no uptake of prison cessation services following the policy roll-out.[98] Healthcare staff noted that prisoners were not eligible to complete the cessation course if they were a current vaper due to concerns over dual use of e-cigarettes and NRT and for fear of prisoners trading NRT products. Staff responsible for the roll-out of smoke-free policies nationally and regionally felt that the exclusion of e-cigarettes from the healthcare provider's smoking cessation course required revisiting. Sales of NRT products across all sites in England and Wales in 2020 suggest that only around 100 prisoners per week purchase their own NRT products (HMPPS canteen figures shared with author).

Only a few global jurisdictions permit the use of e-cigarettes while incarcerated: some US states, England, Wales and Scotland.[91,92,99,100] E-cigarettes are not currently available to those living within the NIPS.[95] Across England, Wales and Scotland, e-cigarettes became available for prisoners to purchase in anticipation of the implementation of smoke-free polices. The places where e-cigarette use is permitted mirror the places where prisoners were allowed to smoke tobacco prior to implementation of the smoke-free policies (in designated rooms and in some outdoor spaces). The availability of e-cigarettes has been identified by those leading the smoke-free implementation (at national and local levels), and by prisoners, as a key contributor to the success of smoke-free policy implementation across UK prisons.[98,101,102]

Across the UK, prisoners are able purchase e-cigarettes (and associated paraphernalia) from the prison shop (known as 'canteen') once a week; a disposable product or a rechargeable vape pen with pre-filled capsules containing up to 18 mg nicotine is available in several flavours.[97,103–105] These closed-system devices with disposable, pre-filled, sealed capsules were chosen to safeguard against individuals refilling devices with unauthorised substances. Most prisoners choose the rechargeable pen over the disposable option and the initial outlay for a rechargeable vape 'starter kit' (device, charging plug, three capsules) in English prisons is around £18. An advance purchase

of an e-cigarette starter kit is offered to those entering prison with insufficient funds, to try and reduce debt and trading. Many smokers entering prison have never used an e-cigarette before; data collected across three prison sites in England found that over half of vapers were regularly using an e-cigarette for the first time.[106]

The latest SPS prisoner survey found that 60% of prisoners are now regularly using an e-cigarette.[107] HMPPS canteen sales in 2020 suggest that around 70% of prisoners regularly purchase capsules for rechargeable e-cigarettes, the most popular strength and flavour across all prison sites being 18 mg nicotine, tobacco flavour (HMPPS canteen figures shared with author). Research in Scotland found that following the introduction of the smoke-free policy, prisoners spend less per week on canteen purchases for e-cigarette-related products than they previously did on tobacco-related products, although this reduced amount still represented a large proportion of the total amount spent by prisoners each week.[108]

UK prison staff have suggested that issues historically relating to tobacco smoking prior to the smoke-free policy have now shifted onto e-cigarettes since the move; pre-filled e-cigarettes capsules have become a new form of currency leading to debt and bullying, alongside being a vehicle for drug use, and there are ongoing issues with policing e-cigarette use outside permitted areas of the prison.[98,102] Due to the e-cigarette capsules becoming a new form of currency, prisons have introduced limits on the amount of capsules that people can purchase each week (set by each prison). Given the high percentage of vapers in prison, SPS staff have also highlighted concerns over workplace exposure to e-cigarette vapour and, on occasions, vapour from e-cigarettes used to inhale drugs.[102]

Some prisoners and staff have outlined concerns over what they perceive as heavy or excess e-cigarette usage (frequency of vaping and/or number of the highest strength e-liquid capsule consumed). Factors have been suggested as to why this might be occurring: poor nicotine delivery of the prison-issue vapes resulting in them not being 'strong enough'; the majority of prisoners vaping 18 mg capsules (regardless of how much they smoked prior to prison) due to this strength being predominantly what prisoners trade in (with lower strength capsules being perceived as having a lower monetary trading value); and as a strategy for managing negative emotions in prison, especially boredom.[98,102,109] Staff and prisoners in these studies have gone on to voice the need for a greater range of e-cigarette products from the canteen, including more powerful, robust devices, offering improved nicotine delivery and a greater variety of e-liquid strengths and flavours.

Prison staff working in smoke-free prisons across the UK anticipate that most prisoners will simply return to combustible tobacco upon release.[98,102] One study has recorded relapse to smoking upon release from smoke-free prison in the UK, with 60% of former (pre-prison) smokers regularly using combustible tobacco 3 months after release, with the majority of these returning to combustible tobacco on the day of release.[106] Over half of prisoners also reported not taking their prison-issue e-cigarette into the community. Staff working in the English prison estate have commented upon how few prisoners take their prison e-cigarette home, but highlighted that giving or selling possessions was often a rite of passage for prisoners before their release.[98]

Since UK research suggests that over half of prisoners want to stop smoking,[110,111] the shift to e-cigarette use in this disadvantaged population offers an opportunity to promote a tobacco-free life (both inside and outside of prison) in a group who experience huge health inequalities. Providing education on the use of e-cigarettes as a cessation device in prison may go some way to support this; NHS Scotland has recently released guidance on how to cut down or quit vaping for those supporting people living in a prison environment.[105] In addition, reviewing the efficacy of the vapes available to prisoners could help to prevent resumption of tobacco smoking after release. A complex intervention is currently being piloted to support prison leavers to remain tobacco-free upon release. Part of this intervention involves providing a new e-cigarette, offering improved nicotine delivery, to prisoners at the point of release.

### 4.3.7 Social housing

At the time of writing, there is limited evidence regarding tobacco smoking and cessation within social housing. Most research on socio-economic inequalities in smoking and cessation has focused on other socio-economic variables such as occupation and income.[112] However, analysis of data from the Smoking Toolkit Study (a monthly cross-sectional survey representative of adults in England) examined a range of socio-economic status predictors for smoking cessation and found the strongest predictor to be housing tenure.[113,114] Approximately one-third of social housing residents in England smoke combustible tobacco (37%), more than twice the prevalence of other housing tenures.[114] This disparity is increasing, due to a relatively muted reduction in smoking prevalence among social housing residents compared with the general population.[114] Despite overlap with other indicators of socio-economic inequality, this discrepancy is not fully explained by these other markers.[113] As such, the health and economic problems caused by smoking are disproportionately high in this population, with

246,000 (~5%) of socially rented households in England estimated to be in poverty as a direct result of tobacco smoking.[115] However, evidence suggests that the majority of social housing residents who smoke want to quit, are as motivated as the rest of the population to do so, are more likely to have made a serious quit attempt in the past year, and to have used evidence-based support to do so.[114] As social housing could also provide an opportune setting to embed smoking cessation support, this is an area that deserves more attention. In April 2023, the UK's Department of Health and Social Care announced addressing smoking in social housing as a priority area for action.[116]

In a 2022 report, Action on Smoking and Health (ASH) and the Housing Learning and Improvement Network (LIN) reported on case studies of local authorities beginning to implement smoking cessation guidance and support within local social housing teams.[115] A strategy developed by the Greater Manchester Health and Social Care Partnership resulted in two e-cigarette pilot projects that aimed to recruit people who smoked tobacco living in deprived areas in the north-west of England.[36,117] Recruitment for both pilots took place throughout the wider community, through organisations such as pharmacies, stop smoking services and workplaces, with targeted efforts in social housing. In both studies, participants were provided with reusable e-cigarettes, chargers and e-liquids (e-cigarette starter kits) through community stop smoking services or pharmacies. Providers were also encouraged to provide participants with behavioural support.[36,117]

In the first of these studies (Swap to Stop, n=1,022), the most popular flavour e-liquid chosen by participants was mixed fruit (a median of six bottles per person distributed), compared with tobacco (median zero bottles) and menthol (median one bottle) flavours.[36] At 4-week follow-up, 37% of participants were confirmed to be using an e-cigarette and abstinent from tobacco smoking (biochemically validated using exhaled carbon monoxide (CO) of less than 10 parts per million (ppm)); assuming those lost to follow-up continued to smoke tobacco. Of those who still smoked tobacco and were in contact at 4 weeks (n=226), the average number of cigarettes smoked per day had reduced from 19 to nine. A comparison of the cost of the Swap to Stop approach versus standard support (including provision of NRT rather than e-cigarettes) found that Swap to Stop was considerably cheaper; £159.73 compared with £322.65 per quitter. This new approach, incorporating e-cigarettes, increased demand for stop smoking services and the number of people making a quit attempt, increased nearly threefold compared with the same quarter in the previous year. The difference was most notable in the most deprived quintile.[118]

The second study provided e-cigarettes to 871 participants. 21.1% were biochemically confirmed (exhaled CO <5 ppm) abstinent from tobacco smoking at 4-week follow-up, assuming those lost to follow-up were still smoking.[117] As with the Swap to Stop study, participants who reported still smoking at follow-up approximately halved the average number of cigarettes they smoked per day (from 19 to nine; n=178) and reduced their exhaled CO levels (from 15 to 9 ppm, n=104).[117] In both studies, people in the least deprived quintiles were more likely to benefit from the intervention than people in the most deprived quintiles, and the follow-up periods were short (4 weeks).[36,117] It is likely that some people may take longer than 4 weeks to switch entirely to e-cigarettes. Participants in the second pilot were followed up via text message after 12 months; however, loss to follow-up was high at 91%.[117]

Qualitative participant insights resulting from the second pilot and from further insights work (surveys, focus groups and interviews) in 2022 within social housing in Greater Manchester found that, as well as health, motivators for using e-cigarettes included saving money and lessening smell indoors.[117,119] However, concerns have been raised over the potential long-term health impacts of vaping across studies.[117,119,120] For example, the English Housing Survey found that 17% of people who smoked and lived in social housing reported safety concerns as the main reason they had not tried e-cigarettes, compared with 10% of private renters and 7% of homeowners who smoked.[120]

Within the social housing population that took part in the Greater Manchester insights project, 28% of people who currently smoke tobacco and 33% of people who had previously smoked tobacco reported using nicotine e-cigarettes.[119] People reporting mental health issues were more likely to use e-cigarettes. Of the people who reported e-cigarette use, 88% said that they had used them to cut down or stop smoking tobacco and, of this group, 32% had remained abstinent from tobacco smoking, 42% were using an e-cigarette and sometimes smoking combustible cigarettes, and 26% had gone back to cigarette smoking only. After quitting using willpower alone (52%), e-cigarettes were the most commonly reported smoking cessation method used (46%).[119] The Smoking Toolkit Study found that rates of e-cigarette use during a quit attempt were similar in social housing residents (33.9%) to those residing in other housing types (32.1 %) between 2015–20.[114]

E-cigarette starter kit provision has proved popular among social housing residents who smoke tobacco.[36,117] 49% of participants in the Greater Manchester insights work reported that being provided with an e-cigarette starter pack would encourage them to access a smoking cessation service.[119] Modelling by University College London estimates that providing targeted quitting support, including an offer of a free e-cigarette starter kit, to people who smoke and live in social housing across England would result in approximately 298,000 additional long-term ex-smokers between 2022–30.[121] This could result in a 3.9% reduction in the number of people who smoke living in social housing and positively contribute to reducing disparity in the prevalence of tobacco smoking in social housing compared with other housing tenures.

## 4.4 Contribution of e-cigarettes to quitting smoking in the general population

This section summarises a new analysis that aims to estimate the contribution of e-cigarettes to smoking cessation in England using time-series data from the Smoking Toolkit Study (STS) from Q1 2007 through Q4 2022.[122]

As summarised in the first section of this chapter, there is high-certainty evidence from randomised controlled trials that using an e-cigarette increases quit rates compared with NRT. While randomised controlled trial evidence is the gold standard, its 'real-world' generalisability is limited, but can be augmented through observational studies in the general population.[123,124] Observational studies are particularly relevant for e-cigarettes due to the rapid change in device types, patterns of uptake and usage, evolution of e-cigarette promotion and regulation, and public perceptions since e-cigarettes first started to become popular around 2011 in England.[125,126] The STS, which is a monthly household survey representative of adults in England, has been measuring e-cigarette use and smoking cessation from 2006 through to 2024. This offers a unique opportunity to assess the impact of changes in the prevalence of e-cigarette use on key population-level measures of quitting among smokers, and thereby provides an up-to-date estimate of their contribution to smoking cessation in England.

Previously published time-series analyses up to 2015 and subsequently 2017 established that population-level changes in e-cigarette use in England were positively associated with quitting.[127,128] The new analysis extends these time-series for a further 23 quarters (up to the end of 2022). The longer time-series provides increased power to estimate associations between e-cigarette use and key quitting outcomes, and to assess whether associations have remained stable despite substantial changes in the types of e-cigarette devices being used. This analysis aimed to: (i) provide up-to-date estimates of how changes in the prevalence of e-cigarette use have been associated with changes in smoking cessation activities and use of licensed treatments among smokers in England, and (ii) explore changes in these associations over time.

Details on the design of the STS are provided in chapter 3 and elsewhere.[129,130] Data from the STS were aggregated quarterly on 70,240 past-year smokers (aged 18 and over) between Q1 2007 and Q4 2022. Explanatory variables were prevalence of (i) current e-cigarette use among smokers and (ii) e-cigarette use during a quit attempt. Outcomes were rates of quit attempts and overall quits among past-year smokers, and the quit success rate and use of licensed treatments among those who made a quit attempt. Autoregressive Integrated Moving Average with Exogenous Input (ARIMAX) modelling was used to estimate unadjusted and adjusted associations of e-cigarette use with quitting activity.[131,132] The adjustments included were government mass media spending, tobacco control policies and onset of the COVID-19 pandemic.

The success rate of quit attempts increased by 0.040% (95% CI: 0.019, 0.062) for every 1% increase in the prevalence of e-cigarette use during a quit attempt in England, after adjustment for a range of confounding variables. No clear evidence was found for an association between current e-cigarette use and the quit attempt rate ($B_{adj}$=0.008, 95% CI: -0.045, 0.061) or overall quit rate ($B_{adj}$=0.063, 95% CI: -0.031, 0.158); or between use of e-cigarettes during a quit attempt and the overall quit rate ($B_{adj}$=0.030, 95% CI: -0.054, 0.114), use of prescription medication ($B_{adj}$=-0.036, 95% CI -0.175, 0.102), or use of over-the-counter NRT ($B_{adj}$=-0.052, 95% CI: -0.120, 0.015). In analyses restricted to including only new data since Q2 2017, there was no clear evidence that this pattern of associations has changed substantially over time. Finding an association between use of e-cigarettes in a quit attempt and quit success, but no clear evidence of an association with the overall quit rate, may appear contradictory. However, the point estimates (0.040 and 0.030 respectively) were consistent with each other; the difference is that the latter had a wider 95% CI and was not statistically significant. The overall quit rate is a function of the rate of quit attempts and quit success, and insofar that the use of e-cigarettes in a quit attempt primarily affects quit success, quit

success would be a more sensitive outcome than the overall quit rate.

Consistent with previous analyses based on data up to 2015[127] and 2017,[128] the success rate of quit attempts increased significantly as the percentage of smokers using e-cigarettes during a quit attempt increased (eg 2017: $B_{adj}$ = 0.060 (0.043–0.078); 2022: $B_{adj}$ = 0.040 (0.019–0.062)). Results for quit attempts and use of licensed smoking cessation treatments were in line with previous analyses, which also showed no clear evidence for an association with e-cigarette use, implying that e-cigarettes have not subsumed the use of other pharmacological treatments in England.[127,128]

Based on the latest results and the changing smoking population, the estimate for the contribution of e-cigarettes to the numbers of people stopping smoking in England, over and above what could otherwise have been expected, was updated. While these findings are associations and not causal, the data suggest each 1 percentage point increase in e-cigarette use in quit attempts could result in a 0.040 percentage point increase in quit success rate. It is estimated that 710,622 smokers used e-cigarettes during a quit attempt (5,820,000 smokers in England × 0.37 making a quit attempt × 0.33 e-cigarette prevalence in those making a quit attempt), which equates to approximately 28,400 (710,622 × 0.040) additional past-year smokers who reported no longer smoking as a consequence of e-cigarette use in a quit attempt in 2022 in England.

This estimate is lower than the 2017 estimate (50,700) because of the numerical difference in the effect size used in the calculation (0.040 vs 0.060, although there is no evidence that this is a significant decline) and the reduction in the overall population of smokers (5.82 million vs 7 million). Collectively, these analyses suggest that the use of e-cigarettes in quit attempts has helped in the region of 30,000–50,000 additional smokers to quit successfully each year in England since they became popular during 2013.

This estimate assumes that the mechanism by which e-cigarettes help smokers transition to ex-smokers is to support a quit attempt. However, it may be that some smokers use e-cigarettes and end up cutting down and stopping without an intention to quit cigarettes and do not report a 'quit attempt'. A previous paper showed a positive association between changes in current e-cigarette use and overall quit rate, and used this to calculate an alternative estimate for the additional number who were helped by e-cigarettes directly or indirectly to quit smoking, which produced a larger figure of ~70,000 in 2017.[128]

Although the point estimate for the association between current e-cigarette use and overall quit rate in this new analysis was similar to the 2017 figure (0.063 vs 0.054 respectively), because it was not statistically significant, this calculation has not been updated.

In conclusion, changes in prevalence of e-cigarette use in England through to 2022 have been positively associated with the success rate of quit attempts, but not clearly associated with the quit attempt rate, overall quit rate or use of licensed smoking cessation treatments. If the association is causal, then the use of e-cigarettes in quit attempts appears to have helped in the region of 30,000–50,000 additional smokers to quit successfully each year in England since 2013.

## 4.5 Relapse prevention

As described in section 4.1, e-cigarettes with nicotine have been shown to be more effective than traditional NRT products to help people to stop smoking.[2] This may be because they afford better control of nicotine intake than NRT products and allow smokers to retain some of the enjoyment and other subjective rewards that they previously obtained from smoking. The higher appeal of e-cigarettes to smokers compared with other stop-smoking aids has an important corollary: more smokers who successfully stop smoking with the help of e-cigarettes continue to use them. For example, in a large UK trial, 80% of stop-smoking service clients who stopped smoking with the help of e-cigarettes were still using them at 1 year (with a third of them using nicotine-free e-cigarettes), while only 9% continued to use NRT.[133]

Post-cessation use of e-cigarettes raises an important question of whether it affects relapse back to smoking. Theoretical arguments can be made that such use may protect from relapse, eg by satisfying the user's needs or reducing the risk that an occasional lapse translates into a relapse;[134] but also that it may facilitate relapse, eg by maintaining sensitivity to smoking cues[134] or making users who continue to want to use a nicotine product vulnerable should new regulations or perceptions make e-cigarettes less attractive or less available than cigarettes.

Several cohort studies compare relapse rates in ex-smokers who do and do not use e-cigarettes, mostly using the US Population Assessment of Tobacco and Health (PATH) longitudinal cohort.[136–141] The PATH study follows up a representative US sample that started with 49,000 participants in 2013. A meta-analysis of these studies reported that e-cigarette use is associated with relapse (RR=2.03 (95% CI: 1.39, 2.96).[142] The causal nature of

this association is unclear, in part because smokers who have quit unaided are likely to have been less dependent smokers and so less vulnerable to relapse than those who needed nicotine-containing aids to stop smoking. In addition, most ex-smokers in the PATH cohort stopped smoking before e-cigarettes became widely available. As duration of abstinence is a strong predictor of relapse, non-e-cigarette users in this cohort would be expected to be less likely to relapse than e-cigarette users who quit much more recently. The only study that controlled for duration of abstinence found no association between e-cigarette use and relapse.[140]

In the absence of randomised trials of e-cigarettes for relapse prevention, randomised trials of relapse prevention using NRT can provide some indication of the likely effects. Four trials examine effects of NRT in relapse prevention. Two studies examined relapse rates at 2 and 6 months in smokers abstaining for 1 or 2 days without any aids and then for 3 months, using nicotine chewing gum vs placebo or no NRT; these found the NRT intervention effective.[143,144] The other two studies included abstainers assisted by treatment who were randomised to NRT or alternatives after the initial 2–3 months' abstinence.[145,146] Their combined results did not show an effect, but actual use of NRT was very low.[147]

The latest Cochrane review does not contain data on relapse rates in early abstainers who did and did not use e-cigarettes,[2] but new (unpublished) secondary analyses of two large trials are presented here.[9,133] Both trials found e-cigarettes more effective than NRT for smoking cessation. The data were first examined to see whether the difference between the study arms increased or decreased over time, as this would indicate different relapse rates. This is not the same as comparing ex-smokers who do and do not use e-cigarettes, because not all participants randomised to the e-cigarette arm were using e-cigarettes post-cessation, while some allocated to the NRT did, and some NRT arm participants used NRT in the long term. However, long-term e-cigarette use was much more common in the e-cigarette arms and so this approach can provide some relevant information. In a trial in smokers accessing stop-smoking services, the effect sizes at 4 weeks and 12 months were RR=1.45 (95% CI: 1.22, 1.74) vs RR=1.83 (95% CI: 1.30, 2.58); the relapse rate tended to be lower in the e-cigarette arm.[133] In a trial that included pregnant smokers, only self-reported point prevalence rates were available at 4 weeks and so this was also used for quit rates at the end of pregnancy.[9] Effect sizes at 4 weeks and at the end of pregnancy were RR=1.45 (95% CI: 1.07, 1.97) vs RR=1.51 (95%, CI: 1.16, 1.96). Next, relapse rates in participants abstinent at 4 weeks, who used e-cigarettes daily at that time, were compared with those of the rest of the 4-week abstainers. In the first study, the relapse rates at 6 months were 33% and 44% (RR=0.76, 95% CI: 0.57, 1.00), while at 1 year the figures were 59% vs 72% in these two groups (RR=0.83, 95% CI: 0.71, 0.97). E-cigarette use was thus associated with reduced relapse, with the effect increasing over time. In the second study, relapse rates between 4 weeks and the end of pregnancy were similar; 32% in abstainers using e-cigarettes daily vs 35% in the rest of the abstainers at week 4.

It is difficult to design a randomised controlled trial that would provide a clear indication of the effects of continued e-cigarette use on relapse back to smoking. One approach would be to randomise recent ex-smokers not using any nicotine product to use e-cigarettes or not, as was done with NRT in the studies mentioned above. The question about e-cigarettes' effects on relapse, however, concerns primarily smokers in the general population who stopped smoking with the help of e-cigarettes and decided to continue e-cigarette use, rather than the scenario in which people who quit smoking unaided are asked to start using e-cigarettes. Another approach would be to start with a cohort of smokers who are quitting with the help of e-cigarettes and randomise those who successfully quit and still use e-cigarettes at 1 month to either continue e-cigarette use or not. This, however, raises the ethical issue of asking successful quitters who wish to continue using e-cigarettes to stop such use, and risk relapse to smoking.

A more informative approach is for trials that include e-cigarettes to compare short- and long-term effect sizes to see whether e-cigarette arms, where the majority of abstainers are likely to continue to use e-cigarettes, differ in relapse rates from non-e-cigarette arms. Finally, in cohorts of people using e-cigarettes to stop smoking within stop-smoking services, relapse rates can be compared in early quitters who do and do not use e-cigarettes. This would face some of the problems of cohort studies and could not rule out the influence of unmeasured differences between these groups, but it would include ex-smokers who stopped smoking at the same time and who are roughly matched for tobacco dependence and a desire to quit as they were all seeking help with stopping smoking.

In conclusion, the limited data currently available offer a mixed picture and further studies are needed to provide clearer answers.

## 4.6 Supporting cessation of e-cigarette use

There are various reasons why people who have used e-cigarettes for smoking cessation may ultimately want to stop using e-cigarettes. Commonly cited reasons include cost, concerns around health, perceptions of friends and family, concerns about dependence, and stigma.[148] General advice is that people who use e-cigarettes to quit smoking should consider stopping using e-cigarettes when they are no longer at any risk of relapsing to smoking. However, there is a dearth of evidence on how to do this and how to minimise any risk of smoking relapse. As smoking is considerably more harmful than vaping, it is critical that vaping cessation efforts do not lead to re-uptake of smoking.

There have been trials of interventions for quitting vaping in current smokers, ex-smokers and people with no history of regular smoking.[149] The largest trial of vaping cessation to date was conducted in the USA by Graham ***et al*** and recruited 2,588 young adult (18–24 years of age) current e-cigarette users. Participants were randomised to an 8-week tailored interactive text programme or to assessment only. At 7 months, treatment was found to be effective compared with control (24.1% 3-day self-reported vaping abstinence, compared with 18.6% in the control group).[150] In a small pilot study, 24 adults were randomised to 12 weeks of treatment, in the form of either a) NRT and behavioural counselling, b) tapering nicotine delivery via e-cigarettes and behavioural counselling, or c) self-guided quitting. The study was not powered to investigate effectiveness but found that people in the tapering arm were more likely to be e-cigarette and nicotine free at 6 months.[151] In another small study, 30 participants were randomised to either a 28-day supply of combination NRT (patch and lozenges) and a supportive booklet, or a referral to the state stop smoking 'Quitline'. Again, the study was not powered to evaluate effectiveness, but initial findings favoured NRT over the Quitline services.[148] Preliminary evidence from an unpublished trial in 140 adult e-cigarette users found that abstinence rates were higher for those randomised to varenicline rather than a placebo at all time points.[152]

Vaping cessation apps currently on the market have been found to have limited features developed specifically for vaping cessation, instead drawing on content from smoking cessation apps.[153] A recent pilot trial in 58 adults (aged 20–43 years) tested a text messaging programme designed to support vaping cessation versus a link to an e-cigarette cessation website. The participants who received the text messaging programme were further randomised to receive automated text messaging alone or automated texts plus live counsellor-delivered messages. Findings suggest that the text programmes, particularly with live support, show promise for e-cigarette cessation, but a larger trial is warranted to assess efficacy.[154]

In summary, there is little evidence on best ways to support people to quit vaping, and even less evidence for the subgroup of people who have used vaping to quit smoking. Further studies are required.

## 4.7 Cost-effectiveness of e-cigarettes for smoking cessation

Cost-effectiveness analysis is a valuable tool for evaluating health interventions by weighing their health benefits against their financial or resource costs.[155] This analysis is instrumental in discerning which interventions make the most efficient use of NHS resources, especially in the context of supporting e-cigarettes as a smoking cessation aid using public funds, particularly in comparison to NRT. In the UK, licensed smoking cessation options encompass various doses of NRT, bupropion and varenicline.[156] Simultaneously, e-cigarettes and combination approaches, although not officially licensed, are offered through programmes providing subsidised starter packs for individuals seeking to quit smoking. Standard practice entails tailoring NRT to a smoker's level of nicotine dependence, with the standard NRT dose tending to serve as a reference point for cost-effectiveness evaluations. The outcomes of comparisons among aids to quitting smoking based on cost-effectiveness analysis depend on four key factors: the intervention's lifetime costs, its effectiveness in achieving sustained smoking cessation and its overall health impact, considering both cessation benefits and any adverse effects, as well as the long-term healthcare cost impacts. Utilities are frequently used to quantify health gains in economic analyses, assigning numerical values to health states through population surveys. Utilities are anchored on two numerical points, with 1 denoting perfect health and 0 denoting a health state equivalent to death. Quality-adjusted life years (QALYs) are calculated by multiplying a patient's life expectancy by their expected utility. Cost-effectiveness is enhanced when interventions yield greater QALY gains at lower costs. Central to cost-effectiveness analysis is the incremental cost-effectiveness ratio (ICER). The ICER estimates the extra cost of gaining each additional QALY through the use of one intervention versus another. In the UK, NICE typically considers a 'willingness to pay' threshold of between £20,000 and £30,000 per QALY

gained.[157] This threshold is used to calculate the expected net benefit of an intervention, where the expected net benefit is the expected QALY gain per patient multiplied by the willingness to pay threshold (eg by £20,000), from which the average cost per patient of the intervention is subtracted. Another way of thinking about the difference in net benefits between an intervention and usual practice is that the difference in net benefit is the economic gain to society if the difference is positive, or loss to society if the difference is negative, of adopting the intervention rather than continuing usual practice. Interventions with higher net benefits are judged to be more cost-effective.

To date, few studies have investigated the cost-effectiveness of e-cigarettes for smoking cessation; however, existing evidence shows that when smoking cessation interventions in general are effective (ie they produce health gains), they are typically also cost-effective.[158–160] This is in large part due to their relatively low cost and the significant impact that smoking cessation has on long-term health outcomes. Current evidence, though limited, indicates that e-cigarettes are likely to be cost-effective.

An economic evaluation comparing e-cigarettes with NRT in English stop smoking services found evidence that offering e-cigarette starter packs within the standard services is a cost-effective approach compared with NRT.[158] The cost-effectiveness analysis was based on a randomised controlled trial involving 886 adult participants enrolled in, and receiving support sessions from, the English stop smoking services. The primary objective was to compare the effectiveness and cost-effectiveness of e-cigarettes with NRT in aiding smoking cessation. The study also investigated whether participants incurred higher expenses on smoking cessation when using e-cigarettes. One group received up to 3 months NRT, either provided for free or with a prescription charge, while the other group received a reusable 'One Kit' e-cigarette device, along with a starter kit of e-liquid (18 mg/mL nicotine) and instructions on where to purchase more. One unusual aspect of smoking cessation from a cost-effectiveness perspective is that NICE only considers NHS expenditure, so if one option costs individuals more, then that is not a consideration for the cost-effectiveness calculation, but it is relevant for the individual's motivation to quit. From a cost-effectiveness perspective, the primary analysis revealed an ICER of £1,100 per QALY gained when considering a 12-month time horizon, ie the decision maker would need to spend £1,100 and over providing e-cigarettes for e-cigarettes to be considered a cost-effective option. This was based on the average cost of treatment being £11 higher with an e-cigarette than NRT. When extending the evaluation to a lifetime perspective using a model of smokers aged 41 and over, the study estimated the lower ICER of £65 per QALY, indicating that offering e-cigarettes as a treatment option is highly cost-effective compared with NRT. This was based on smokers using e-cigarettes having a slightly higher estimated remaining lifetime cost of treating smoking-related diseases of £3,184 per smoker, compared with £3,175 for smokers using NRT. However, in addition, smokers using e-cigarettes were estimated to have a higher expectation of remaining QALYs of 24.28 per smoker who used e-cigarettes, compared with 24.14 QALYs for smokers who used NRT. Sensitivity analysis that factored in the uncertainty around these marginal differences supported the finding that e-cigarettes are cost-effective from a lifetime perspective, estimating that there is an 85% probability of the ICER falling below the £20,000 per QALY threshold. Examining the participant expenditure on smoking cessation aids in the e-cigarette and NRT groups, the study found no substantial differences. Furthermore, the costs associated with smoking cessation borne by the Stop Smoking Services and NHS were lower in the e-cigarette group. This suggested that implementing e-cigarette interventions could potentially reduce financial burdens on stop smoking services and the NHS without imposing additional costs on individuals attempting to quit smoking.

A further modelling study, which took care to account for the health outcomes and costs due to depression and self-harm that can be associated with the use of smoking cessation aids, also found e-cigarettes to be cost-effective compared with other smoking cessation medications available in the UK.[160] The modelled population consisted of individuals aged 18 and above who were smokers in the UK. In the base case scenario, the study compared various licensed interventions, including different doses of NRT, bupropion and varenicline. Additionally, e-cigarettes and combinations of interventions, though not currently licensed in the UK, were included in a sensitivity analysis. Notable findings from the study included the observation that low-dose e-cigarettes consistently emerged as the most cost-effective option, outperforming other interventions in terms of QALYs gained and lower costs. At a willingness-to-pay threshold of £20,000, low-dose e-cigarettes had the highest expected net benefit (£7,085 per patient), followed by specific combinations of standard-dose varenicline and bupropion, or standard-dose varenicline with NRT. When considering all interventions, low-dose e-cigarettes consistently proved to be the most cost-effective choice for willingness-to-pay values exceeding £56, ie the model estimated an ICER of £56 per QALY. This indicated that low-dose e-cigarettes

provided optimal value for money. Furthermore, the study found that when adverse events were not considered, the combination of varenicline and NRT was the most cost-effective option. However, when adverse events were factored in, low-dose e-cigarettes and the combination of standard-dose varenicline and bupropion became more cost-effective.

In summary, the studies underscore the high cost-effectiveness of low-dose e-cigarettes as a smoking cessation aid and highlight the importance of conducting trials that compare e-cigarettes with other smoking cessation aids to assess their safety and efficacy in both short- and long-term contexts.

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# 05

# Health effects of e-cigarettes

## Key points

- Vaping exposes vapers to a far narrower range of toxins than does smoking cigarettes, and levels of toxins absorbed from vaping are generally low. It is therefore likely that vaping poses only a small fraction of the risk of smoking.
- Blood levels of nicotine and its metabolites in vapers are similar to or lower than those in smokers, and carbon monoxide levels are lower.
- Levels of tobacco-specific nitrosamines, volatile organic compounds and polycyclic-aromatic hydrocarbons are lower in vapers than in smokers and are higher or similar to non-vapers/non-smokers.
- There is inconsistent evidence whether vapers have higher levels of lead, cadmium, arsenic or mercury than smokers. Levels of lead and cadmium were higher, and levels of arsenic lower or equal between vapers and non-vapers/non-smokers.
- Vapers show similar or lower levels of markers of oxidative stress and inflammation to those in smokers and similar levels compared with non-vapers/non-smokers.
- Findings of research into disease-specific biomarkers has yielded mixed results.
- There is some evidence that passive exposure to vaping aerosol results in some nicotine absorption, and in one study, evidence of inflammatory change in those exposed.
- Evidence on the effects of vaping in pregnancy remains mixed.
- Vaping nicotine is not associated with a high frequency of adverse health effects after accounting for past smoking history.

## Recommendations

- Agreement needs to be reached on the methods for vaping health risks research, including which biomarkers are the most relevant to study regarding the relative and absolute risks of vaping.
- Large longitudinal cohort studies are needed: firstly, of people who vape and have never smoked, and secondly, of former smokers who vape and which adequately account for their smoking history.

# 5.1 Introduction

In this chapter we discuss the health effects of vaping. We draw on several sources of published evidence (see Box 5.1), including a new systematic review conducted specifically for this report. We do not include cannabis vaping or vaping of other illicit substances.

**Box 5.1 Evidence sources**

1. McNeill *et al. Nicotine vaping in England: an evidence update including health risks and perceptions, 2022*.[1] A report commissioned by the Office for Health Improvement and Disparities drew on the systematic literature review of studies exploring vaping associations with exposure to toxicants and change in biomarkers of potential harm.
2. A new systematic review, funded by Cancer Research UK, updating the McNeill *et al* report[1] using a more refined set of criteria for study selection.
3. A new systematic review on the health consequences of vaping in pregnancy.[2]
4. Adverse and serious adverse event data in a Cochrane living systematic review on e-cigarettes for smoking cessation by Hartmann-Boyce *et al*.[3]
5. Drug analysis prints on e-cigarettes by the Medicines and Healthcare products Regulatory Agency.[4]

In this chapter we investigate two categories of biomarkers. The first set are biomarkers of exposure, which are tobacco-related chemicals or their metabolites that can be detected in the human body; these include nicotine, tobacco-specific nitrosamines, volatile organic compounds, aromatic amines, polycyclic-aromatic hydrocarbons and metals. The second category are biomarkers of potential harm, sometimes referred to as biomarkers of effect, such as markers of oxidative stress and inflammation, which are signs of the effect of vaping or smoking in the body, for instance heart rate, blood pressure or lung function. Key diseases associated with these biomarkers include cancer and respiratory and cardiovascular diseases. These biomarkers are compared between people who vape, people who smoke, people who do both (dual use) and people who do neither (non-use).

The health effects of vaping have been the subject of multiple systematic reviews, including the National Academies of Sciences, Engineering and Medicine (NASEM) report on the public health consequences for e-cigarettes,[5] the Committee on Toxicity statement on the potential toxicological risks from electronic nicotine (and non-nicotine) delivery systems[6] and McNeill *et al*'s recent evidence update on nicotine vaping in England commissioned by the Office for Health Improvement and Disparities (OHID), Department of Health and Social Care, England.[1] As this is a rapidly evolving field, we have updated the comprehensive systematic review and meta-analysis of studies of health risks reported by McNeill *et al*[1] with some adaptions to the eligibility criteria for this report. This updated review focuses on health biomarkers, like the original review. We also include a summary of a systematic review on the health consequences of vaping in pregnancy. We did not assess self-reported symptoms, which constitute a much greater literature, but are also often assessed subjectively and retrospectively. The temporality of self-reported symptoms in relation to vaping or smoking exposure is frequently unclear and unaccounted for and, as a result, these studies have been the subject of criticism. We did, however, include data on safety of vaping, drawing on two additional sources: 1) adverse event data reported in intervention studies, taken from the Cochrane living systematic review on e-cigarettes;[7] and 2) the UK's Medicines and Healthcare products Regulatory Agency (MHRA) Yellow Card data on e-cigarettes, which cover suspected adverse events believed to be associated with e-cigarettes reported to the MHRA by health professionals or members of the public.

## 5.1.1 Overview and findings of a systematic review commissioned by OHID

McNeill *et al*'s systematic review of biomarkers of absolute and relative exposure and potential harm of vaping identified 231 (human) studies published between August 2017 and July 2021.[1] The review included 60 studies on exposure to nicotine and its metabolites, 28 on tobacco-specific nitrosamines (TSNAs), 23 on volatile organic compounds (VOCs), 10 on other potential toxicants (aromatic amine, polycyclic aromatic hydrocarbons (PAHs) and ortho-toluidine), 10 on metals, 32 on carbon monoxide (CO) and six on second-hand exposure. The most frequent studies were of acute or short- to medium-term exposure, with the maximum exposure length being a study of 5 years (2 years retrospective and 3 years prospective).

Regarding exposure to nicotine and its metabolites (cotinine, total nicotine equivalents, 3-hydroxycotinine), McNeill *et al* reported finding generally lower acute exposure to nicotine after short-term use (up to 7 days) of e-cigarettes compared with smoking, but similar exposure to nicotine over studies of medium- to longer-term duration (longer than 7 days).[1] This indicated that, with experience, people who vape can achieve similar levels of nicotine exposure to when they were smoking cigarettes. There were differences in nicotine exposure across devices, with higher exposure being associated with tank and modular vaping devices. Although assessed in few studies, there was evidence of compensatory puffing behaviour to achieve preferred nicotine levels when using lower nicotine strength liquids, and in one longitudinal study this was evident among people who vaped who reduced their e-liquid nicotine concentrations over time, the reasons for which were unknown. Regarding exposure to TSNAs, findings were generally consistent that 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and N'-nitrosonornicotine (NNN) levels among people who vaped were substantially lower than among people who smoked, and slightly higher than or similar to those in non-users.

For exposure to VOCs, findings varied by biomarker, although in general most studies showed statistically significantly lower levels of VOC metabolites among people who vaped than in people who smoked, with substantial reductions in some biomarkers such as the acrolein metabolite 3-hydroxypropylmercapturic acid (3-HPMA), the acrylonitrile metabolite 2-cyanoethyl mercapturic acid (CNEMA) and 1,3-butadiene metabolite monohydroxybutenylmercapturic acid (MHBMA). Limited evidence on exposure to formaldehyde and toluene suggested no difference between vaping product use, smoking and non-use. Metabolites of benzene also did not differ statistically significantly between people who vaped, people who smoked and non-users. In relation to absolute exposure, all VOC biomarkers except CNEMA showed no significant differences between people who vaped and non-users. One study of CNEMA showed that average levels of CNEMA for people who vaped were over three times higher than those among non-users.

Findings across the studies that assessed heavy metals were inconsistent; some finding higher, similar or lower levels in those who vaped compared with those who smoked or non-users. Due to long half-lives of some metals, a history of smoking can greatly affect the levels of metals among people who stop smoking but vape.

McNeill *et al* examined four aromatic amines: 1-aminonaphthalene (1-AN), 2-aminonaphthalene (2-AN), 3-aminobiphenyl (3-ABP) and 4-aminobiphenyl (4-ABP), and from two RCTs reported statistically significant reductions in these four metabolites within a week of switching from smoking to vaping. The magnitude of exposure reduction was similar to those who switched to neither smoking nor vaping. One study reported statistically significantly higher levels of 2-AN compared to non-users. McNeill *et al* also examined ortho-toluidine (o-Tol) and reported statistically significant reductions within a week of switching to vaping. The evidence regarding exposure difference to o-Tol between people who vaped and non-users was not clear.[1]

Results for PAHs (pyrene and its metabolite 1-HOP, and benzo[a]pyrene and its metabolite 3-OH-B[a]P) found that exposure was significantly reduced after switching from smoking to vaping for at least 5 days. Greater reductions were seen in studies that were conducted in confinement rather than in ad libitum studies in real-world settings, possibly due to other environmental sources of PAHs apart from smoking. Studies reported lower exposure to PAHs among non-users compared with vapers, however findings were not consistent and participants' past or concurrent tobacco use may be contributing to some of the study findings.[1]

CO was substantially reduced after completely switching from smoking to vaping. Among people who smoked and vaped, the degree of CO exposure reduction was dependent on the amount of tobacco cigarettes smoked. Some interventional studies suggested that exposure to CO in smokers who completely switched to vaping might be reduced to levels similar to those in non-users. Reviewed evidence on second-hand exposure to vaping products showed that, after atypical overexposure, non-users demonstrated detectable biomarker levels of potential toxicants, but biomarkers of toxicants were usually non-detectable in shorter exposure situations.

Regarding biomarkers of potential harm, McNeill *et al*[1] also included 23 studies that assessed oxidative stress, 25 on inflammation, 11 on endothelial function and four studies on platelet activation. However, these studies were methodologically heterogeneous and findings were mixed. Regarding biomarkers of oxidative stress, there were no significant differences in low-density lipoprotein (LDL) cholesterol levels between people who vaped, people who smoked and non-user groups. Findings on high-density lipoprotein (HDL) cholesterol levels were inconsistent and studies with larger samples showed

statistically significantly higher HDL cholesterol levels among non-users than people who smoked or vaped; meta-analyses of cross-sectional studies, however, found no difference in blood HDL cholesterol levels between people who vaped and each of the other two groups. Evidence for 8-isoprostane level changes after vaping product use was mixed, with several confounders identified. There was limited evidence for the other oxidative stress biomarkers included.

There were mixed findings regarding the effect of vaping on inflammation biomarkers. Evidence from one RCT suggested that levels of interleukin-6 (IL-6), interleukin-8 (IL-8), tumour necrosis factor alpha (TNF-α) and white blood cell count (WBC) did not change after non-users vaped propylene glycol and vegetable glycerine liquid without nicotine for 4 weeks. A longitudinal study of 2 years also did not find changes in WBC counts after people who smoked switched to vaping, although many continued smoking. Results from other studies regarding IL-6, IL-8, TNF-α and WBC were mixed. Another RCT found no significant differences in high-sensitivity C-reactive protein (CRP) levels within or between groups, 4 weeks after people who smoked switched to vaping products with or without nicotine, or continued smoking. These latter findings were not confirmed by other interventional or cross-sectional studies; indeed, meta-analyses of three cross-sectional studies showed lower blood CRP and soluble intercellular adhesion molecule 1 (siCAM-1) levels among people who vaped than people who smoked, and levels of these inflammation markers were similar between people who vaped and non-users. There was also little evidence that vaping was associated with increased platelet activation biomarkers compared with smoking or not using tobacco or nicotine products and some evidence that endothelial function might deteriorate after acute exposure to vaping compared with non-use, but improves when people who smoke switch to vaping for a short- to medium-term period of time.

The systematic review by McNeill *et al*[1] also included an additional nine studies specifically on cancer-specific biomarkers related with gene expression, non-coding RNAs and DNA methylation. As highlighted above, exposure to potential carcinogens from vaping was significantly lower than smoking tobacco cigarettes, but greater than non-use.[1] There was a small amount of evidence that vaping might alter gene expression and DNA methylation, but it was not clear how much this may overlap with the alteration of gene expression and DNA methylation related to previous or current smoking. There was no available evidence on how vaping affected disease progression in people with an existing or a prior cancer condition. There were 25 studies relating to risks to respiratory health. Overall, the findings showed no immediate short- to long-term detrimental effects for people who vaped, whereas a clear worsening of lung function was seen in one small study of vapers who switched back to smoking for 7 days. Studies that assessed fractional exhaled nitric oxide had mixed findings, but most reported no significant differences across the user groups. However, McNeill *et al*[1] advised caution in interpreting the findings because of the heterogenous study designs, groups and duration of exposure, which limited any firm conclusions. Among people with existing respiratory conditions, four studies that included people with a diagnosis of asthma had very small sample sizes and the findings were inconclusive. Two longitudinal study papers including the same group of patients with COPD indicated that there was some evidence for reduction of COPD exacerbations among adult smokers with COPD who switched to vaping completely and continued vaping for up to 5 years. However, sample sizes were small and larger studies are needed to confirm these findings.

There were 41 studies that assessed biomarkers specific to cardiovascular health, most of which assessed heart rate or blood pressure. In meta-analyses, heart rate immediately after vaping was statistically significantly lower than immediately after smoking and not statistically different than no vaping or smoking. In a meta-analysis of longer-term vaping and smoking, a lower heart rate was also detected in people who vaped. Other longer-term studies not included in the meta-analyses mostly found no differences between groups who vaped and smoked; however, those categorised as vapers often also smoked. There were mixed results comparing people who vaped with people who smoked over the longer term. A meta-analysis of two longer-term cross-sectional studies found that people who vaped had a lower heart rate than non-users; however, one further cross-sectional study found the opposite and a longitudinal study found no significant differences in heart rate between people who vaped and people who did not use any nicotine products when followed up after 12, 24 and 42 months. Meta-analyses found no differences in blood pressure after acute exposure to vaping, smoking or non-use, with the exception of a small difference between vaping and non-use for diastolic blood pressure. Meta-analyses comparing groups with longer exposure found that people who vaped had

lower blood pressure than people who smoked and that there was no difference between people who vaped and people who did not vape or smoke. Studies that assessed pulse wave velocity found a general increase after acute exposure to vaping nicotine, but not after non-nicotine vaping. Studies that assessed flow-mediated dilation (FMD) found that, while acute exposure showed similar short-term reductions in FMD parameters after vaping (with and without nicotine) and smoking sessions, a single RCT showed that switching from smoking to vaping for 4 weeks significantly improved (increased) participants' FMD function.

The review by McNeill *et al*[1] concluded that vaping carries a small fraction of the health risks of smoking and, given the evidence from Cochrane reviews that they support people to stop smoking, people who smoke should be encouraged to use vaping products (or medicinally licensed products) for stopping smoking or as alternative nicotine delivery devices to reduce the health harms of smoking. The review also concluded that people who had never smoked or were long-term former smokers should be discouraged from taking up vaping (unless the person would otherwise relapse to smoking) as the degree of any long-term residual risk from vaping compared with non-use of tobacco or nicotine products remained unclear. McNeill *et al*.[1] stated that evidence was mostly limited to short- and medium-term effects and studies assessing longer-term vaping (for more than 12 months) were necessary; more standardised and consistent methodologies in future studies would improve interpretation of the evidence. Varying definitions of exclusive vaping across studies was one of the key methodological limitations noted by McNeill *et al*; therefore, the update of the review for this report included a stricter criterion for defining user groups, including minimum length and frequency of vaping.

For the updated systematic review, an investigation of two categories of biomarkers, as by McNeill *et al*,[1] is included but using a more focused list of biomarkers in both groups. The first set of biomarkers are biomarkers of exposure, the second are biomarkers of potential harm. These biomarkers are compared between people who vape, people who smoke, people who do both (dual use) and people who do neither (non-use). Stricter criteria for these groups are used than by McNeill *et al*[1] so that people in the vaping or smoking groups were using each product exclusively and regularly. Additionally for the non-user groups, where feasible, only people who had never smoked or vaped were included; where this wasn't possible, the possibility of confounding by prior smoking is noted. Second-hand exposure to vape aerosols was compared with second-hand exposure to tobacco smoke, and no second-hand exposure was also considered.

## 5.2 Methods for updated systematic review

A detailed description of the methods used for this updated systematic review, including stricter criteria for definition of vaping and narrower set of biomarkers investigated, and an algorithm to assess whether we could conduct meta-analyses, are provided in appendix 1. The funding sources of the studies included in the systematic review are included in Table A2.35 in appendix 2.

## 5.3 Results

Overall, the review identified 30 new studies for inclusion (Table 5.1). Two were controlled trials, one an RCT and one a non-randomised controlled trial (NRCT),[8–9] three were longitudinal cohort studies,[10–12] four were longitudinal cohort studies that reported cross-sectional findings or trends over time[13–16] and 21 were cross-sectional studies, some with multiple time points.[17–37] Two studies were from the UK,[24,33] 22 studies were conducted in the USA,[8–18,20–23,25,28–30,35,37] one in Spain,[27] one in South Korea,[26] one in Indonesia,[34] one in Russia[31] and one in four European countries – Spain, Greece, Italy and the UK.[19]

Twenty-nine studies assessed first-hand exposure, and two studies assessed second-hand exposure (one studied both).

**Table 5.1. Studies identified in the updated review**

| Biomarkers of exposure | Biomarkers of potential harm (cross-cutting and disease specific) | | | |
|---|---|---|---|---|
| | Cross-cutting | Cancer | Respiratory | Cardiovascular |
| Amalia 2023*[19] | AlMubarak 2021**[18] | Mori 2022[29] | Edmiston 2022[8] | Amraotkar 2023[20] |
| Addicott 2023[17] | Christensen 2021[22] | Reeve 2021[32] | Higham 2022[24] | Mohammadi 2022[28] |
| Amraotkar 2023[20] | Edmiston 2022[8] | Richmond 2021[33] | | Podzolkov 2021[31] |
| Anic 2022[10] | Hickman 2022[23] | Tommasi 2021[35] | | |
| Chaffee 2022[21] | Higham 2022[24] | Tommasi 2023[36] | | |
| Dai 2022[11] | Kamal 2022[25] | | | |
| Dai 2022[13] | Kim 2022[9] | | | |
| Edmiston 2022[8] | Lizhnyak 2022[15] | | | |
| Feng 2022[14] | Payton 2022[30] | | | |
| Hickman 2022[23] | Wang 2022[37] | | | |
| Lee 2022[26] | | | | |
| Lizhnyak 2022[15] | | | | |
| Melero-Ollonarte 2023[27] | | | | |
| Mohammadi 2022[28] | | | | |
| Mori 2022[29] | | | | |
| Morris 2022[12] | | | | |
| Payton 2022[30] | | | | |
| Sosnoff 2022[16] | | | | |
| Pamungkasningsih 2021[34] | | | | |
| Tommasi 2021[35] | | | | |

*First- and second-hand exposure studies, **Second-hand exposure study

## 5.3.1 Biomarkers of first-hand exposure

### 5.3.1.1 Nicotine and its metabolites

Nicotine is the major active component of tobacco, is addictive and acts as a stimulant (see chapter 2). Most adults and young people who vape use e-cigarettes containing nicotine. This updated review identified 20 new studies published since July 2021 that measured levels of nicotine (n=6), cotinine (n=16) and/or total nicotine equivalents (TNE, n=9). One was an RCT,[8] three were longitudinal cohort studies,[10–12] four were longitudinal cohort studies that reported cross-sectional findings or trends over time[13–16] and 12 were cross-sectional studies, some with multiple time points.[17,19,20,21,23,26–30,34,35] Sixteen studies were conducted in the USA[8,10–17,20,21,23,28,29,30,35] one in Spain,[27] one in South Korea[26] and one in Indonesia.[34] and one in four countries—Spain, Greece, Italy and the UK.[19] It is notable that two of the longitudinal observational studies were around 10 years old (and with a small number of people who switched to vaping at the 1-year follow-up). Similarly, many of the cross-sectional studies were also carried out several years ago. These data do not therefore reflect the performance of the newer nicotine vaping devices currently on the market.

#### 5.3.1.1.1 Vaping versus smoking

##### Longitudinal studies

One RCT[8] and one longitudinal study[12] reported non-significant increases in urinary TNE levels in people who smoked at baseline and switched to exclusive vaping for 24 weeks or 14 days, respectively. Following the algorithm, we meta-analysed data (Fig 5.1) from two randomised studies (one from the updated review[8] and one from a study included by McNeill *et al*[1]) that compared urinary TNE levels between people who vaped and people who smoked.

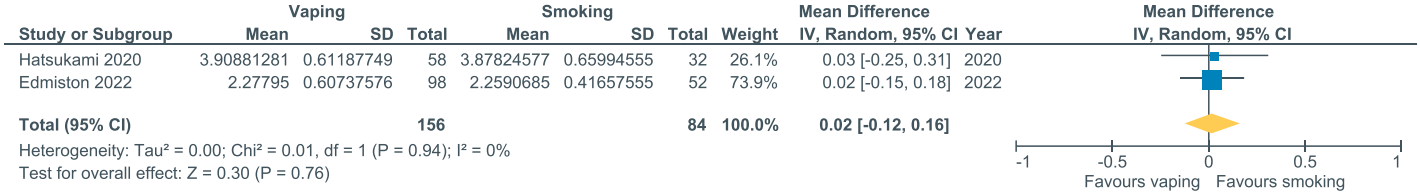


**Fig 5.1. Meta-analysis of randomised studies reporting on urinary total nicotine equivalent levels between people who vaped and people who smoked.**

The pooled data across two RCTs (mean differences on the log-transformed scale LMD = 0.02, 95% CI: -0.12, 0.16; 240 participants) showed that the geometric mean urinary TNE levels (GMR = 1.02, 95% CI: 0.89, 1.17) were approximately 2% higher among people who vaped than people who smoked, which was not a statistically significant difference.

Two studies reported findings from the Population Assessment of Tobacco and Health (PATH) study, a longitudinal survey in the USA, over a 1-year period beginning in 2013,[10,11] but used different inclusion criteria for the baseline samples. Both studies indicated that urinary levels of nicotine, cotinine and TNE reduced among people who smoked at baseline and had switched to vaping at follow-up a year later; only Anic *et al*[10] tested and found the reduction in nicotine to be statistically significant, and both studies reported statistically significant reductions in cotinine and TNE2 levels. However, only a small number of people had switched from smoking to vaping, so these data should be treated with caution. Similarly, measuring changes in a small subgroup of participants (n=14) who switched from vaping at baseline to smoking at follow-up, Dai[11] reported significant increases in urinary levels of TNE and cotinine. Finally, among participants who vaped at baseline and 1 year later, a 40% increase, a 35% decrease, a 34% decrease and a 20% increase, all statistically non-significant changes, were reported in urinary nicotine, cotinine, TNE2 and TNE7 levels respectively.[11]

A further study that assessed linear trend data from repeated cross-sectional PATH waves 1–5 (2013–14 to 2018–19) reported statistically significant increases in mean urinary cotinine and TNE2 levels in the vaping groups and non-significant change among the smoking groups over the 5-year study period.[13] For instance, urinary cotinine and TNE2 levels in the vaping groups were nearly twice as great in PATH wave 5 (collected in 2018–19) than in wave 1 (collected in 2013–14), whereas cotinine and TNE2 levels among smoking groups increased non-significantly by 14.4% and 12.8%, respectively. The study findings also show that urinary cotinine and TNE2 levels were statistically significantly lower among people who vaped compared with people who smoked in the first three waves only (2013–16) and did not differ in the last two waves (2016–19) – a likely result of the proliferation during the study of vaping products with high nicotine concentrations and nicotine salt formulation.[13]

## Cross-sectional studies

Cross-sectional data from two US studies reported lower urinary nicotine levels among people who exclusively vaped compared with people who exclusively smoked, but neither tested the statistical significance of these results.[14,28] Following the algorithm, data on urinary nicotine levels from these studies were combined with two studies from the McNeill *et al* review[1] (Fig 5.2).

The pooled data across the four studies (LMD = -0.17, 95% CI: -0.65, 0.30; 2,744 participants) showed that the geometric mean urinary nicotine levels (GMR = 0.84, 95% CI: 0.52, 1.35) were approximately 16% lower among people who vaped than people who smoked, but the difference was not statistically significant, and the heterogeneity between the included studies was high at I2=84%.

Ten cross-sectional studies assessed cotinine levels in urine, blood or saliva: eight were carried out in the USA,[14,16,20,21,23,28,30,35] with single studies carried out in South Korea[26] and Spain.[27] One study reported saliva cotinine levels to be over twice as high among high school students (mean age 15 years) who vaped compared with those who used tobacco products (cigars, cigarettes, smokeless tobacco or hookah), but the difference was not tested for statistical significance.[21] In the remaining nine studies, cotinine levels were lower among those who vaped than those who smoked, but only four tested this statistically – one finding the difference to be statistically significant,[16] the other three not so.[23,28,35]

Following our algorithm, we meta-analysed six cross-sectional studies (Fig 5.3) comparing urinary cotinine levels between people who vaped and people who smoked – three were from the updated review[14,20,28] and three from the McNeill *et al* review.[1]

| | Vaping | | | Smoking | | | | Mean Difference | |
|---|---|---|---|---|---|---|---|---|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | Year |
| Keith 2020 | 5.364278 | 1.191569 | 17 | 5.436299 | 1.66409 | 237 | 20.6% | -0.07 [-0.68, 0.53] | 2020 |
| Smith 2020 | 6.458338 | 1.285548 | 124 | 6.196444 | 1.28008 | 127 | 27.3% | 0.26 [-0.06, 0.58] | 2020 |
| Mohammadi 2022 | 6.60904027 | 0.92242697 | 42 | 6.84692266 | 1.06493909 | 28 | 23.5% | -0.24 [-0.72, 0.25] | 2022 |
| Feng 2022 | 6.66568372 | 1.45891302 | 148 | 7.28000825 | 2.09825463 | 2021 | 28.6% | -0.61 [-0.87, -0.36] | 2022 |
| **Total (95% CI)** | | | **331** | | | **2413** | **100.0%** | **-0.17 [-0.65, 0.30]** | |

Heterogeneity: Tau² = 0.19; Chi² = 18.34, df = 3 (P = 0.0004); I² = 84%
Test for overall effect: Z = 0.72 (P = 0.47)

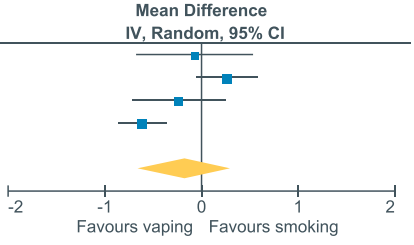


**Fig 5.2. Meta-analysis of cross-sectional studies reporting on urinary nicotine levels after exposure to vaping and smoking.**

The pooled data across the six studies (LMD = -0.20, 95% CI: -0.60, 0.20; 3,052 participants) showed that the geometric mean urinary cotinine levels (GMR = 0.82, 95% CI: 0.55, 1.22) were approximately 18% lower among people who vaped than people who smoked, but the difference was not statistically significant. Additionally, we meta-analysed two cross-sectional studies (Fig 5.4) assessing blood serum cotinine levels between people who vaped and people who smoked.[16,23]

The pooled data across two studies (LMD = -0.64, 95% CI: -1.05, -0.22; 1,541 participants) showed that the geometric mean blood serum cotinine levels (GMR = 0.53, 95% CI: 0.35, 0.80) were approximately 47% lower among people who vaped than people who smoked, and the difference was statistically significant. Levels of blood cotinine better reflect recent exposure to nicotine, while levels of urinary cotinine better reflect exposure over a longer period. These differences suggest that nicotine exposure is lower from vaping than smoking over a short period and similar over longer exposure.

Three cross-sectional studies reported lower levels of TNE2, TNE3 and TNE7 in people who vaped compared with people who smoked,[14,15,29] but no significant difference was detected in the one study that tested the difference statistically.[29]

#### 5.3.1.1.2 Vaping versus dual use

Dual use data were not compared with other user groups in McNeill *et al*[1] due to varying definitions of dual use, and the following results are from newly included studies only (because of the tighter criteria used in this updated review).

### Longitudinal studies

The two longitudinal studies using PATH cohort data over a 1-year period starting in 2013 reported changes in levels of urinary nicotine and its metabolites among smokers or vapers at baseline who switched to dual use at follow-up, and changes among participants who were dual users at baseline.[10,11] For people who were vaping at baseline and switched to dual use 1 year later, mean urinary nicotine level increased by 69% (non-significant change), cotinine levels increased by 164% (significant) and TNE2 levels increased by 160% (significant)[11] (see Tables A2.3, A2.5 and A2.8 in appendix 2).

Both studies reported similar results for dual users at baseline who switched to vaping only at follow-up. Dai[11] and Anic *et al*[10] reported small, non-significant changes in urinary nicotine levels (see Table A2.3 in appendix 2), and reductions (significant in Dai,[11] non-significant in Anic *et al*[10]) in urinary cotinine and TNE2 levels (see Tables A2.5 and A2.8 in appendix 2) among those exclusively vaping at follow-up.

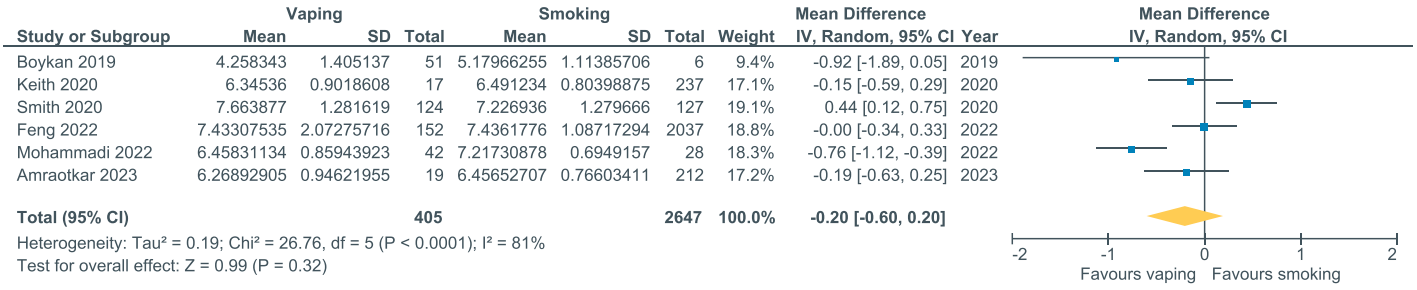


**Fig 5.3. Meta-analysis of cross-sectional studies reporting on urinary cotinine levels between people who vaped and people who smoked.**

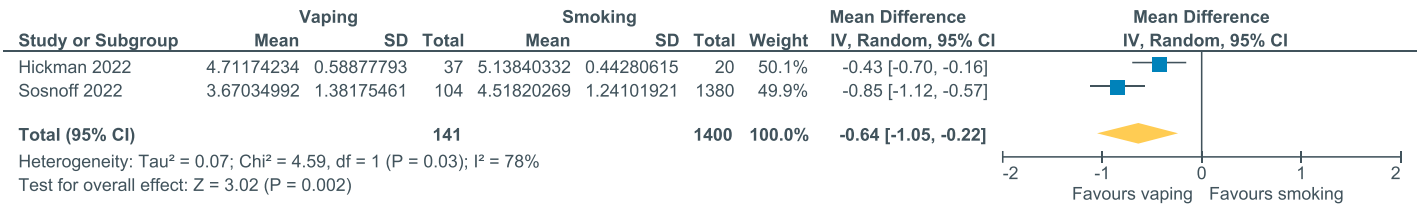


**Fig 5.4. Meta-analysis of cross-sectional studies reporting on blood serum cotinine levels between people who vaped and people who smoked.**

Definitions of dual use differed between the two studies, and numbers of dual users who switched to vaping in PATH wave 2 were small, so these estimates should be treated with caution.

Both studies also examined changes from dual use at baseline to exclusive smoking at follow-up, reporting decreases in urinary nicotine and its metabolites, with only nicotine levels reducing statistically significantly in the Anic *et al* study.[10] Both studies found that smokers who switched to dual use showed slight increases in urinary nicotine levels (see Table A2.3 in appendix 2) and slight decreases in urinary cotinine (see Table A2.5 in appendix 2) and TNE2 levels (see Table A2.8 in appendix 2); Anic *et al* tested for statistical significance and found that these changes were not statistically significant.[10]

### Cross-sectional studies

Nicotine levels in urine between vaping and dual use groups were compared in two cross-sectional studies from the USA. Both studies reported lower levels of nicotine among people who vaped than those who vaped and smoked,[14,17] and Feng *et al*[14] reported that the difference was statistically significant (see Table A2.4 in appendix 2).

Cotinine levels between vaping and dual use groups in urine, blood or saliva were compared in five cross-sectional studies: three were carried out in the USA,[14,17,20] one was conducted in South Korea[26] and one in Spain.[27] Four studies reported urinary cotinine levels to be higher among dual use than vaping groups, but none tested for statistical significance (see Table A2.7 in appendix 2).[14,20,26,27] Addicott *et al* reported lower urinary and blood plasma cotinine levels among dual use than vaping groups but did not test for statistical significance (see Table A2.7 in appendix 2).[17]

Data from five cross-sectional studies (two from the updated review and three from the McNeill *et al* review assessing urinary cotinine levels between dual use and vaping groups were meta-analysed (Fig 5.5).

The pooled data across five studies (LMD = -0.29, 95% CI: -0.77, 0.19; 403 participants) showed that the geometric mean urinary cotinine levels (GMR = 0.75, 95% CI: 0.46, 1.21) were approximately 25% lower among people who vaped than people who vaped and smoked; the difference, however, was not statistically significant and heterogeneity between studies was high at $I^2$=80%.

Two cross-sectional studies reported on urinary TN2, TNE3[14] and urinary TNE7[14] levels between dual use and vaping groups using the same PATH wave 1 data (see Table A2.10 in appendix 2). All three TNE measures were lower in the vaping group than the dual use group; Lizhnyak *et al* tested and reported that the difference in TNE7 levels was statistically significant (see Table A2.10 in appendix 2).[15]

#### 5.3.1.1.3 Vaping vs non-use

### Longitudinal studies

One longitudinal study exploring PATH waves 1 and 2 reported on changes in urinary nicotine and its metabolite levels after people who vaped at baseline switched to non-use at follow-up.[11] Participants' levels of nicotine decreased by 44% (see Table A2.3 in appendix 2), levels of cotinine decreased by 85% (see Table A2.5 in appendix 2), and levels of TNE2 decreased by 84% (see Table A2.8 in appendix 2).

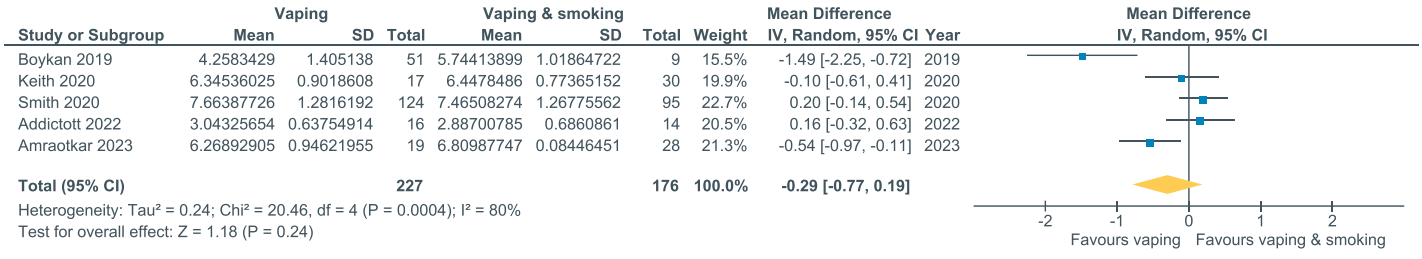


**Fig 5.5. Meta-analysis of cross-sectional studies reporting on urinary cotinine levels between people who vaped and people who vaped and smoked.**

## Cross-sectional studies

Two cross-sectional studies, one from the USA[28] and one from four European countries—Spain, Greece, Italy and the UK,[19] compared nicotine levels in urine or saliva between people who vaped and non-users of tobacco products. In line with expectations, both studies reported statistically significantly lower levels of nicotine among non-users than people who vaped.

Data on urinary nicotine levels from the two studies were combined with data from two studies identified by McNeill *et al*,[1] and meta-analysed (Fig 5.6).

The pooled data across four studies (LMD = 4.40, 95% CI: 3.74, 5.06; 449 participants) showed that the geometric mean urinary nicotine levels were approximately statistically significantly 82 times lower (GMR = 81.5, 95% CI: 42.1, 157.6) among non-users than people who vaped.

Twelve cross-sectional studies compared cotinine levels in urine, blood or saliva between people who vaped and non-users: eight were conducted in the USA,[14,16,20,21,23,28,30,35] two studies covering Spain,[19,27] one in Indonesia[34] and one in South Korea.[26]. All 12 reported lower cotinine levels among non-users than people who vaped, and three studies that tested the differences statistically found them to be statistically significant.[19,34,35]

Data on urinary cotinine levels between people who vaped and non-users reported in six cross-sectional studies (four from the updated review and two from McNeill *et al* review1) were meta-analysed (Fig 5.7). The pooled data across the six studies (LMD = 7.24, 95% CI: 6.02, 8.47; 2,787 participants) showed that the geometric mean urinary cotinine levels were approximately statistically significantly 1,394 times lower (GMR = 1394.1, 95% CI: 411.6, 4,769.5) among people who did not vape or smoke compared with people who vaped.

Additional meta-analysis from three cross-sectional studies assessing salivary cotinine levels between people who vaped and non-users was conducted (Fig 5.8).

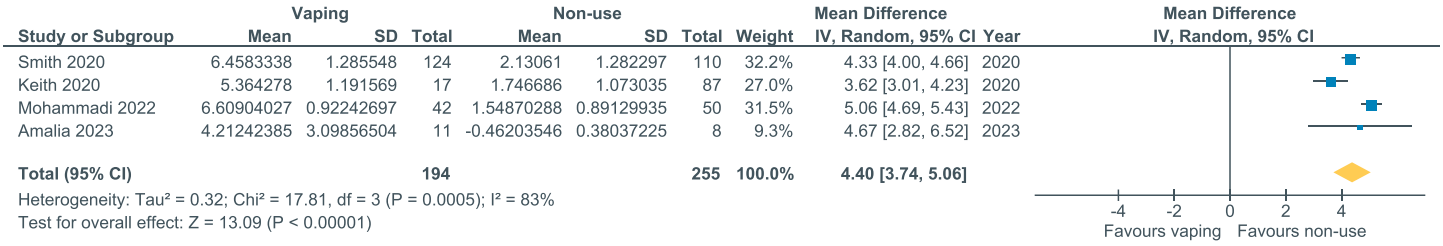


**Fig 5.6. Meta-analysis of cross-sectional studies reporting on urinary nicotine levels between people who vaped and non-users.**

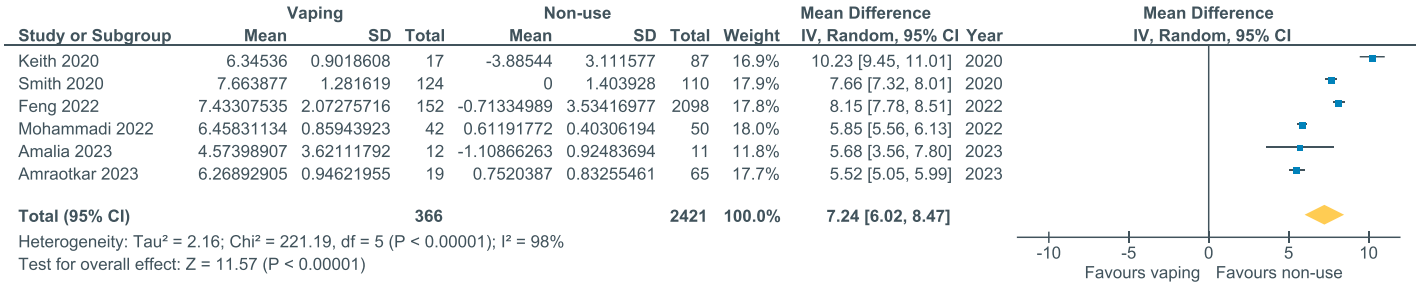


**Fig 5.7. Meta-analysis of cross-sectional studies reporting on urinary cotinine levels between people who vaped and non-users.**

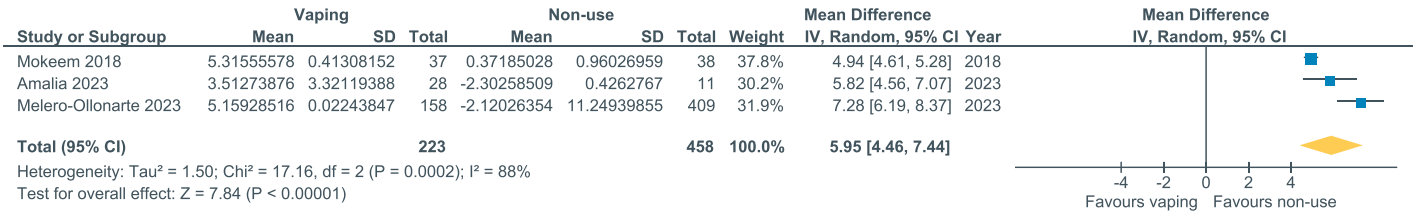


**Fig 5.8. Meta-analysis of cross-sectional studies reporting on salivary cotinine levels between people who vaped and non-users.**

The pooled data across the three studies (LMD = 5.95, 95% CI: 4.46, 7.44; 681 participants) showed that the geometric mean salivary cotinine levels were approximately statistically significantly 383 times lower (GMR = 383.8, 95% CI: 86.5, 1,702.[8]) among people who did not vape or smoke compared with people who vaped.

Three cross-sectional studies, all from the USA, reported lower urinary TNE2[14,29] and TNE7[15] levels among non-users than in people who vaped; only Mori *et al* tested statistically and found the difference to be statistically significant.[29]

#### 5.3.1.1.4 Nicotine: summary

The updated review identified 20 new studies that measured nicotine and/or its metabolites. Three meta-analyses (which, where appropriate, included studies from McNeill *et al*[1]) found no statistically significant differences in urinary nicotine, urinary cotinine or urinary TNE levels between people who vaped and people who smoked, although levels were lower among the people who vaped in each comparison. A fourth meta-analysis of blood serum cotinine levels found that levels were statistically significantly approximately 47% lower among people who vaped than people who smoked. These results suggested lower exposure among people who vape than smoke over a short period, and similar over longer exposure periods. In line with expectations, three meta-analyses indicated that urinary nicotine, urinary cotinine and saliva cotinine levels were statistically significantly lower among non-users than among people who vaped. These findings were broadly consistent with those reported by McNeill *et al*, who reported similar exposure to nicotine when studies were over medium- to longer-term periods. Potentially consistent with this, in the updated review, one study which examined the linear trend in urinary cotinine and TNE levels in multiple cross-sectional waves found that these were nearly twice as great in 2018–19 than in 2013–14.[11] The authors indicated that these changes were likely due to a proliferation of vaping products with high nicotine concentrations and nicotine salt formulation. Duration of vaping was not assessed, but increases could also reflect a greater proportion of long-term users in the later samples.[13] The updated review did not include any cross-country analyses which, given different regulations on nicotine content, could throw light on issues such as nicotine compensation in jurisdictions like the UK, where a nicotine cap is in place.

### 5.3.1.2 Tobacco-specific nitrosamines (TSNAs)

Tobacco-specific nitrosamines (TSNAs) are a group of toxicants that are specific to tobacco and are formed through nitrosation of nicotine alkaloids during the tobacco curing and fermentation process. TSNA levels may be very low in e-liquid due to the purified tobacco derived, or synthetic, pharmaceutical-grade nicotine that is typically used and TSNA exposure may occur from vaping if there are impurities in the nicotine that is used. TSNAs that have been classified as group 1 carcinogens by the International Agency for Research on Cancer (IARC)[38], ie 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and its metabolite 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and N′ -nitrosonornicotine (NNN) formed through nitrosation of nornicotine were included in this review. TSNAs not classified as carcinogenic to humans are excluded here, but further information can be found in the studies by McNeill *et al*[1] and Taylor *et al*.[39]

Eight new studies published since July 2021 investigating exposure to TSNAs were identified: one RCT,[8] one longitudinal observation study in confinement,[12] two from the observational longitudinal PATH study,[10,11] one comparing trends over time in cross-sectional waves from the PATH longitudinal survey,[13] one study reporting from PATH wave 1[15] and two other cross-sectional studies.[19,27] All eight reported levels of NNAL, six reported levels of NNN[10,12,13,15,19,27] and one reported levels of NNK.[27] Most studies measured TSNAs in urine only,[8,10–13,15] Melero-Ollonarte *et al* reported on TSNAs in saliva only[27] and Amalia *et al* measured TSNAs in saliva and urine.[19]

Table A2.11 in appendix 2 gives details of the findings of the one RCT and three observational longitudinal studies reporting on TSNA levels, and Tables A2.12 and A2.13 in appendix 2 report findings on TSNAs from one study reporting linear trend data and the three cross-sectional studies, respectively.

#### 5.3.1.2.1 Vaping vs smoking

##### Longitudinal studies

One RCT reported on levels of NNAL after participants who smoked at baseline switched to vaping for 24 weeks.[8] Urinary NNAL levels were reported to reduce statistically significantly by 73–84% (depending on flavour and device type used) after 24 weeks of switching from smoking to vaping exclusively.[8]

Data from two RCTs were meta-analysed (Fig 5.9) – one from the updated search[8] and one from the RCT included in the McNeill *et al* report,[1] which measured urinary NNAL levels after 8 weeks of switching from smoking to vaping and therefore fitted our inclusion criteria (see Table A1.2 in appendix 1). The pooled data across two RCTs (LMD= -1.27, 95% CI: -3.10, 0.55; 238 participants) showed that the geometric mean urinary NNAL levels (GMR = 0.28, 95% CI: 0.05, 1.73) were approximately 72% lower among people who vaped at follow-up than among people who smoked at follow-up. The difference was not statistically significant, heterogeneity was high at I2=98%, and the direction of the difference was consistent across the two studies.
One longitudinal observational study conducted in confinement reported that urinary NNAL levels reduced statistically significantly by 71.8% and 75.7% in two study sites 14 days after participants switched from smoking to vaping. The same study reported that urinary NNN levels also reduced significantly by 89% and 92% in exclusive vaping groups at follow-up.[12]

Two cohort studies from the PATH study investigated changes in urinary NNAL levels among people who smoked and switched to vaping over a 1-year period beginning in 2013. NNAL levels among those who smoked and had switched to vaping fell statistically significantly by 92% and 93%; the reductions among those who quit smoking without vaping were 84% and 85% respectively.[10,11] Similarly, urinary NNN levels also reduced by 82% and 83%, while reductions among those who quit smoking without vaping were 44% in both studies. Smokers who switched to vaping at wave 2 had smoked on average 11 cigarettes per day (CPD), while smokers who switched to non-use had smoked 5 CPD, which potentially explains the higher percentage reduction seen among those who vaped compared with non-users at wave 2. Moreover, the mean urinary NNAL level was still higher among those who switched from smoking to vaping than among those who just quit smoking, whereas NNN levels were similar; however, neither comparison was tested for statistical significance.

Only a small number of people had switched from smoking to vaping, so these data should be treated with caution. Both studies reported data from the same source, therefore meta-analysis was not conducted.
In the only study to examine the vaping group at PATH wave 1, among those who switched to smoking, urinary levels of NNAL increased statistically significantly by 367%, and urinary levels of NNN increased by 42%.[11]
In a further PATH study which assessed linear trends from wave 1 to wave 4 (2013–14 to 2016–18), urinary NNAL levels in the vaping groups decreased by 19% over time but this was not statistically significant. For comparison, in the smoking groups, urinary NNAL levels increased non-significantly by 11% from wave 1 to wave 4.[13]

### Cross-sectional studies

Two cross-sectional studies compared urinary NNAL and NNN levels between people who vaped and people who smoked.[15,27] In the PATH study of Wave 1 data[15] compared to people who smoked, among people who vaped urinary NNAL levels were 98% lower and urinary NNN levels 68% lower (these comparisons were not tested statistically). In a further cross-sectional study saliva NNAL levels were 73% lower and saliva NNN levels 81% lower among people who vaped compared to people who smoked.[27]

In the Dai PATH study comparing multiple cross-sectional waves, urinary NNAL levels were statistically significantly lower (by 97–98%) among people who vaped compared with people who smoked in all waves.[13]

Melero-Ollonarte also examined salivary NNK levels, finding that these were 31% lower among people who vaped than in people who smoked.[27]

## 5.3.1.2.2 Vaping vs dual use

### Longitudinal studies

The two studies using PATH cohort data over a 1-year period starting in 2013 reported that smokers who switched to dual use showed decreases in urinary NNAL levels of around 15% (statistically significantly so in one

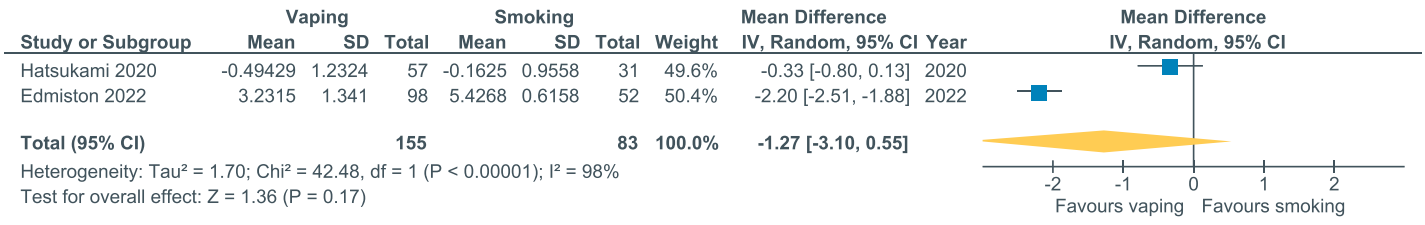


**Fig 5.9. Meta-analysis of randomised controlled trials reporting on urinary NNAL levels between people who vaped and people who smoked.**

study) and statistically significant decreases in urinary NNN levels of 13–14% in both studies.[10,11] For people who were dual users at baseline, in those who switched to vaping only at follow-up, statistically significant reductions in NNAL levels were observed across the two studies of 95%[10] and 96%,[11] and non-statistically significant reductions in urinary NNN levels of 25%[10] and 28%.[10] Again, the numbers who switched to vaping were small, so these estimates should be treated with caution. Both studies also examined changes from dual use to exclusive smoking at follow-up, with very small changes being observed in both directions for NNAL, neither statistically significant, and non-statistically significant decreases of 8%[10] and 6%[11] being reported in both. Both studies reported data from the same source, therefore meta-analysis could not be conducted.

Only one study assessed changes among those who were vaping at baseline and switched to dual use at follow-up – findings showed a 327% statistically significant increase in urinary NNAL levels, and a non-statistically significant increase in urinary NNN levels.[11]

#### Cross-sectional studies

Two cross-sectional studies assessed urinary NNAL and NNN levels among people who vaped compared with dual users. In the PATH study of wave 1 data, among people who vaped urinary NNAL and NNN levels were statistically significantly lower than those in dual users by 98% and 63%, respectively.[15] In a further cross-sectional study, saliva NNAL levels were non-statistically significantly lower by 34%, and saliva NNN levels statistically significantly lower by 56%, among people who vaped than in people who smoked and vaped.[27]

### 5.3.1.2.3 Vaping vs non-use

#### Longitudinal studies

In the PATH cohort study that examined people who vaped at wave 1, among those who had quit vaping at wave 2, urinary NNAL and NNN levels decreased non-significantly by 35% and 25% respectively. Among participants who vaped exclusively at wave 1 and at wave 2, urinary NNAL levels decreased non-significantly by 28% and NNN levels increased non-significantly by 4%.[11]

#### Cross-sectional studies

Three cross-sectional studies compared NNAL levels in people who vaped with those in people who neither vaped nor smoked.[15,19,27] Urinary and salivary NNAL levels in one study did not differ statistically significantly between people who vaped and people who neither smoked nor vaped, although most participants within these groups had NNAL levels below the limit of quantification.[19] Levels of NNN could not be compared *et al* because too many were below the level of quantification. Another study used PATH wave 1 data (2013–14) and reported that urinary NNAL levels were approximately 85% lower and NNN levels were approximately 58% lower among people who neither vaped nor smoked than in people who vaped exclusively – these comparisons were not tested for statistical difference.[15] Melero-Ollonarte *et al* reported that salivary NNAL levels were approximately 10% lower and NNN levels approximately 56% lower among people who neither vaped nor smoked than in people who vaped. The study also found that NNK levels were 19% lower among people who neither vaped nor smoked than in people who vaped.[27]

### 5.3.1.2.4 Tobacco-specific nitrosamines (TSNAs): summary

Across the eight new studies, TSNA levels were substantially lower among people who vaped than in people who smoked. Only one meta-analysis on TSNAs was possible, which was of urinary NNAL levels in two RCTs (one with 8 weeks follow-up from the earlier review, and the second a new study with 24 weeks follow-up). The meta-analysis found lower NNAL levels among people who vaped than in people who smoked, but the difference was not statistically significant. The studies in this updated review found that TSNA levels among people who neither vaped nor smoked were lower than or similar to levels among people who vaped, and frequently below the level of quantification. No meta-analyses were possible. Findings from the eight new studies were broadly consistent with the findings from 28 studies on TSNAs reported by McNeill *et al*.[1] However, McNeill *et al*, in their meta-analysis, found that vaping groups were exposed to significantly lower NNAL levels than smoking groups. As the direction of both meta-analyses were similar, the difference might be due to fewer participants in the updated meta-analysis and due to increased likelihood that participants in vaping groups could have been exposed to tobacco smoke over the longer follow-up period. Other differences in overall study findings may be due to the length of time since stopping smoking, as there was some suggestion of declines in TSNAs among exclusively vaping groups over time.

Comparisons between people who vaped and those who vaped and smoked (dual users) were new. Across all studies, TSNA levels were consistently lower among people who vaped than in people who smoked and vaped. No meta-analyses were possible.

### 5.3.1.3 Volatile organic compounds (VOCs)

Volatile organic compounds (VOCs) are a diverse group of chemicals formed by incomplete combustion of organic materials such as tobacco. It has been suggested that the thermal degradation of e-liquid constituents may result in exposure of VOCs in people who vape. The updated review identified four new studies examining levels of VOC biomarkers. One observational longitudinal open label study conducted in confinement reported on biomarker changes in people who switched from smoking at baseline to vaping for a 14-day period.[12] From the PATH surveys, there were two cohort longitudinal studies reporting on biomarker changes between waves 1 and 2,[10,11] and one study that reported cross-sectional data from wave 1.[15] Across these studies, five VOCs and their metabolites were assessed: acrolein (3-HPMA, CEMA); 1,3-butadiene (MHBMA3, DHBMA); acrylamide (AAMA, GAMA); benzene (S-PMA); and, not included in the prior review, ethylene oxide (HEMA).

#### 5.3.1.3.1 Vaping vs smoking

All the studies reported lower levels of all VOC biomarker metabolites among people who vaped than people who smoked, but the amount of change varied across the studies and metabolites.

##### Longitudinal studies

Morris *et al* reported on several VOC metabolites after people who smoked had vaped exclusively for 14 days; two measures are given for each metabolite, as there were two identical study recruitment sites reported separately (site 1 (14 participants) and site 2 (11 participants)).[12] All the reductions in exposure to VOCs were statistically significant, but the small sample sizes mean that the estimates should be treated with caution. Levels of acrolein metabolites across the two study sites reduced by 86% and 69% (3-HPMA) and 85% and 86% (CEMA); 1,3-butadiene by 85% and 60% (MHBMA3); benzene by 95% and 92% (S-PMA); ethylene oxide (HEMA) by 70% and 46%.

Two studies used the longitudinal PATH study in the USA and identified a small number of participants who smoked at baseline (2013–14) and reported vaping at the follow-up point 1 year later (28 participants;[10] 32 participants[11]). Given these small sample sizes, estimates should be treated with caution. One of the studies only tested for differences in CEMA (acrolein) and AAMA (acrylamide) levels.[11] Levels of acrolein metabolites reduced by 72% (3-HPMA) in both studies (this was a statistically significant reduction in one study10) and statistically significantly by 56% and 57% (CEMA); 1,3-butadiene reduced by 6% (non-significant decline[10]) and 9%[11] (DHBMA), and by 77% (a significant decline[10]) and 80%[11] (MHBMA3). Acrylamide reduced statistically significantly by 48% and 46% (AAMA), and 41% (a significant decline[10]) and 39% (GAMA).[11] For benzene metabolite S-PMA, reductions of 22% (not significant[10]) and 15%[11] were reported. For ethylene oxide metabolite (HEMA), a 66% reduction was reported in both studies (statistically significant in one[10] and not tested in the other[11]).

Dai also assessed participants who vaped exclusively at baseline and had switched to smoking at 1-year follow-up, and VOC biomarkers increased over this time period.[11] Levels of acrolein metabolites increased by 17% (3-HPMA) and a non-statistically significant increase of 61% (CEMA); 1,3-butadiene metabolites increased by 11% (DHBMA) and 235% (MHBMA3); acrylamide metabolites increased statistically significantly by 51% (AAMA) and 26% (GAMA); benzene metabolites reduced by 55% (S-PMA); and levels of ethylene oxide metabolite (HEMA) increased by 74%.

Dai also assessed participants who vaped exclusively at baseline and 1 year later. Acrolein metabolites reduced by 4% (3-HPMA) and 6% (CEMA, non-significant); 1,3-butadiene metabolites reduced by 4% (DHBMA) and 2% (MHBMA3); acrylamide metabolites reduced non-significantly by 9% (AAMA) and increased by 5% (GAMA); benzene metabolites reduced by 8% (S-PMA); ethylene oxide increased by 4% (HEMA).

##### Cross-sectional studies

The one cross-sectional study assessed metabolites of three VOCs using PATH wave 1 data collected in 2013–14. Comparisons were not tested statistically between the exclusive vaping and exclusive smoking groups, and levels of the biomarkers assessed (3-HPMA, CEMA, MHBMA3, AAMA) were all lower among those who vaped than in those who smoked.[15]

#### 5.3.1.3.2 Vaping vs dual use

All the studies reported lower levels of most VOC metabolites among people who vaped than in people who smoked and vaped, but the amount of change varied across the studies and metabolites.

##### Longitudinal studies

The two longitudinal PATH studies examined people who were smoking and vaping at baseline and reported switching to vaping only at follow-up, but again the numbers were small (30–36 participants) so the estimates should be treated with caution.[10,11]

Acrolein metabolites reduced by 67% (HPMA) in both studies (statistically significant reduction in one[10]), and statistically significantly by 57% and 62% (CEMA); 1,3-butadiene reduced by 25% (DHBMA) in both studies (statistically significant[10]), and by 85% (statistically significant[10]) and 84%[11] (MHBMA3). Acrylamide statistically significantly reduced by 25%10 and 63%[11] (AAMA) and by 65% (statistically significant10) and 26%[11] (GAMA); benzene reduced non-significantly by 11%[10] and increased by 8%[11] (S-PMA); ethylene oxide reduced by 57% (statistically significant[10]) and 60%[11] (HEMA).

The Dai study also assessed changes among those who were vaping at baseline and reported smoking and vaping at follow-up. In most cases, increases in VOC metabolite levels were observed. Exposure to acrolein increased by 163% (3-HPMA) and statistically significantly by 83%; (CEMA); 1,3-butadiene metabolite levels decreased by 4% (DHBMA) and 2% (MHBMA3); acrylamide metabolites statistically significantly increased by 96% (AAMA) and 23% (GAMA); benzene metabolites increased by 19% (S-PMA); ethylene oxide metabolite HEMA increased by 101%.[11]

The two studies also assessed changes after switching from dual use to exclusive smoking and smoking to dual use; results are reported in Tables A2.14, A2.16, A2.18, A2.20 and A2.21 in appendix 2.

#### Cross-sectional studies

In the Lizhnyak *et al* cross-sectional analysis of PATH wave 1 data, differences in VOC metabolite levels between people who exclusively vaped and people who vaped and smoked regularly were tested statistically. Levels of 3-HPMA, CEMA, MHBMA3 and AAMA were all statistically significantly lower among people who vaped than people who vaped and smoked.[15]

#### 5.3.1.3.3 Vaping vs non-use

Overall, there was no consistency in the findings for the metabolites between people who vaped and people who neither smoked nor vaped, and again the amount of change varied across the studies and metabolites.

#### Longitudinal studies

One PATH cohort study identified 44 people who vaped at wave 1 and who reported neither vaping nor smoking at the follow-up 1 year later. Levels of acrolein metabolites increased by 9% (3 HPMA) and 10% (CEMA) (the latter statistically significant); [1,3] butadiene metabolites increased by 3% (DHBMA) and 7% (MHBMA3); acrylamide metabolites decreased non-significantly by 18% (AAMA) and increased by 9% (GAMA); benzene metabolite S-PMA decreased by 36%; and ethylene oxide metabolite HEMA decreased by 29%.[11]

#### Cross-sectional studies

In the Lizhnyak *et al* cross-sectional analysis of PATH wave 1 data, metabolite levels between people who vaped exclusively and people who neither vaped nor smoked were not tested statistically. Levels of 3-HPMA, CEMA and AAMA were lower, and MHBMA3 higher, among people who neither smoked nor vaped than among people who vaped.[15]

#### 5.3.1.3.4 Volatile organic compounds (VOCs): summary

Across the four new studies, VOC levels were substantially lower among people who vaped compared with people who smoked. No meta-analyses were possible. In the two studies that compared VOC levels between people who neither vaped nor smoked and people who vaped, there was no consistency between the two groups. No meta-analyses were possible.

Findings from the four new studies were generally consistent with the findings from 25 studies on VOCs reported by McNeill *et al* for vaping vs smoking. Meta-analyses carried out by McNeill *et al* generally found no statistically significant differences across vaping and non-use groups for biomarkers of VOCs included in the updated review.[1]

Comparisons between people who vaped and those who vaped and smoked were new. Across all studies, levels of most VOC metabolites were significantly lower among people who vaped than people who smoked and vaped. No meta-analyses were possible.

### 5.3.1.4 Metals

There are many environmental sources of metal exposure to people, such as soil, food or water contamination. Exposure to certain metals (eg cadmium, lead, arsenic and mercury) is considered carcinogenic and can adversely affect cardiovascular and respiratory systems.[38]

People who smoke have higher levels of some metals in their bodies than people who do not smoke. Tobacco plants absorb metals from the soil and fertilisers, while combustion of tobacco liberates the metals that are further retained in ash or transferred to tobacco smoke. Most heavy metals have long excretion half-lives (eg years in the case of cadmium); therefore, traces of metals can be detected in human biosamples for many years after stopping smoking.

Metals have also been found in the aerosols from e-cigarettes. Exposure to metals and metalloids when vaping may originate from the atomiser, batteries or other vaping device parts that may leach into vaping liquid.[1]

In the updated review, we identified four new studies (two longitudinal and two cross-sectional) which assessed levels of metals in urine. From the US PATH surveys, there were two cohort longitudinal studies reporting on biomarker changes between waves 1 and 2[10,11] and one study that reported cross-sectional data from wave 1.[15] The findings from these studies should be interpreted in consideration of overlapping datasets, small sample sizes, early versions of vaping products and long elimination periods of certain metals from the human body. One further cross-sectional study from Spain collected data in 2019 and compared exposure to metals between people who vaped and people who neither smoked nor vaped.[19] All four studies assessed exposures to cadmium and lead; two studies assessed exposure to arsenic[11,19] and one assessed exposure to mercury.[19]

#### 5.3.1.4.1 Vaping vs smoking

##### Longitudinal studies

Both PATH longitudinal studies reported little change in metals among people who smoked at baseline and switched to vaping at the 1-year follow-up.[10,11] For urinary cadmium levels, there were no statistically significant differences (0% and 3% increase); for urinary lead levels, small non-significant increases of 6%[10] and 7%[11] were reported; for urinary arsenic levels, a non-statistically significant reduction of 14% was observed.[11]

Dai *et al* also reported changes in metal biomarkers among people who vaped at baseline and switched to smoking at follow-up 1 year later. For urinary cadmium levels, there was a statistically significant increase by 15%; for urinary lead a statistically significant decrease of 24%; and for urinary arsenic a reduction of 27% (not tested for statistical significance).[11]

Dai *et al* also assessed participants who vaped exclusively at baseline and continued vaping 1 year later. For urinary cadmium levels, there was a non-statistically significant increase of 2%; for urinary lead, a non-statistically significant decrease of 9%; for urinary arsenic, a reduction of 15% (not tested for statistical significance).[11]

##### Cross-sectional studies

The cross-sectional study by Lizhnyak *et al*[15] used PATH wave 1 data (2013–14) and reported slightly lower urinary cadmium levels and slightly higher lead levels among people who vaped than people who smoked, but did not test these differences for statistical significance.

#### 5.3.1.4.2 Vaping vs dual use

##### Longitudinal studies

The two longitudinal PATH studies also examined people who were smoking and vaping at baseline who reported switching to vaping only at follow-up. Urinary cadmium levels increased non-statistically significantly by 21%[10] and 19%;[11] urinary lead levels decreased statistically significantly by 25%[10] and non-statistically significantly by 6%;[11] urinary arsenic decreased by 6%[11] (not tested for statistical significance).

One study also assessed changes among those who were vaping at baseline and reported smoking and vaping at follow-up. Urinary cadmium levels did not change; urinary lead increased non-significantly by 6%; urinary arsenic levels decreased by 11% (not tested for statistical significance).[11]

The two studies also assessed changes from dual use to exclusive smoking and from smoking to dual use; results are reported in Tables A2.22, A2.24 and A2.26 in appendix 2.

##### Cross-sectional studies

In the Lizhnyak *et al* cross-sectional analysis of PATH wave 1 data, differences in urinary metal levels between people who exclusively vaped and people who vaped and smoked regularly were tested statistically. Urinary levels of cadmium were statistically significantly lower and lead levels non-statistically significantly lower among people who vaped than people who vaped and smoked.[15]

#### 5.3.1.4.3 Vaping vs non use

##### Longitudinal studies

One PATH cohort study identified people who vaped at wave 1 and who reported neither vaping nor smoking at the follow-up 1 year later, finding that there was a 15% non-significant increase in cadmium levels, no change in urinary lead levels and a reduction by 28% in urinary arsenic levels (not tested for statistical significance).[11]

### Cross-sectional studies

In the Lizhnyak *et al* cross-sectional analysis of PATH wave 1 data, metabolite levels between people who vaped exclusively and people who neither vaped nor smoked were not tested statistically. Urinary cadmium and lead levels were lower among people who neither vaped nor smoked compared with people who vaped.[15] In the Amalia *et al* cross-sectional study, urinary cadmium, arsenic and mercury levels were lower among people who vaped than non-users, but none of these comparisons were statistically significant. Urinary lead levels were higher among people who vaped than non-users, but again this difference was not statistically significant.[19]

Following the algorithm, we conducted meta-analyses of the two studies (Fig 5.10) reporting cross-sectional data for urinary cadmium and lead levels between people who vaped and non-users. The pooled data across these two studies (LMD = 0.62, 95% CI: 0.53, 0.72; 1,889 participants) showed that the geometric mean urinary cadmium levels (GMR = 1.86, 95% CI: 1.70, 2.05) were approximately 86% higher among people who vaped than among people who did not smoke or vape; the meta-analysis result was largely based on PATH wave 1 data collected in 2013–14,[15] as the Amalia *et al* study included only 23 participants.[19]

The pooled data across these two studies (LMD= 0.43, 95% CI: 0.28, 0.58; 1,889 participants) (Fig 5.[11]) showed that the geometric mean urinary lead levels (GMR = 1.54, 95% CI: 1.32, 1.79) were approximately 54% higher among people who vaped than among people who did not smoke or vape; the meta-analysis result was largely based on PATH wave 1 data collected in 2013–1415 as the Amalia *et al* study included only 23 participants.[19] For urinary arsenic levels, we meta-analysed cross-sectional data from the new Amalia study[19] and from a study reporting data from PATH wave 1, which was included in the McNeill *et al* report[1] (Fig 5.12).

The pooled data (LMD= -0.02, 95% CI: -0.12, 0.08; 1,923 participants) (Fig 5.13) showed that the geometric mean urinary arsenic levels (GMR = 0.98, 95% CI: 0.89, 1.08) were approximately 2% lower among people who vaped than among people who did not smoke or vape, which was not a statistically significant difference. The meta-analysis result was largely based on PATH wave 1 data collected in 2013–14, as the Amalia *et al* study included only 23 participants.[23]

#### 5.3.1.4.4 Metals: summary

Across four identified studies, results were inconsistent for metals between people who vaped compared with people who smoked, finding non-statistically significant decreases or increases. No meta-analyses were possible

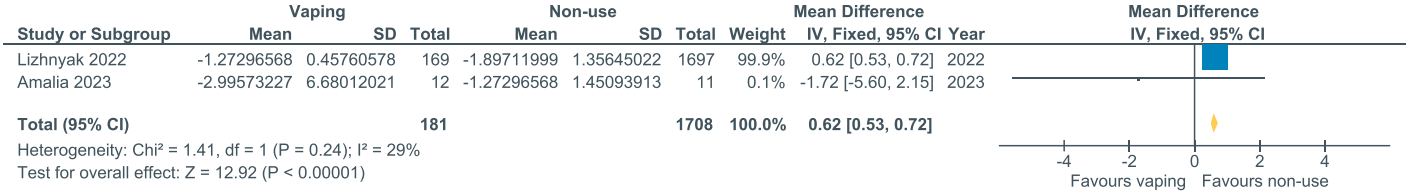


**Fig 5.10. Meta-analysis of cross-sectional data reporting on urinary cadmium levels between people who vaped and non-users.**

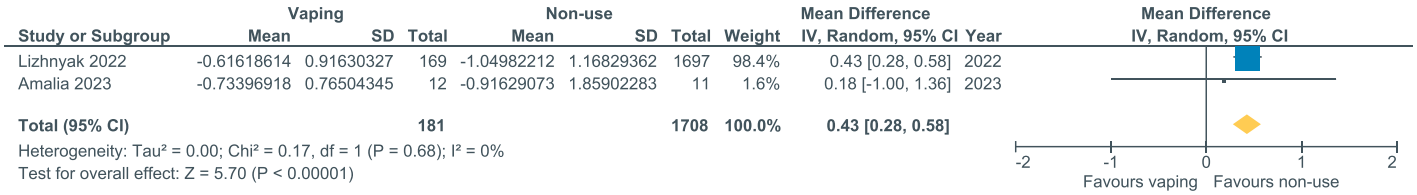


**Fig 5.11. Meta-analysis of cross-sectional data reporting on urinary lead levels between people who vaped and non-users.**

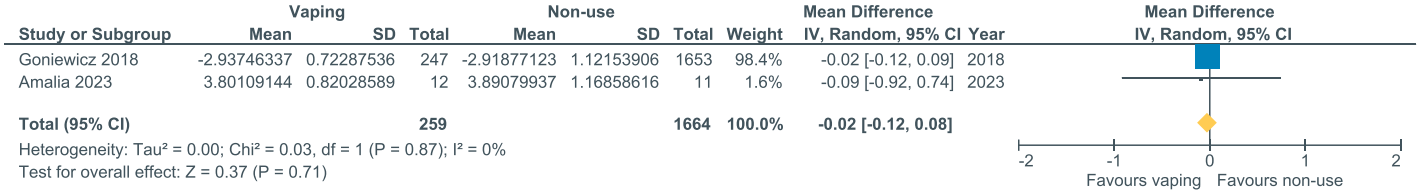


**Fig 5.12. Meta-analysis of cross-sectional data reporting on urinary arsenic levels between people who vaped and non-users.**

comparing vaping with smoking. Meta-analyses, each of two studies, comparing people who vaped with non-users, found approximately 86% higher urinary cadmium levels (statistically significant), approximately 54% higher urinary lead levels (statistically significant) and lower arsenic levels (but not statistically significant) among people who vaped than among people who did not smoke or vape, with these results largely based on much larger US studies where data were collected in 2013–14. Findings from the four new studies were similar to those from 10 studies of metals reported by McNeill *et al*.[1] Due to long half-lives of some metals, a history of smoking can greatly affect the levels of metals among people who stop smoking and vape.

Comparisons between people who vaped and those who vaped and smoked were new. Findings were again mixed. Overall, the data were limited in relation to date of collection, small sample sizes and few studies, so are inconclusive at this stage.

### 5.3.1.5 Aromatic amines

Aromatic amines are formed during tobacco pyrolysis, and bladder cancer is one of the risks associated with exposure to aromatic amines in tobacco smoke.[1] Aromatic amines have been identified as components of e-liquids.[40]

We identified one observational longitudinal open label study conducted in confinement in the USA, which compared urinary levels of two aromatic amines, 2-AN and ortho-toluidine (o-Tol), among people who switched to exclusive vaping for a period of 14 days.[12]

Morris *et al* found that urinary levels of 2-AN were statistically significantly reduced by 89.5% and 85.5% after smokers at baseline switched to exclusive vaping across two study sites at day 14. Similarly, urinary levels of o-Tol were statistically significantly reduced by 77.1% and 45.2% across two study sites at day [14,12]

#### 5.3.1.5.1 Aromatic amines: summary

The updated review identified only one observational longitudinal study assessing two aromatic amines, carried out in confinement and with a short-term follow-up (14 days); statistically significant reductions were identified for both. This study is consistent with the three studies in McNeill *et al* that reported statistically significant lower levels of aromatic amines among people who vaped than in people who smoked (two RCTs with 1-week follow-up and a cross-sectional study).[1] The updated review identified no studies assessing aromatic amines among people who vaped, compared with non-users or people who vaped and smoked.

### 5.3.1.6 Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) are a large class of chemicals formed of two or more benzene rings. They are formed during the incomplete burning of organic materials, such as tobacco, coal, oil and wood. PAHs are also found in food that has been smoked or cooked by grilling or frying. They are widely accepted to be a major contributor to lung cancer among people who smoke.[41] PAHs have also been identified in e-liquids and vaping products aerosols, generally at very low levels.[6]

The most well-known PAH is benzo[a]pyrene (BaP), which is classified as carcinogenic to humans according to IARC.[42] The metabolite of BaP is 3-hydroxybenzo[a] pyrene (3-OH-B[a]P). Another PAH, pyrene is classified as not carcinogenic to humans but is always a component of mixtures of other PAHs that are carcinogenic. Therefore, the metabolite of pyrene, 1-hydroxypyrene (1-HOP), is considered an accepted biomarker of carcinogenic PAH dose.[43] This review, therefore, focused on the metabolites of BaP and pyrene.

Four studies published since July 2021 were identified – three observational longitudinal studies[10–12] and one cross-sectional study[15] that assessed urinary levels of PAHs. Morris *et al* carried out a randomised, open-label, two-part study in confinement that assessed both 3-OH-B[a]P and 1-HOP.[12] The remaining three all used data from the longitudinal PATH study and assessed 1-HOP only: two used cohort data from the 2013–14 and 2014–15 waves[10,11] and one used cross-sectional data only from the 2013–14 wave.[15]

#### 5.3.1.6.1 Vaping vs smoking

Longitudinal studies

Morris *et al* reported changes in urinary 3-OH B[a]P levels after people who smoked at baseline changed to vaping only for 14 days. Authors reported a statistically significant reduction in 3-OH B[a]P levels (87.0% and 79.8% in the two study sites) and in 1-HOP levels (83.9% and 69.2%) 14 days after switching from smoking to vaping exclusively.[12]

Both the other longitudinal studies used data from PATH wave 1 (2013–14) and wave 2, 1 year later (see Table A2.30, appendix 2). Among people who smoked at baseline and switched to vaping at follow-up 1 year later, both studies reported a statistically significant decrease in urinary 1-HOP levels by 55.2%[10] and 55.3%.[11] However, only a small number of people had switched from smoking to vaping, so these data should be treated with caution.

Dai *et al* also reported that 1-HOP levels increased by 63%, not statistically significantly, among 14 participants who transitioned from vaping at baseline to smoking at follow-up.[11]

Dai *et al* also assessed urinary 1-HOP levels in participants who vaped exclusively at baseline and, 1 year later, observed a small decline that was not statistically significant over this time period.[11]

#### Cross-sectional studies

A study by Lizhnyak *et al* analysed cross-sectional data from PATH wave 1 (2013–14) and reported that urinary 1-HOP levels were approximately 50.5% lower among people who vaped than people who smoked, but this was not tested for significance.[15]

#### 5.3.1.6.2 Vaping vs dual use

#### Longitudinal studies

Two longitudinal studies that analysed the same PATH data from waves 1 and 2 reported a statistically significant reduction in urinary 1-HOP levels among dual users at baseline who switched to exclusive vaping at follow-up (48.6% to 51%, see Table A2.30 in appendix 2), but again sample sizes were small.[10,11]

Dai *et al* also reported that people who exclusively vaped at baseline and switched to dual use at follow-up showed a statistically significant increase of 47% in urinary 1-HOP levels, although the number who switched was small.[11]

#### Cross-sectional studies

A cross-sectional PATH wave 1 data reported by Lizhnyak *et al* showed that urinary 1-HOP levels were statistically significantly 48.6% lower among people who vaped than people who frequently smoked and vaped.[15]

#### 5.3.1.6.3 Vaping vs non-use

#### Longitudinal studies

A longitudinal study by Dai *et al* reported a statistically significant reduction of 20% in urinary 1-HOP levels among people who vaped at baseline and were non-users at follow-up 1 year later.[11]

#### Cross-sectional studies

Lizhnyak *et al* reported that urinary 1-HOP levels were 26.5% higher among people who vaped than people who did not vape or smoke at PATH wave 1; the difference was not tested for statistical significance.[15]

#### 5.3.1.6.4 Polycyclic aromatic hydrocarbons (PAHs): summary

Across four identified studies, urinary levels of PAHs were substantially lower (and, where tested, these differences were statistically significant) among people who vaped compared with people who smoked. No meta-analyses were possible. People who vaped had higher urinary PAH levels than those who neither smoked nor vaped. The findings were generally consistent with the eight studies on PAHs reported by McNeill *et al*.[1]

Comparisons between people who vaped and those who vaped and smoked were new. Three studies identified that people who smoked and vaped had statistically significantly higher PAH levels than those who only vaped. In general, sample sizes of the vaping or vaping and smoking groups were small across the four studies.

### 5.3.1.7 Carbon monoxide (CO)

Carbon monoxide (CO) is formed from incomplete combustion of tobacco and is categorised as a reproductive or developmental toxicant[44] and exposure to CO contributes to an increased risk of myocardial infarction and sudden death from coronary heart disease.[45] Exposure to CO is assessed using expired air CO and carboxyhaemoglobin (COHb).

The updated review identified only two longitudinal studies; one an RCT that assessed changes after people who smoked switched to ad libitum exclusive use of cartridge-type vapes (tobacco or menthol flavours) for 24 weeks,[8] and the second an observational longitudinal study carried out on two sites in confinement for 14 days.[12]

One study reported a statistically significantly higher reduction in blood COHb levels in the two vaping groups (60% and 56%)8 than the smoking group (25% reduction), and the other study reported that blood COHb levels reduced by 73.2% and 71.5% when participants who were smoking at baseline switched to vaping exclusively at day 14 at follow-up, across two study sites.[12]

#### 5.3.1.7.1 Carbon monoxide (CO): summary

We identified two longitudinal studies that reported statistically significant reductions in CO among people who switched from smoking after 14 days and 24 weeks. Findings from these two new studies were consistent with the five studies reported by McNeill *et al*.[1] The updated review identified no studies assessing CO among people who vaped, compared with non-users or people who vaped and smoked.

#### 5.3.1.8 Summary of meta-analyses

A table illustrating the results of the meta-analyses in the updated review and McNeill *et al* can be found in Table A2.34 in appendix 2.

## 5.3.2 Cross-cutting biomarkers of potential harm

The next section focuses on biomarkers that are implicated in more than one disease.

### 5.3.2.1 Oxidative stress

Oxidised low-density lipoprotein (LDL) cholesterol is one of the blood lipid profile indicators that can contribute to the development of cardiovascular disease (CVD) and atherosclerosis.[46] Tobacco smoking (as well as diet, physical activity and genetics) is associated with increased LDL cholesterol levels. High-density lipoprotein (HDL) cholesterol levels are also known to be associated with diet, physical activity and genetics, and blood levels are inversely related to CVD. F2-isoprostane and 8-isoprostane (8-iso-prostaglandin F2α, a type of F2 isoprostane) are markers of oxidative stress and lipid peroxidation, and levels of these biomarkers tend to increase after smoking.[46]

In the updated review, two studies in the USA assessed oxidative stress markers: an RCT by Edmiston *et al*,[8] which assessed changes after people switched to ad libitum exclusive use of cartridge-type vapes (tobacco or menthol flavours) for 24 weeks, and one cross-sectional study using PATH wave 1 (2013–14) data.[22]

#### 5.3.2.1.1 Vaping vs smoking

Longitudinal studies

Edmiston *et al* reported statistically significant approximately 9% and 7% increases (ie improvement) in serum HDL cholesterol levels for tobacco- and menthol-flavoured vaping groups respectively after switching from smoking at 24 weeks, and a non-significant decrease of 8% in the smoking group, but changes between the vaping and smoking groups were not statistically significant.[8]

Cross-sectional studies

Christensen *et al*, using the PATH cross-sectional wave 1 data, reported that people who vaped had statistically significantly approximately 25% lower F2-isoprostane levels than people who smoked.[22]

#### 5.3.2.1.2 Vaping vs dual use

Cross-sectional studies

Christensen *et al* did not compare F2-isoprostane levels between vaping groups and people who were smoking and vaping. However, they reported that levels were statistically significantly higher among a frequent dual use group than a non-user group (57% higher) and a smoking group (9% higher).[22]

#### 5.3.2.1.3 Vaping vs non use

Cross-sectional studies

Christensen *et al* reported that there was no statistically significant difference in F2-isoprostane levels between the vaping and non-user groups (former smokers who did not vape and never smoked tobacco).[22]

Christensen *et al* also reported that the F2-isoprostane concentration decreased statistically significantly depending on time since stopping smoking, among participants who vaped (linear trend $p=0.03$) and among participants who stopped smoking and did not vape ($p<0.0001$).[22]

#### 5.3.2.1.4 Oxidative stress: summary

Two indicators of oxidative stress from two new studies were identified in the updated review – HDL cholesterol and F2-isoprostane. Findings on HDL cholesterol from an RCT showing no significant differences in improvements among people who vaped than people who smoked over a 24-month period were broadly consistent with findings from the McNeill *et al* review.[1] For F2-isoprostane, one study indicated lower levels among people who vaped than smoked, and greater reductions were associated with increased time since stopping smoking, both among people who vaped and among people who stopped smoking without vaping. This study also found no statistically significant differences in F2-isoprostane levels between vaping and non-use.

### 5.3.2.2 Inflammation

There are multiple markers of inflammation. Interleukin-6 (IL-6) is a pro-inflammatory cytokine upstream of C-reactive protein (CRP), which is involved in inflammation and infection responses including the regulation of metabolic, regenerative and neural processes.[47] Interleukin-8 (IL-8) is a chemoattractant cytokine produced by multiple tissue and blood cells in response to inflammation, which specifically attracts and activates neutrophils in inflammatory regions.[48] Elevated levels of both IL-6 and IL-8 have been associated with tobacco smoking. Interleukin-1-beta (IL-1β) is another

pro-inflammatory cytokine. White blood cell (WBC) count is a marker of systemic inflammation, and its increase is dose dependent and positively associated with tobacco exposure. CRP is an acute-phase, non-specific marker of systemic and vascular inflammation detected in blood.[46] Tumour necrosis factor alpha (TNF-α) is a pro-inflammatory cytokine involved in the acute phase reaction and implicated in many human diseases. Soluble intercellular adhesion molecule 1 (siCAM-1) is expressed in response to injury or inflammation of the endothelia. Fibrinogen is an inflammation marker and a protein formed in response to vascular injuries and infections.[49] Higher prostaglandin E2 metabolite (PGE-M) levels are associated with tobacco smoking and contribute to the development and progression of a number of cancers.[46,50] Elevated levels of monocyte chemoattractant protein-1 (MCP-1) in blood are associated with hypertension and increased CVD risk.

In the updated review, two RCTs and seven publications from five cross-sectional studies examined inflammation markers. An RCT by Edmiston *et al* reported on WBC counts and siCAM-1 levels,[8] and an NRCT reported on TNF-α levels.[9] Three publications assessed IL-1β levels from two cross-sectional studies,[23,25,30] and two of these also reported IL-6 and IL-8 levels from the same (small) cross-sectional study.[23,30] Two further publications[15,22] also reported IL-6 levels from one cross-sectional PATH study and additionally high-sensitivity CRP, fibrinogen and siCAM-1 levels;[15,22] two additional cross-sectional studies reported on CRP.[23,31] Hickman *et al* also reported siCAM-1 levels;[23] one cross-sectional study reported TNF-α levels,[30] and a further cross-sectional study by Wang *et al* reported on WBC count.[37]

Due to different methodologies/biosamples, reviewed data could not be meta-analysed for the different indicators.

#### 5.3.2.2.1 Vaping vs smoking

##### Longitudinal studies

In their RCT study, Edmiston *et al* reported statistically significant reductions of approximately 10% in blood plasma siCAM-1 levels among participants who switched from smoking to vaping (tobacco- and menthol-flavoured vaping groups) for 24 weeks, and a non-significant increase of 1% in those who continued smoking. The difference between the changes in the vaping group and the smoking group was statistically significant.[8]

Edmiston *et al* also reported that WBC levels decreased statistically significantly in both vaping groups after switching (9% and 10% decreases for tobacco- and menthol-flavoured groups respectively) and there was a non-significant increase of 5% in those who continued smoking. Again, the difference between the changes in the vaping group and the smoking group was statistically significant.[8]

An RCT by Kim *et al* assessed the relative expression levels of TNF-α in the upper airways of people who smoked at baseline and either continued to smoke or switched to vaping or non-use for 12 weeks. They reported that TNF-α levels did not change statistically significantly in the smoking or vaping groups.[9]

##### Cross-sectional studies

Christensen *et al* reported statistically significantly lower siCAM-1 levels among people who vaped compared with people who smoked.[22]

Wang *et al* reported no differences in WBC counts between smoking and vaping groups in their cross-sectional study.[37]

Hickman *et al* and Payton *et al* reported results from the same cross-sectional study assessing effects of self-reported smoking and vaping for at least 6 months on airway biomarkers of potential harm, including a range of cytokines.[23,30] Payton *et al* reported no statistically significant differences in TNF-α levels between vaping and smoking groups across four biosamples – nasal lavage fluid, epithelial lining fluid, sputum and blood serum.[30]

Hickman *et al* reported no statistically significant differences in sputum IL-623 and Payton *et al*, from the same study, reported no statistically significant differences in sputum IL-1β, IL-6 or IL-8 levels between people who smoked and people who vaped.[30]

Christensen *et al*, using PATH wave 1 data collected in 2013–14, reported that IL-6 levels were statistically significantly approximately 16% lower among people who vaped (all former smokers) compared with people who smoked.[22] One additional study, however, did report statistically significantly higher salivary IL-1β levels among people who smoked than those who vaped.[25]

Using PATH wave 1 data, Christensen *et al* reported statistically significantly lower CRP levels among people who vaped compared with people who smoked, but no statistically significant difference in fibrinogen levels.[22] By contrast, Podzolkov *et al* reported no statistically significant differences in serum CRP levels between participants who vaped and participants who smoked,[31] as did Hickman *et al*.[23]

However, among participants who vaped, Hickman *et al* found the lowest CRP levels among people who vaped fourth-generation vaping products (low-powered with nicotine salts) that statistically significantly differed from people who vaped third-generation vaping products (users of vape pens or box mods with freebase nicotine). Hickman *et al* also reported statistically significantly lower siCAM-1 levels among fourth-generation vape models compared with third-generation models.[23]

#### 5.3.2.2.2 Vaping and dual use

##### Cross-sectional studies

Lizhnyak *et al* reported that people who smoked and vaped had significantly higher siCAM-1 levels than people who exclusively vaped, but there was no statistically significant difference for IL-6, CRP or fibrinogen.[15] Wang *et al* reported no statistically significant differences in WBC count between vaping and dual use groups.[37]

#### 5.3.2.2.3 Vaping and non-use

##### Longitudinal studies

Kim *et al* reported that TNF-α levels did not change statistically significantly in the group that switched to vaping, but significantly reduced in people who stopped smoking with NRT or varenicline.[9]

##### Cross-sectional studies

The cross-sectional study by Payton *et al* reported no statistically significant differences in TNF-α levels between vaping and non-use groups across the four biosamples collected.[30]

Using PATH wave 1 data, Christensen *et al* reported no statistically significant differences between people who exclusively vaped (all former cigarettes smokers), former cigarette smokers who did not vape and never tobacco users, in high-sensitivity CRP levels (people who vaped were 14% lower), fibrinogen or siCAM-1 levels. There were also no statistically significant differences in CRP between never-users and people who smoked (17% higher).[22]

Similarly, Payton *et al* and Hickman *et al*, using the same cross-sectional study, found no significant differences in sputum CRP levels between people who vaped and non-users.[23,30] However, Podzolkov *et al* found statistically significantly lower serum CRP levels among participants who were not using tobacco or nicotine products than those who were vaping (or smoking).[31]

Using PATH wave 1 data, Christensen also reported no statistically significant differences between people who exclusively vaped, former cigarette smokers who did not vape and never tobacco users, in IL-6 (people who vaped had 2% lower levels).[22] In comparison, both Payton *et al* and Hickman *et al* reported that IL-6, but not IL-1β or IL-8, levels were statistically significantly higher among participants who smoked than non-users.[23,30] However, a further cross-sectional study reported higher IL-1β levels among people who vaped than non-users.[25]
Wang *et al* reported statistically significantly higher WBC counts in people who vaped than non-users.[37]

#### 5.3.2.2.4 Inflammation: summary

Overall, seven new studies in nine publications reported mixed findings for inflammatory biomarkers. The findings on IL-6 and IL-8 levels from the new cross-sectional studies remain mixed, as they were in the McNeill *et al* review.[1] Two studies with a small sample size[23,30] found no differences between people who vaped, people who smoked and non-users for IL-6, IL-8 and IL-1β. However, data from the larger PATH wave 1 sample indicated that people who vaped had lower IL-6 levels than people who smoked, and no difference was found between people who vaped and non-users. An additional cross-sectional study also found lower IL-1β levels among people who vaped than people who smoked, but higher levels than among non-users.

New evidence from PATH suggests that CRP levels are highest among people who smoke and people who both smoke and vape, and there is no difference between people who vape and non-users.[15,22] Podzolkov *et al*, however, found no difference between people who smoked and people who vaped,[31] and another study that reported no significant differences between vaping, smoking and non-user groups did, however, find that CRP levels might differ depending on the type of vaping device or nicotine type used.[23] The evidence on CRP therefore remains mixed, similar to findings reported by McNeill *et al*.[1]

In the updated review, similar to the prior review, studies reported significantly lower siCAM-1 levels among people who vaped than people who smoked. New to this review is a finding (from one study) that people who smoked and vaped had significantly higher siCAM-1 levels compared with people who exclusively vaped.

No statistically significant differences in fibrinogen levels were reported between people who vaped, smoked or were non-users in two new studies using the same PATH wave 1 data. This is consistent with findings reported by McNeill *et al*.[1]

An RCT reported a statistically significant reduction in WBC counts in participants who switched from smoking to vaping for 24 weeks, which was also significantly

different from changes in those who continued smoking.[8] However, a new cross-sectional study found no differences in WBC counts between smoking, dual use and vaping groups, and reported statistically significantly higher WBC counts in people who vaped than in non-users.[37] As in McNeill *et al*, the evidence on vaping and WBC therefore remains mixed.

## 5.3.3 Disease-specific biomarkers of potential harm

### 5.3.3.1 Cancer

#### 5.3.3.1.1 How might vaping affect cancer?

The possible biological pathways for how vaping (and smoking) may theoretically influence the development of cancer, respiratory and cardiovascular disease are described in detail by McNeill *et al*.[1] For cancer, NASEM hypothesised that exposure to toxicants in vaping products (for example, aldehydes) may cause inflammation, leading to cytotoxicity and cell death, potentially influencing tissue repair and immune response.[5] Toxicant exposure might also theoretically lead to reactive oxygen species and/or their reactive intermediates that bind to DNA. This may cause damage to DNA and no or incorrect DNA repair. It is hypothesised this may then lead to activation of oncogenes (mutated genes that contribute to the development of a cancer) and/or loss of function of tumour suppressor genes (normal genes that slow down cell division, repair DNA mistakes or tell cells when to die). When tumour suppressor genes do not work properly, cells can grow out of control, which in the long term can lead to cancer. Advances in epigenetic studies (the study of how behaviours and the environment can cause changes that affect the way that our genes work) are increasingly helping our understanding of how smoking and vaping may influence health risks. Epigenetic changes affect gene expression to turn genes 'on' and 'off'. Types of epigenetic changes include DNA methylation and non-coding RNA (methylation turns genes 'off' and demethylation turns genes 'on'). DNA methylation is a type of epigenetic modification involving the addition of methyl groups to the DNA, which influences how the underlying sequence is interpreted and expressed. Some, but not all, altered DNA methylation is reversible after stopping smoking.

#### 5.3.3.1.2 Findings from the review

In the updated search, four studies were identified that provide information on DNA methylation and gene expression related to vaping, all cross-sectional. One study was conducted in England[33] and three in the USA. Sample sizes ranged from 2732 to 350.[33] Ages ranged from 18–65 years, though across studies most of the participants who vaped were in their 20s and had been vaping for around 2–3 years.

Richmond *et al* evaluated associations between e-cigarette use and epigenome-wide methylation from saliva of 116 people who exclusively vaped, 117 who smoked and 117 who did neither. Participants in the vaping group had used an e-cigarette at least weekly for the past 6 months and had smoked fewer than 100 times in their lifetime. Those in the smoking group had smoked at least weekly for the past 6 months and used an e-cigarette fewer than 100 times in their lifetime; and the never-smokers were defined as not having smoked and/or used an e-cigarette <100 times in their lifetime. The DNA methylation profile of participants who vaped was less pronounced than that of participants who smoked. Methylation at cg05575921 was 8.2% (95% CI: 5.7, 10.5) lower in participants in the smoking group than those in the non-using group, and 7.1% (95% CI: 4.6, 9.6) lower in those who smoked than in those who vaped. The DNA methylation profile for e-cigarette use was largely distinct from that of cigarette smoking, did not replicate in independent datasets, and was unable to discriminate lung cancer from normal tissue (unlike the smoking profile).[33]

Tommasi *et al* investigated the differential expression of genes and alteration of pathways and gene networks in blood leukocytes of 37 people who vaped, 22 who smoked and 23 who did neither. The number of differentially expressed genes of those in the smoking group was around 7.4 times higher than that in those who vaped (683 vs 92). The differentially expressed genes of participants in the vaping group consisted of 59 upregulated (64.1%) and 33 downregulated (35.9%) genes, and more than half (66.3%) were protein-coding genes. In the smoking group, there were 471 upregulated (69.0%) and 212 (31.0%) downregulated genes; 54.8% were protein-coding, while the remaining belonged to several classes of gene/transcript biotypes, including short and long non-coding RNAs. Just under a third (n=25/92) of genes were differentially expressed in the vaping group only; 616/683 (90%) were expressed in the smoking group only and 67 genes were differentially expressed in both groups. Tommasi *et al* conducted a sensitivity analysis using estimated cumulative e-liquid and pack-year modelling and reported that past smoking was not associated with gene dysregulation in participants who smoked, but current vaping was. He suggested that the overlap of differentially expressed genes in both vapers and smokers was likely due to exposure to similar chemicals (possibly aldehydes and heavy metals) present in both e-cigarette and combustible cigarette emissions.[35]

Advancing their work further, Tommasi *et al* assessed DNA damage in the oral cells of 24 people who exclusively vaped and had never smoked, 24 people who smoked and 24 who had never smoked or vaped, matched for age, gender and race. Participants in the vaping group reported current use of e-cigarettes at least 3 times a week for a minimum of 6 months and no use of combustible cigarettes or any other tobacco products in their lifetime. Those in the smoking group reported currently smoking tobacco cigarettes at least 3 times per week for a minimum of 1 year, no or less than five vaping sessions in their lifetime, and no use of any other tobacco products (except for combustible cigarettes) in the past 6 months. Non-users reported smoking no or fewer than 100 cigarettes or having no or less than five vaping sessions in their lifetime (no vaping or smoking in the past 6 months). DNA damage in oral epithelial cells was collected from brushings and was quantified using a long-amplicon quantitative polymerase chain reaction assay (LA-qPCR). The levels of DNA damage in the polymerase beta (POLB) gene in the oral cells of participants in the vaping and smoking groups were not statistically significantly different. There were 2.6- and 2.2-fold increases, respectively, in mean levels of DNA damage in the POLB gene in the oral cells of participants in the vaping and smoking groups compared with participants in the non-using group. These results were also confirmed in an LA-qPCR analysis of an independent gene target (HPRT). Among the participants who vaped, users of pod-based devices had the highest levels of DNA damage in their oral cells as compared to non-users, followed by users of mod-based devices and multiple device users (only one participant used a first-generation 'cig-a-like' device and none used modern 'disposables'). Those who used sweet-, mint or menthol-, and fruit-flavoured e-liquids showed the highest levels of DNA damage. The nicotine content of e-liquid was not a predictor of DNA damage in vapers.[36]

Reeve *et al* compared the histology and transcriptome (mRNA and miRNA) in oral epithelium cells among 24 healthy participants who vaped and 23 participants who served as a healthy non-smoking control group (non-users). Among the 24 participants who vaped, 17 participants exclusively vaped (15 of whom had formerly smoked and had not smoked in the past 6 months) and seven concurrently vaped and smoked. They were compared with 23 participants who had never smoked or vaped. Oral biopsies were obtained from the buccal mucosa and an examination of tissue and cells in the vaping group appeared normal. Genome-wide mRNA assessment of the oral epithelium transcriptome of participants who vaped compared with non-users found no genes that were differentially expressed.[32]

#### 5.3.3.1.3 Cancer risk: summary

There is a growing albeit still small number of studies of how vaping relative to smoking and vaping compared with non-use may affect cancer risk. Most cancers have several rather than a single cause and have a long latency period. Four studies were identified that provide information on DNA methylation and gene expression related to vaping. Early indications of impact on DNA and gene expression from good-quality research studies can be informative about potential future risk. The more recent study by Tommasi *et al*,[36] for example, considers several confounding factors that can influence DNA damage, eg frequency of use. Gene expression and DNA methylation are more pronounced in people who smoke than vape and there is evidence of a small amount of overlap with people who smoke.[36] However other studies did not find a significant difference in the oral cells of people who vaped compared with people who did not vape or smoke. These findings are consistent with those of McNeill *et al*, in that there is some, but currently insufficient, evidence that vaping alters gene expression and DNA methylation. Further clarity is still needed on how much this overlaps with the alteration of gene expression and DNA methylation related to smoking and why, as well as absolute effects. There remains no research in humans about how vaping affects disease progression in people with an existing or prior cancer condition relative to smoking or in comparison to never smoking.

### 5.3.3.2 Cardiovascular health

#### 5.3.3.2.1 How might vaping affect cardiovascular health?

There are several possible biological pathways for how vaping may theoretically influence the development of cardiovascular disease (CVD). One plausible pathway suggests that exposure to metals, oxidant chemicals and particulate matter could increase, among other things, inflammation, oxidative stress, platelet activation and thrombosis, endothelial dysfunction and atherosclerosis. This in turn would increase the risk of myocardial ischaemia and coronary heart disease via reduced myocardial blood, oxygen and nutrient supply.[5]

As e-cigarettes can deliver similar levels of nicotine to tobacco cigarettes (with experienced use), exposure to nicotine can produce the same sympathomimetic effects, including increased heart rate, blood pressure and myocardial contractility. A rise in the demand for oxygen and nutrients may subsequently increase the risk of myocardial ischaemia and coronary heart disease.[51]

#### 5.3.3.2.2 Findings from the review

Three studies were identified that provide information on the biomarkers of potential harm with specific relevance to cardiovascular health, all cross-sectional. Two of the studies were conducted in the USA[20,28] and one in Russia.[31] Sample sizes ranged from 51[28] – 396.[31] Average ages ranged from 21 to 34 years and participants had been vaping for about 1.7[28]– 4 years[31] (not reported by Amraotkar *et al*).[20] Participants were 'healthy' and excluded if they had symptoms of CVD. Mohammadi *et al* assessed brachial artery flow-mediated dilation (FMD), a marker of endothelial function and an early predictor of cardiovascular disease, among a subsample (n=51) of participants from a larger study.[22] participants vaped, 13 smoked and 16 were non-users. Frequencies of use are provided for the larger sample and included vaping (5 or more times a week for mean (SD) of 1.7 (0.7) years); exclusive smoking (5 or more times a week for a mean (SD) of 10.2 (10.4) years); non-using group (smoked less than 1 pack a year or quit more than 5 years ago).[28]

FMD was significantly lower in both those who vaped (5.3±2.3%) and those who smoked (6.5±2.8%), relative to the non-using group (10.7±5.2). The authors also argue that these results are clinically significant, as an absolute reduction in FMD of 2 percentage points has been associated with a 15% increase in CVD risk.[52]

Podzolkov *et al* assessed the ankle-brachial index, a marker of peripheral arterial disease, among 396 participants, 90 of whom vaped, 83 who smoked and 196 who had neither smoked nor vaped in the previous 12 months. It is unclear whether the vaping and non-using groups had a history of smoking. The average ankle-brachial index was 0.85 (95% CI: 0.79, 0.93) in the vaping group, 0.98 (95% CI: 0.91, 0.99) in the smoking group and 1.12 (95% CI: 1.01, 1.18) in the non-smoking/non vaping group. The average index in both the smoking and vaping groups was statistically significantly lower than the non-smoking/vaping group and the average index in the vaping group was statistically significantly lower than in the smoking group.[31] An ankle-brachial index of less than 0.9 is associated with an increased risk of CVD.[53]

Both Mohammadi *et al* and Podzolkov *et al* also assessed heart rate, systolic and diastolic blood pressure. In the study by Mohammadi *et al*, there was no statistically significant difference between vaping, smoking and non-using groups.[28] In the study by Podzolkov *et al*, heart rate was statistically significantly higher in the group that smoked than in the group that vaped.[31] Systolic blood pressure and heart rate were statistically significantly higher in the vaping and smoking groups than in the non-using group.

Amraotkar *et al* assessed circulating angiogenic cells (CACs), biomarkers of vascular injury and of capacity for vascular repair in 324 participants aged 21–45 years of age. Participants in the vaping group (n=19) were defined as currently vaping at least 5 days per week and had not used combustible cigarettes for at least 3 months (the authors reported that most had previously smoked). Those in the smoking group (n=212) were defined as currently smoking at least 5 days per week, having smoked more than 100 cigarettes in their lifetime, and had not vaped for at least 3 months. Those who dual used (n=28) were defined as participants who reported current use of both combustible and e-cigarettes, at least 5 days per week, with a lifetime usage of more than 100 cigarettes. Participants were classified as never tobacco users (n=65) if they had smoked fewer than 100 cigarettes in their lifetime, were not current smokers or users of other tobacco products and had a urinary cotinine level less than 10 ng/mL.[20]

There were no statistically significant associations with any CAC subtypes between the vaping and smoking groups. The vaping group showed significantly higher circulating levels of two CAC subsets compared with never tobacco users and the dual use group showed four CAC subsets significantly higher than never tobacco users, two of which overlapped with the smoking group. Those in the smoking and dual use groups had higher circulating levels of CACs characterised by endothelial surface markers, and lower circulating levels of CACs with stem surface markers. Among the vaping group, there was an association with higher levels of two CAC subpopulations, one with endothelial surface markers and one with leukocytic surface markers. The authors suggested that the use of e-cigarettes and combustible cigarettes has differential associations with circulating populations of cells with regenerative potential; however, they also point out that that participants in the vaping group had smoked in the past.

#### 5.3.3.2.3 Cardiovascular health: summary

Two cross-sectional studies, identified in the updated review that assessed differences in heart rate and blood pressure among people who vaped compared with those who smoked or did neither, are consistent with the findings of McNeill *et al*.[1] Heart rate was lower or similar among people who vaped compared with those who smoked, and similar or higher in vaping groups compared with non-using groups. Systolic blood pressure was similar between those who vaped or smoked and higher among people who vaped or smoked compared with those who did neither. Only one new cross-sectional study was identified that assessed brachial artery FMD; its results were inconsistent with the findings of the one

cross-sectional study and seven other studies identified by McNeill *et al* that found no difference in FMD between people who vaped, smoked or did neither. Following the RCT reported by McNeill *et al* showing that participants' FMD function improved after switching from smoking to vaping for a relatively short time (4 weeks), no further longitudinal studies have been published.

The updated review identified studies reporting on CVD-specific biomarkers not included by McNeill *et al*, specifically ankle-brachial index scores and CACs. Both would benefit from being researched further, with efforts made to test these biomarkers in exclusive vapers who have never smoked.

### 5.3.3.3 Respiratory diseases

#### 5.3.3.3.1 How might vaping affect respiratory health?

NASEM proposed possible pathways through which vaping might affect respiratory disease. Ultrafine particle exposure could damage airways through DNA damage, inducing pro-inflammatory cytokine expression, producing free oxygen radicals that affect the immune system.[5] Exposure to ultrafine particles could also increase asthma exacerbations. Nicotine may decrease viral and bacterial clearance, impair cough, and cause α7 nicotinic acetylcholine receptor activity and cystic fibrosis transmembrane conductance regulator (CFTR) dysfunction in the airways. E-liquid flavourings could induce pro-inflammatory cytokine expression. Although aversive to people who vape, a high temperature of vaping devices could cause the production of toxic formaldehyde. The possible effects of vaping on respiratory health may vary depending on whether a person's airways had previously been damaged by smoking.[1]

#### 5.3.3.3.2 Findings from the review

Three studies were identified that provide information on biomarkers of potential harm with specific relevance to respiratory health. Two studies collected spirometry measures (forced expiratory volume in 1 second (FEV1); forced vital capacity (FVC); FEV/FVC ratio),[8,24] and one assessed mitochondrial DNA copy numbers (mtCN) using bronchoscopies.[29] Two studies were conducted in the USA[8,29] and one in the UK.[24] Sample sizes ranged from 84–228, ages ranged from 21–69 years, and one of the studies included people with a diagnosis of COPD.[24]
One RCT reported on lung function measures after 150 participants who smoked at baseline switched to menthol- or tobacco-flavoured vapes for 24 weeks. From baseline to 24 weeks, a significantly slower decline in FEV1 and FVC in those who switched to vaping menthol products and no difference in the FEV1/FVC ratio was reported compared with those who continued to smoke. There were no statistically significant differences in the group switching to tobacco-flavoured vapes compared with those continuing to smoke, and no significant differences between the two vaping groups on any lung function measure.[8]

In a retrospective analysis of data collected in 2014–20, Higham *et al* compared airway inflammatory cell count among patients with COPD who were currently smoking (n=72), patients who stopped smoking for a median of 14 years (n=133) and patients who stopped smoking for a median of 3 years and were currently vaping (n=23).[24] Mean age across the three study groups ranged from 64–69 years and groups differed statistically significantly in mean (SD) smoking pack-years: 38 in people who had stopped smoking and were not vaping,[20,46] in the vaping group[13] and 51 in the smoking group.[19] The COPD assessment test results and spirometry measures (FEV1, FEV1/FVC) did not differ statistically significantly between the three groups. The study reported several significant differences in airway inflammation profiles between the smoking, vaping and non-use groups. The percentage of neutrophils in sputum was statistically significantly lower in the smoking compared with the vaping and non-use groups, and the percentage of macrophages was significantly higher in the smoking group than in other two groups. The lower rate of neutrophils among patients with COPD who smoked might suggest that acute toxic effects of cigarette smoke may influence lung neutrophil numbers,[24] while a higher percentage of neutrophils and lower percentage of macrophages in sputum of patients with COPD who stopped smoking or were vaping indicate a different type of airway inflammation than when patients with COPD are smoking.

A cross sectional study by Mori *et al* used bronchoscopy biospecimens to assesses mitochondrial DNA copy numbers (mtCN), and the association with nuclear biomarkers, such as DNA methylation and gene expression in 84 participants aged 20–31 years of age. The smoking group (n=26) was defined as smoking more than 10 cigarettes a day for more than 6 months and additionally had not used an e-cigarette for at least a year. The vaping group (n=15) used nicotine-containing e-cigarettes daily for at least 1 year and had not smoked a cigarette for more than 6 months; a majority of the vaping group were people who had formerly smoked (n=11). The group that had never smoked (n=43) had smoked fewer than 100 cigarettes in their lifetime and also had not smoked a cigarette or vaped for at least one year prior to enrolment. mtCN was significantly

higher in the smoking compared with the never smoking group and mtCN in the vaping group was numerically intermediate between the other two groups.[29] Positive associations between mtCN and lung disease-associated cytokines such as IL-2 and IL-4 were seen in the vaping group but not the smoking and never smoking groups, and the authors commented that additional research was needed to investigate the clinical relevance of these findings. E-cigarette specific mtCN-CpGs (regions in DNA sequences where methylation can appear and influence gene expression) and transcript genes were found to be differentially expressed in respiratory diseases such as asthma, COPD and lung cancers, including genes involved in cellular movement, inflammatory response, metabolisms and airway hyperresponsiveness. Mori *et al* concluded that smoking may elicit a toxic lung effect through mtCN. Also, mtCN was significantly associated with inflammation and nuclear DNA methylation and gene expression in the lungs of healthy individuals. While a toxic effect in mtCN by participants who vaped (and used to smoke) was less clear, vaping-specific associations of mtCN with nuclear biomarkers were found. The authors cautioned that their cross-sectional study design could not assess the causal relationship of mtCN with nuclear biomarkers, which may be influenced by unknown confounders.[29]

#### 5.3.3.3.3 Respiratory diseases: summary

Three new studies on respiratory health were identified. While the newly identified RCT followed up participants at 6 months,[8] which was twice the follow-up time in the RCT[54] reviewed by McNeill *et al*,[1] findings were mixed but changes in lung function studies may require several years to detect.

A novel cross-sectional study identified for the review update assessed mitochondrial DNA copy numbers via bronchoscopies, which identified potential mechanisms for toxic lung effects of vaping requiring further research.[29]

Regarding participants with existing smoking-related lung disease, authors reported in one cross-sectional study identified in the updated review that spirometry measures (FEV1, FEV1/FVC) did not differ statistically significantly between a group of patients with chronic obstructive pulmonary disease (COPD) who were smoking, who stopped smoking, and who stopped smoking and were vaping.[24] However, there were differences in smoking history and duration since stopping smoking between groups. The findings from cross-sectional data contrast with the prior review by McNeill *et al*.[1] Further research that follows people up long term or among people who have quit smoking and switched to vaping is still needed among people with pre-existing respiratory conditions.

### 5.3.4 Second-hand exposure

Two new cross-sectional studies investigating second-hand exposure to vape aerosols among non-users of tobacco or vaping products were identified. Amalia *et al* compared people who used e-cigarettes daily and exclusively for at least a month (vaping group, n=29) to people who were not using tobacco or vaping products (or had not used for at least 1 month) and either lived in the same home as someone in the vaping group (exposed group, n=29) or did not live with someone who vapes (non-exposed group, n=21).[19] It should be noted that individuals in the 'non-user' groups may have been using tobacco products up to a month before sample collection. AlMubarak *et al* compared young adults who did not smoke or vape and either reported no second-hand exposure to tobacco or vaping products (non-exposed group, n=24) or reported daily at least 5-minute exposure to vape aerosols for at least a year (exposed group, n=24).[18]

The exposed group from Amalia *et al* had statistically significantly higher levels of salivary cotinine than participants in the non-exposed group (0.24 ng/mL, 95 % CI: 0.09, 0.60, vs 0.01 ng/mL, 95 % CI: 0.00, 0.12; p=0.003), although urinary cotinine levels did not differ statistically significantly between these groups (1.04 ng/mL, 95 % CI: 0.28, 3.87, vs 0.33 ng/mL, 95 % CI: 0.19, 0.57; p=0.24). The salivary nicotine concentrations of the exposed group were lower than those of non-exposed non-users (0.17 vs 0.28 ng/mL); however, 90.5 % of samples from the exposed group were below the limit of quantification compared with 62 % in the non-exposed group. The vaping group had statistically significantly higher levels of cotinine and nicotine than the exposed group, both in saliva and in urine.[19] The exposed group from AlMubarak *et al* had higher levels of salivary cotinine than the non-exposed group (M(SD)=17.5 (3.1) ng/mL vs M (SD)=0.17 (0.006) ng/mL; p<0.001).[18]

Additionally, Amalia *et al* measured other biomarkers of exposure, including TSNAs (NNA, NNN, NNK) in saliva and urine, and metals (arsenic, cadmium, lead, and mercury) in urine. No statistically significant differences between the exposed and non-exposed groups were identified for these biomarkers. The authors found that out of 27 metal elements analysed in urine, only levels of cobalt were higher in the exposed than the non-exposed group (M=0.60 µg/L, 95 % CI: 0.19, 1.86, vs M=0.22 µg/L, 95 % CI: 0.12, 0.38; p=0.031);[19] nevertheless, these findings should be treated with care, as the half-life for

cobalt is around 5 years and prior tobacco product use might also be associated with assessed cobalt levels. Finally, AlMubarak *et al* measured salivary levels of IL-1β, which was statistically significantly higher among the exposed group than the non-exposed group (M(SD)=26.2 (6.4) pg/mL vs M(SD)=0.12 (0.005); p<0.001), suggesting a possible effect of exposure to second-hand vape aerosol on this inflammatory cytokine.[18]

#### 5.3.4.1 Second-hand exposure: summary

Of the two new studies in this updated review, both found higher levels of salivary cotinine among non-users who were exposed to vaping than in those not exposed. Levels of saliva cotinine were very low and unlikely to potentiate dependence. Regarding biomarkers of potential harm, one new study found significantly higher salivary IL-1β levels among exposed than non-exposed participants, suggesting that this may be a possible effect of exposure to second-hand vape aerosol. Levels of other biomarkers of exposure to toxicants did not differ between the exposed and not exposed groups. These findings were in line with conclusions made by McNeill *et al* that shorter exposures to second-hand vaping aerosol do not result in detectable increases in toxicant exposure among non-users.[1]

## 5.3.5 Pregnancy

Ussher and colleagues recently conducted a systematic review on the health consequences of vaping during pregnancy. They searched six databases up to February 2023 and included quantitative, English language, human studies that assessed vaping and maternal or fetal/infant outcomes. The authors summarised relative risk (vaping compared with smoking) and absolute risk (vaping compared with no use of nicotine or tobacco).[2] Twenty-one cohort studies included a total of about 534,474 women and one RCT, which compared vaping and nicotine replacement therapy (NRT) for smoking cessation among 1,140 pregnant women. Fifteen studies were conducted in the USA, four in the UK, one in Italy, one in Ireland and one in the Netherlands.

Study quality was assessed with the mixed-methods appraisal tool, which includes five criteria that differ according to study type. For the cohort studies, study quality was poor – for example, none of the studies adequately assessed exposure to smoking and vaping and many did not have representative samples or provide information on whether the exposure occurred as intended. The RCT met four out of five quality criteria, missing the last one because of contamination, specifically because every participant in the NRT arm who successfully stopped smoking also used vaping products. Five studies assessed pregnancy outcomes; one found no evidence of increased absolute risk of exclusive vaping and inconclusive evidence for relative risk. Another reported increased relative and absolute risk for miscarriage, which could be a spurious finding as the study included only 10 exclusive vapers, with three using non-nicotine vapes. The other three studies were not designed to assess relative or absolute risk.

Only two studies assessed biomarkers of exposure, one among people who vaped exclusively, the other among people who smoked and vaped; both had small sample sizes (7 and 11, respectively). One reported that various toxicant and carcinogenic urinary biomarkers were substantially lower among people who were exclusively vaping than people who smoked or people who smoked and vaped, although no statistical tests were reported. The other study reported on NNK and NNAL levels and reported that these were not significantly different for people who smoked and vaped, smoked exclusively or who neither smoked nor vaped; this study did not include people who exclusively vaped.

Among the 14 cohort studies assessing the key fetal or infant outcomes of pre-term birth or gestational age, small-for-gestational-age and (low) birthweight, there were 14 reports of outcomes with no increased absolute risk and eight of increased absolute risk; there were four reports of lower relative risk compared with smoking and six observations of comparable risks. The one RCT included in the review observed no difference in adverse outcomes except that babies in the vaping arm had significantly less risk of low birthweight than in the NRT arm, most likely due to more successful smoking cessation. Neurological outcomes were assessed in three studies, mostly finding risks of vaping similar to smoking and, depending on the outcome, similar or higher than for non-use.

In conclusion, while overall more studies found no evidence of increased absolute risk of vaping, findings for relative risk were less clear for most outcomes. However, the quality of the evidence limited conclusions. The only good-quality RCT indicated positive outcomes on birthweight.

The authors identified that large, longitudinal, naturalistic studies examining risk of vaping are needed, particularly with women who exclusively vape throughout pregnancy compared with non-users and exclusive smokers. Also, risks need investigating in RCTs of smoking cessation in pregnancy, comparing nicotine and placebo vaping, for example. Adequate assessment of levels of vaping and smoking are needed to address current limitations where, for example, a majority of low-level vaping may have masked any effects of vaping, while previous or

concurrent smoking may have caused heightened risk in groups categorised as vaping.[2]

## 5.3.6 Adverse reactions to vaping reported in clinical trials

As indicated at the start of the chapter, we did not assess self-reported symptoms as these are often assessed subjectively and retrospectively, and the temporality of the symptoms in relation to the exposure to vaping or smoking is frequently unclear and unaccounted for. Instead, we report here a summary of adverse and serious adverse events from clinical studies evaluating the effect of vaping on smoking cessation, included in the Cochrane living systematic review on e-cigarettes.[3] The review by Hartmann-Boyce *et al* includes 55 studies that reported data on adverse events and 38 studies on serious adverse events published between 2004 and 2022.[3]

### 5.3.6.1 Adverse and serious events reported in studies comparing nicotine e-cigarettes with nicotine replacement therapy (NRT)

In their meta-analyses, Hartmann-Boyce *et al* reported pooled data from four studies that were low risk of bias and included 1,702 participants. The analysis showed no evidence of a statistically significant difference in adverse events between those who used an e-cigarette and those who used NRT (RR 1.02, 95% CI: 0.88, 1.19), nor a statistically significant difference in serious adverse events (RR 1.12. 95% CI: 0.82, 1.52).[3] In their narrative review of studies not included in the meta-analysis, Hartmann-Boyce *et al*[7] described a further two studies that had followed up participants for 6–12 weeks. One study reported that there was a trend towards decreased dyspnoea and COPD symptoms among participants in the e-cigarette arm compared with the NRT arm, and in the other study most respiratory adverse events were lower among e-cigarette participants than those in the NRT arm. Five studies that were low risk of bias and included 2,411 participants showed a small increased number of serious adverse events in participants receiving an e-cigarette, but with wide confidence intervals incorporating no difference (RR 1.12, 95% CI: 0.82, 1.52). The narrative review included one study that followed up participants for 6 months with no serious adverse events.

### 5.3.6.2 Adverse and serious events in studies comparing nicotine e-cigarettes with e-cigarettes without nicotine or behavioural support only or no support

Pooled data from five studies (none at high risk of bias) including 840 participants showed no significant difference in the number of participants experiencing adverse events when comparing e-cigarettes with nicotine to e-cigarettes without nicotine (RR 1.01, 95% CI: 0.91, 1.11). In the narrative review of studies not included in the meta-analysis and comparing e-cigarettes with and without nicotine, one found similar adverse event rates between groups, and two reported more adverse events in the nicotine e-cigarette group. Eight studies involving 1,272 participants reported on serious adverse events for e-cigarettes with nicotine compared with those without nicotine; four of these reported no serious events. In the other four studies in the meta-analysis (three low risk of bias, one unclear) there was no evidence of a difference between groups (RR 1.00, 95% CI: 0.56, 1.79).

When comparing e-cigarettes with nicotine to behavioural support only or no support, in four studies including 765 participants (with a high risk of bias), more people assigned to nicotine e-cigarette groups reported experiencing adverse events (RR 1.22, 95% CI: 1.12, 1.32). Findings from the narrative review of six studies comparing nicotine e-cigarettes with behavioural or no support were mixed. Some found that participants who used e-cigarettes experienced throat irritation, cough and dry mouth more than participants who continued to smoke, whereas another study found a reduction in respiratory symptoms among people using e-cigarettes compared with those who smoked. One study found an increase in throat irritation, palpitations and dizziness in the e-cigarette group, and decreases in cough, headache, nausea, dry mouth, shortness of breath and stomach pain. In other studies where primary authors had provided frequencies, the most common adverse events among vaping groups were cough, reported roughly by a third, and sore throat or throat irritation reported by around a quarter of participants.

Nine studies, including 1,993 participants, compared e-cigarettes with nicotine versus behavioural support only or no support and reported data on serious adverse effects. In five of these studies, no events occurred. Pooled results from the four studies in which events occurred showed no clear evidence of a difference between groups (RR 1.03, 95% CI: 0.54, 1.97). In the narrative review, six studies reported that no serious adverse events occurred. In one study that recruited participants from mental health settings, five serious adverse events were recorded during the study, all of which were psychiatric hospitalisations. None were considered related to study treatment.

### 5.3.6.3 Adverse reactions to vaping reported in clinical trials: summary

Hartmann-Boyce *et al* concluded that there was moderate certainty of no difference in rates of adverse events in participants who received nicotine-containing e-cigarettes compared with either NRT or non nicotine e-cigarettes. There was low/insufficient evidence that rates of adverse events were higher in participants using nicotine e-cigarettes compared with behavioural or no support (eg throat irritation, cough and dry mouth). A limitation with the data is that the longest follow-up was 2 years.[3]

## 5.3.7 Adverse reactions to vaping reported to the Medicines and Healthcare products Regulatory Agency

Healthcare professionals and the public are able to report suspected adverse reactions relating to e-cigarettes through the UK's Medicines and Healthcare products Regulatory Agency's (MHRA) Yellow Card scheme. This is a voluntary reporting scheme that collects and monitors information on safety concerns or incidents involving medicines or medical devices in the UK. Although a submitted report of adverse reactions does not necessarily mean that an e-cigarette has been proven to cause a reaction, they can be useful in helping to identify possible safety issues. Reporting suspected adverse events related to vaping to the Yellow Card scheme is recommended by the National Institute for Health and Care Excellence (NICE).[55]

The MHRA identified that, between 1 January 2020 and 14 August 2023, it received 347 reports covering 958 suspected adverse reactions to vaping (Table 5.2). Five fatalities linked to e-cigarettes (two cardiac and three respiratory) have been reported to the MHRA in the past 12 years. However, the MHRA is careful to point out that causation was not proven, as healthcare professionals are asked to report even if they only have a suspicion that the e-cigarette may have caused the adverse event.

**Table 5.2. All suspected adverse reactions associated with e-cigarettes reported in the UK from January 2020–August 2023**

| Reaction name | Number of reactions |
|---|---|
| Blood disorders | 1 |
| Cardiac disorders | 31 |
| Ear disorders | 4 |
| Endocrine disorders | 1 |
| Eye disorders | 9 |
| Gastrointestinal disorders | 122 |
| General disorders | 115 |
| Hepatic disorders | 1 |
| Immune system disorders | 24 |
| Infections | 20 |
| Injuries | 18 |
| Investigations | 9 |
| Metabolic disorders | 4 |
| Muscle and tissue disorders | 19 |
| Neoplasms | 1 |
| Nervous system disorders | 82 |
| Pregnancy conditions | 1 |
| Product label/physical/quality issues | 31 |
| Psychiatric disorders | 18 |
| Respiratory disorders | 411 |
| Skin disorders | 31 |
| Vascular disorders | 5 |
| **Total reactions for drug** | **958** |
| **Total reports*** | **347** |
| **Total fatal outcome reports** | **5 (2 cardiac, 3 respiratory)** |

* The number of reports is lower than the total reactions because each report constitutes an individual for whom more than one adverse reaction could have been reported.

The review by McNeill *et al* included reports up until January 2022.[1] Since then there have been a further 90 reports, including 238 reactions. Two fatalities were noted in previous reviews by McNeill *et al* and classified as 'acute lung injury' and 'non-infective endocarditis'.[1] The three newly identified fatalities were classified as 'cardiac arrest', 'pneumonia lipoid', and 'idiopathic pulmonary fibrosis'.

## 5.3.8 Limitations of the reviewed evidence

The Nicotine vaping in England review by McNeill *et al* identified key methodological issues limiting the conclusions that could be made based on the reviewed evidence.[1] To address some of these limitations, the updated review used stricter inclusion criteria for definition and duration of exclusive vaping and focused specifically on biomarkers of exposure that are directly associated with the development of cancer. Nevertheless, the new evidence was also restricted by the following limitations.

First, there remains a lack of research exploring longer-term health risks of vaping. Only two new controlled trials—one RCT with 24-week follow-up and an NRCT with 12-week follow-up – were published since July 2021, and their findings mostly focused on relative (vs smoking) but not absolute (vs non-use) health risks of vaping. Secondly, most of the recently published longitudinal observational studies analysed data from the same source that were around 10 years old and hence did not adequately represent exposure to newer vaping products. Thirdly, sample sizes were often small. Finally, very few new studies explored vaping associations with changes in disease-specific biomarkers of potential harm or vaping effects on people with existing health conditions. Due to these recurring limitations, an international standard for assessing vaping health risks should be established and followed.

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# 06

# Regulation of tobacco and nicotine products

## Key points

- E-cigarette policy varies substantially between countries, ranging from supporting their use as an aid to quitting and harm reduction to prohibition.
- Regulation of e-cigarettes should be designed to prevent harmful products from reaching consumers and to prevent, as far as possible, children who do not smoke from becoming vapers.
- Nicotine product regulation in the UK has evolved to enable and encourage smokers to quit smoking, either by quitting all nicotine use or by cutting down on the route to quitting, or by switching to a less harmful nicotine product.
- The UK regulates e-cigarettes as a consumer product in line with the requirements of the EU Tobacco Products Directive.
- The main levers for e-cigarette regulation are related to sales, product standards including nicotine content, flavours, colours, added ingredients, packaging, labelling, advertising, promotion, product registration/notification, authorised use (eg if a prescription is required) and price.
- Notification of content and emissions to the Medicines and Healthcare products Regulation Agency (MHRA) is mandatory for all e-cigarettes sold in the UK, but the reporting system lacks standardisation and reports are not independently validated. Responsibility for investigating non-compliance and enforcing regulation rests with trading standards departments in local authorities.
- Current UK regulations have been insufficient to prohibit packaging and labelling from including bright colours, cartoon characters and sweet names, which increase the attractiveness of vaping products to children.
- Compliance with advertising regulations appears to be high for adverts in traditional media, but significantly lower on social media sites. Point-of-sale advertising and display of e-cigarettes is not covered by current regulations.
- Price regulation is a potential means to discourage the use of disposable e-cigarettes by children. However, the elasticity and cross-elasticity of e-cigarette purchasing are not well defined in the UK, making it difficult to predict the likely effect of price regulation on vaping in general, on use of disposable vapes in particular, or the use of e-cigarettes by adult smokers who are trying to quit.
- To maximise the potential impact of an e-cigarette policy in priority socio-economic groups of smokers, the development of any national policy should take a health equity-informed approach during its design and implementation.
- The extent to which illicit vapes are used in the UK is unknown but seizure data suggest that availability is significant and growing. Penalties for illicit sale are currently very low and therefore offer little disincentive to sellers.
- Disposable vapes present significant environmental and safety hazards, and recycling of these products has been widely neglected.
- Formulating policy to maximise the public health benefit of vaping should be evidence-based, but predicting the magnitude of intended and unintended consequences of new policy can be difficult as policy decisions typically need to be made within timescales that do not align well with traditional academic research.

## Recommendations

- Since leaving the EU, the UK parliament lacks legislative powers to amend the UK Tobacco and Related Products Regulations. The government must introduce legislation to take such powers as an urgent priority.
- Regulatory restrictions on the promotion, price and availability of all consumer nicotine products should be proportionate to the health risk they represent and designed to discourage uptake among young people and reduce, rather than perpetuate, tobacco smoking.
- The MHRA notification process should be revised to require a standardised system of content and emission reporting, and to require random sampling of products for independent validation of content and emission data.
- Regulations should be revised to enable competent authorities such as the MHRA to raise and use notification fees to carry out systematic validation of notified data, and to fund enforcement activity.
- Trading standards services should be sufficiently resourced to effectively enforce e-cigarette sales legislation and reduce underage sales.
- A register of tobacco and nicotine retailers should be established along with requiring age verification and meaningful sanctions for breaching the law, with the aim of limiting access to young people.
- Regulations on advertising and promotion of e-cigarettes should be introduced to restrict online platforms, content generators and point-of-sale advertising to limit advertising of e-cigarette products to young people.
- A gradation of taxes at levels in broad relation to likely harm should be imposed on nicotine products in the UK.
- E-cigarette price and taxation strategies should target the products that are the cheapest and most commonly used by youth vapers while ensuring that the products most likely to be used by adult smokers/quitters remain affordable.
- Consideration should be given to banning e-cigarette price promotions and discounts; and minimum pricing for e-cigarettes.
- The government should consider a range of policy options to address the challenges of vape recycling from an environmental perspective, including:
  - prohibiting disposable e-cigarettes
  - amending product standards, descriptors and notification to the MHRA to support recycling
  - registration with environment agencies via producer compliance schemes as a mandatory component of MHRA notification
  - amending electrical and battery waste regulations to include disposable vapes
  - ensuring vendors comply with recycling costs for vapes
  - providing accessible drop-off points.

# 6.1 Nicotine or 'no-nicotine' tobacco control policies: a review of international approaches

## 6.1.1 Introduction

As the main cause of preventable nicotine-related harm, reducing tobacco smoking has been a priority health policy focus in most high-income countries. However, the increase in non-smoker nicotine use via e-cigarettes, particularly among young people, has led some countries to broaden their policy goals from minimising smoking to minimising all nicotine use. For example, the objective of Finland's Tobacco Act is 'to end the use of tobacco products and other nicotine-containing products that are toxic to humans and cause addiction',[1] in keeping with the national prevalence goal of reducing both smoking and use of other nicotine products to less than 5% by 2030. In contrast, England's Tobacco Control Plan maintains the focus on goals related to smoking prevalence, with e-cigarette use supported as a strategy to achieve a smoking prevalence of less than 5% by 2030.[2–4] Some governments have aimed to balance protection of young people from addiction and any potential longer term health impacts of vaping, with the potential benefits of allowing adults who smoke to switch to a lower-risk substitute product for cigarettes, while some countries consider e-cigarettes only as a threat to public health. Hence, there is wide international variation in e-cigarette regulations applied to sales, product standards, including nicotine content, flavours, colours and added ingredients, packaging and labelling, advertising and promotion, product registration/notification, and authorised use (eg if a prescription is required).[5,6] International trends of smoking prevalence and e-cigarette use are described in chapter 3, section 3.9. This section discusses selected international examples of e-cigarette regulation and how they developed in their respective countries. A detailed description of regulation of vaping products in the UK follows in section 6.2.

The regulation of nicotine-containing products, particularly e-cigarettes, has been and continues to be highly dynamic in many countries as governments contend with rapid innovation in the e-cigarette market. England was an early adopter of policies that supported tobacco harm reduction as recommended by the RCP in 2007, initially using nicotine replacement therapy and subsequently e-cigarettes for harm reduction purposes,[7] while other Commonwealth countries, particularly Australia, New Zealand and Canada, initially adopted a prohibitionist regulatory stance by applying medicines regulations.[8] New Zealand and Canada subsequently moved to more expansionist policies, amending laws to create a legal market for nicotine-containing e-cigarettes to be sold as consumer products, while Australia retained its original policy approach of prohibiting the sale of nicotine-containing products outside of medicines regulations.[9] Initially, all three countries only permitted nicotine-free e-cigarettes to be sold as consumer products with some of the restrictions on sales that apply to tobacco products (eg minimum purchase age), while requiring any e-cigarettes containing nicotine to be approved as a medicine prior to sale.

## 6.1.2 Australia

In 2012, the Australian medicines regulator, the Therapeutic Goods Administration (TGA), amended the classification applied to nicotine-containing e-cigarettes to require consumers to obtain a medical prescription to import nicotine e-cigarettes under the Personal Importation Scheme.[10] However, medical practitioners were not encouraged to prescribe them. For example, during a government inquiry into the regulation of e-cigarettes, the head of the TGA acknowledged that nicotine-containing e-cigarettes could be used legally if prescribed, but emphasised, 'In that situation, the individual doctor is taking the responsibility, both for making sure that there is informed consent and that it is appropriate, and that alternatives have not been effective in that case.... The individual doctor, who is the prescribing doctor, comes very much into the frame'.[11] In 2015, the Australian Medical Association issued a position statement listing multiple concerns about e-cigarettes, concluding that 'Currently there is no medical reason to start using an e-cigarette'.[12]

Some state and territory health departments provided conflicting advice that nicotine-containing e-cigarettes were dangerous poisons and could not be imported or used, even with a prescription.[13] Numerous government inquiries and consultations at both federal and state and territory levels have considered the issue of how to regulate e-cigarettes. In 2020, the federal health minister announced that all imports of nicotine-containing e-cigarettes would require a permit from the Office of Drug Control, which would effectively end personal importation as a legal pathway for individuals wishing to use nicotine-containing e-cigarettes.[14] A streamlined process would be developed by the TGA to facilitate prescribing and pharmacy dispensing of e-cigarettes that had not been approved as medicines, which was modelled on the pathway for accessing medicinal cannabis products. The importation ban was subsequently abandoned but the reforms to

domestic access to nicotine-containing e-cigarettes (the prescription model) proceeded, culminating in the development of a product standard (TGO 110)[15] and a streamlined process for medical practitioners to become authorised prescribers for e-cigarettes.[9] This new regulation was implemented in October 2021 along with regulatory amendments clarifying that nicotine-e-cigarettes were classed as prescription-only medicines (rather than dangerous poisons). The TGA did not define e-cigarettes that did not contain nicotine as medical devices, hence they continued to be sold as consumer products. During this period, the Australian e-cigarette market expanded substantially, as did under-the-counter sales of nicotine e-cigarettes and anecdotal reports of a large increase in youth vaping. The prescription model, implemented in 2021, was considered to have failed because it did not prevent a growing illicit market in nicotine e-cigarettes and uptake by youth.[16] In 2023, a new federal health minister announced further regulatory reforms for e-cigarettes, including a more extensive importation ban that would also apply to e-cigarettes that do not contain nicotine (whereby only pharmacies are permitted to import and supply e-cigarettes regardless of nicotine content), conservative packaging requirements (similar to medicines) for e-cigarette products, and a ban on non-tobacco flavours and disposable e-cigarettes.[17] An implementation date has not been announced.

E-cigarettes first arrived in Australia during a time when national tobacco policy would have been expected to have supported reshaping regulations in favour of e-cigarettes under the 2004–2009 National Tobacco Strategy, which included harm reduction objectives. The overarching framework of the National Drug Strategy, under which the National Tobacco Strategy sits, is one of harm minimisation with the approach aiming to achieve balance across the three pillars of demand, supply and harm reduction.[18] Successive National Tobacco Strategies have been less supportive of harm reduction than the 2004–2009 strategy and the most recent strategy only mentions harm reduction as being tobacco industry rhetoric, rather than a principle supported by government policy.[19] In rejecting an application to reschedule nicotine in 2017 to allow nicotine-containing e-cigarettes to be used for harm reduction purposes, the Australian regulator stated 'government policy supports the cessation of smoking rather than harm reduction'.[18]

### 6.1.3 New Zealand

Having initially prohibited electronic cigarettes that did not have a medicines licence, in practice an illicit under-the-counter market in nicotine-containing e-cigarettes was tolerated from an early stage in New Zealand due to challenges in enforcement of illicit sales.[20] In 2016, the government announced an intention to reverse the ban on domestic sales of non-smoked nicotine products, which would also apply to heated tobacco products.[21] Expanding legal access to these products was considered as a harm reduction measure in the context of supporting the country's 2011 national smokefree 2025 goal.[20]

However, while regulations were under development, Philip Morris International (PMI) commenced selling its heated tobacco product in the country. Legal action taken by the Ministry of Health against PMI resulted in a court decision that the sales ban on smokeless tobacco did not apply to tobacco products that were inhaled.[8] The government interpreted the ruling to apply also to nicotine-containing e-cigarettes, which immediately made them legal to sell before any regulations or product standards were in place. Regulations were subsequently implemented in November 2020 and a Vaping Regulatory Authority was established. These regulations restrict general retailers to selling e-cigarettes in tobacco, mint and menthol flavours in nicotine concentrations up to 50 mg/ml for nicotine salt products that have been notified to the Vaping Regulatory Authority. Specialist vape retailers may allow vaping on the premises, sell e-cigarettes in any flavour, and discuss e-cigarette products with customers; however, they must also restrict access to people aged 18 and over and maintain 70% of their turnover from selling e-cigarettes. Further regulations have been announced with anticipated commencement in August 2023 in response to growing concerns about an increase in youth vaping. Namely, new specialist vape shops will be prevented from operating near schools and marae (traditional Māori meeting grounds), only generic flavour descriptions will be permitted for e-cigarettes, the allowable maximum nicotine strength of disposable vapes will be reduced, and e-cigarettes must have removable batteries and child-safety mechanisms.[22] These marketing restrictions will maintain greater accessibility to nicotine-containing e-cigarettes than tobacco cigarettes if the country's

full Smokefree Action Plan is implemented by 2025, which includes reducing the number of tobacco retailers nationally by at least 90% (to around 600), a smoke-free generation law that bans sales to anyone born after 2008, and a maximum nicotine content limit for smoked tobacco products of 0.8 mg/g.[23] In December 2023 the new coalition government of New Zealand announced plans to repeal the smoke-free generation law.

### 6.1.4 Canada

As in New Zealand, an illegal domestic nicotine-containing e-cigarette market developed and expanded in Canada during the time that medicines regulations applied to nicotine-containing e-cigarettes. Health Canada sent vendors selling nicotine-containing e-cigarettes 'cease-and-desist' letters and seized products, but did not actively shut down e-cigarette retailers.[8] The lack of regulation of e-cigarettes that were being widely and blatantly sold was considered unacceptable. In 2018, Canada's Tobacco Act was amended (now the Tobacco and Vaping Products Act),[24] which made nicotine-containing e-cigarettes legal to sell and imposed some restrictions on their sales, marketing and use. Similar to the European Union Tobacco Products Directive legal e-cigarettes in Canada have a maximum nicotine concentration of 20 mg/ml.[25] E-cigarette manufacturers and importers must also report sales and ingredient information to the regulator. Packaging and labelling requirements and a single prescribed health warning are also imposed. Advertising and promotion activities are regulated to prevent exposure to young people. Some limited advertising to adults is permitted, such as in product brochures distributed to consumers in retail outlets. Provinces can also impose further restrictions on e-cigarette retailing. Consistent with the harm reduction approach that underpinned the regulations, fewer restrictions are applied to e-cigarettes than are applied to tobacco cigarettes.

### 6.1.5 USA

Like Australia, New Zealand and Canada, the US regulator also initially applied medicines regulation to nicotine-containing e-cigarettes. In 2008, the Food and Drug Administration (FDA) seized shipments of e-cigarettes, stating they were unapproved drugs.[26] However, legal action by the e-cigarette manufacturers led to rulings that the FDA could only regulate e-cigarettes as tobacco products unless marketed with therapeutic claims (which require a different regulatory process). To be legally sold in the USA, e-cigarette manufacturers need to submit applications with supporting evidence to the FDA, demonstrating that sale of their products are appropriate for the protection of the public health. As at mid-2023, only 23 tobacco-flavoured e-cigarettes had been authorised.[27] Hence, most e-cigarettes on the US market are being sold without authorisation, including Juul, which was issued a Marketing Denial Order in 2022.[26] Similar to New Zealand and Canada, maintaining consumer access to nicotine-containing e-cigarettes has received some support in the context of greater restrictions on smoked tobacco products, namely a proposal to impose a very low nicotine content standard on combustible cigarettes that was advocated by the FDA commissioner and the head of the agency's Centre for Tobacco Products.[28]

### 6.1.6 Other countries and regions

India prohibited the production, manufacture, importation, exportation, transport, sale, distribution, storage and advertisement of e-cigarettes in 2019.[29] This complete prohibition applies to all e-cigarettes regardless of whether they contain nicotine. Before this prohibition e-cigarettes were unregulated. Penalties for breaching the prohibition include fines and possible jail terms of up to 3 years for repeat offences. There is limited information available on the prevalence of e-cigarette use in India, though prior to the ban use among adults (aged 15 and older) was estimated to be 0.02% (95% CI: 0.01%, 0.04%) in 2016–17.[30] There are reports that an illicit market operates in the country since the ban came into force.[31,32]

China is the world's largest producer and exporter of e-cigarettes, but the prevalence of e-cigarette use in China is low. In 2018–19, only 1.6% (95% CI: 1.4%, 1.8%) of adults reported having used an e-cigarette in the past month.[33] However, use of e-cigarettes among middle school students increased to 2.7% in 2019.[34] China imposes a minimum sales age for e-cigarettes and sale of non-tobacco flavoured e-cigarettes is banned, as are use of terms such as 'safety', 'harm reduction', 'smoking cessation' etc on packaging.[35] Sales near some educational facilities, via vending machines and online are banned. A maximum nicotine concentration of 20 mg/ml applies to e-cigarette products sold in China. There are also requirements for e-cigarette devices, such as leak-proof design. Refillable devices are banned.[35] Non-compliance with laws have been noted, such as for online sales.[36] Hong Kong prohibits the import, manufacture, sale and possession of e-cigarettes for commercial purposes, unless approved as a pharmaceutical product.[37,38]

Since 2010, Japan has regulated nicotine-containing e-cigarettes as medicines and medical devices, hence they are not available for sale.[39] A limited quantity of e-cigarettes containing nicotine can be brought into the

country for personal use. Nicotine-free e-cigarettes are not regulated, including any age restrictions. There is limited information available on e-cigarette use in Japan, but prevalence appears to be low, with a population survey conducted in 2019 of people aged 15–29 finding that only 2.9% had used an e-cigarette in the last 30 days.[40] While nicotine-containing e-cigarettes cannot be sold in Japan without being approved as medicines, heated tobacco products may be sold. Japan was a test market for Philip Morris International's IQOS product. These more limited restrictions on heated tobacco products compared with e-cigarettes, as well as being an early test market, have led to a rapid increase in prevalence of heated tobacco product use between 2015 and 2019 to around 11% of the population aged 15–74.[41,42]

### 6.1.7 International approaches – conclusions

In conclusion, Australia, New Zealand, Canada and the USA share some similarities in how nicotine-containing e-cigarettes were initially classified, with regulators attempting to regulate them as medicinal products. In all countries, an illicit market of nicotine-containing e-cigarettes developed. In the USA, legal action initiated by e-cigarette importers led to a change in regulatory approach from classification as a drug delivery device to a tobacco product. Legal action initiated by the government in New Zealand similarly led to overturning regulation as a medicine ahead of finalisation of regulatory reforms that were underway to create a legal domestic e-cigarette market. Canada amended its tobacco control laws to incorporate e-cigarettes. Australia retained the medicines regulation framework but developed a unique regulatory approach that allows access to nicotine-containing e-cigarettes when prescribed by a medical practitioner, without requiring the products to be approved as medicines prior to supply, so long as they comply with a quality standard.

Government representatives in New Zealand, Canada and the USA have framed nicotine-containing e-cigarettes as being able to contribute to achieving national goals of minimising tobacco smoking. Australian policymakers have increasingly rejected e-cigarettes as having a role as a tobacco harm reduction strategy, other than in a limited capacity as a short-term cessation aid delivered in a medical context to people who have been unable to quit smoking with approved methods. Other examples of the range of regulatory approaches internationally include a complete prohibition in India; regulation as a medicinal product in Japan and Hong Kong, which effectively bans their supply; and some restrictions on sales and marketing in most of China.

## 6.2 Regulatory frameworks for nicotine-containing products in the UK

### 6.2.1 Introduction

There is a wide range of nicotine products available on the UK market, which can be broadly grouped into six categories (see chapter 2, Fig 2.2 Nicotine products and the likelihood of risk). The first, and by far the most harmful, includes manufactured cigarettes, hand-rolling tobacco, pipe tobacco and cigars, consumption of which involves tobacco combustion. A second category includes a new generation of tobacco-based products which generate an aerosol for inhalation by heating rather than burning tobacco (heated tobacco products) and which, although as yet relatively untried and tested, are likely to represent a lesser hazard to health than smoked tobacco. The third comprises products that contain tobacco but do not involve heating or combustion, and although harmful these typically represent a much lower health hazard than combustible products, particularly in the case of the Swedish oral moist tobacco product manufactured to defined standards and known as snus.[43,44] A fourth category, which in terms of risk will generally fall between smokeless and medicinal products, includes products that deliver nicotine without tobacco but do not meet medicines manufacturing standards and/or have a medicines licence, being marketed instead as consumer products. E-cigarettes are by far the most popular product in this category. Sales of nicotine pouches are growing which comprise the fifth category. The sixth category of products, which has by far the lowest risk, is that of medicinally licensed nicotine formulations that deliver highly purified nicotine.

UK nicotine regulatory systems have long recognised the importance and potential health gains that could be achieved by encouraging nicotine users, particularly smokers, who cannot quit without using nicotine, to switch to an alternative, less harmful, nicotine product. The result is a regulatory system which now imposes tight controls on the supply and marketing of all tobacco products, especially smoked tobacco; allows relative market freedom to non-tobacco nicotine consumer products such as e-cigarettes; and affords additional marketing freedoms to medicinally licensed nicotine products. This section reviews the current status of nicotine product regulation in the UK, particularly in relation to e-cigarettes, aims to identify failings of current UK legislation in relation to these products, and offers suggestions as to how this might be improved.

## 6.2.2 Outline of current nicotine regulation in the UK

### 6.2.2.1 Tobacco

The pre-eminent tobacco product of the past century has been the traditional manufactured cigarette. Cigarettes became popular in the UK before the advent of modern consumer protection laws and were that not the case it is inconceivable that cigarettes or other tobacco products would have been allowed on the market. Regulation of cigarettes and other tobacco products has, therefore, developed reactively and particularly in response to growing understanding of the harm that tobacco consumption, and particularly smoking, causes to individual users and non-users, and to wider society. Since the millennium, and in particular following the ratification of the WHO Framework Convention on Tobacco Control (FCTC) in 2004,[45] and the Illicit Trade Protocol to the FCTC in 2018,[46] the UK has applied extensive regulation to tobacco products including, among other measures, bans on advertising, displays of tobacco, smoking in enclosed public places, high rates of taxation increased annually above inflation to reduce affordability over time, standardised packaging, and tracking and tracing down to pack level. Together these comprise the most comprehensive regulatory package in Europe.[47] Although there remains considerable scope to extend and improve these regulatory controls, as recommended by the RCP, the All Party Parliamentary Group on Smoking and Health, and an independent review commissioned by the UK government, tobacco regulation in the UK is extensive.[48,49,50] Crucially, it uses regulatory incentives to encourage smokers to quit smoking and non-smokers not to start.

Commensurate with this approach, heated tobacco products, which are likely to be less toxic than smoked tobacco,[51] have been allocated a slightly lower level of excise duty than cigarettes or other combustible tobacco products.[52] To date in the UK, however, heated tobacco products have gained little popularity, with a prevalence of use below 0.5% in the general population and rarely higher than 1% among current and former smokers since their emergence in 2016 (see chapter 3, section 3.6.3).[53] The sale of smokeless tobacco in the form of oral snuff, is however prohibited in the UK and, although chewing tobacco remains legal, consumption is low and largely confined to the South Asian community.[54]

### 6.2.2.2 Nicotine medicines

Since 1980, the range of nicotine-containing products available to consumers has expanded with the development of products designed to help smokers to quit smoking. Licensed as medicines for this purpose and known as nicotine replacement therapy (NRT), these products are designed to be used to alleviate nicotine withdrawal symptoms and hence help smokers to stop smoking tobacco. Over the past 25 years, licensing restrictions on these medicines have been relaxed substantially, such that they are now widely available for over-the-counter purchase, for use by pregnant smokers and children aged over 12 years, and latterly for 'harm reduction' (which in this context means support for cutting down before quitting, and temporary or long-term smoking abstinence). Commensurate with medicines licensing requirements, these products remain tightly regulated in relation to manufacturing standards but their medicines status means that manufacturers are allowed, in promoting and providing NRT, and within constraints on all medicines promotion applied by the MHRA,[55] to advertise products using all channels and make the health claim that these products help smokers to quit.

### 6.2.2.3 Other non-tobacco, non-medicinal nicotine-containing products

Over the past three decades, a variety of non-tobacco unlicensed nicotine products have entered the UK market – an oral spray, oral nicotine pouches and nicotine lollipops, among others – and have been marketed under general consumer regulations. To date, none has been commercially successful in the UK other than the e-cigarette, which unlike other products in this category is designed to deliver nicotine in an aerosol for inhalation (referred to as vaping). In the 17 years or so that have passed since the first e-cigarettes became available, they have evolved into the most popular non-tobacco nicotine product in the UK and are widely used globally.[53] As outlined in section 6.1, different countries have adopted different regulatory approaches to them, ranging from endorsement by health agencies (as in the UK) to prohibition (as in Australia, India and others).[56] The evolution of UK nicotine product regulation was summarised in detail in chapter 10 of the 2016 RCP *Nicotine without smoke* report.[57] This section, therefore, focuses on how vaping devices are currently regulated in the UK, what regulation of these products should be aiming to achieve and how UK regulation might be improved in relation to those aims.

#### 6.2.2.4 What should non-tobacco nicotine product regulation aim to achieve?

The RCP has long argued that nicotine product regulation should be designed to discourage tobacco smoking, both by encouraging quitting among smokers able and willing to quit, and to promote substitution of tobacco with less hazardous non-tobacco nicotine products among those who are not.[57,58,59] It is also important that regulation protects non-smokers of any age from commencing nicotine use while recognising that those who do will be at much lower risk if they choose non-combustible nicotine products. The RCP has, therefore, argued that regulatory restrictions on the promotion, price and availability of nicotine products should be proportionate to the health risk they represent and thus designed to reduce, rather than perpetuate, tobacco smoking.[57] It is, therefore, right that tobacco products be subject to the most restrictive nicotine regulations of all, as is now the case, and that that these regulations be tightened further to minimise tobacco appeal, accessibility, promotion and use, along the lines articulated in the Khan review.[49] It is also right that, given the high standards of manufacture and purity, long experience of use, safety and evident low appeal of currently available medicinal nicotine products to non-smokers, these products are made as cheaply and readily available as possible. It also follows that e-cigarettes, which although markedly less harmful than tobacco are also likely to pose a greater long-term risk than NRT, are regulated to a degree that falls somewhere between the above product groups, but much closer to NRT than tobacco. Since a fundamental objective of all product regulation is to ensure that products are safe and fit for purpose, it is also important that e-cigarette regulation should require the monitoring of safety and patterns of use.

#### 6.2.2.5 Consumer versus medicines regulation of nicotine products

Until the advent of e-cigarettes in around 2007, the most widely used non-tobacco nicotine products were licensed NRT. Medicines licensing guarantees to the user that the product is of very high quality, purity, dose consistency and safety. However, the need to apply for and obtain a medicines licence, and to manufacture and distribute products in adherence with defined good practice,[60] imposes substantial financial and opportunity costs on manufacturers and particularly to new entrants to the market without a background in pharmaceutical medicines. The manufacturing costs of medicinal products, and their retail price to consumers, tend to be high. Furthermore, when the technology of products is evolving rapidly, as has been the case for e-cigarettes, there is a risk that products will be relatively redundant by the time a licence has been obtained and compliant manufacturing established. A major advantage of medicines licensing is that without this, suppliers are legally forbidden from marketing their products as a smoking cessation aid, and that health professionals can prescribe the products with confidence that they are not recommending a risky or even dangerous product. After NRT was made reimbursable on prescription; the proportion of smokers using NRT as a cessation aid grew substantially,[61] suggesting that making e-cigarettes reimbursable on prescription could have a similar impact. Although the MHRA has actively encouraged e-cigarette manufacturers to apply for medicines licences, and attempted to streamline the process, at the time of writing and over 17 years after the first e-cigarettes appeared on the market there is no licensed e-cigarette available in the UK. E-cigarette manufacturers and suppliers have instead continued to make their products available using the alternative consumer product route to market. This applies general standards of safety and purity which are much lower than those required for a medicines licence and are generic rather than product specific. However, as a result, manufacturing and consumer prices are also much lower, and the regulations present much less of a barrier to rapid technological development and thus overall can achieve much higher population reach and uptake than medicinal nicotine.

### 6.2.3 Evolution to date of UK regulation of electronic cigarettes

E-cigarettes were initially marketed in the UK under general consumer regulations.[62] In 2010, the MHRA extended the indication for NRT to include 'harm reduction', to reflect the fact that it has become widely accepted that there are no circumstances in which it is safer to smoke than to use NRT. The MHRA launched a consultation on whether or not to bring all non-tobacco nicotine-containing products within the medicines licensing regime, either immediately or after a grace period of 1 year or more to allow time for manufacturers and importers to comply.[63] However, this was superseded by the 2014 EU Tobacco Products Directive,[64] which allowed two routes to market for e-cigarettes (no other unlicensed nicotine-containing products were included in the TPD): the medicinal route and a consumer route. The consumer approach set specific regulations for nicotine-containing e-cigarettes[64] transposed into UK law by the 2016 regulations.[65] The legislation was revised to take into account Britain's exit from the European Union in 2020, but without significant change.[66] Consumer e-cigarettes have since been subject to this regulatory system in relation to generic product standards, as well as advertising and promotion restrictions,[65] imposed by

the Advertising Standards Authority.[67] In 2023, the UK government announced a consultation on youth vaping[68] and a review of vaping regulations,[69] with the subsequent announcement of the intention to introduce a Tobacco and Vapes Bill and publication of the consultation response in January 2024.[70,71]

#### 6.2.3.1 MHRA notification

Since 2016, MHRA notification has been mandatory for all vaping products sold in the UK and over 42,000 products had been registered as compliant with UK law by the end of 2020, and more than 20,000 since that date.[72] In the registration process, manufacturers and suppliers of e-cigarette products are required under the 2016 Act[65] to report the following information to the MHRA:

- A list of all ingredients in, as well as emissions resulting from the use of, the product by brand and variant name, including quantities.
- Toxicological data regarding the product's ingredients (including in heated form) and emissions, referring in particular to their effects on the health of consumers when inhaled and taking into account, among other things, any addictive effect.
- Information on the nicotine dose and uptake when consumed under normal or reasonably foreseeable conditions.
- A description of the components of the product including, where applicable, the opening and refill mechanism of the electronic cigarette or refill container.
- A description of the production process and a declaration that the production process ensures conformity with the requirements of this Part.
- A declaration that the producer bears full responsibility for the quality and safety of the product when supplied and used under normal or reasonably foreseeable conditions.

Manufacturers and suppliers must also, every year, submit the following information:

- Comprehensive data on the producer's sales volumes in the UK, by brand and variant name.
- Any information available to the producer, whether published or not, on the preferences of consumer groups in the UK, including young people, non-smokers and the main types of current users.
- The mode of sale of the producer's products in the UK.
- Executive summaries of any market surveys carried out by the producer in respect of the above three paragraphs.

Nicotine-containing liquids can be sold in disposable or refillable e-cigarettes and in containers of refill solutions. The tank capacity of any disposable or refillable e-cigarette is limited to 2 ml, and that of refill solutions to 10 ml.[65] The maximum permitted concentration of nicotine in nicotine solutions is 20 mg/ml, thus limiting the total nicotine content of any e-cigarette to 40 mg. The 20 mg/ml limit was justified on the basis that this had been shown to be adequate for the majority of smokers that use an e-cigarette to substitute for smoking, though no evidence was provided in support of this claim.[73] Addition of vitamins, caffeine or other stimulants, products intended to add colour to emissions or any substance known to be carcinogenic, toxic or mutagenic, is prohibited, as is inclusion of ingredients other than nicotine known to pose a risk to human health in heated or unheated form. Ingredients at trace levels technically unavoidable during manufacture are permitted and not required to be reported to the MHRA. E-cigarette and refill containers must be child-resistant and tamper-evident; protected against breakage and leakage; and refillable e-cigarettes and refill containers must have a mechanism to prevent leakage during refilling, such as a nozzle and flow control on the refill container or a docking system that only allows refilling when the e-cigarette and refill container are connected.

Flavour additives in notified e-cigarette products have to be included in the EU list of flavouring substances[74] and cannot include respiratory sensitisers, vitamins, stimulant additives (eg caffeine), or certain chemicals such as diacetyl.[75] Below the level of 0.1 % of the final product formulation, the MHRA will allow ingredients to be considered as confidential in the notification.[75]

The MHRA notification database is available to the public, so consumers, retailers and others can check if any individual product has been notified.[72]

#### 6.2.3.2 Packaging, labelling and information

In addition to compliance with general regulations on the classification, labelling and packaging of chemical substances,[76] and on disposal or recycling of batteries,[77] packets containing e-cigarettes or refill containers must include a leaflet listing instructions for use and storage of the product, including a reference that the product is not recommended for use by young people and non-smokers; contraindications; warnings for specific risk groups;

possible adverse effects; addictiveness and toxicity; and contact details of the producer.[65] Packs are also required to list ingredients in descending order of weight, an indication of the nicotine content of the product and the delivery per dose, and a recommendation to keep the product out of reach of children.[65]

Every e-cigarette or refill pack is also required to carry a health warning stating 'This product contains nicotine which is a highly addictive substance', which appears on both the front and back surfaces of the pack, covers 30% of the area of each of those surfaces, is in black Helvetica bold type on a white background in a font size which ensures that the text occupies the greatest possible proportion of the surface area reserved for it, and appears at the centre of that area.[65]

E-cigarette or refill packs are not permitted to in any way create an erroneous impression about their characteristics, health effects, risks or emissions; that they are less harmful than other e-cigarettes or refill containers; have vitalising, energising, healing, rejuvenating, natural or organic properties, or other health or lifestyle benefits; refer to taste, smell or other additives (except flavourings) or the absence of any such thing; resemble a food or a cosmetic product; or suggest that a particular e-cigarette or refill container has improved biodegradability or other environmental advantages. Packs must also not contain any element or feature that offers discounts, free distribution, two-for-one or other suggestions of economic advantage.[65] However, at the time of writing, giving out free samples of vaping products is not illegal, although the government has committed to ban free samples for children.[78]

### 6.2.3.3 Safety vigilance and oversight

The 2016 regulations require producers of e-cigarettes or refills to establish and maintain a system for collecting information about all suspected adverse effects on human health of their products.[65] Producers who become aware that a product is not safe, of good quality, or compliant with the 2016 regulations, must either correct the product to ensure compliance or withdraw and/or recall the product from sale. In those circumstances the producer is immediately required to notify the MHRA as to the nature of any risk to health or safety, the corrective action taken and the result of that action. Where the secretary of state for health and social care has reasonable grounds to believe that an electronic cigarette or refill product could present a serious risk to human health, they may take measures to address the risk by prohibiting the product or requiring it to be recalled. In these circumstances the MHRA checks that the submission is compliant and meets the standards required. However, the MHRA does not have powers to carry out pre-emptive checks on the products themselves to ensure that they are compliant.

Independent of the above regulation, a degree of safety vigilance is provided to the MHRA via the Yellow Card reporting scheme.[79]

### 6.2.3.4 Advertising and promotion

The 2016 regulations prohibit e-cigarette advertising in broadcast media, newspapers, periodicals and magazines (with the exception of trade publications), and the placing of advertising in 'information society services' (which covers internet search engines, social media platforms, streaming services, online games or other online services) provided to a recipient in the UK.[65] The regulations also prohibit sponsorship of cross-border events in the EU, but permit domestic advertising and sponsorship through billboards, at point of sale, on public transport or other local media.

Where UK advertising of e-cigarettes is allowed, it is further regulated by the Committee on Advertising Practice (CAP), which publishes advertising codes, and the Advertising Standards Authority (ASA), responsible for enforcement of the codes, apart from point of sale which is not within their remit. Their initial guidance required that marketing communications for e-cigarettes comply with a number of content restrictions and must:[67, 80]

- be socially responsible
- contain nothing which promotes any design, imagery or logo style that might reasonably be associated in the audience's mind with a tobacco brand
- contain nothing which promotes the use of a tobacco product or shows the use of a tobacco product in a positive light
- make clear that the product is an e-cigarette and not a tobacco product
- not contain medicinal claims unless the product is authorised for those purposes by the MHRA. E-cigarettes may be presented as an alternative to tobacco but marketers must do nothing to undermine the message that quitting tobacco use is the best option for health
- not use health professionals to endorse e-cigarettes
- state clearly if the product contains nicotine. They may include factual information about other product ingredients
- not encourage non-smokers or non-nicotine-users to use e-cigarettes

- not be likely to appeal particularly to people under 18, especially by reflecting or being associated with youth culture. They should not feature or portray real or fictitious characters who are likely to appeal particularly to people under 18. People shown using e-cigarettes or playing a significant role should not be shown behaving in an adolescent or juvenile manner. People shown using e-cigarettes or playing a significant role must neither be, nor seem to be, under 25. People under 25 may be shown in an incidental role but must be obviously not using e-cigarettes
- not be directed at people under 18 through the selection of media or the context in which they appear. No medium should be used to advertise e-cigarettes if more than 25% of its audience is under 18 years of age.

Under these regulations, factual claims about products are allowed to be made on marketer's own websites and, in certain circumstances, in other non-paid-for space online under the marketer's control. Unless targeted exclusively to the trade, marketing communications with the direct or indirect effect of promoting nicotine-containing e-cigarettes and their components which are not licensed as medicines are not permitted in newspapers, magazines, periodicals, online media and some other forms of electronic media. Further guidance expands on the use of marketing via online media to clarify that marketing communications are likely to be prohibited if they involve:[80]

- commercial email, commercial text messaging and other electronic messaging service
- marketing activities online, for example on their website and on social media (except for permissible activities described in the sections below)
- online (display) advertisements in paid-for space (including banner or pop-up advertisements and online video advertisements)
- paid-for search listings; preferential listings on price comparison sites; viral advertisements
- paid social media placements, advertisement features and contextually targeted branded content
- in-game advertisements (including augmented reality and virtual reality environments)
- commercial classified advertisements
- advertisements which are pushed electronically to devices
- advertisements distributed through web widgets
  - promotional marketing online
  - affiliate links
  - in-app advertising.

The guidance also prohibits promotion of non-nicotine e-cigarettes or solutions under the same brand name or other characteristics shared with nicotine products.[80] The guidance makes clear that, so long as compliant with the above content restrictions, advertising of nicotine-containing e-cigarettes is permitted (that is, not prohibited) in:

- outdoor advertising, including digital outdoor advertising
- posters on public transport
- cinema
- direct hard copy mail
- leaflets
- private, bespoke correspondence between a marketer and a consumer
- media which are targeted exclusively to the trade.

In 2018, the Advertising Standards Authority relaxed the guidance on health and medicinal claims, limiting these to medical claims only. This change allows manufacturers to make limited advertising claims, presenting e-cigarettes as an alternative to tobacco, while not undermining 'the message that quitting tobacco use is the best option for health.[81] However, any health claims must be backed up by robust evidence to substantiate them, in line with CAP's Advertising Guidance on Substantiation for Health Claims.[82]

In 2022, the Scottish government consulted on tightening rules on advertising and promoting of vaping products, but at time of writing no further action had been taken.

Exposure to e-cigarette advertising and its impact on e-cigarette use among young people is reviewed in chapter 8, section 8.5 and suggests additional advertising and promotion regulations are required.

#### 6.2.3.5 Minimum age of sale and prohibition of proxy purchase

Since 2015, it has been illegal in England and Wales to sell nicotine-inhaling products, and specifically nicotine-containing e-cigarettes or e-liquids, to persons aged under 18 years[83] or to purchase such products on behalf of a person aged under 18 years (proxy purchase).[84] Subsequently, age of sale restrictions have been extended to Scotland in 2017 and Northern Ireland in 2022. Age verification is mandatory for retailers of tobacco and nicotine-containing e-cigarettes in Scotland but not elsewhere in the UK. In Scotland it is also illegal to purchase tobacco or nicotine-containing e-cigarettes below the age of 18,[85] which is not the case in the other nations of the UK.

#### 6.2.3.6 Tax and duty

Taxation is a major lever that can be used to encourage market choices and a gradation of taxes at levels in broad relation to likely harm are imposed on nicotine products in the UK. Thus, UK tobacco products are subject to an excise tax in addition to VAT, which is set at a high level. The regular imposition of a tobacco tax escalator above inflation has ensured that tobacco is now less affordable than it was in the 1960s.[86] Taxes include the standard 20% VAT, and in the case of factory-made cigarettes (the most hazardous product) a specific tax which (as of November 2023) is £316.70 per 1,000 cigarettes plus an ad valorem tax of 16.5% of the retail price, and a specific tax on hand rolling tobacco of £412.32 per kg[52] and for heated tobacco products of £325.53 per kg. The government also levies a minimum excise tax level for factory-made cigarettes, such that if the manufacturer prices products below this, it has to pay any additional tax due. In addition to taxes, minimum pack sizes of 20 cigarettes, and 30 grams for hand rolling tobacco (HRT), prevent manufacturers from making products cheaper by reducing pack sizes. NRT medicines bought over the counter, which are widely accepted to be the least hazardous nicotine products, have for some years now benefited from a reduced VAT rate of 5%, while NRT on prescription, like other prescription medicines, is not subject to VAT.

E-cigarettes and e-liquids, as consumer products and with a much lower likely hazard than tobacco, are currently subject to standard 20% VAT only. Since e-cigarettes are not subject to excise taxes, and do not have to comply with complex and costly medicines regulations[60] making them less expensive to produce and distribute than NRT, they are also significantly cheaper than both NRT and cigarettes. However, the availability in shops of disposable vapes which can be bought for under £5, and online for as little as £2.99 (at the time of writing), associated with growth in youth vaping since 2021,[87] has led to growing concern that the affordability, accessibility and appeal of disposable vapes is a factor in the fuelling youth uptake and needs to be addressed.

### 6.2.4 Review of the status and effectiveness, and of opportunities to improve, existing UK e-cigarette regulation

Following a review of evidence on the effectiveness of tobacco regulation introduced under the EU Tobacco Products Directive in 2015–16, which still represents the great majority of e-cigarette regulations in place today, the government concluded in 2022 that 'The regulations were found to be fit for purpose and to be retained in their current format'.[88] However, following more recent growth in youth vaping, the government launched a further review of the regulations in autumn 2023,[68,69,89] and subsequently published proposals for new regulations to limit flavours, advertising, packaging, promotion of e-cigarettes and a ban of disposable e-cigarettes,[90] the legislative process is expected to be completed in 2024.[90]

#### 6.2.4.1 MHRA notification and enforcement

There have been few evaluations of the data submitted to the MHRA in the notification process, or of the extent to which manufacturers and suppliers comply with them. The MHRA scheme is a direct transposition of the EU Tobacco Products Directive (TPD) and, as a result under current legislation, the MHRA as competent authority has powers only to require notification and can only charge manufacturers and importers 'proportionate fees for receiving, storing, handling and analysing the information submitted to them'.[91] Responsibility for investigating non-compliance with the TPD, and enforcing the regulations where necessary, rests with trading standards departments in local authorities. However, trading standards resources have been severely reduced by cuts in funding, from £213 million in 2009 to £105 million in 2018/19 (a real terms cut of approximately 60%), and lost 56% of full-time equivalent staff between 2009–16.[92] In April 2023 the UK government announced £3m investment to support enforcement of vaping legislation, with a further announcement in October 2023 of an additional £30m of funding to support enforcement activity of both vaping and tobacco laws.[69]

For the MHRA to be able to carry out systematic validation of the notified data, and to fund enforcement activity, it will be necessary to revise the legislation so that the MHRA can raise fees to cover these costs, as

'It is Government policy to recharge costs of regulating e-cigarettes back to the e-cigarette industry and MHRA may not cross-subsidise this work from the taxpayer or other business sectors'.[93]

An analysis of reported content and emission data for 40,785 products notified during the first year after notification became a legal requirement found that data were submitted without standardisation in relation to units of measurement or constituent names.[94] Over 1,500 ingredients were listed in the notifications, with the typical product including 17 ingredients including nicotine, propylene glycol and glycerol. The most widely used flavours were ethyl butyrate, vanillin and ethyl maltol. The most widely reported emissions were nicotine, formaldehyde and acetaldehyde. The lack of standardisation of emissions reporting, in particular, made analysis of emission quantities extremely difficult, but where estimation was possible levels of emissions other than nicotine were typically below European Chemicals Agency Long Term Exposure and US Department of Labor Occupational Safety and Health Administration (OSHA) limits.[94] These findings indicate that levels of emission of typical notified e-cigarettes at that time were unlikely to present a significant health hazard. However, the lack of standardisation and growing evidence that un-notified (that is, illicit) products are being sold on the UK market precludes generalisation of this conclusion to all e-cigarette and e-liquid products.[95] Given the rapid evolution of e-cigarette products, regular monitoring and update is essential.

The MHRA notification process could, therefore, be improved to likely practical public health advantage by introducing a standardised system of content and emission reporting, and by regularly subjecting a random sample of products to independent validation of content and emission data. Data on the extent to which illicit (that is, products without MHRA notification) are available on the market is only collected ad hoc and needs to be monitored consistently and regularly by Trading Standards and Border Force agencies over time to identify trends.

### 6.2.4.2 Packaging, labelling and information

There is little information on the extent to which e-cigarettes and liquids on sale in the UK are compliant with existing labelling and information requirements. However, a study of 30 products (21 e-liquids and nine e-cigarettes) reported in 2017,[96] and therefore probably predating the introduction of MHRA notification, found that up to 40% did not comply with general classification, labelling and packaging of chemical substances legislation,[76] and none complied with regulations on disposal or recycling of batteries.[77] These data, although based on a small sample, indicate that enforcement of labelling and information has been lax.

Current regulations require that packaging and labelling should not resemble food or a cosmetic product, but do not cover the vaping product itself. These regulations have been insufficient to prohibit packaging and labelling including bright colours, cartoon characters and sweet names, which increase the attractiveness of vaping products to children relative to standardised packaging.[97] Changing regulations to make packaging, labelling and product design less appealing will require primary legislation, but an amendment to the Health and Social Care Bill 2021 to 'give powers to the Secretary of State to prohibit branding on e-cigarette packaging which is appealing to children', tabled by a cross-party group of MPs, was voted down by the government.[98] However, the review of e-cigarette regulations announced in October 2023.[69] asked for recommendations on how to make products less appealing, and these are now under consideration.

This is another area where, with legislative changes to allow funding from notification fees, increased trading standards supervision could be used to identify non-compliant products.

### 6.2.4.3 Safety vigilance and oversight

We are not aware of any data on the extent to which manufacturers or retailers check the safety of the products they produce or sell, or the extent to which products have been withdrawn from the market on safety grounds. However, it is also questionable that a system based on self-report of unsafe products is likely to be particularly effective as a means of public protection, while illicit products, which are by definition non-compliant with regulation, perhaps represent the greatest risk in terms of adverse effects and access for young people.

Data on adverse health effects from reports to the MHRA Yellow Card scheme indicate, however, that reported serious adverse effects from vaping are rare in absolute terms (see chapter 5, section 5.37). Between 1 January 2010 and 15 June 2023, the MHRA received reports of 942 adverse effects in 339 people. There were five fatalities (two cardiac and three respiratory)[99] in an at-risk population (ie those who have ever used e-cigarettes), which has grown rapidly from under a million at the outset to over 5 million people in Great Britain in 2023, including 370,000 children aged 11–17 years.[87]

As the MHRA is careful to point out, causation is not proven in these cases as healthcare professionals are asked to report cases even if they only have a suspicion that the e-cigarette may have caused the adverse event.[100] While the extent to which adverse effects from vaping go unreported to the Yellow Card scheme is unknown, the extremely low numbers reported indicate that serious adverse events are likely to be very rare.

Hospital admissions for respiratory conditions linked to vaping are small in number, although they have grown significantly since they were first collected in 2020–21. A provisional count of finished admission episodes, where an ICD-10 code indicating a vaping related disorder has been recorded as the primary or secondary diagnosis, for hospitals in England rose from 177 in 2020–21 to 337 in 2021–22.[101] However, these events are also not necessarily causally related, as growing awareness of vaping, and the impact of current or former tobacco smoking among those recorded as having a vaping-related disorder are likely to be a confounding factor in the growth of reporting.

### 6.2.4.4 Advertising and promotion

ASH survey data find that children's awareness of e-cigarette promotion is greatest at point of sale, (up from 37% to 53% awareness between 2022 and 2023), as was the case with tobacco before the display ban; the main source of promotion is displays. Advertising, promotion and displays at the point of sale are not subject to Advertising Standards Authority regulation and have become as potentially powerful a source of promotion for e-cigarettes as they were for tobacco prior to the implementation of the display ban. This could be addressed by prohibiting advertising, promotion, sponsorship and e-cigarette displays at point of sale in shops frequented by children and allowing exemptions for specialist vape shops where children are not permitted to enter. At the current time there is no prohibition for under 18s to enter specialist tobacconists, which are not required to comply with the tobacco display legislation, and this should also be made a legal requirement.

There is limited information on the extent to which e-cigarette advertising and promotion is legally compliant in advertising channels regulated by the Advertising Standards Authority. An evaluation of 130 advertisements from traditional (billboards, cinema, direct mail, door drops, internet and press channels) found compliance was high for advertisements on traditional channels, with 5% or fewer breaching any single rule.[67,80]

Online advertising of e-cigarettes is illegal, but e-cigarette marketers are allowed to provide factual information about e-cigarette products online. Among 10 top EC brand websites in England, marketing elements that might appeal to young people were commonly identified and CAP code compliance was low. A sample of 30 Instagram posts found they were in breach of the advertising code.[102] This is consistent with ASH data, which found relatively low awareness of promotion of e-cigarettes through traditional channels such as billboards (14%) and buses (11%), with significantly higher and growing awareness of online promotion, from 24% in 2022 to 32% in 2023. Of those reporting seeing e-cigarettes promoted online, the most common location was TikTok (49%), followed by YouTube (29%), Instagram (28%), Snapchat (24%) and Google (21%).

For traditional media and for marketer's own websites the ASA will act on complaints about breaches of the advertising code, where the advertiser, publication or platform has failed to act. However, for social media this can be more difficult, as content is often created by 'social influencers'; proof that they have been paid may be difficult to secure and online platforms have often been difficult to reach and unresponsive. In response to growing concerns, particularly concerning TikTok, in 2023 CAP published an enforcement notice, instructing vaping companies to follow the advertising rules and remove any adverts for vapes that are appearing on social media.[103]

Data from the Advertising Standards Authority indicate that at the time of writing, 23 potential breaches of electronic cigarette advertising regulations had been reported to the authority, of which 17 including some user-generated content on Instagram and TikTok, were upheld.[104]

### 6.2.4.5 Age of sale

Data from ASH surveys of 11–17-year-olds indicate that among the 7.6% of people in this age group who were currently vaping, nearly half (48%) purchased e-cigarettes from shops, with around a quarter (26%) purchasing from friends or other informal sources. The proportion purchasing from shops for the 3.6% of current smokers was 40% (25% purchased from friends or other informal sources).[87] Buying from the internet was far less frequent, with only 7.6% of current e-cigarette users and 7% of smokers citing this as a source.

As a result of growing concern about underage vaping, in 2022 the Chartered Trading Standards Institute (CTSI) was commissioned to carry out a rapid one-off review of sales compliance. A total of 442 test purchases, using young people under the age of 18, to attempt to purchase disposable vapes were conducted in shops. Illegal sales were made on 145 occasions, a non-compliance rate of 33% (underage sales were highest in mobile phone and discount shops at 50% and 52% respectively).[105] A quarter of the products purchased were not up to UK standards and should not have been on sale in this country. The maximum penalty for selling a nicotine inhaling product to a person under 18 years is a fine of £2,500. If convicted and further offences occur in a 2-year period, Trading Standards can make an application to a Magistrates' Court for a restricted premises order and/or a restricted sales order. As at April 2022 no such orders have been issued.[105]

Responsibility for policing underage sales, along with other products retailed in breach of existing regulations, lies with local authority trading standards officers, for whom non-compliant and underage sales have become a significant challenge.[106] The CTSI is arguing for additional measures to assist in preventing non-compliant and underage sale, including mandatory age verification, taking vaping products out of sight and reach of children, tougher packaging regulations to reduce appeal to children, retailer registration, higher penalties for underage sale, and more resourcing of trading standards services to enforce these measures.[106] In 2022, the Khan review recommended an additional investment into local trading standards tobacco enforcement of £15 million a year,[49] which was not implemented. However, in April 2023 the government committed £3 million of new funding over 2 years to create a specialised 'illicit vapes enforcement squad', to enforce the rules on the underage sale and sale of illicit vapes.[107] It is proposed that this national programme will gather intelligence, coordinate efforts across the country, undertake test purchasing and develop guidance to build regulatory compliance. At the time of writing the initiative was still under development, while additional funding of £30m for enforcement of both vaping and tobacco laws was announced in October 2023.[69]

However, the CTSI argues that, even if sustained, enforcement activity will not alone be sufficient and that making e-cigarettes an excisable product is also necessary. Imposing excise duty would not only make cheap disposable vapes less affordable but also give Border Force and His Majesty's Revenue and Customs (HMRC) additional powers to tackle the growing illicit market for e-cigarettes. These powers are already in place for illicit tobacco and allow collaborative work more effectively to prevent illegal imports and distribution and sale inland. For example, in 2021–2 Border Force and HMRC seized 213,000 kg of hand rolling tobacco and 1.35 billion illegal cigarettes, of which around 180 million were seized overseas, 1.1 billion at the border and 80 million inland.[108] HMRC has a well-funded network of criminal investigators, and a Fiscal Crime Liaison Officer (FCLO) network overseas to identify illicit product before it reaches the UK and works closely with Border Force to stop illicit tobacco arriving at our ports.[109]

Currently, there is no retail licensing for tobacco or nicotine vaping products in England and no centralised, publicly available information about how many outlets sell these products to enable effective monitoring and surveillance. In Scotland there is a retail register which provides this information, although it is not regularly updated. Mandatory age verification for all sales of tobacco and nicotine-inhaling products is also a legal requirement in Scotland, which aids enforcement as any retailer failing to carry out age verification checks has immediately committed an offence.[110]

### 6.2.4.6 Tax

The UK tax system currently imposes the highest level of tax on the most hazardous (combusted tobacco) nicotine products and the lowest on the least hazardous (NRT), with e-cigarettes subject to the same tax as other consumer products. However, while taxes are applied in approximate relation to product hazard, the retail cost of vaping is substantially lower than that of both NRT and tobacco. There is, therefore, a case for abolishing all VAT on NRT to try to reduce the cost difference from vaping, but little to be gained in terms of relative retail price advantage by reducing VAT on e-cigarettes. The current widespread use of disposable e-cigarettes among children[87] has, however, led to calls for a specific excise duty on the disposable products that are most widely used by children and, through their disposable nature, are environmentally more harmful than refillable devices.[111] Evidence on e-cigarette price elasticity based on US data indicates that price increases do generate modest decreases in vaping among young people.[112] There is therefore a case for taxing disposable products to reduce use by children and to encourage vapers to use more sustainable products.

In March 2024, the government announced a new duty on vaping which will be introduced from October 2026. The revenue is projected to raise £445 million in 2028–29. From that same date, the government also plans to introduce a one-off increase to the tobacco duty by £2 per 100 cigarettes or 50 grams of tobacco, which is an equivalent quantity to 10 ml of e-liquid to maintain the current financial incentive to choose vaping over smoking. This is projected to raise a further £170 million in 2028–29. A consultation has been announced on these proposals.[71,113]

For a more extensive review of e-cigarette price and taxation policy, see section 6.3.

#### 6.2.4.7 Flavours

Concerns have been expressed about the proliferation of flavours in e-cigarettes on the UK market and the extent to which these are a factor in young people's uptake (see chapter 7). In current circumstances with a free choice of flavours, almost no one who vapes chooses to use unflavoured vapes. For adults, the ASH surveys find that the most frequently chosen flavour is fruit (47%), followed by menthol/mint (17%), then tobacco (12%) with sweets (chocolate, dessert, sweet or candy) used by 6%.[114] There is also evidence to show that use of non-tobacco flavours (largely fruit and menthol) is associated with higher success in quitting (see chapter 7). For children, fruit flavours are the flavour of choice for 60%, followed by sweet flavours (17%), with just under 5% choosing tobacco/menthol or tobacco and just under 3% choosing menthol/mint.[87] Further research is needed about the impact of banning specific flavours (unless there are concerns about their health impact), which needs to include assessing the risks of unintended consequences, including an increase in tobacco sales as reported by Friedman *et al*.[115] However, this warrants further investigation, particularly for flavours which are far more popular with children than adults, such as sweet flavours.

## 6.3 E-cigarette price and taxation policy options

### 6.3.1 Introduction

While most adult vapers use reusable e-cigarette devices, so-called disposable vapes (which can't be refilled or recharged) have gained popularity among users in recent years.[116] Price is an important component of the product characteristics that can encourage smokers to transition to e-cigarettes for smoking cessation.[117] The evidence suggests that the price of e-cigarettes significantly influences consumption; studies on price elasticity of demand indicate that higher prices are associated with lower e-cigarette use.[118–122] However, there is limited evidence for the UK and limited evidence to help understand how the price responsiveness of consumers is affected by other aspects of e-cigarette product design and marketing.

Taxation has a long history of use for reducing the accessibility of tobacco products and preventing the health and economic burdens of tobacco use,[123,124] and is part of an extensive package of tobacco regulation in the UK intended to incentivise smokers to quit and discourage non-smokers from starting. Tax is now also being discussed as a tool to influence consumer demand for products in the e-cigarette market.[125] In the UK, e-cigarette products (whether they contain nicotine or not) are currently subject to the standard rate of VAT at 20%. Medicinally regulated products that are formally approved as therapies to help people stop smoking are subject to the reduced rate of VAT at 5%. Thus, while e-cigarettes are subject to VAT in the UK, unlike tobacco, they are not currently subject to excise duties, although the UK government has announced plans to introduce an excise tax from October 2026.[71,113]

The rapid rise in the use of disposable e-cigarettes in the UK,[116] which are most popular among young people,[126] brings issues around safeguarding young people who have never smoked from nicotine addiction and preventing the negative environmental impact when large amounts of products that constitute electrical waste are used once and then discarded. There is now a large volume of disposable e-cigarettes being purchased,[127] which is causing problems with litter and of the proper disposal of components. Although recycling of e-cigarettes by producers is required under environmental legislation, there has been insufficient investment in recycling infrastructure, which will entail a cost to the public. However, the development of more effective and accessible recycling schemes for e-cigarettes is needed regardless, and would still be needed in the absence of disposable e-cigarettes.[127]

Six policy options are discussed in section 6.5 of this report: increasing the affordability of reusable e-cigarettes for quitting smoking by reducing VAT or providing subsidised products, a new excise tax on disposable e-cigarettes, levies and fee schemes for manufacturers, importers or retailers of e-cigarettes, banning price promotions and discounts, and setting a minimum price for e-cigarettes. These options are discussed in relation to a complete ban on disposable e-cigarettes and regulations short of a ban that would introduce restrictions on how e-cigarettes are marketed to young people. In practice, new price regulations are

likely to form part of a suite of regulations applied to e-cigarette products. The goal of this suite of regulations is to minimise the harm to non-smokers, especially children, that could happen if they take up e-cigarette use; maximise the potential for e-cigarettes to increase the rate at which smokers quit tobacco use; and reduce the environmental harms of e-cigarette waste.

## 6.3.2. Avoiding new price regulations making it less likely that smokers will quit smoking

It is important also to consider how smokers who use e-cigarettes to support quit attempts might respond to new price regulations. Data from the Smoking Toolkit Study help to understand the situation,[53] indicating that 37.9% of smokers used some form of e-cigarette to support their latest quit attempt, and disposable e-cigarettes comprised around 41.5% of this nicotine-containing e-cigarette use (Fig 6.1). This indicates that around 15.7% (41.5% of people using disposable e-cigarettes out of the 37.9% using some form of e-cigarette) of recent quit attempts are currently supported by a disposable e-cigarette.[128]

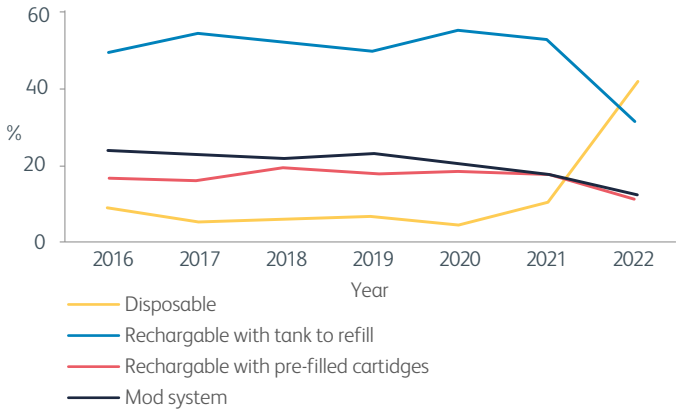


**Fig 6.1. Types of e-cigarette used to support quitting.[53]**

The extent to which e-cigarette price rises affect quit attempts and quit success will depend on the importance of having access to an affordable e-cigarette, and then on the importance of price for the decision of what type of e-cigarette to use. There is currently limited evidence available to understand the choices that people might make in this situation. For instance, when the price of disposable e-cigarettes rises, it may dissuade smokers from attempting to quit. However, those smokers who aim to use e-cigarettes as a tool to aid in quitting might opt for rechargeable refillable e-cigarettes instead. These reuseable devices were the preferred choice before the surge in popularity of disposable e-cigarettes.

It is important to consider that smoking rates are highest among economically disadvantaged individuals with low disposable incomes. Thus, e-cigarette price rises might disproportionately affect those who stand to benefit the most from quitting. Moreover, raising the price of e-cigarettes could be seen as stigmatising people who might want to quit using an e-cigarette but need an easily affordable option.[129]

## 6.3.3 The potential benefits from new e-cigarette price regulation

Price regulations for harmful commodities are a way to reduce their affordability and consequently the harm that they cause. If consumers are very responsive to the consequent price rise, then demand for the product will fall substantially. The less that consumers respond to the price rise, the more they will pay and the more tax revenue the government will get, which could be used to mitigate the harm caused by consumption of the commodity.

New price regulation, which includes tax changes, subsidies for healthy commodities and setting minimum pricing thresholds, has a role in this, specifically regulating access by changing product affordability. Price regulation is also achieved by reducing the illicit market which gives access to cheaper products. Although there is limited information on the scale of the illicit market for disposable e-cigarettes, the available evidence suggests that this illicit market is large and actively used by children.

The key question for the price regulation of e-cigarettes is how pricing policies, including tax, can be used as a tool to optimise access to products across tobacco, disposable e-cigarettes, and reusable e-cigarettes. The criteria for this optimisation considered here are: 1) minimise the use of e-cigarettes among non-smokers, especially children; 2) encourage the use of e-cigarettes among smokers for whom e-cigarettes might be an effective option to help them quit smoking; 3) either minimise or recoup money to offset for the economic and environmental costs to society, which could be done by reducing e-cigarette use, increasing their reusability or generating tax revenue to cover the costs to society; 4) ensure people who currently vape do not switch to smoking as a result of increasing e-cigarette prices. Disposable e-cigarettes are the cheapest products most commonly used by youth vapers, while adult smokers/quitters more commonly use reusable e-cigarettes, which are less damaging to the environment. This suggests that optimal price regulation would raise the price of disposable e-cigarettes while keeping reusable e-cigarettes affordable.

For example, a new excise tax on disposable e-cigarettes could raise their price high enough to significantly reduce consumption and consequently also reduce their negative environment impacts. The less responsive that consumer demand is to price rises caused by a new tax, the more additional tax revenue is generated for government. From a 'tax and spend' perspective, the revenue raised could be used to support the case for more investment in new recycling initiatives, and for enforcement activities to minimise the illicit market. In addition, having a new excise tax on e-cigarettes would provide a basis for HMRC and Border Force to invest resources alongside Trading Standards in enforcement activities to minimise the illicit market.

## 6.3.4 Price policy options that could be considered

### 6.3.4.1 Reduce VAT on e-cigarette devices in line with other nicotine products

The Kahn review recommended reducing the VAT on e-cigarette devices in line with other nicotine products.[130] This reduction in VAT could potentially be applied to reusable e-cigarette devices and refills to increase their accessibility to smokers using them to support a quit attempt.

### 6.3.4.2 Provide subsidised e-cigarettes to people who access stop smoking support

One solution to this problem would be to provide subsidised e-cigarettes to people who access support to help them to stop smoking. There are a number of existing initiatives funded by local government that aim to increase access to e-cigarettes for people who want to use them to quit, which include contributions to the cost.[131] The UK government has also recently announced a 'Swap to stop' scheme that will provide free vaping starter kits to help to encourage and support smokers to make a quit attempt.[132] A medically licensed e-cigarette available on prescription[133] would be free to people who qualify for free prescriptions. As an added benefit, government initiatives to provide affordable e-cigarettes could ensure that the products provided meet minimum standards of quality, safety and efficacy, which could include standards of environmental impact.

### 6.3.4.3 A new excise tax on disposable e-cigarettes

In their submission of evidence to inform the UK's 2023 Spring Budget, Action on Smoking and Health (ASH) and the SPECTRUM UK Prevention Research Partnership consortium called for a new excise tax on disposable e-cigarettes.[125] They proposed adding an excise tax of approximately £4 per disposable e-cigarette to bring the price up to the same level as the cheapest reusable vapes, while still keeping the price below tobacco cigarettes. The idea is that this would raise the price of the cheapest disposable e-cigarettes out of the price range found to be easily affordable by young people who have never smoked tobacco. ASH and SPECTRUM also called for a zero rating (ie 0% excise tax), in effect a price subsidy, to be applied to reusable e-cigarettes, which are the main products used by adult ex-smokers who used e-cigarettes to help them quit smoking. Worldwide, e-cigarettes have been taxed in a variety of ways, eg in the USA, individual states vary in how they tax e-cigarettes with some levying a tax on liquid and containers, others ad valorem taxes on wholesale prices and others sales taxes.[134] However, there is a risk that some approaches to taxation could be sub-optimal in placing the higher burden of tax on e-cigarette products that are associated with higher reusability, such as liquid refills, and on e-cigarette products that are relatively more expensive, which could indicate higher quality and greater longevity.

### 6.3.4.4 Levies and fee schemes for e-cigarette retailers, manufacturers and importers

A tax levy could be placed on retailers selling disposable e-cigarettes in the form of a payment linked to e-cigarette sales volume. This levy could be linked to a registration scheme for retailers selling e-cigarette products, which in turn would aid enforcement efforts by providing a list of e-cigarette sellers in each locality.

The current situation is that all manufacturers and importers of e-cigarettes must notify the competent authority, the Medicines and Healthcare products Regulatory Agency, and pay a notification fee. This fee cannot currently be used to pay for enforcement but could be extended to do so with primary legislation.

#### 6.3.4.5 Banning price promotions and discounts on disposable e-cigarettes

Price regulation might also look to ban price promotions and discounts for disposable e-cigarettes, especially when part of marketing activities targeted at young people. The Tobacco and Related Products Regulations includes attempts to do this[135] but it is limited to the promotion on the pack of any such offers rather than the offers themselves, which represents a legal loophole in need of revising with further legislation.

#### 6.3.4.6 Minimum pricing for e-cigarettes

An alternative to introducing a new tax on a specific category of e-cigarettes products would be to introduce a minimum price for e-cigarettes that applies to all products. However, implementing the policy would require a definition of what 'unit' the minimum price applied to, eg would it be a minimum price per millilitre of e-liquid? Would it be a minimum price for the e-cigarette device? The heterogeneity of the e-cigarette market means that a way to standardise the measurement of price is needed in order to then clearly define the minimum threshold. We suggest that there are three options for defining the price per unit of e-cigarette use. The most intuitive approach, which has already been developed and tested as a way to standardise e-cigarette taxes in the USA, is the price per millilitre of e-liquid.[134] Other approaches might include a minimum price per e-cigarette device, which would exclude the cost of recharging or refilling reusable e-cigarettes; or a minimum price per 'puff', which would include the expected costs of recharging, refilling and replacing devices over a defined period (eg 4 weeks of use).

### 6.3.5 How price regulations in general might interact with bans on availability

The policy debate has contrasted the range of potential price regulation options that aim to change product affordability, to the alternative set of options that aim to limit product availability by removing certain products from the marketplace, ie by introducing total or partial bans on legal e-cigarettes. However, it is unclear exactly what definition of e-cigarette products the potential price regulations would affect and how this compares to the products that would be affected by a ban. Understanding what products would be affected, and by how much, is key to understanding whether price regulations and bans would affect the same products, or whether a combination of policies on affordability and availability would be optimal.

The Local Government Association has argued for a ban on disposable e-cigarettes, primarily for environmental reasons (like plastic litter and batteries causing fires).[136] France is rolling out a ban of legally sold disposable e-cigarettes from December 2023.[137] If such a ban were implemented in the UK it would remove disposable e-cigarettes from the legal market but they could remain in the illicit market. If such a ban on disposable use e-cigarettes were implemented then the potential to introduce price regulations that specifically targeted disposable e-cigarettes would be removed. However, a diverse product range of reusable e-cigarettes would still remain on the market, and price regulations might still be a useful tool to increase smokers' access to the products that are most effective at supporting quit attempts and that carry the least environmental cost. It is also important to recognise that the e-cigarette market is constantly evolving at a fast pace. As a result, new products might appear that effectively circumvent the specific product definitions associated with a ban or certain price regulations, resulting in definitions having to be regularly reviewed and updated.

### 6.3.6 How the e-cigarette industry might respond to a new excise tax on disposable e-cigarettes

This section considers how the e-cigarette industry might respond to a new excise tax on disposable e-cigarettes. It is important to give this special consideration because a long history of evidence from tobacco taxation policy shows that manufacturers and importers of tobacco products respond to tax changes by changing the revenue that they get from product sales, in order to modify the effects that a tax change has on the price distribution of products in the marketplace.[138–141] It is reasonable to expect that in order to maintain the affordability of the cheapest products, the e-cigarette industry might employ similar tactics by responding to a new excise tax by reducing the profits that they make. The value to the e-cigarette industry of doing so would depend on how responsive the consumers of disposable e-cigarettes are likely to be to price rises. If the demand for a product is very responsive to price changes (this is called elastic demand), then it is likely that suppliers will end up mitigating the effects of the tax rise on product prices by reducing their profits. However, if the demand for a product is not very responsive to price changes (this is called inelastic demand), then suppliers are more likely to pass the entire value of the new tax rise onto consumers, who would consequently pay more.

Due to the importance to the industry of having cheap products that are affordable to people who smoke many of whom have limited budgets, they might even choose to make a loss on sales of disposable e-cigarettes. In response to a tax rise on disposable e-cigarettes, the industry might also diversify products. For example, industry might develop products that fall outside the formal regulatory definition of a disposable e-cigarette, thereby falling outside of the category of products that are subject to the tax. There is currently limited evidence on how the e-cigarette industry might respond with their pricing and distribution strategies to a new tax on e-cigarettes.

### 6.3.7 How consumers might respond to increases in the sales price of disposable e-cigarettes

The most important thing to consider is the extent to which current users of disposable e-cigarettes will reduce their use of these products in response to a price rise (the 'own-price' elasticity of demand), and the extent to which they switch to other products as a result (the set of 'cross-price' elasticities of demand).

International studies have found that the own-price elasticity of demand for e-cigarettes in general varies depending on several factors. Most of the studies are from the USA and no studies have estimated price responsiveness specifically for disposable e-cigarette use in the UK. Recent US evidence by Cotti *et al* found that e-cigarettes have an own-price elasticity of -2.2,[118] ie that a 1% price rise would result in a 2.2% decrease in consumption, with a particularly large own-price elasticity of demand for flavoured e-cigarettes. Another US study of the effect of price on youth vaping found that a 1% increase in the price of 1 ml of e-liquid decreased past 30-day e-cigarette use by 0.36% to 0.45%, and decreased total e-cigarette demand by 0.92% to 1.16%.[119] A US study that used retail store scanner data estimated own-price elasticities for disposable e-cigarettes at -1.2,[112] which means that a 1% increase in price would reduce consumption by 1.2%; this was compared to an own-price elasticity of -1.9 for reusable e-cigarettes. Another study in the USA found that a 1% increase in the price of disposable e-cigarettes was associated with a reduction in the number of days vaping among school-age e-cigarette users by approximately 0.97%.[121] The same study found that changes in the price of refillable e-cigarettes did not have a statistically significant effect on vaping. A further study in the USA estimated e-cigarette price elasticities alongside price elasticities for tobacco and other nicotine-containing products. It found that the estimated own-price elasticity for disposable e-cigarettes was -1.560, compared to an own-price elasticity for reusable e-cigarettes of -1.363.[142] Notably, this study also found that if cigarette prices went up, then the consumption of disposable e-cigarettes sold in convenience stores also went up, indicating that these products are substitutes. An exploratory study of European data also indicated that e-cigarettes sales are responsive to price changes and that e-cigarettes and regular cigarettes are substitutes.[122]

This raises an important research question; if disposable e-cigarette prices go up, what products will users switch to and to what extent, if at all, could this drive people to smoke more tobacco? Due to the already high levels of tax on tobacco in the UK, price rises on disposable e-cigarettes may limit the number of e-cigarette users switching to tobacco cigarettes. In addition, for long-term e-cigarette users, reusable e-cigarettes represent a much cheaper option than disposable e-cigarettes, and it is possible that some users might turn to other nicotine replacement products, like patches or gum, if they find e-cigarettes too expensive. Some individuals might try to maintain their consumption of disposable e-cigarettes by looking for discounts and promotions to save money and, therefore, maintain their use of disposable e-cigarettes. Usage might also switch to the illicit market for disposable e-cigarettes, bringing the added dangers of unregulated and potentially dangerous products. However, insufficient data are available to determine how different categories of nicotine products could be complements or substitutes, and to what extent consumption might shift among these products if the price of disposable e-cigarettes rises. Given the complexity of the e-cigarette market, targeted behavioural psychology experiments might be useful to gain deeper insights (eg hypothetical purchasing tasks).[143] These experiments can help to answer questions such as how a ban on certain e-cigarette flavours or marketing directed to young people might affect consumer responses to price changes.

### 6.3.8 Keeping track of product definitions and prices

Understanding how price regulations would impact the e-cigarette market requires data on the prices at which products are currently available to consumers. This requires the definition of product categories (see also chapter 2, section 2.3), for which the distribution of product prices is then estimated (see for example descriptive work on the prices that consumers pay for tobacco and alcohol products, which is then used to inform modelling of the effects of price policies).[144,145]

Product categories might be defined in terms of key aspects of product design, eg disposable vs reusable, or whether they contain certain flavours, characteristics of packaging and branding, or aspects of quality, safety and efficacy in supporting tobacco smokers to quit. ASH suggests the creation of a separate category for e-cigarettes that falls within waste electrical and electronic equipment (WEEE) regulations to ensure that producers, importers and retailers are required to fully finance takeback.[146] Product categories might also be defined based on the channel of distribution, for example distinguishing e-cigarettes sold in specialist vape shops and lounges from multiproduct retailers such as supermarkets.

The main data source would be retail scanner data, but these data would need to cover the main sources of purchase in order to be representative (Fig 6.2). To include the costs of all e-cigarettes available to consumers, further information would be needed on the cost of e-cigarettes provided by stop smoking services, which could be subsidised or free, eg the UK government's 'Swap to stop' plan, to give smokers free e-cigarette starter packs containing a device and e-liquid.[132]

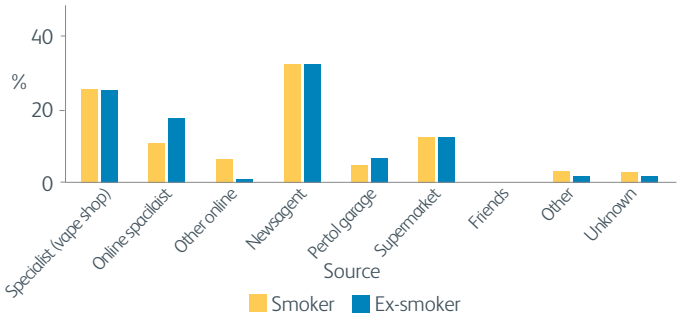


**Fig 6.2. Source of purchase of e-cigarettes.[53]**

The product categories would ideally need to be defined broadly enough so that they are 'future proof' to new product innovations that enter the market but would likely need to be reviewed regularly. Having clearly defined and up-to-date product categories is likely to be particularly important if these categories are to be the basis for new price regulations.

## 6.3.9 Appraisal of policy options

It is clear from the discussion above that there is no obvious or perfect policy option. It is also clear that we are far from having sufficient evidence to be able to appraise the potential effects of any price policy options in any detail. Thus, we provide an incomplete but illustrative assessment of the policy options currently 'on the table' in Table 6.1 on the basis that these are a step in the process of regulating the general course of the e-cigarette market, and that further market and policy developments are likely to need further policy responses. We conclude that any policy that attempts to limit access to disposable e-cigarettes should be accompanied by pricing policies that increase access to safe and effective reusable e-cigarettes. Ideally, policies that aim to make reusable e-cigarettes more affordable would be targeted to smokers in key population groups who would benefit from using them to support a quit attempt (see chapter 4, section 4.2).

**Table 6.1. Appraisal of policy options**

| | Reducing VAT on reusable e-cigarettes | Provide subsidised e-cigarettes to smokers using them to quit | A new excise tax on disposable e-cigarettes | Industry levies and fee schemes | Banning price promotions and discounts | Regulations on marketing to young people with a minimum unit price |
|---|---|---|---|---|---|---|
| **Pros** | | | | | | |
| Would likely reduce youth vaping and the environmental impact of disposable e-cigarettes | | | x | x | x | x |
| Could immediately remove the impact of disposable e-cigarettes on youth vaping and the environment | | | | | | |
| Could generate government revenue to fund administration, enforcement, and public health initiatives | | | x | x | | |
| Could lead to HMRC and Border Force having greater enforcement powers | | | x | x | | |
| Could lead to increased successful attempts to quit smoking | x | x | | | | |
| **Cons** | | | | | | |
| Could hinder smokers' attempts to quit, depending on the extent of switching from disposable e-cigarettes to other quitting aids | | | x | x | | x |
| Could increase the size of the illicit e-cigarette market, requiring more investment in enforcement | | | x | | | x |
| Difficult to define (and update) the category of products that are subject to t he policy | | | x | x | | |
| Could lead to manufacturers creating a new range of products to bypass regulations | | | x | | | |

### 6.3.10 Summary

The price of e-cigarettes is a crucial factor in determining consumption. Higher prices are generally associated with lower use, based on studies of the price elasticity of demand. Price regulation of e-cigarettes should focus on raising the price of the disposable e-cigarettes that are most commonly used by young people and have the greatest negative environmental impact, while keeping reusable products more affordable than tobacco smoking for adult smokers. The effect of a new tax will depend on consumers' responsiveness to the price of disposable e-cigarettes, and there is limited evidence to inform what this price response might be for the UK population.

New price regulation on disposable e-cigarettes would likely have only a partial effect on removing access to young people who are not using them to quit tobacco smoking, ie it would reduce but not remove e-cigarette consumption. However, this could also be true of a ban, depending on the effectiveness of enforcement of any new ban. Additionally, a tax on disposable e-cigarettes or industry levies/fee schemes could raise government tax revenue and at the same time give HMRC and Border Force greater enforcement powers to minimise the illicit market. However, removing or reducing access to disposable e-cigarettes would also require a significant proportion of smokers making a quit attempt to have to immediately choose a different aid to support them. Furthermore, reducing the availability of disposable e-cigarettes could lead to a significant increase in the illicit market in disposable e-cigarettes. It is therefore likely to be important that any new measures that increase the price of disposable e-cigarettes are accompanied by policies that decrease the price of reusable e-cigarettes, in a way that targets products used by current tobacco smokers who might want to use them to support a quit attempt.

A practical way to consider the best mix of e-cigarette pricing policies is to assess which combination would be either cost-neutral or cost-saving from a wider societal perspective. Implementing a new excise tax on disposable e-cigarettes is likely to generate additional tax revenue for the government, which would not be achieved through a minimum price requirement or an outright ban. The amount of tax revenue generated would increase as more people continue to use disposable e-cigarettes despite the price increase. This added revenue could be instrumental in building the political support for increased investments in several important initiatives, including: 1) raising awareness among young people about the risks of e-cigarette use and smoking; 2) minimising the illicit trade in disposable e-cigarettes; 3) making reusable e-cigarettes more accessible to individuals seeking to quit tobacco smoking; 4) enhancing the accessibility of e-cigarette recycling facilities. Furthermore, raising the price of disposable e-cigarettes may also contribute to reducing the recent surge in use among young people. Depending on how we value the societal impact of this reduction, it could further strengthen the case for increased investments in the above initiatives.

## 6.4 Health inequalities and specific population groups

### 6.4.1 Low socio-economic status and homelessness

In the UK, most national policy approaches have been 'blanket approaches', targeting all people who smoke. Because smoking is more concentrated among the most deprived communities,[147,148] it is expected that national policies will have some impact on reducing smoking prevalence in these groups. Whether a policy reduces absolute or relative inequalities in smoking depends on it having a comparably greater impact in priority groups than in more advantaged groups. In the context of national policy on e-cigarettes, the UK government recently announced their plans to fund the delivery of a new scheme called 'Stop to swap'.[149] Under this scheme, approximately 1 million e-cigarettes will be offered to people who smoke to help them to quit smoking. The details of the scheme are still being developed, but because more people experiencing disadvantage smoke, and face greater barriers to sustaining quit attempts, the policy may consequently reach individuals in more deprived communities. Another example of e-cigarette policy that was sensitive to inequalities in smoking occurred during the COVID-19 pandemic, when people experiencing homelessness were offered e-cigarettes and other nicotine replacement therapies, as part of the 'Everyone in' initiative. The scheme rapidly responded to the lockdowns by bringing people who were insecurely housed into hotels and hostels. To date, there has been no national evaluation of the impact of this scheme on smoking cessation, though some evidence of effects at local level is available.[150]

There is growing evidence that e-cigarettes may appeal to people across a range of sub-populations experiencing disadvantage because they offer a way of using nicotine without having to quit.[151–153] For example, for people experiencing homelessness or accessing substance use services, e-cigarettes are another form of harm reduction, a concept with which service users and staff

are familiar.[154] While there is no national policy on offering e-cigarettes in these health services *per se*, the drug misuse and dependence UK guidelines on clinical management (also known as 'the Orange Book') does include a section on tobacco harm reduction where it recommends e-cigarettes.[155] In addition, the National Centre for Smoking Cessation and Training (NCSCT) has recently developed a training module for professionals working with people who are homeless on how to offer Very Brief Advice.[156] Both resources recognise the need to reduce smoking within priority groups and the potential role of e-cigarettes as a tool to help people quit.
Finally, because the vast majority of those experiencing disadvantage are on low or sometimes no income, for e-cigarettes to fulfil their potential as a smoking cessation tool they need to be an accessible, affordable and pleasurable alternative to cigarettes.[151,154,157] If not, then individuals who smoke will likely find ways to smoke cigarettes even under stronger regulation. For instance, research shows that people on low incomes are more likely to use roll-your-own (loose) tobacco cigarettes when factory-made cigarette prices increase.[158] There are also implications for restricting product characteristics such as e-liquid flavour, which has been associated with a return to smoking.[159] Altogether, to maximise the potential impact of an e-cigarette policy in priority socio-economic groups of smokers, the development of any national policy should take a health equity-informed approach during its design and implementation.

## 6.4.2 Mental health

In recent years, increasing attention has been paid to the existing and widening tobacco-related health inequalities among people with mental illness. As briefly summarised in chapter 4, section 4.2.2, the links between smoking and mental illness are strong and characterised by complex biopsychosocial factors.[160] Both smoking prevalence and tobacco dependence are substantially increased among people with mental illness compared to the general population, and despite similar motivation and ability to quit smoking, smoking rates are declining much more slowly in this population than on average in the national population.[161,162] In 2013, national public health guidance[163] and a joint report by the Royal College of Physicians and the Royal College of Psychiatrists[164] highlighted the importance of addressing tobacco-related health inequalities in people with mental illness. Since then, the last Tobacco Control Plan for England (2017)[165] and the NHS Long Term Plan (2019)[166] have identified the matter as a national health priority. The NHS Long Term Plan pledged that by 2023/24, all people admitted to hospital who smoke, including those admitted for the treatment of mental illness, will be offered NHS-funded tobacco treatment services. Notably, it also committed that 'a new universal smoking cessation offer will also be available as part of specialist mental health services'.[166]

### 6.4.2.1 E-cigarettes in tobacco dependence treatment for people with mental illness

The latest national clinical guidelines on tobacco expressly include smokers with a mental illness in their recommendations on promoting quitting and treating tobacco dependence.[167] These recommendations also cover harm reduction ('cutting down to quit'). Thus, they arguably remove a historical divide between the way support offers for smokers with and without mental illness were sometimes viewed in terms of appropriateness and effectiveness,[168] acknowledging that interventions that 'work' in the general population, also 'work' for people with mental illness.[169] However, they clarify that, based on the limited existing evidence in the field,[170] smokers with severe mental illness (SMI) such as schizophrenia may require smoking cessation or harm reduction support that is tailored in duration and intensity to the person's need, which should be provided by a tobacco specialist adviser with mental health expertise. Tailoring smoking cessation and harm reduction offers to the needs of smokers with mental illness could arguably be expected to be increasingly focused on e-cigarettes use, seeing as vaping appears attractive to and prevalent in this population and has been argued to be particularly suited to support highly dependent smokers with difficulties to quit by other means.[171–173] Notably, the Royal College of Psychiatrists released a position statement according to which psychiatrists should advise patients who smoke that e-cigarettes may help them to quit, particularly when used with stop smoking treatments, and are safer than continuing to smoke.[174] The clinical guidelines on tobacco recommend the inclusion of nicotine-containing e-cigarettes in the provision of smoking cessation and harm reduction support.[167] In the currently prevailing absence of such medicinally licensed products, which are however expected to become available in due course, advice on the use of other nicotine-containing e-cigarette products should be given to all smokers. Further evidence on the effectiveness and cost-effectiveness of e-cigarettes for sustained smoking cessation and harm reduction in smokers with mental illness is, however, needed (see chapter 4, section 4.6).[175] In view of indications that long-term dual use of e-cigarettes and combustible cigarettes,[175] or return to using combustible cigarettes when e-cigarettes are no longer provided for free, are common in this population.[171,175] research should also focus on these aspects to explore and prevent potential e-cigarette-related health inequalities for people with mental illness.

With regard to the use of e-cigarettes in mental health settings, guidelines recommend that when admitted to acute and mental health secondary care, smokers should be advised on the local policies on indoor and outdoor use of nicotine-containing e-cigarettes.[167] The use of e-cigarettes (vaping) is not subject to UK restrictions on smoking, but advice from Public Health England (PHE – now the Office for Health Improvement and Disparities)[176] stated that NHS organisations should seek to develop approaches to e-cigarettes that support completely smoke-free NHS sites as recommended by NICE.[163] Quoting the Care Quality Commission (CQC), advice specifically directed at NHS mental health trusts states that 'it is not appropriate to prohibit e-cigarettes use in health services as part of smoke-free policies', and states that, seeing as most people use e-cigarettes in the attempt to quit or cut down smoking, it is 'never acceptable' to require vapers to share the same outdoor space with smokers.[177] It goes further to suggest that mental health services should consider permitting the use of e-cigarettes indoors to make it more accessible than smoking and avoid any potential impact on social norms through increased (outdoor) visibility.[176,177]

### 6.4.3 E-cigarettes, mental health and inequalities: evidence of current practice

Reviewing the impact of national guidelines and policies involving e-cigarettes on tobacco-related health inequalities in mental health populations is limited by the scarcity of published studies in the field. As pointed out in a comprehensive review of the evidence,[175] further studies that involve representative samples of UK mental health populations are required to enhance understanding of the experience of e-cigarette use, its challenges and impact for smokers with mental illness, both within and outside of supported cessation and harm reduction attempt contexts. Formal evaluations of new tobacco dependence treatment pathways implemented as part of the NHS Long Term Plan, which will include information on e-cigarettes, are expected in due course. In terms of practice relating to e-cigarette use in mental health settings and spaces, ASH conducted a survey of mental health trusts in England and found that the great majority (82%) of the 45 respondent trusts reported having a comprehensive smoke-free policy (covering buildings and grounds), and 91% permitted the use of e-cigarettes, 44% of which permitted their use indoors (most commonly in private bedrooms) and 76% in ward courtyards. Almost half (42%) reported providing e-cigarettes free to their patients. Three trusts (7%), however, only permitted vaping in the hospital grounds, and one only off-site. Discrepancies between reports on organisational smoke-free policies and practice have been reported before.[178,179] To understand the impact of varying organisational approaches to vaping on smokers, non-smokers, vapers and tobacco-related inequalities, further research is required.[180]

## 6.5 Smoke-free places

Article 8 of the WHO Framework Convention on Tobacco Control (FCTC) requires parties to adopt effective legislation providing for 'protection from exposure to tobacco smoke in indoor workplaces, public transport, indoor public places and, as appropriate, other public places'.[181,182] Indeed, the obligation is one of a small number of convention requirements that are time bound, with parties committing to implement legislation within 5 years of the convention coming into force. The explicit rationale for legislation is that 'Parties recognise that scientific evidence has unequivocally established that exposure to tobacco smoke causes death, disease and disability'.[181] A large body of evidence demonstrates not only that second-hand smoke is harmful but that the prohibition of exposure in indoor places results in measurable reductions in harm at a population level such as acute coronary events.[183]

The Article 8 Guideline recommendations for smoke-free indoor places, such as workplaces, are stronger than those for outdoor places, reflecting the more consistent and compelling evidence of harm from indoor exposure and the benefits arising from effective measures to prevent exposure.[184] Political and ethical justification for the infringement on the rights of the individual is provided by JS Mill's harm principle 'That the only purpose for which power can be rightfully exercised over any member of a civilized community, against his will, is to prevent harm to others. His own good, either physical or moral, is not a sufficient warrant. He cannot rightfully be compelled to do or forbear because it will be better for him to do so, because it will make him happier, because, in the opinions of others, to do so would be wise, or even right'.[185] Simply preventing offence or nuisance to others would not be consistent with the principle. The invocation of Mill served to allay concerns among libertarian politicians.

FCTC Guidelines to the implementation of Article 8 clearly justify the requirements and recommendations for indoor public places with the evidence of harm stating that 'only the creation of 100% smoke-free environments provides effective protection from the health risks of exposure to tobacco smoke'. The guideline recommendations for outdoor public places are less universal and suggests that extension of prohibition is required 'possibly' and 'where appropriate'. Published in 2017, the guidelines recognise

that circumstances and evidence are likely to evolve and Principle 7 makes provision for 'measures to reflect new scientific evidence and case-study experiences'.[182] In the same year that the guidelines were published, Wilson *et al* asked 'Should e-cigarette use be included in indoor smoking bans?'.[186] They proposed two arguments for vaping, that permitting vaping may encourage smokers to quit and that permitting vaping could minimise discomfort to users. They posed five arguments against: that from a distance vaping might be confused with smoking; that exposure of those who have recently quit smoking might trigger relapse to smoking; that passive exposure to vaping may have adverse health consequences; that regardless of harm some might experience exposure as a nuisance; and that legislation prohibiting both vaping and smoking would be more easily understood and so result in greater compliance.[186] As they neither demonstrate harm from exposure nor benefit from prohibition and, as including the avoidance of nuisance as equal to the protection from harm, these arguments fall somewhat short of the high ethical and evidential bars set by smoke-free legislation. Nonetheless, Wilson *et al* concluded that 'central and local governments should adopt regulations that effectively determine that all designated indoor smoke-free areas are also vape-free areas.'[186] A single rule that always applies to both behaviours will be clearer and easier to implement, they argue.

In 2015, a coalition of UK health bodies led by ASH and the Chartered Institute of Public Health published a briefing, 'Will you permit or prohibit the use of e-cigarettes on your premises'.[187] While not adopting a single universal recommendation, they offered 5 questions to ask before making a decision: What are the issues you are trying to deal with? What do you think you need to control? Do you have concerns about the possibility of harm from electronic cigarettes? Will restricting or prohibiting the use of electronic cigarettes support compliance with smoke-free policies? Do you want your policy to help to improve people's health?[187] In 2016, Public Health England responded with an online 'public conversation' concluding with the following 5-point guide to policy making: Make a clear distinction between vaping and smoking; ensure that policies are based on evidence of health risks to bystanders; identify and manage risks of uptake by children and young people; support smokers to stop smoking and remain smoke-free; and support compliance with smoke-free legislation and policies.[188] Both PHE and ASH documents avoid a universal rule and propose that rules should reflect the evidence and the context of the behaviours.[188] Five years after the Wilson and ASH recommendations, Semple *et al* made a range of recommendations for strengthening smoke-free places but concluded, 'Restrictions and policies on use of e-cigarettes in smoke-free settings require more research to determine the benefits and implications of bystanders' exposure to second-hand e-cigarette aerosol, dual use and smoking cessation'.[189] Smoke-free policies that do not include the use of e-cigarettes have been found to be effective with benefits in certain settings, including reducing fires.[190] Wilson's recommendation of a direct application of smoke-free laws to vaping in all smoke-free places[186] is not widely enshrined in law outside the USA but specific prohibitions are widespread. In Europe, 28 countries have some legal prohibition of vaping in public places, most commonly in educational establishments, public transport and workplaces, with 12 countries prohibiting vaping in some private places.[191] By contrast, in the USA, which is not a party to the FCTC, as at 1 January 2023 over 1,000 municipalities and 26 states had restricted the use of e-cigarettes in all smoke-free places.[192]

Evidence suggests that, while effective in achieving the goal, some policies intended to reduce vaping among young people (such as taxation, minimum legal age of sale and flavour bans) may have adverse unintended consequences. In their investigation into the impact of extending smoke-free legislation in the USA, Friedman *et al* found adding vaping restrictions to smoke-free worksite laws 'was not associated with a reduction in recent vaping among emerging adults and may have attenuated the smoke-free policy's impact on current smoking in this age group'.[193] Gibson *et al* have offered a framework for assessing the direct and indirect impact of specific vaping policies on the health and welfare of young people. It may be appropriate to subject 'vape-free' policies to similar analysis.[194]

## 6.6 Illicit vaping products

### 6.6.1 Introduction

Illicit vaping products comprise products that have not been notified to and listed by the MHRA.[72] Some such products may meet MHRA requirements but simply have not been notified; some have not been notified and contravene one or more regulations applying to vaping products such as tank size, the display of health warnings or nicotine content; while others have been notified but are found to be non-compliant.[195] Some products that are illicit in the UK are legal in other jurisdictions, such as the USA.

Although a recent surge in illicit sales of vaping products by specialist vape shops, convenience stores and corner shops has been reported,[196] comprehensive national data on the scale of the illicit vaping market are not currently

available. However, local data on seizures indicate that the size of the market is significant with, for example, 1.4 tonnes of illegal vapes being seized in the North East of England in the last 6 months of 2022 alone.[105] A recent programme of test purchasing by the Chartered Trading Standards Institute carried out by young people under 18 found that a quarter of the products purchased did not comply with UK requirements.[95] No research has investigated consumer incentives for purchasing illicit vapes; however, anecdotal evidence from Trading Standards officials suggests that circumventing product restrictions, particularly on tank size, may be a key reason for purchasing these products.

An outbreak of serious respiratory illness among vapers in North America, which was attributed to vitamin E acetate contained in illicit tetrahydro-cannabinol (THC, which is illegal for recreational use in the UK) e-liquids, rather than nicotine-containing e-liquids, has led to concern that illicit vapes may be more harmful than legal products. There is, however, no published peer-reviewed evidence that this is the case in the UK. Some illicit e-liquids may not meet UK regulatory standards, which prohibit the use of ingredients that pose a risk to human health in heated or unheated form, such as vitamin E acetate and diacetyl. There is anecdotal evidence that some illicit products may exceed safe levels of metals,[197] which requires further exploration. The safety of illicit vaping products, as with legal products, should be monitored.

## 6.6.2 Tackling illicit vaping products

Trading Standards services are responsible for the enforcement of vape product sale regulations, and in most local authorities undertake this work as part of a broader programme of measures to tackle illicit tobacco and enforce age of sales legislation for tobacco products. This includes activities such as surveillance and intelligence, test purchasing and seizures. The Chartered Trading Standards Institute has called for additional support to help enforce regulations and advise businesses, and has highlighted the need for clarity on the scale of the problem across the country.[198]

The 2023 government announcement of £3 million funding for an 'illicit vapes enforcement squad', as part of a national programme to tackle illicit vapes and underage sales,[107,199] may provide an opportunity for more effective work to counter illicit sales, though the specific details of how and where this funding will be used have yet to be set out. The programme is expected, however, to include providing additional resources to support activities that are already being undertaken, such as knowledge and intelligence gathering and sharing, seizures in local areas and borders, and test purchasing.

Testing of products, the cost of which can be prohibitive in relation to current Trading Standards working budgets, is also likely to form part of the programme of work and will potentially lead to better understanding of the content of illicit e-liquids. Activity to tackle online sales of illicit products is also expected to be part of the squad's remit.

## 6.6.3 Learning lessons from tobacco enforcement

Although tobacco and vaping products raise different issues in relation to enforcement of regulations, there are clear parallels between the two. Lessons can therefore be learned from the UK's approach to tackling illicit tobacco and preventing underage sales of tobacco.

From 2000, the UK implemented a comprehensive illicit tobacco strategy focusing predominantly on supply-side measures, characterised by operational responses including disrupting the supply and distribution chains for illegal products and by increasing sanctions.[200] The illicit tobacco strategy has been underpinned by strong governance, including monitoring data, to increase transparency and is widely regarded to have been a success, with the estimated combined illicit market share for manufactured cigarettes and hand-rolling tobacco down from 21.7% in 2005 to 17.7% in 2021,[201] with larger decreases in the first decade of the strategy. Measures to address the sale of illicit vaping products should, where appropriate, be aligned with those already implemented to reduce sales of illicit tobacco. Much of this activity is already being undertaken by Trading Standards, but with limited resources. As such, effective efforts to reduce the availability of illicit products will involve significant investment in human resources to develop intelligence, detect illegal products, undertake test purchasing and undertake criminal investigations. A formal strategy setting out a comprehensive national approach should be implemented and subsequently monitored and evaluated. The vaping market changes quickly, and any strategy should be reviewed and revised regularly to allow changes and responses to newly emerging threats, such as new products and new supply chains.

Given resource constraints, there is a risk that efforts to address illicit vaping may overshadow efforts to tackle illicit tobacco. Illicit tobacco continues to be a major public health problem, undermining tobacco control policy and allowing the sale of tobacco to children.[200] As such, it is important that efforts to tackle illicit vaping do not come at the expense of efforts to combat illicit tobacco.

## 6.6.4 Future regulation and sanctions

As described in earlier sections of this report, the main priority in the development of policies on vaping and vaping products is to seek to maximise any potential benefits of e-cigarettes for smoking cessation while minimising the risks of e-cigarettes, particularly among non-smokers and children. Anecdotal evidence suggests that, unlike tobacco, for which the primary incentive for purchasing an illicit product is the low price, illicit vaping products may often be purchased to circumvent specific regulations, such as tank size restrictions. To the extent that the rational for illicit purchase is to obtain a more effective or convenient product, enforcing regulations could be counterproductive to effective substitution of vaping for smoking. However, preventing the sale of illicit products that represent a greater health risk than licit products, or are intended to be appealing to children, is a priority. The UK's exit from the EU has created the possibility of changes to the regulatory framework for vaping products and so the current proposals for new regulations is warranted.[90]

One area that needs urgent reform is that of sanctions for sellers operating illegally. As stated earlier, the current penalty for selling vaping products to people under the age of sale is currently £2,500, however, test purchasing suggests that the existing penalty is insufficient to deter businesses from illicit sales, and prosecutions are rare. Fixed penalty notices would make it less costly for enforcement authorities to levy fines. A registration scheme which requires retailers to register to sell both tobacco and vaping products, incorporating significant sanctions for non-compliant businesses, would provide comprehensive data on where e-cigarettes are being sold in local areas. This, together with requiring mandatory age verification for tobacco and e-cigarette sales, would facilitate enforcement and reduce sales to under 18s.

## 6.6.5 Evaluation, research and data

The illegality of the illicit vape market makes it difficult to study. As such, there are currently no comprehensive data on the scale and nature of the illicit vape market and a lack of research exploring topics such as the supply chain of vaping products and the characteristics and motivations of illicit vape users.

Independent data on the illicit vape market is needed to validate media claims, both in the UK and beyond, by tobacco companies and tobacco industry-affiliated actors that illicit vapes are a growing issue.[202,203] As claims about the illicit vape market mirror the industry's long-held strategy of using the illicit tobacco market as a threat against tobacco control regulation,[204,205] it is crucial that there is sufficient independent data to compare them with in order to identify any potential exaggeration of the problem.

This concern applies not just to claims about illicit vapes but also industry-affiliated data on the vaping market more broadly. The Phillip Morris International (PMI)-funded 'Foundation for a Smoke-Free World'[206] has provided funding for work on topics such as 'estimation of the global number of vapers' and 'interventions to mitigate vaping misinformation',[207] creating a risk that such research will influence understandings of vape use and thus vape regulation, despite being financially supported by commercial entities with clear vested interests in the debate.

One such vested interest is transnational tobacco companies having an incentive to influence policy on vaping products, with several having made investments in the vaping market in recent years, both via developing their own products and by investing in pre-existing companies.[208] Further, tobacco industry-affiliated claims regarding vape products should be seen within the context of industry efforts to conflate what they refer to as 'heat not burn' devices which contain tobacco, such as PMI's IQOS, with vapes which do not contain tobacco.[209] Such conflation aids the industry's efforts to lobby governments into providing softer regulation on heated tobacco products than on conventional tobacco products,[210] under unsubstantiated claims that they are effective cessation tools.[209] For a broader analysis of transnational tobacco company claims and conduct around harm reduction, see chapter 9.

Effective monitoring and evaluation of efforts to tackle illicit vapes requires independent nationwide data which are routinely collected over time and available at local authority level. Drawing lessons from how the illicit tobacco market is estimated in the UK, setting the groundwork for potential tax gap analysis of vaping products could be one way forward. A first step here would be to require duty on vapes, returns from which could then be used alongside existing vape consumption data published by the Office for National Statistics[211] to produce regular estimates of the proportion of the UK's vape market that is illicit. Additionally, further independent research on vaping products currently found on the UK market and their individual health impacts, such as exploration of which products exceed legal thresholds for potentially harmful metals, would be beneficial for informing vape regulation.

Independent research on the supply chain of illicit vapes, such as investigation into where illegal vapes are manufactured and the regulatory framework within those contexts, could also provide insight into the extent to which any existing supply chain control measures in the legal vape market are effective, and of the role of organised crime networks in the production and distribution of illicit vaping products. The regulatory debate may also benefit from research exploring consumer motivations in more detail, eg the main incentives for using illicit vapes and how comparable these are with incentives for illicit tobacco use (eg price) by providing insight into which policy measures would be most effective for curtailing the illicit vape market.

# 6.7 The environmental impact of disposable vapes

## 6.7.1 Introduction

The use of disposable vapes presents a range of environmental challenges, particularly in relation to recycling and fire risks. These are growing problems: one-fifth of UK adults have now bought either a disposable, rechargeable with a single-use pod, or rechargeable with a refillable tank vape.[212] Non-reusable disposable vapes, such as brightly coloured sticks that are reminiscent of highlighter pens, are increasingly prevalent with nearly 14 million disposable vapes bought each month.[212] The number of MHRA-notified disposable vape products available on the market has increased from none in 2016 to just over 2,000 in 2021, and almost 10,000 by the end of 2022 (see Fig 6.3 ).[213] Two brands (Elf Bar and Lost Mary) accounted for a majority of disposable vape sales in the year to January 2023 (Fig 6.4).[213]

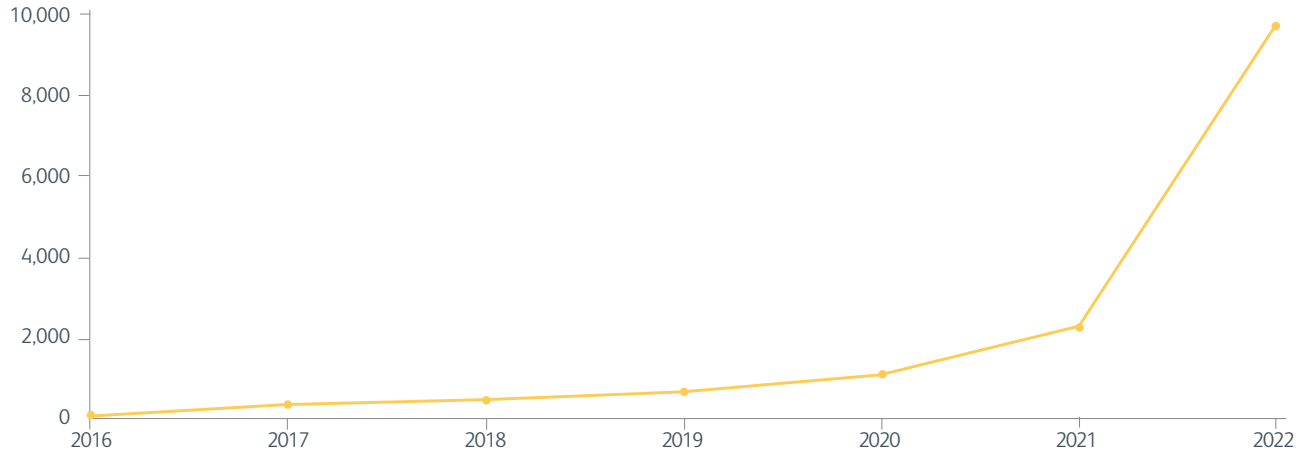


**Fig 6.3. Cumulative number of MHRA-notified UK disposable vape products.[213]**
Figure courtesy of *Financial Times*; MHRA data provided by Vape-Click.com

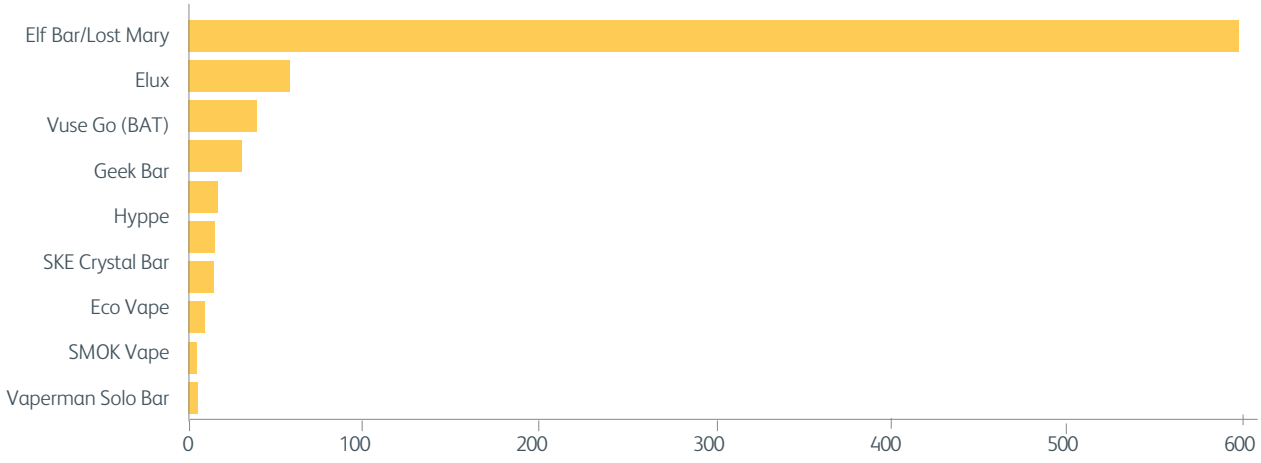


**Fig 6.4. UK disposable vape sales by value (£m) in year to end of January 2023.[213]**
Figure courtesy of *Financial Times*; data source Nielsen IQ

### 6.7.2 Waste and recycling implications

Discarded unwanted electricals are the fastest growing waste stream in the UK and the world.[214] Waste electrical and electronic equipment (WEEE) and portable batteries are regulated by the UK government to reduce the amount of old and unwanted electricals that are incinerated or sent to landfill sites.[215] The government sets annual targets for the recycling of all waste electricals and portable batteries to ensure that UK producers and importers are compliant. All electricals, that is anything with a plug, battery or cable, are covered by the regulations. This includes all vapes.

Research commissioned by Material Focus as part of an investigation with the Bureau of Investigative Journalism in May 2022 identified that at least 1.3 million disposable vapes are thrown away every week, equivalent to over 67 million a year.[212] Sales of disposable vapes have risen considerably since then, so the true number now is likely to be significantly higher, thus representing a rapidly growing source of electronic waste. There are numerous models, shapes and sizes of disposable vapes which include a mix of materials including plastic, steel, aluminium, copper, lithium, nicotine liquid and synthetic absorbent materials. Aside from these constituents, the plastic components in disposable vapes contribute to the growing problem of plastic pollution. Improper disposal of these devices can result in them ending up in landfills, polluting water bodies, or posing a threat to wildlife and ecosystems. A typical disposable vape contains an average 0.15 g of lithium and 1.9 g of copper, all of which is lost forever if not recycled.

Recycling disposable vapes can be challenging due to their complex design and mixed materials. The lack of standardised products, recycling processes and collection systems specifically for vapes contributes to their low recycling rate. This results in a significant proportion ending up littered, in landfills or being incinerated. However, in July 2023 a commercial waste management company announced a 'takeback' scheme for disposable vapes, with a plan to introduce a national disposal, collection and recycling service for disposable vapes.[216]

### 6.7.3 Fire risks

The lithium-ion batteries in vapes represent a fire safety risk if disposed of incorrectly, either as a result of crushing in waste vehicles or at waste sites, or as a result of heat in vehicles or sunlight on public or household dustbins. It is essential to dispose of these devices safely to reduce this hazard. An estimated 700 fires a year in the UK are caused by the incorrect disposal of electricals with hidden batteries, including vapes.[217]

### 6.7.4 Non-compliance with extended producer responsibility regulations

An examination of the company records of over 150 of the largest UK e-cigarette producers in January 2023 identified that only 16 had registered to comply with environmental regulations for producer responsibility for waste electricals, portable batteries, and packaging,[218] despite being members of a vape industry trade association and having registered their products with the MHRA. Larger vape producers and importers which have only recently begun to register are not covering the legacy clean-up costs of the hundreds of millions of vapes already sold in the UK. Vapes currently fall under cheaper-to-process small electricals rather than under their own special category, so even if producers have registered for waste electricals, they are currently not covering the significant present and future costs of collecting and recycling the products they place on the market. Material Focus analysis has identified that if all of the 138 million disposable vapes that are bought in the UK every year were recycled, this could cost up to £69 million per year.[218]

### 6.7.5 Illegal vapes

There is a significant and widely reported growing market in illegal vapes, and from an environmental and safety perspective illegal vapes may be of a lower quality and therefore pose greater risks. Impounded tobacco products are generally managed by being sent for incineration for energy from waste, but vapes are electrical products and, as confirmed by the Environment Agency, must be recycled.[219] Trading standards teams across the UK are thus now presented with the challenge of having to cover the high costs of recycling impounded vapes, with very limited financial support to do so.

## 6.7.6 Policy responses to vape recycling

The scale of the challenges set out above are significant. Possible policy options to help tackle some of these challenges are set out below.

### 6.7.6.1 Banning sales

Prohibition of the sale of disposable e-cigarettes has the potential to markedly reduce environmental and safety hazards arising from these products, but success would rely on effective policing and enforcement, which would be particularly difficult for online sellers. Banning disposable vape sales would also remove any mechanism for producer, importer and retailer financing for takeback and recycling costs. Furthermore, if disposable vape users all switch to, for example, pod-based vapes with a rechargeable battery unit, the volume of waste – likely to run into tens of millions of battery units and hundreds of millions of vape pods each year – would remain substantial in the absence of more radical and effective takeback schemes.

### 6.7.6.2 Amending the waste electrical and battery regulations

Existing environmental regulations require disposable vape producers and importers to properly fund end-of-life takeback.[215] However, the current product categories allow vape producers, even if they have registered, to avoid these significant compliance costs because they can report sales as a general small electrical goods with compliance recycling costs being significantly lower than the costs for recycling vapes. Defra are reportedly planning to review the WEEE regulations and have indicated that they will consult on adding disposable vapes as a new separate category.[220] It is not clear whether, if adopted, this approach will be followed up by strong producer compliance enforcement by the UK environment agencies to ensure that takeback and recycling of vapes is properly financed by producers, importers and retailers.

### 6.7.6.3 Providing accessible drop-off points

Setting up more public recycling drop-off points and educating users about the importance of proper disposal, such as using designated e-waste, vape and battery recycling points, would be likely to increase the extent to which these products are recycled. As a minimum, and required by legislation, retailers need to make it possible for the public to drop off their vapes in-store for recycling. Public drop-off-points in and near to parks, town centres, bars, clubs, colleges and universities might also encourage recycling and could be financed by vape producers and importers as part of their waste electricals and portable batteries compliance charges.

### 6.7.6.4 Amending product standards, descriptors and notification

Disposable vape product standards could be used to impose some standardisation of design to make recycling easier, and perhaps to end the use of disposable as a marketing descriptor. Proof of compliance with WEEE, batteries and packaging regulations could also be made a condition of market notification with the MHRA. Effective recycling systems could also be made a requirement of supply into the 'Swap to stop' scheme.[149]

# 6.8 An e-cigarette decision-making tool to support policymakers

Formulating policy to maximise the public health benefit of vaping should be evidence-based, but predicting the magnitude of intended and unintended consequences of new policy can be very difficult. For example, banning flavours in e-cigarettes to reduce appeal to non-smoking young people could have the intended impact by reducing youth vaping uptake, but could have negative consequences for established smokers and/or vapers. In addition, policy decisions typically need to be made within timescales that do not align well with traditional academic research. A decision-making aid established to help policymakers make rapid, informed decisions on the potential net impact of a ban on e-cigarette flavours estimated the number of non-smoking young people who would be deterred from ever vaping and subsequently ever smoking, and the number of smokers and ex-smokers who would be deterred from quitting or encouraged to relapse, to determine whether the benefits to youth outweigh the costs to existing smokers and vapers.[194] The aid produces a report with the results graphically depicted to aid interpretability. The tool will be updated as data emerge and is not intended to provide a definitive answer, but rather a readily interpretable snapshot given the extant data at any given time. It demonstrates how decision aids can be used to help policymakers arrive at evidence-based decisions efficiently and can be used to quickly obtain up-to-date estimates as new data become available. An example output from the decision-making tool is shown in Fig 6.5.

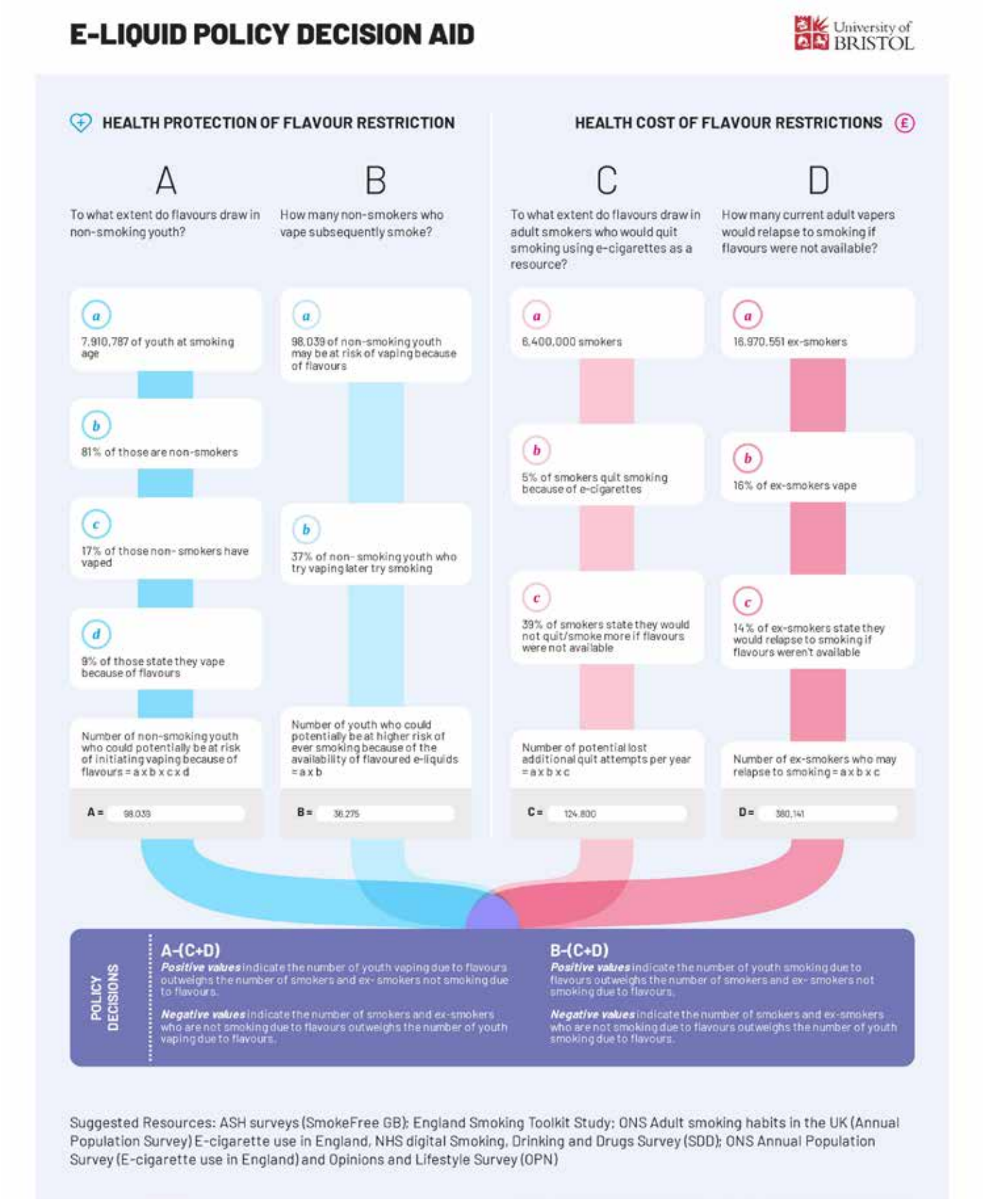


**Fig 6.5. An example output from the policymaker decision-making tool.**
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# 07

# Encouraging uptake of e-cigarettes for smoking cessation

## Key points

- E-cigarettes are an effective treatment for tobacco dependency, but despite wide retail availability they are under-utilised by people who want to quit or reduce smoking. This represents a large missed opportunity to reduce morbidity and premature mortality caused by smoking.
- Many commissioned stop smoking services do not currently utilise e-cigarettes as part of their treatment interventions.
- Public perceptions of the risks of vaping relative to smoking do not reflect current evidence.
- Misinformation in the media is likely to contribute to misperceptions about vaping.
- Misperceptions about vaping and nicotine need to be addressed because the evidence suggests that correct perceptions encourage people who smoke to switch to vaping.
- Nicotine addiction warnings on e-cigarette packaging are infrequently noticed but may affect harm and addictiveness perceptions and reduce intentions to vape among youth but also adults who smoke.
- Reduced risk messages presented on e-cigarette packs alone (without an addiction message) may increase uptake of vaping by smokers without influencing non-smokers.
- The availability of a range of device types and flavours can encourage the use of e-cigarettes to quit smoking.
- Smoking cessation is more likely if vapes are used daily and frequently.
- Dual users who are predominantly vapers are more likely to reduce tobacco consumption compared with those who are predominantly smokers.
- A person's identity in relation to smoking and vaping may play an important role in smoking cessation. Vaping offers an identity that may be attractive to some smokers who wish to quit or stay quit.
- The price of e-cigarettes is likely to be an important determinant of their consumption; higher prices are generally associated with lower use.
- There is very limited evidence on the impact of e-cigarette advertising on use of e-cigarettes; however, some studies suggest that advertising may help to encourage e-cigarette uptake among smokers.
- The vast majority of brand adverts comply with UK advertising standards, which prohibit explicit messages that e-cigarettes could help with stopping smoking.
- Regulating e-cigarettes as medicines to limit their availability would create a barrier to use by people who smoke and are contemplating or attempting to quit.
- There is an opportunity to proactively support smoking cessation by promoting vaping as a treatment for tobacco dependency in all NHS settings.
- Despite national guidelines that clinicians should offer e-cigarettes as a treatment for tobacco dependency to their patients who smoke, a high proportion of health professionals report that they would not advise their patients to use e-cigarettes due to concerns about addiction and uncertainty about long-term harms.
- There is a need to work with clinicians to integrate the harm reduction mindset into routine clinical practice.

## Recommendations

- Measures that encourage e-cigarette use for smoking cessation, encompassing policies that address availability, affordability, access to nicotine-containing e-cigarette together with information and support to use these products, should be expanded to improve smoking quit rates in the UK.
- Measures to encourage e-cigarette use by smokers should be used together with measures to discourage uptake of e-cigarettes by people who do not smoke, especially children and young people.
- Interventions to increase accurate perceptions of the risks of vaping, especially relative to smoking, are important, but more research is needed to identify the most effective ways of doing this.
- A range of flavours should be available to facilitate quitting among adults who are using e-cigarettes to quit smoking.
- More research is needed to directly explore the effects of device type , nicotine concentration and other features on smoking cessation.
- Messages on the relative risks of vaping and smoking should be required on cigarette packs and on package inserts, thus reaching smokers but not non-smokers.
- Reduced risk messages should be included on e-cigarette packs.
- More research is needed to explore how to maximise credibility of reduced risk messages, ensure that smokers notice and attend to them, and understand the extent to which message exposure can promote actual use behaviour.
- Detailed research is needed to understand how e-cigarette advertising can increase the uptake of e-cigarettes among people who smoke to support and maintain quit attempts.
- In all healthcare settings, trained specialists should offer support for smoking cessation using e-cigarettes and other evidence-based therapies.
- Smoking cessation interventions should support positive identity change in relation to vaping. Research is needed to identify the most effective ways to do this.
- Smokers who are trying to quit using e-cigarettes should be encouraged and supported to adopt patterns of e-cigarette use most likely to lead to successful smoking cessation.

# 7.1 Introduction

As described in chapter 4, evidence from randomised trials and systematic reviews shows that e-cigarettes containing nicotine are an effective aid to smoking cessation. Most people who smoke and attempt to quit do so without utilising behavioural support or quit aids such as e-cigarettes or pharmacotherapy, while for those who do make use of quit aids, e-cigarettes are the most popular (see chapter 1, Fig 1.2).[1] However, data from local government-commissioned stop smoking services (LG SSS) from 2022/23 indicate that only approximately 5 % of quit attempts supported by LG SSS, utilised e-cigarettes (Table 7.1)[2] implying that a large proportion of people who smoke are not receiving the most cost-effective treatment and comparable in effectivness to varenicline and cytisine for tobacco dependency treatment.[3] Of the 5.3 million people who smoke in England,[4] it is estimated that 1.8 million (34 %) have not tried e-cigarettes in a quit attempt, therefore prolonging their use of combustible tobacco and its consequences.[5] Individual and population benefits of e-cigarettes for smoking cessation will be maximised by encouraging more current smokers to take up e-cigarettes and give up combustible tobacco use.

A number of factors affect the extent to which people who smoke will be willing to use e-cigarettes in smoking quit attempts and continue using them to maintain abstinence. This includes public attitudes towards e-cigarettes and their perceived risks and benefits, information provided by public officials and agencies such as the Department of Health and Social Care, reporting in mass media and the influence of social media, the appeal of the vaping products, ease of access, affordability and availability of vaping products, advice and support from healthcare professionals, public health and NHS organisations, and individual-level factors including patterns of use and people's identities in relation to smoking and vaping. This chapter considers the evidence on these factors and makes recommendations, which will support maximal e-cigarette uptake and successful quitting among people who smoke, while balancing these against the need to minimise uptake of e-cigarettes among non-smokers, particularly children (discussed in chapter 8).

# 7.2 Public attitudes and perceptions of e-cigarettes

## 7.2.1 Risk perceptions

This section aims to summarise the evidence on risk perceptions of the risks of vaping among adults who smoke, building on findings from the 2022 Nicotine vaping in England evidence update.[7] We first present data from national surveys, and then summarise peer-reviewed literature with respect to a) how risk perceptions

**Table 7.1 Type of stop smoking support, associated success rates and proportion of quit attempts using this support in England from April 2022 to March 2023 (NHS digital, n= 176,566)[2,6]**

| Type of stop smoking support | Self-reported 4-week quit success rate, % | Quit attempts using the type of support, % |
|---|---|---|
| Licensed medication and an unlicensed nicotine-containing product (NCP) consecutively | 67 | 1 |
| Combination of a licensed medication and an unlicensed NCP concurrently | 61 | 7 |
| Unlicensed NCP | 59 | 5 |
| Single NCP only | 56 | 23 |
| Buproprion only | 54 | 4 |
| Combination of licensed NCPs concurrently | 53 | 45 |
| Varenicline only | 50 | <1 |
| Did not use any licensed medication or unlicensed NCP | 49 | 9 |
| Licensed NCP and/or bupropion and/or vareniciline consecutively | 48 | 1 |
| Pharmacotherapy not known | 46 | 4 |

influence vaping and quitting smoking, and b) interventions that can change vaping risk perceptions. To update the 2022 review we have included articles published up to January 2023, identifying 57 studies from among adults that examine a) or b) above (an increase from the 32 identified in 2022). Evidence on risk perceptions of the risks of vaping among youth and people who have never smoked is presented in chapter 8. Risk perceptions can include perceptions of the relative harms of vaping and smoking, perceptions of absolute harms of vaping (ie relative to not using cigarettes), and perceived addictiveness. Relative risk perceptions were considered accurate if vaping was perceived to be lower risk than smoking, or inaccurate if vaping was perceived to be of equal, greater, or unknown harm relative to smoking.

### 7.2.1.1 How risk perceptions influence vaping and quitting smoking among adults

#### 7.2.1.1.1 National survey data

Perceptions of the risks of vaping relative to smoking are increasingly out of kilter with current evidence. In 2023, only a third (34%) of adults who smoke perceived vaping to be less harmful than smoking, down from 60% in 2014. [8] Meanwhile, the proportion who inaccurately perceived that vaping is equally or more harmful than smoking has risen over this period, from 10% in 2013 to 39% in 2023, while the proportion who 'don't know' has remained at 25%.[8] In 2022, 14% of adults who currently smoked and/or vaped accurately believed that none or a small amount of the risks of smoking were due to nicotine, with the least accurate perceptions observed among adults who currently only smoked (11%) compared with those who currently only vaped (20%).[9]

#### 7.2.1.1.2 Peer-reviewed literature

Misperceptions of vaping and nicotine are important to address because they could deter people who smoke from switching to vaping or to other less harmful forms of nicotine consumption. A systematic review on this topic among adults who smoke published in 2020 identified 31 studies, all of which were either experimental or cross-sectional and none of which examined changes in vaping or smoking behaviours as an outcome.[10] The review found that messages accurately communicating that vaping is less harmful than smoking can help to improve the accuracy of vaping risk perceptions and increase intentions to quit smoking or intentions to switch to vaping.[10]

The 2022 Nicotine vaping in England evidence update included a systematic review that assessed whether vaping risk perceptions predicted changes in vaping or smoking behaviours.[7] A total of seven studies from among adults were identified; and an additional 15 studies published up to January 2023 were also included, totalling 22 studies. The impact of perceptions on vaping initiation, as well as smoking cessation, were assessed. Of the 22 included studies, the majority were from the USA with only four from or including the UK. The four studies that included the UK found that perceptions that vaping is less harmful than smoking predicted vaping for the purposes of smoking cessation,[11] switching away from smoking to Juul use (in one study funded by Juul),[12] and trying vaping among adults in the UK who currently or formerly smoked,[13] and also predicted vaping certain flavours (eg non-tobacco/menthol rather than tobacco/menthol) in a study among adults who currently vaped.[14]

The literature suggests that overall, vaping risk perceptions predicted subsequent changes in vaping behaviours and smoking behaviours among adults. Specifically, numerous studies now suggest that accurately perceiving vaping as less harmful than smoking predicts subsequently starting vaping among adults who smoke. While there are fewer studies that examine smoking behaviours as an outcome, those that do assess this have found that accurately perceiving vaping as less harmful than smoking predicts switching from smoking to vaping as well as quitting smoking among adults who smoke.[7] Moreover, perceiving vaping as equally or more harmful than smoking predicts subsequent relapse to smoking among adults who had previously quit smoking.[7]

### 7.2.1.2 Interventions that can change vaping risk perceptions among adults

The 2022 Nicotine vaping in England evidence update included a systematic review that assessed interventions that have been effective in changing vaping risk perceptions.[7] A total of 25 studies from among adults were identified; an additional 10 studies published up to January 2023 have also been included, totalling 35 studies.

Of the 35 included studies, the majority were from the USA with only nine that included the UK (five were from the UK as well as another country), which are summarised here. One study found that the 2019 'EVALI' (e-cigarette or vaping use-associated lung injury) outbreak increased misperceptions that vaping is equally or more harmful than smoking,[15] a second found that exposure to a reduced risk warning label (for example,

'Use of this product is much less harmful than smoking') decreased perceptions of the harms of vaping and perceptions that vaping is addictive.[16] A further study found that perceptions that vaping is 'healthy' increased after viewing e-cigarette advertisements (including advertisements that vaping is healthier than smoking),[17] and three additional papers using the same data found that misinformation about vaping that is available online (eg tweets suggesting that vaping is equally or more harmful than smoking) can increase inaccurate vaping perceptions and subsequently reduce interest in trying vaping among adults in the UK who smoke.[18–20] Despite this, other studies in the UK have found insufficient evidence at the population level that a mass media campaign in Manchester (see section 7.2.2)[21] or the introduction of e-cigarette warning labels[22] changed vaping risk perceptions, and one experimental study found little evidence that vaping advertisements can change the perception that vaping is harmful.[23]

The literature suggests that overall, interventions targeted at adults who smoke that focused on communicating information about the reduced risks of vaping relative to smoking – typically via information in writing (eg nicotine fact sheets) or warning labels[7] – were generally effective in increasing perceptions that vaping is less harmful than smoking. However, information that focused on communicating that vaping is harmful and addictive were also generally effective,[7] suggesting information that mentions absolute risks of vaping to adults who smoke must be balanced with information about risks relative to smoking for more accurate risk perceptions.

### 7.2.2 Public health campaigns

Public health campaigns have provided information about vaping in several countries, including absolute harms (ie compared with not vaping) and harms relative to smoking cigarettes, and could also help to encourage uptake of vaping among adults who smoke while reducing the appeal of vaping to youth and those who have never smoked.

In the USA and Canada, vaping campaigns and associated messages from public health organisations have focused predominantly on youth vaping prevention.[24–32] (see chapter 8, section 8.2.2). In England, since 2017, vaping has featured in national campaigns aiming to help adults quit smoking,[33,34] and, since 2015, there have been regional vaping campaigns[21] containing messages that vaping is less harmful than smoking but is not risk-free, and that people who have never smoked should not take up vaping.

There is little evidence on the impact of vaping education campaigns among adults who smoke at the population level. As mentioned above, one study that examined a regional mass media campaign in Manchester[21] found little evidence that the campaign improved accurate perceptions that vaping is less harmful than smoking among adults who smoke. An experimental study among adults who smoke in England found that exposure to videos highlighting that vaping is less harmful than smoking (either a Cancer Research UK text-only video, or a video featuring e-cigarette experts) increased the accurate perception that vaping is less harmful than smoking but also increased misperceptions that vaping is safe.[35]

### 7.2.3 Media coverage

Information about vaping in the media is widespread and can change vaping harm perceptions as well as encourage uptake of vaping among adults who smoke while reducing the appeal of vaping to youth and those who have never smoked. Research suggests that exposure to anti-vaping news can increase the perceived harmfulness of vaping among US adults.[36,37] The portrayal of vaping in the media has also been found to be associated with harm perceptions of vaping relative to smoking among adults who smoke.[38] As noted above, one study found that the 2019 'EVALI' outbreak increased misperceptions that vaping is equally or more harmful than smoking among adults who smoke in the UK,[15] and this finding has since been replicated among youth.[39] As highlighted above, misinformation about vaping that is available online (eg tweets suggesting that vaping is equally or more harmful than smoking) have also been found to increase inaccurate vaping perceptions and subsequently reduce interest in trying vaping among adults in the UK who smoke. [18–20]

## 7.3 Product characteristics

### 7.3.1 Product design

E-cigarettes can help adults who smoke to stop smoking and a recent Cochrane review concluded with high certainty evidence that quit rates to 6-months+ are higher with e-cigarettes compared to NRT.[40] However, even with the support of e-cigarettes , long-term quit rates remain modest and people who smoke who have tried but no longer use e-cigarettes report lack of satisfaction with continuing to use e-cigarettes.[41] There is therefore interest in determining what aspects of product design (eg device type, nicotine concentration, e-liquid composition, pack messages) are associated with encouraging uptake among people who smoke and maximising smoking cessation. Much of the evidence

on the appeal of different e-cigarette product design characteristics has been undertaken in adolescents and young adults. This is described in chapter 8, which focuses on discouraging e-cigarette use in non-smokers.

### 7.3.1.1 Device types

Adult smokers and ex-smokers' preferences in terms of product design can be observed based on survey data on e-cigarette use (see chapter 2, section 2.3). The ASH Smokefree GB survey has included questions about e-cigarette use since 2010 and provides data on preferences over time. Two-thirds of adult vapers (of whom less than 7% were never-smokers) reported using a rechargeable device as their main device in the 2023 survey; 50% used a refillable tank system.[41] This has decreased since 2021 when 77% of current vapers mainly used a tank-type e-cigarette. During this period there has been a corresponding increase in the main use of disposable e-cigarettes, from 2.3% in 2021 to 31% in 2023. This increase is predominantly driven by use of disposable devices by younger adults aged 18–24.

Very few studies have directly compared smoking cessation rates between different device types and other product characteristics. The Cochrane review planned to undertake comparisons but there were too few studies for viable analyses. Nevertheless, randomised controlled trials (RCTs) that used tank-style refillable rather than cig-a-like (cartridge) devices tended to be associated with higher odds of quitting.[40] In experimental studies that have compared cig-a-likes with tanks on smoking reduction, no differences between device types were found[42,43] but tanks have been associated with higher levels of satisfaction.[42,44] Among cross-sectional and longitudinal surveys, findings consistently show that use of tank devices (vape pens and/or mods), is associated with greater smoking cessation success compared with cig-a-likes.[45–47]

Pods, and especially, disposable vape bars, have received less attention since they have not been on the market as long as cig-a-likes and tanks. In one survey of smokers who used an e-cigarette in a recent quit attempt that did include pod-users, abstinence duration was similar between pod and mod users, and longer than for cig-a-like users.[48] Although no studies have directly compared pod-based devices with other e-cigarettes for smoking cessation, one single-arm pilot study reported a 40% 12-week cessation rate smokers among smokers with serious mental illness unwilling to quit using a Juul pod device.[49] A similarly high quit rate of 31.6% at 6 months was reported in an online survey of over 15,000 adult smokers who had purchased a Juul in the USA.[50] These studies, however, used high nicotine concentrations that are not available on the UK market.

In order to maximise smoking cessation rates, e-cigarette products need to appeal to smokers. Qualitative studies reveal that tank and mod devices can constitute a barrier for some due to their conspicuous appearance and complexity. Common themes reported include: challenges in maintaining the device;[51] difficulties learning about the technical aspects; accumulating skills to vape;[52,53] difficulties finding the right combination of device and liquid[53] involving a steep learning curve[54] as well as descriptions of devices as 'bulky' and 'scary'.[55] Pod-based devices and, particularly, newer disposable vape bars may overcome many of these barriers as they are discreet, easy to use and do not require recharging or replacing components. Few studies have explored the importance of such components for smoking cessation but convenience and low maintenance have been reported as facilitators to switching by cigarette smokers.[56] Moreover, such features may be particularly important for smokers who have found other e-cigarette products hard to navigate including those with manual dexterity problems, visual difficulties, physical or mental health problems, other addictions, or those with a learning disability.

Features such as simplicity, discreetness and aesthetics may have contributed to the rapid rise in popularity of the Juul pod vaping device in the USA in February 2018. At the time it accounted for an estimated 49.6% of all US e-cigarette products – an estimated 652.6% increase in sales over 12 months.[57] Juul was one of the first products to use a salt-based (aka protonated) nicotine formulation, another characteristic that may have increased its appeal. Nevertheless, use of Juul in England has remained low (with less than 1% of adults reporting using the device in 2023,[58] despite availability of the same product and nicotine formulation. This may be due to the difference in the nicotine concentration (available at 30 and 59 mg/mL in the USA and 18 mg/mL in the UK due to legal limits) or differences in the marketing strategy in individual countries.

### 7.3.1.2 Nicotine delivery and e-liquid nicotine concentration

Different device types may be associated with better or worse cessation efficacy due to differences in the amount of nicotine they deliver. While few studies have directly compared smoking cessation rates by device type, numerous pharmacokinetic studies have compared e-cig devices, nicotine concentrations, and formulations (salt vs. freebase) on nicotine delivery to the user. More effective nicotine delivery may be an important proxy for smoking cessation insofar as it can reduce craving and produce a 'cigarette-like' hit to the user. Following a review of the literature, the McNeill *et al* report

concluded that in general, compared to cartridge type devices (cig-a-likes and 'disposables'), tank and mod devices were associated with higher levels of nicotine delivery.[7] A number of these studies included pod-based devices with some evidence of effective nicotine delivery[59–61] although conclusions are difficult to draw due to confounding effects of nicotine formulation and concentration. No studies to date have explored nicotine delivery from the newer disposable vape bars.

The report by McNeill *et al* also reviewed pharmacokinetic studies comparing different nicotine concentrations. Higher nicotine e-liquid concentrations across a variety of different device types were consistently associated with higher nicotine delivery to the user.[7] In studies where subjective measures were taken, higher nicotine delivery has been accompanied by greater satisfaction and craving/withdrawal symptom relief[61–63] but not always[64,65] particularly those with very high nicotine concentrations which can be harsh on the throat; an effect that may be attenuated with nicotine salt.[66] In the only RCT comparing the effects of different e-liquid nicotine concentrations on smoking cessation,[67] 7-day abstinence rates at 24 weeks were highest among those in the 36 mg/mL concentration (10.8%) compared with 4.6% in the 8 mg/mL concentration and 0.8% in the 0 mg/mL concentration. Finally, a recent systematic review exploring the effects of nicotine concentration (and flavour) on e-cigarette abuse potential and appeal (abuse potential is the 'likelihood that [intentional, nontherapeutic use to achieve a desired psychological or physiological effect] will occur with a particular drug or substance with CNS activity'), concluded that higher nicotine concentrations are likely associated with greater abuse potential but this might facilitate complete switching from smoking to vaping due to increased appeal to users.[68]

### 7.3.1.3 Other product characteristics and interactions

Other studies have explored the effects of nicotine formulation (salt versus freebase), composition (propylene glycol vs vegetable glycerin), power and wicking material on nicotine delivery. In one study, 100% PG e-liquid was associated with better nicotine delivery but reduced satisfaction[69] and in another, salt-based e-liquid was associated with higher nicotine delivery but this was confounded by a higher nicotine concentration.[66] In the only study to directly compare salt-based and freebase formulations using the same device and nicotine concentration, quit rates were similar between formulations.[70] Isolating the effect of device type, nicotine concentration, e-liquid composition or other product features on nicotine delivery or smoking cessation is complicated by the complex interactions between these factors as well as flavour (section 7.3.2) and usage patterns (section 7.9.1), making it difficult to draw conclusions. Mod devices and newer tank models usually have larger, higher power output batteries and lower atomiser resistance, features that are associated with higher nicotine delivery.[71–74] This produces more vapour allowing the user to use a lower nicotine e-liquid concentration. Pod devices (and newer disposable vape bars) have smaller batteries with lower power output and produce less vapour, hence higher nicotine e-liquid concentrations are needed. Given the complexities for some users, associated with using more advanced tanks or mods for some users, simple pod-based and disposable products with higher nicotine strength have a valuable place on the market. For more information on e-cigarette devices see chapter 2, section 2.3.

### 7.3.1.4 Summary

Evidence that any particular device type or characteristic can encourage uptake for smoking cessation is limited, although pods, mods and tank systems appear to be associated with better nicotine delivery and higher quit rates than the older cartridge/cig-a-like types. There is clear evidence that higher nicotine e-liquid concentrations can deliver higher nicotine levels to the user, and emerging evidence that this may improve cessation rates. Some smokers find tanks and mods easy to use, while for others, these products are a barrier to uptake due to their complexity. This suggests the need for a range of products, including simple easy-to-use products such as pods and disposables, to be available.

## 7.3.2 Flavours

Concern about the potential harm of flavouring additives in e-cigarette products and the perceived effect of flavours on attracting young people to start vaping have prompted some jurisdictions to restrict or ban flavours.[75] Limiting access to flavour options may impede the uptake of e-cigarettes to quit smoking, whereas the variety and customisation of flavours can be an enabler to helping people switch from smoking to vaping.[7] Here, following a general overview of flavourings in e-cigarette products, we describe the concerns about the potential harmfulness of flavourings, the possible effects of flavour restrictions and the evidence that flavours are useful in uptake of e-cigarettes to support quitting smoking. The evidence on the appeal of flavours to youth and the potential impact of flavour restictions are discussed in chapter 8.

### 7.3.2.1 Overview of flavours in e-cigarettes

Flavours play an important role in shaping our experience of food and drink, as well as perceptions of combustible tobacco cigarettes and e-cigarettes. A flavouring is an additive (or chemical) used to create a flavour (a sensory experience). For example, vanilla flavour in e-cigarettes is created by using the flavouring vanillin. Flavour enhancers can also be added to food, drinks, tobacco and e-cigarette products to modify the flavour that the product already has. In the case of e-liquids, sweeteners or cooling agents may be added as flavour enhancers.

Flavouring chemicals and enhancers in e-cigarettes sold in the UK are regulated by the Medicines and Healthcare products Regulatory Agency (MHRA). Nyakutsikwa ***et al*** (2021) analysed ingredients and emissions data reported to the MHRA via the EU Common Entry Gate system, an IT tool through which manufacturers and importers of tobacco and vaping products are required to report detailed information to the European Commission and European Union Member States on products which they intend to place on the market.[76] A total of 40,785 e-liquid-containing products were notified to the MHRA from November 2016 to October 2017. Of the 1,500 ingredients notified, 803 were flavourings. The most common flavouring ingredients were ethyl butyrate (which produces a fruit flavour) and vanillin (which provides a sweet vanilla flavour). Fix *et al* (2023) tested the chemicals in 234 e-cigarette product refill liquids and prefilled cartridges bought in England, Canada, USA and Australia in 2017.[77] The number of flavouring chemicals identified in products varied substantially across products and countries. Those purchased in England contained more identifiable chemicals than the products bought in other countries and those purchased in the USA contained the lowest number of chemicals. The number of flavourings is likely to have increased since these studies were conducted.

### 7.3.2.2 What flavours do people who vape use?

Based upon the chemical composition of the e-liquid, categories of commonly marketed flavours include: tobacco, menthol/mint, fruit, candy, dessert, other sweets, alcohol, coffee/tea, other beverages, spices, nuts, and unflavoured.[78] According to surveys among adults and young people (11–17 years of age in England,) who vape, fruit flavour followed by menthol is the most popular. Among adults, tobacco flavour is the third most popular and in young people, candy/sweet flavours come third.[5,9] Preferences for non-tobacco flavours among adults and young people are also reported in the international literature.[79] Although the majority of people who vape choose to use flavoured e-liquids, around 3 % of adults who vape, and fewer than 1 % of 11–17 year olds use 'unflavoured' products (ie just the carrier solution of propylene glycol and glycerine with or without nicotine,[5,9] which has a natural sweet taste).[7].Regulation of flavours is discussed in chapter 6, section 6.2.4.7.

### 7.3.2.3 Concerns about the harmfulness of flavours and impact of flavour restrictions

Flavouring chemicals have a long safety history when used in a wide variety of foods, drinks and medicines. There are international standards for assessing intake levels, absorption and toxicity of thousands of individual flavourings and these are referred to as 'generally considered safe for ingestion'. The fact that few have been tested for their effects when heated, inhaled or when combined with each other is commonly cited as a cause for concern and caution regarding their use in vaping products. Although the routes of flavour exposure from e-cigarettes (via the mouth and upper respiratory tract) and foods (via the digestive tract) are different, the systemic toxicological effects will be the same for equivalent concentrations once flavourings are absorbed by the body.[80]

Studies assessing the health risks of inhaling flavours in humans are lacking. A systematic review of 38 *in vitro* and *in vivo* studies published between 2006 and 2021 on the effects of flavoured e-liquids on the respiratory system reported that cinnamon, strawberry and menthol flavours had adverse effects compared with other flavours.[81] Effects included perturbations of pro-inflammatory biomarkers and enhanced cytotoxicity. Other reviews highlight the potential toxicity of cinnamaldehyde flavouring,[7,82] though all highlight lack of appropriate controls in many *in vitro* and *in vivo* studies and overexposure, leading to ambiguity over the physical effects of flavourings among people who vape.

Several countries or regions within countries have restricted the sale of flavoured e-cigarettes, to either tobacco-only flavoured e-liquids or tobacco and menthol/mint flavours.[83] Most of the research about the impact of this originates from the USA, where the US Food and Drug Administration announced measures to curb youth e-cigarette use, including a nationwide ban on any non-tobacco and non-menthol flavoured vaping products that used pod or cartridge systems.[84] Also, the FDA has issued marketing denials through its Premarket Tobacco Product Application process for millions of e-cigarette products, and has only approved a small number of tobacco-flavoured e-cigarettes.[85] At the time of writing no non-tobacco flavoured products have been approved.

When people who vape are surveyed about how they might respond to hypothetical flavour restrictions, study findings suggest that there may be a decrease in the use of e-cigarettes, an increase in cigarette smoking, or that people may evade restrictions and obtain illicit products.[86,87] Studies that have evaluated the impact on individuals' smoking and vaping behaviour after restrictions have been implemented have mixed findings, with some studies reporting a decrease in e-cigarette sales but an increase or no change in cigarette sales.[88] A study of retail sales data across 44 US states between January 2018 and March 2023 that compared outcomes in states before and after flavour restrictions or bans were implemented found that banning flavoured e-cigarettes led to a larger rise in cigarette sales after restricting flavours.[89]

#### 7.3.2.4 Role of flavours in quitting smoking

Access to a variety of flavours can encourage the uptake of e-cigarettes to quit smoking. It is important for people considering switching from smoking to vaping to experiment with flavours (as well as nicotine strength and device type) until they find one that is suitable for them.[7] Very few people just use one flavour and preferences usually change between when an individual starts to vape and long-term use.[90] Flavour preferences and their effect on quitting are also influenced by smoking status.[90] Vaping non-tobacco flavours is associated with increased smoking cessation in adults. In a longitudinal survey of the Population Assessment of Tobacco and Health Study (collected from 2013 to 2018), including 5,984 adults aged 18–54 years of age who smoked and began vaping, the odds of smoking cessation for those using non-tobacco flavours were 2.3 times that of those who used tobacco-flavoured e-cigarettes.[91] Among 886 people in the USA, Canada, England and Australia between 2016–18 who concurrently smoked and vaped, those who used fruit/sweet-flavoured e-cigarettes were more likely to stop smoking than those who used tobacco-flavoured e-cigarettes.[92]

There are several possible reasons why non-tobacco flavoured e-cigarettes might enable adults to switch from smoking to vaping. The palatability of flavourings and the range of available flavourings allow individuals to select flavours that align with their taste preferences. Use of flavours other than tobacco is associated with greater satisfaction and enjoyment of vaping.[91] Pleasure and enjoyment of vaping (as well as nicotine delivery and relief of the urge to smoke) may increase adherence to using e-cigarettes as a smoking cessation aid and are likely to be key factors in helping people transition from smoking to vaping and continuing to vape. Sustaining satisfaction may reduce the likelihood of relapsing back to smoking.

Balancing regulation to maintain access to a variety of flavours for adults who smoke while addressing concerns about uptake among youth and possible health risks, is important for encouraging and maintaining uptake of e-cigarettes to quit smoking.

### 7.3.3 Packaging

E-cigarette packaging varies substantially across devices type and brands, with many brands featuring vibrant colours and images to promote products.[93,94] As well as bright colours, it is not uncommon for brands to also use images, cartoons characters, popular themes such as unicorns, and novel brand and flavour names on e-cigarette and e-liquid packaging.[95,96] E-cigarette packaging is very different to that of cigarette products, as unlike cigarettes which are stored in their packaging, people who vape do not tend to keep devices or liquids in their packaging, and the boxes that they come in are often discarded shortly after purchase.

Product packaging plays an important role in a brand's advertising, identity, and appeal, particularly for the tobacco and e-cigarette industry where advertising through other mediums, such as mass media, is restricted.[97–101] Historically, the tobacco industry's cigarette packaging design has been found to encourage smoking, particularly among youth, through its appeal and influence on harm perceptions.[102–105] Packaging of e-cigarettes has also been found to influence the appeal of vaping products to youth and young adults who smoke,[106] and there is concern that the way in which e-cigarettes are packaged may also appeal to youth who have never smoked and entice them to start vaping. However, e-cigarettes and tobacco cigarettes present distinctly different harms and benefits.[7,107] Therefore, e-cigarette packaging regulation needs to strike a balance of attracting people who smoke to use the products to quit without attracting people who have never smoked to try them.

#### 7.3.3.1 Current policy

E-cigarette and nicotine-containing e-liquid packaging is currently regulated by the Medicines and Healthcare products Regulatory Agency (MHRA) (see chapter 6, section 6.2.3.1). Policies concerning e-cigarette specific packaging were first introduced by the European Union Tobacco Product Directive in 2014, and later enshrined in UK law under the 2016 Tobacco and Regulated Products Regulation (TRPR).[108] Overall, packaging regulations generally concern product labelling, such as requirements

that packs include nicotine content, a nicotine warning label, the ingredients list, and manufacturer information.[108] Products must also display the relevant classification labelling and packaging regulation (CLP) hazard symbols and be in child-safe packaging. There are also regulations on the claims and themes that can be presented on packaging, however, these can be quite conceptual and difficult to define and enforce. For example, product packaging cannot include claims that they provide any health or lifestyle benefits, or have vitalising, energising, healing, rejuvenating, natural or organic properties. Smell and taste references should only relate to the flavour of the product, and it should be clear that the products are not food or cosmetics. They also cannot suggest that a particular e-cigarette or refill container has improved biodegradability or other environmental advantages.[108] A recent report that analysed the information on 156 different e-cigarette and e-liquid packs, found good compliance with regulation on product information and labelling. However, compliance with more conceptual concepts was unclear, with some products claiming energising or natural properties.[109] Current policy for packaging of vaping products is set out in further detail in chapter 6, section 6.2.4.2.

### 7.3.3.2 Health warning labels

Health messages are widely used to communicate the risks of smoking. Vaping is substantially less harmful than smoking (see chapter 5) but there are widespread public misperceptions around relative risks (see section 7.2). Messages focusing on e-cigarette harms (eg on packs) may contribute to these misperceptions, whereas presenting accurate reduced risk information (to the extent that they are noticed) may help to correct them and encourage uptake to quit smoking. This section considers effects of health messages on individuals who smoke; effects on non-smokers is considered in chapter 8 (section 8.3.4).

#### 7.3.3.2.1 Current nicotine warning labels

E-cigarette and nicotine-containing e-liquid packaging must include the following warning: '*this product contains nicotine which is a highly addictive substance*'. The nicotine health warning label must be displayed on 30% of the front and back of e-cigarette devices and nicotine-containing e-liquid packaging, in bold black Helvetica font[108] (see also chapter 6, section 6.2.3.2 for more information on warning labels). Warnings were introduced in England and the European Union in May 2016, and mandated in May 2017, allowing for an implementation period. Since then, nicotine health warning labels have been introduced in many other countries, such as Canada, the USA and Israel, all using a different variation of wording surrounding the theme of nicotine and addiction. Survey research from England in 2018 found that adults and youth reported low levels of noticing warnings on e-cigarette packaging, with only 30% of adults who vape reporting noticing warnings.[22,110]

Overall, nicotine addiction warnings are rated as believable and easy to understand.[108,111] As misperceptions about the harm of nicotine to health are common,[20] with many people perceiving that nicotine contributes to most harms from smoking,[112] there are concerns that nicotine warning labels may deter adults who smoke from using e-cigarettes in a quit attempt. Experimental research from the USA has reported that the warnings may decrease willingness to try e-cigarettes among adults who smoke[113,114] and do not smoke;[115] however, this was not supported by findings from survey research.[116] The effect of warnings on intentions to vape are likely to be mediated by their effect on risk perceptions. Experimental research has reported that warnings increase perceptions of harm and addictiveness among both adults who smoke and adults who do not smoke.[16,113] This was also reflected by survey research in the Netherlands, where perceptions of addictiveness of vaping increased among people who smoke and vape after the Tobacco Products Directive (TPD) was mandated.[117] However, it is unclear if these perceptions are attributable to the introduction of nicotine vaping product (NVP) warnings, as other TPD measures were implemented over the same period. Moreover, surveys in England from 2018 did not find associations between noticing warnings and risk perceptions.[116] Research among youth and young adults from the US reports that nicotine warnings decrease appeal and intentions to use e-cigarettes, some research also reports increased perceptions of addictiveness and harm to health.[110,118] Overall, warnings are infrequently noticed by adults and youth. Their inclusion on packaging may affect harm and addictiveness perceptions and, in turn, reduce intentions to vape among youth but also adults who smoke. However, evidence for this is mixed.

#### 7.3.3.2.2 Proposed relative risk warning messages

In an early (2015) discrete choice experiment exploring e-cigarette preferences in Canadian smokers and non-smokers,[119] different health warnings were presented alongside other attributes (flavour, nicotine content, price). Health warnings predicted harm perceptions and were more influential in predicting intentions to try e-cigarettes and perceptions of quit efficacy than flavour, nicotine content or price. Among people who smoke specifically, nicotine addiction warnings were

associated with lower interest in trying e-cigarettes, and a Health Canada statement (not approving the product for quitting) was associated with greater interest in trying. In another online experiment, non-smokers, smokers and transitioning smokers (recent quitters or trying to quit) were exposed to one of four health warnings designed to deter e-cigarette use.[120] In the whole sample, increases in perceived risk were found for most messages. The message focusing on harmful chemicals (formaldehyde) significantly decreased intentions to use e-cigarettes in smokers and transitioning smokers (but not in non-smokers) and evoked the highest levels of negative emotions.

These studies focused on messages designed to convey information about e-cigarette harm and uncertainty which may reduce appeal and uptake among non-smokers (see section 8.3.4) but might also deter uptake among smokers who may benefit from switching to a reduced risk product. Due to a high proportion of adults who smoke having inaccurate risk perceptions of vaping,[7] it has been proposed that e-cigarette packaging could be a vessel for reduced risk messaging. Other studies have included relative risk messages highlighting the reduced health risks associated with vaping compared with smoking. A systematic review including 31 articles published up to April 2020 aimed to explore whether different e-cigarette risk messages influence harm perception and behavioural intentions.[10] Messages were categorised by content into those focusing on i) (negative) health effects, ii) addiction, iii) relative risk, iv) chemical constituents, and v) scientific uncertainty. Compared with nicotine addiction messages, relative risk messages increased the perception that e-cigarettes are less harmful than smoking and in current smokers, increased intentions to purchase, try or switch to e-cigarettes. Many different messages have been trialled, with a focus on the reduced health risks of vaping compared with smoking. The addition of relative risk messaging to packs has been reported to reduce absolute harm and addictiveness perceptions of vaping among adults who do and do not smoke.[16] However, they have been found to not increase purchase intentions for e-cigarettes among adults who smoke in New Zealand.[115]

Some studies have included a 'relative/reduced risk' message either alone or alongside the standard nicotine addiction or harmful chemical warnings. Such messages, rather than focusing on the presence of harmful chemicals or nicotine addiction, convey information that vaping is considerably less harmful than smoking. Using such language implies that the products are designed for smokers and can reduce interest or relevance of the product for non-smokers.[121] However, when a vaping prevention message and a relative risk message are presented together, they are perceived as less believable, less credible, are recalled less accurately, and increase ambiguity and risk perceptions.[16,122–124]

One study examined perceptions of reduced risk and exposure health messages in 32 adult smokers and 25 young adult non-smokers.[45] Language and claims around 'switching completely' were well understood but participants expressed the need for greater message specificity, quantitative information (statistics) and evidence. In a similar study of smokers' interpretations of relative risk messages, uncertainty tended to be interpreted as an indicator of significant unknown risk (even sometimes greater than the health risks of tobacco smoking).[125] Combining a nicotine addiction message with a reduced risk message (which may be perceived as contradictory) was associated with greater harm perceptions and lower quit intentions compared to viewing a reduced risk message alone,[16] further highlighting the need for clear, specific, quantitative messages.

Another study looked looked specifically at the '95% less harmful' message as an example of a specific message which quantifies the extent of reduced risk.[121] Participants agreed that the information (that e-cigarettes are less harmful than cigarettes) was clearly conveyed and 'could' be convincing but scepticism was expressed around the source, accuracy, and possible appeal to young people. Including the source of the message (eg as from a public health agency) may increase perceived credibility[41,42] but only insofar as the recipient has trust in such agencies.[10]

In one of the few UK studies exploring the effects of e-cigarette health messages, Kimber and colleagues compared the presence and absence of the EU TPD message (this product contains nicotine which is a highly addictive substance) and a reduced risk message (use of this product is much less harmful than smoking) on smokers' and non-smokers' risk perceptions and behavioural intentions.[16] While the TPD message increased perceptions of harm and addictiveness in both smokers and non-smokers, the reduced risk message when presented alone, reduced harm perceptions and increased intentions to purchase in smokers but not in non-smokers. Together these findings suggest that reduced risk messages using smoker language may increase appeal and use intentions among smokers but not in non-smokers.

#### 7.3.3.2.3 Conclusions

Warning labels that focus on nicotine addiction may appear to increase smokers' perceptions of harm and reduce intentions to use; however, evidence is mixed. Reduced risk messages can improve accurate perceptions but messages need to be clear and specific, perhaps with quantitative information from a credible source. Nevertheless, the extent to which people who smoke are exposed to such messages on e-cigarette packs, especially if they are resistant to trying the product, may limit their effectiveness. Finally, intentions are not always reliable predictors of action, so further research is needed to explore the effects of message exposure on actual behaviour (ie e-cigarette uptake).

### 7.3.3.3 Flavour and brand name descriptors

E-cigarette and e-liquid packaging often use images, sensory descriptors, flavour blends (eg strawberry ice or vanilla custard) and conceptual names (eg 'blue voltage' or 'solar') to describe flavours,[126,127] all of which have been found to be popular among youth.[128] From a content analysis of 156 UK e-liquid and e-cigarette packs, use of flavour blend names were found among 63.2% of products, and conceptual names among 11% of products.[109] While flavours play a role in youth initiation, they have also been identified as being important in the continuation of vaping among people who switch from smoking.[5,129] Flavour descriptor-related packaging elements have been found to influence perceptions among youth aged 11–14 in the USA, with perceptions of novelty highest among those who were shown packaging with fruit related colours and imagery.[130] Thus, the representation of flavour on packaging and products is likely appealing to youth and a potential avenue for policy.

As well as abstract flavour names, e-cigarette companies often use novel brand names, such as Moreish Puff, Geekvape or Lost Mary. Research on tobacco cigarettes has found that brand identity is important to the appeal and enjoyment of tobacco cigarettes among people who smoke,[131] with youth reporting that brand names can be appealing and encourage purchase and perceptions of coolness and sophistication. Brand names have also been found to influence cigarette taste experiences[132] and be appealing to youth, even when all other elements of the pack are standardised.[133] Therefore, regulation of brand names may be another potential policy opportunity.

### 7.3.3.4 Pack branding and standardisation

As well as the features mentioned above, e-cigarette packaging is made up of many elements including marketing claims, a range of warnings and product information, and variations in size, shape, and colour, as highlighted by Nottage in 2022.[134] Therefore, standardised packaging has been proposed for e-cigarettes. Standardised (plain) packaging for combustible tobacco cigarettes was introduced in the UK in May 2016.[108] This requires cigarettes and rolling tobacco to be manufactured and sold in standardised Pantone 448C olive-green packs with the brand name in standard font and no brand imagery or logos. Standardised tobacco packaging is effective for reducing the appeal of tobacco products, particularly among youth.[104,135]

Israel is currently the only country that has also applied standardised packaging to e-cigarettes, implementing the same green Pantone 448C colour as standardised cigarette packaging.[136] Since the implementation of these policies, there has been little evaluation of their effects. Recent experimental findings from the UK, however, have reported that when youth aged 11–18 were shown pictures of e-cigarette devices in branded, standardised white or plain green packs, they were less likely to report interest in trying e-cigarettes in the white and green packs than those that were branded. Conversely, there was no difference in appeal of products between branded, and plain white or green packs among adult respondents, especially among adults who currently smoked.[137] This suggests that packaging restrictions may make products less appealing to youth but not to adult smokers. However, other findings focusing on e-liquid packaging among youth found decreased appeal of e-liquids in standardised packs, but also increased relative harm perceptions.[138] Therefore, standardising packaging of e-cigarettes may reduce youth appeal, but there is concern that this may increase inaccurate perceptions of e-cigarette harms among people who smoke who would benefit from using e-cigarettes to quit smoking.

It is important that any standardisation of packaging does not inadvertently equate the harm of tobacco cigarettes and e-cigarettes. Therefore, packaging standardisation strategies such as those used in Canada for cannabis packaging, where the size of logos and imagery are restricted, and packs can only use one background colour,[139] could be considered as an alternative to having the same packaging regulations as for combustible tobacco.

## 7.4 Price

E-cigarettes and e-liquids are not tobacco products and are currently exempt from tobacco excise duties in the UK, though they are subject to the standard 20% rate of value added tax (VAT). In March 2024, the

government announced a new duty on vaping which will be introduced from October 2026, with a subsequent consultation announced on these proposals.[140,141] There is evidence that vaping is, on average, less expensive than smoking;[142,143] however, this depends on the products purchased and patterns of use. In the UK, there are significant differences in the prices of different e-cigarette products. For example, in January 2023 the brand of disposable vape most frequently used by youth vapers (Elf Bar) cost £4.99; the equivalent reusable device cost £7.99, and refill pods cost £5.99 for two.[144] Disposable vapes were available for as little as £3.49 in 2023.[144]

The price of e-cigarettes is likely to be an important determinant of their consumption. Although there are limited data on this issue, as described below, existing studies indicate that, as with tobacco, higher prices are generally associated with lower use.

The price elasticity of demand measures the change in consumption of a product in relation to a change in its price. Estimates are likely to vary according to factors such as the type of data used, jurisdiction and study dates; however, several studies indicate that both adults (as well as children, see chapter 6, section 6.3.7) are sensitive to e-cigarette prices. A US study which used retail store scanner data estimated price elasticity for disposable e-cigarettes of around -1.2 ,which means that every 10% increase in price reduces consumption by 12% , and -1.9 for reusable e-cigarettes.[145] A more recent US study using retail scanner data from 2013 to 2019 identified an e-cigarette price elasticity of -2.2.[146] Demand for non-mentholated flavored e-cigarettes was found to be approximately twice as elastic compared with non-flavored and mentholated e-cigarettes. An exploratory study of European data indicated that e-cigarettes sales are responsive to e-cigarette prices and that e-cigarettes and tobacco cigarettes are substitutes, such that if the price of e-cigarettes goes up, consumption of cigarettes increases.[147]

To encourage the use of e-cigarettes for smoking cessation, adult smokers should have access to affordable e-cigarette products. As with many of the issues raised in this chapter, the aim of encouraging the use of e-cigarette for smoking cessation must be balanced against the need to prevent uptake in never-smokers, especially children. As discussed further in chapter 8, this requires taking into consideration the products that are most likely to be used by adults (reuseables) and those that are most frequently used by children (disposables). E-cigarette price and tax policy options are outlined in detail in chapter 6, section 6.3.

## 7.5 Promotion and advertising

In the UK, e-cigarette advertising is regulated through the Tobacco and Related Products Regulations (TRPR) 2016[108] (see chapter 6 section 6.2.3.4). The regulations aimed for balance between encouraging smokers to switch to e-cigarettes, and protecting never-smokers, particularly children, from e-cigarette uptake. The TRPR prohibits the advertising of nicotine-containing e-cigarettes (unless they are licensed as medicines) on TV and radio, in newspapers, magazines and cross-border sponsorship, and online (apart from factual content in non-paid-for space under the marketer's control, which is permitted). Advertising is permitted outdoors (for example on billboards, posters and public transport), and in the cinema, direct mail and leaflets. The UK Advertising Standards Authority (ASA) Committee of Advertising Practice (CAP) Code 22 sets out the TRPR requirements for e-cigarette advertising.[148] The Scottish government is considering further domestic advertising prohibitions covering brandsharing, sponsorship, and free distribution of nicotine vapes.[149]

The CAP Code rules are designed to ensure that e-cigarette advertising is socially responsible. While adverts need to clearly inform consumers about the nature of the product, Rule 22.5 does not allow adverts to make medicinal claims, including anything that may suggest that e-cigarettes are stop smoking products. *'E-cigarettes may be presented as an alternative to tobacco, but must not undermine the message that quitting tobacco use is the best option for health'*.[150] A content analysis of 130 UK adverts appearing in 2019 found that the vast majority (94%) complied with rule 22.5[151] and did not include explicit messages that e-cigarettes could help with stopping smoking. Twenty-seven per cent of adverts explicitly stated that the product is not a cessation product. This contrasts with studies from other countries, which have found smoking cessation is the most reported marketing communication message.[152]

The UK content analysis study also explored the selling propositions and messages contained within the adverts.[153] The majority (86%) of adverts promoted at least one positive attribute of the e-cigarette product or vaping in general. Adverts were found to communicate convenience, ease of use, quality, new products or flavours, device or vaping safety, satisfaction, testimonials from ex-smokers, technological innovation, and taste. Two-thirds of adverts (66%) associated the advertised brand with at least one psycho-social benefit. While the most commonly evoked benefit was that of an attractive lifestyle, a quarter of adverts also evoked ideas of positive

change and self-improvement, typically suggesting making a fresh start by taking up vaping or using the specific brand. Adverts were also found to communicate concepts of individuality and freedom. Almost half (45%) of adverts included norms messages about e-cigarette use, and 43% were judged as targeted to new users of e-cigarettes with messages around 'switching' and 'starter kit' offers. While not a requirement, 43% of the adverts included the message that the product was for adult smokers and vapers only, but these messages were usually small and not clearly differentiated.[153] One UK study which looked at 10 websites, found that all presented e-cigarettes as an alternative to smoking, eight as a smoking cessation aid and six as less harmful than smoking.[154]

The International Tobacco Control (ITC) Four Country Study has explored exposure to e-cigarette advertising in countries with different advertising regulation. Data from surveys conducted between August 2014 and March 2015 in the USA, Canada, Australia and England (pre-implementation of the TRPR) showed that participants in countries with less restrictive e-cigarette advertising regulations were more likely to notice advertisements than those in countries with more restrictive regulations; US and UK participants were more likely to report that they had noticed e-cigarette advertisements than participants in Canada and Australia. Daily smokers were also more likely to have noticed e-cigarette adverts on the radio, perceived what they had seen as positive, and received more free samples than those who had quit smoking.[155] Data from the ITC Four Country Smoking and Vaping Survey in 2016 found that exposure to vaping advertising at point of sale (POS) was higher in England and the USA (where POS e-cigarette advertising is permitted), compared with countries which have a ban on e-cigarette sales and marketing.[156] Data from the ITC Youth Tobacco and Vaping Survey in 2017, found that 16–19 year old smokers and/or vapers were more likely to report ad exposure through most channels and greater appeal of e-cigarette adverts compared to never-smokers/vapers.[157] Young people in England were also less likely to report that e-cigarette adverts targeted non-smokers, compared to participants in the USA and Canada.

Some potential enablers for e-cigarette uptake among smokers can be found in the advertising and promotions literature with UK samples. A qualitative study conducted in London with smokers or ex-smokers who were currently using or had used e-cigarettes, found that some participants had been encouraged to try e-cigarettes from seeing e-cigarette retail displays, or because retailers had suggested that they try them.[55,158] A study in the East Midlands region with vape shop staff and customers, found vape shops frequently ran in-store price promotions of vape products.[158] The authors suggested that in-store promotions may help to communicate vaping as a cheaper alternative to smoking. A study exploring the potential for e-cigarette adverts to reduce barriers to e-cigarettes uptake among UK and US adults found that after viewing an online electronic cigarette ad, smokers scored e-cigarettes as healthier, but there was no change in their scores on e-cigarette desirability or social acceptability.[17]

## 7.6 Access and availability

Encouraging uptake of e-cigarettes to quit smoking is supported by ease of access to e-cigarette products. The availability of e-cigarettes in the UK is spread across a diverse retail landscape: in convenience retail with their extended opening hours, in the large number of specialist stores providing advice accessible on high streets, and in online specialist stores and online marketplaces with next-day home delivery. In 2022, 52% of local authority survey respondents provided e-cigarettes or e-liquids to smokers through the stop smoking services they commissioned or provided.[45]

Retailers may only sell e-cigarettes and nicotine-containing e-liquid products that have been notified to the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK government and that appear in the MHRA's published lists.[159] The products are required to meet technical and safety standards, and Trading Standards bodies have enforcement responsibilities, alongside the MHRA, to ensure acceptable standards of safety.

Purchases of vaping products from supermarkets (stores and online), cooperatives, off-licences, petrol station forecourts and convenience store chains together in the UK increased by 49% between 2021 and 2022, with the value of sales in the product category more than doubling over that year (an increase of 121%) to £793 million (NielsenIQ 2022, cited by[160]). Unlike the more conventional sales settings for tobacco and nicotine replacement therapies where vaping products can also be purchased (eg the stores listed previously, plus market stalls, pharmacies and online marketplaces), their availability extends further. In the UK, between 2017 and 2020, research for the UK Vaping Industry Association estimated that the number of specialised vape stores increased by 61% from 2,280 to almost 3,650.[161] Interviews with trading standards officers have highlighted that vapes are also available in many retail outlets that have not traditionally sold age-restricted

products, such as mobile phone shops and boutiques.[162] Trials of vending machines for vapes, with age-verification technology, in retail, hospitality and NHS locations have been reported by a company in England.[163] In Scotland and Northern Ireland, e-cigarette sales by vending machine were prohibited from April and June 2017, respectively. In addition, vapes can be accessed through some local authority stop smoking services in England, either directly or in the form of vouchers or other arrangements with vape stores.[164]

In spring 2023, adults in Great Britain who vaped (56% ex-smokers, 37% smokers, 7% never-smokers), and purchased their vapes (ie were not given them from other sources), were most likely to buy them online (36%).[8] Other locations included from a newsagent, corner shop or off-licence (18%), from a supermarket (11%) or from some other type of shop (19%). Few purchased them from forecourt shops, street markets or a machine (5%). The typical purchase locations have not changed much since those highlighted in an earlier survey in England in 2016.[165]

Detailed interviews with vape store customers in the East Midlands[166] and south-east England[167] have examined reasons for accessing vapes through specialist vape stores. Interviewees considered vape shop staff to be specialists and reputable suppliers, with standards such as CE marking certifications (Conformité Européenne marking, a regulatory safety standard) adhered to.[166] The stores provided access to a range of diverse products, gave guidance, were trustworthy and provided a community. Other customers of specialist vape shops viewed their high street setting positively, as normalising vaping and making it accessible – purchases could be instantly compared with those made online – and supporting competitive pricing as outlets proliferated.[167] Earlier research in London with adults who vaped, suggested that the visibility and accessibility of e-cigarettes (in shops and online) 'opened their eyes to the possibility' of vaping, as cig-a-like vapes were readily available from newsagents, supermarkets and general stores.[55]

Some store users, however, felt that specialist vape stores just wanted to make a sale and vaping advice was lacking, or that, as a commercial business, the vape shop was an inappropriate location for smoking or vaping cessation advice.[166] Some customers considered the product range overwhelming, so they shopped in a pharmacy or supermarket instead, and a few of the women interviewed described feeling put-off because stores felt like masculine territories.[167]

In terms of policy support in the UK, proposals to regulate vapes as medicines were rejected in discussions by some adults who vape, as being a potential barrier to product availability and choice if they were only available from health professionals.[168] Before the age restrictions were authorised across the UK, in qualitative research with 14–17-year-olds, many endorsed an age restriction, but also raised the issue of undermining smoking cessation attempts using vaping for teenage tobacco users; if sales of vapes were restricted to 18 and over, access to vapes as a tobacco cessation aid would need to be via another source.[169] Other views collected pre-regulation (2013–14), found that adults who smoke and who used to smoke, considered that vapes should be equally or more available than combustible cigarettes (78% and 77%, respectively).[170] Among adults who used vapes, this increased to 92% of daily users and 84% of non-daily users, who believed that vapes should be equally or more available than combustible cigarettes.[170]

## 7.7 Support for vaping in healthcare settings

Healthcare care settings offer a unique opportunity to engage with people who smoke to support quit attempts using e-cigarettes.[171] Primary care clinicians will be familiar with patients who smoke tobacco, and are financially incentivised to make referrals for cessation support as part of the GP contract. There is a positive association with GP incentives and referrals for smoking cessation support.[172] Smoking status is a routinely asked question in primary care health checks,[173] and is recorded in patient notes on screening and admission to hospital if presenting at an emergency care department. Current national guidance following the NHS Long Term Plan[174] recommends promoting smoking cessation at every point of contact with the NHS,[175] including the choice of nicotine-containing e-cigarettes as a quit aid. The British Thoracic Society has published a clinical statement for hospital clinicians clearly stating the role and effectiveness of e-cigarettes for treating tobacco dependency.[176] Primary and emergency care settings offer the greatest opportunity to engage with large numbers of people who smoke who may not otherwise be seeking cessation support. Recent investigative work in a UK hospital emergency department found that approximately 24% of patients were active current tobacco smokers,[177] compared to population-level smoking prevalence of 14.6%,[178] suggesting that these settings are an ideal opportunistic location to meet people who smoke who may not otherwise be seeking support (see chapter 4, section 4.2.5). The offer of an e-cigarette may be particularly helpful in this context, as

a 'no-pressure' opportunity to switch away from using harmful tobacco without having to stop using nicotine, at least in the short term. However, there remain barriers to offering harm reduction support outside of standard NHS smoking cessation care (eg prescribeable NRT), such as concerns from healthcare professionals about potential long-term health harms.[179]

CoSTED (Cessation of Smoking Trial in the Hospital Emergency Department) is a large research trial of people who smoke attending UK hospital emergency departments.[177] This trial recruited 975 patients who were not currently motivated to quit smoking, and randomised them to a switching intervention including brief advice, the offer of a pod-based e-cigarette starter kit, and referral to specialist stop smoking service support. The 6-month biochemically verified abstinence rate was 7.2% in the intervention group and 4.1% in the control group (relative risk, 1.76; 95% confidence interval [CI] 1.03 to 3.01; p=0.038]). Self-reported 7-day abstinence at 6 months was 23.3% in the intervention group and 12.9% in the control group.[180]

Given the potential to reach large numbers of people who smoke and positively intervene across all healthcare care settings, there is an opportunity to proactively support smoking cessation by promoting vaping in these settings.

# 7.8 Health professionals

## 7.8.1 Current practice

The latest version of the NICE guideline on tobacco explicitly suggests clinicians should offer e-cigarettes as a tobacco dependency treatment option to patients,[175] and, as described in section 7.7 above, healthcare settings provide the opportunity to offer smoking cessation support to a high volume of people who smoke. However, existing data show that clinicians are considerably more cautious in their promotion of e-cigarette use than these expert bodies.[181]

A nationally representative Cancer Research UK (CRUK) survey, which included 1,000 practice nurses and 1,000 GPs selected without reference to their interest in tobacco control, took place in 2019.[182] Clinicians reported that e-cigarettes were usually not discussed when the topic of smoking arose in the consultation. Clinicians reported that patients who smoked would often raise the topic of vaping. Just over one in 10 GPs and two in 10 nurses would advise patients to use an e-cigarette either while the patient continued to smoke or in a quit attempt. Clinicians' concerns about recommending vaping centred on their potential for causing harm with them but only four in 10 felt that they were safe enough to recommend as alternatives to smoking. Most believed that e-cigarettes were addictive. Six in 10 clinicians felt that e-cigarettes were less harmful than smoking, but three in 10 were unsure about this. Less than one in 10 believed that dual use, vaping and smoking concurrently, improved health compared with smoking alone.[181]

Clinicians in this survey were asked to appraise their knowledge, with around a quarter feeling that they knew enough to advise on e-cigarettes, while around a third were aware of guidelines on vaping. Most clinicians agreed that more training on e-cigarettes would be helpful but nearly half did not see this as a priority. Clinicians reported that their main source of information on vaping came from news reports, from patients, friends, or family, or from colleagues. Fewer than one in five reported their views were shaped by national or local guidance or training, with GPs particularly unlikely to have had training. These findings from the UK are very similar to those in a 2022 systematic review, which synthesised findings from mostly the USA, Europe, and two studies in Asia.[183] This same review found little evidence that beliefs, feelings, and reported practice on recommending vaping differed substantially between hospital-based and community-based physicians.

Qualitative studies have examined these beliefs in more detail. One UK-based study found that fear of addiction was a salient concern among GPs and practice nurses.[184] They felt uncomfortable recommending e-cigarettes when many patients would continue vaping after stopping smoking. They felt it was not responsible to recommend e-cigarettes in the light of uncertainty about harms and wanted a 'higher authority', such as national guidelines (which were in place at the time of the study) to advocate their use.

## 7.8.2 Improving current practice

There is limited literature examing interventions that improve clinical practice and the utilisation of e-cigarettes to treat tobacco dependency. To our knowledge, only one such study has reported on this – a randomised trial testing a brief opportunistic intervention to promote harm reduction through vaping for people who had just declined help to stop smoking.[185] The patients in this study all had smoking-related disease or serious mental illness. All clinicians were trained with a 1-hour online training course. Fidelity in delivering the intervention was high. Interviews with participating patients and clinicians (doctors and nurses) revealed that they were reassured by the evidence presented to them from guidelines, but still had lingering concerns about long-term harms despite

the evidence presented that sought to allay this.[179] In particular, patients struggled with the apparent newness of e-cigarettes, where the known harms of smoking were contrasted with the uncertainty about the harm of vaping, while clinicians were concerned about the incompatibility of promoting a long-term substitute for smoking that was itself harmful. Their dissonance was between the harm that the patient was choosing to do to themselves by smoking compared with their own active agency in promoting a less harmful but still harmful alternative. However, the study found that clinicians who provided drug misuse services, such as methadone replacement clinics, were comfortable with this approach.

These findings relate to the concept of mindlines, which, unlike linear models of knowledge transmission, appear to better reflect how clinicians learn in practice.[186] While guidelines implicitly balance probabilities of harm against one another, clinicians are particularly swayed by worries about harm they may cause by acting. This probably explains, for example, why prescribing of anticoagulants to older people with atrial fibrillation took so long to become established clinical practice.[187] These considerations suggest that rather than presenting the rational case for e-cigarettes, we need to work with clinicians to integrate the harm reduction mindset into routine clinical practice and to emphasise the ways in which recommendations in national guidelines support this.[188]

## 7.9 Vaping identity

Identity can be defined as 'a cognitive representation by a person or group of themselves'.[189] In the context of using e-cigarettes as a way of quitting smoking, a person's identity (how they see themselves in relation to the behaviour of smoking and/or vaping) has been suggested, primarily through exploratory and qualitative research, to potentially play an important mediating role in smoking cessation.[189,190]

As tobacco smoking becomes increasingly de-normalised in society,[191] it can be observed to have moved from a normative acceptable behaviour, to a minority stigmatised behaviour.[192,193] What was once seen as a positive identity, that of a 'smoker', has shifted to being that of a stigmatised minority.This may encourage people to move away from the behaviour, or alternatively the stigmatised identity could become entrenched. Vaping has simultaneously emerged as a consumer phenomenon with its own unique set of social practices.[194] Just as tobacco smoking has been theorised as a form of social exchange that cements social relationships, the vaping device and its associated paraphernalia may also take on status that has importance in initiating and maintaining certain behaviours.[195] As social groups share in the practice of vaping, perhaps swapping tips, advice and even sharing devices and consumables, the practice becomes embedded within the social milieu, and becomes a defining feature of the social group. In this way, the practice interacts with strong social and group identity formation, that serves, in turn, to potentially facilitate ongoing engagement in the practice, and simultaneously, to prevent engagement in other competing practices that are not associated with the in-group, such as tobacco smoking.[190,196] This thesis may not apply to those who 'dual use' both tobacco and e-cigarettes – a group that might be hypothesised to be less likely to have a strong identity as either a smoker or a vaper. Similarly, some individuals or groups may reject a vaping identity despite quitting smoking, seeing vaping more as a medicinal route to smoking cessation.[197] In contrast, groups with strong tobacco smoking identities may not engage with alternative vaping identities, which could limit the potential of vaping for smoking cessation in particular sub-groups.[198]

In wider smoking cessation literature, moving from an identity as a 'smoker' to that of a 'non-smoker' or an 'ex-smoker' has been suggested to play a key role in one's ability to achieve abstinence. This suggestion is triangulated with quantitative data where measures of identity are associated with smoking status.[199,200] This can work both ways, as ex-smokers retaining a smoker identity may conversely be more vulnerable to tobacco smoking relapse.[201]

For people who make a smoking quit attempt with the support of an e-cigarette, identity and identity change may be especially important, since vaping has its own related identity, or set of possible available identities.[202,203] In this respect, vaping offers an alternative identity that may be attractive to ex-smokers.[189] Shifting away from a stigmatised smoking identity and taking on a new identity as a vaper may support a smoking quit attempt, and potentially be protective against tobacco smoking relapse. As a cultural phenomenon, vaping as it has emerged as a social practice has also attracted particular groups at particular times, making it an attractive option to groups of people who may otherwise have continued to smoke tobacco.[195] There is emergent evidence to suggest that vaping may attract people to consider quitting smoking who were not actively attempting to quit.[204]

As vaping identities may be attractive to ex-smokers, and identity change may support successful smoking cessation and relapse prevention, smoking cessation interventions should address positive identity change to enhance effectiveness.[205]

## 7.9.1 Patterns of use to encourage cessation

The most common pattern of use factor for e-cigarettes in predicting subsequent smoking cessation is frequency of use. Studies consistently find that daily use of e-cigarettes, compared to non-use, is positively associated with smoking cessation whereas non-daily use is negatively associated.[206–208] This is illustrated by a retrospective study from the USA that identified a dose-response association between frequency of e-cigarette use and smoking cessation duration.[48] When using vaping 'once or twice' per day as the comparison, they found that vaping 'several times' per day was associated with an average of 19 more days of abstinence, vaping 'many times' per day with 30 more days and vaping 'almost constantly' throughout the day with 75 more days of abstinence. Similarly, another US study found the number of days of e-cigarette use in the past 30 days, among either exclusive vapers or dual users, was associated with continued or subsequent exclusive e-cigarette use respectively.[209]

The relationship between vaping intensity and smoking is supported by within-person analyses of timeseries data among dual users. In a UK study that tracked dual users daily over 90 days, it was found that, on average, for every additional millilitre (ml) of vaping e-liquid used per day, the rate of cigarette consumption reduced.[210] This reinforces the belief that vaping is substitutive for smoking and vice versa, rather than additive.

There is also evidence that different types of dual user, when defined primarily by which product is dominant, have different smoking cessation trajectories. Dual users who are predominantly vapers are more likely to use e-cigarettes to help them quit smoking[211] and reduce their tobacco intake over time[212] compared to dual users who are predominantly smokers. However, Buu *et al*[212] also found, as part of a 2-year observational study, that individuals who use both e-cigarettes and tobacco heavily, representing an additional type of dual user, reduced tobacco use over time whereas dual users who were predominantly smokers did not.

Dual use patterns are not always stable, however. Longitudinal evidence shows that patterns of dual use will often vary within the same individuals over time.[210,213]

Furthermore, the dominance of either vaping or smoking among dual users is influenced by multiple factors that fluctuate over time, including motivation to vape and vaping satisfaction, urges to smoke, smoking cessation self-efficacy, the social environment and specific activities, places or locations.[210,213,214] In particular, the likelihood of smoking behaviour among dual users is affected by beliefs in the need for cigarettes during times of acute stress.[189]

Other patterns of e-cigarette use associated with smoking cessation include the speed at which smokers switch to e-cigarettes. Abruptly switching to e-cigarettes compared with gradually switching through dual use, is associated with longer durations of abstinence.[48,215] In addition, having fewer previous failed quit attempts through vaping and vaping shortly after waking are also both associated with success in quitting smoking through vaping among those trying to do so.[216]

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# 08

# Discouraging uptake of e-cigarettes in people who do not smoke

## Key points

- There has been a recent increase in e-cigarette use among people who do not smoke, and particularly among children and young people in the UK. This represents a potential health risk as vaping products are addictive and not risk-free.
- Perceiving vaping as less harmful than smoking predicts subsequent vaping uptake among youth and adults who do and do not smoke, while perceiving vaping as harmful is associated with not starting vaping.
- Evidence suggests that campaigns aiming to deter youth from trying vaping can increase perceptions of vaping as harmful.
- Limited evidence suggests that perceiving vaping as equally or more harmful than smoking is not associated with starting smoking among youth or young adults.
- Smaller, discreet, compact and brightly coloured devices (ie disposable vape bars) appeal to young non-smokers; larger tanks and mods appear to be less appealing.
- While higher nicotine concentrations do not appear to be part of the initial appeal of vaping, higher nicotine content may be associated with continued use and/or more frequent use among young people.
- Surveys suggest the appeal of flavours is not the main reason why young people who have never smoked start vaping, rather the names or 'descriptors' of flavours may be a factor in attracting young people who have never smoked to vaping.
- Modelling suggests that restricting flavours could disproportionately lead to more people continuing to smoke or relapsing to smoking rather than preventing uptake of vaping or uptake of smoking.
- Research among people aged 11–18 in England has found that compared to branded and standardised packaging, youth interest in trying e-cigarettes is lowest when standardised packaging is combined with reduced flavour and brand descriptions.
- Higher e-cigarette prices are likely to reduce youth vaping but cross-price elasticity with tobacco cigarettes is associated with increases in smoking.
- Interventions such as increased e-cigarette prices and flavour bans can be effective at reducing vaping use, however, these measures are also associated with increases in smoking.
- Evidence suggests that e-cigarettes are widely advertised to young people. There is evidence that, in the UK, advertising via non-traditional channels such as social media often breaches advertising standards rules. Exposure to advertisements for e-cigarettes in TV and movies may increase uptake of e-cigarettes by 36% in adolescents. Exposure to e-cigarettes in social media may increase uptake of e-cigarettes by 62% in adolescents.
- The annual ASH Smokefree GB Youth Survey shows a significant increase in awareness of e-cigarette promotion predominantly from local shops and online sources among 11–17-year-olds.
- Although it is illegal to sell e-cigarettes to people under the age of 18, a significant proportion of young people who vape report that they purchase their own e-cigarettes. Newsagents, corner shops and off-licences are the most common places for under 18s to purchase e-cigarettes.
- An e-cigarette retail licensing scheme could be used to improve age-of-sale compliance, since licences can be revoked in the case of retailers who sell to underage customers.
- Tailoring models which have worked for smoking prevention in schools for prevention of e-cigarette use might be an effective approach, but research on this is lacking.

## Recommendations

- Measures should be adopted to discourage people who do not smoke from taking up vaping.
- Policy changes to reduce the uptake of vaping among people who have never smoked needs to be carefully focused to minimise their impact on the uptake of vaping for smoking cessation. The shared goal must be to reduce death, disease and disparities.
- Information should be provided to young people and never-smokers on the health risks of vaping, but such information should be carefully designed so it does not misinform people about the relative harms of smoking and vaping, and deter people who smoke from switching to vaping.
- More research is needed on the aspects of product design that a) facilitate smoking cessation in people who smoke and b) reduce appeal among those who do not smoke.
- Standardised plain packaging combined with reduced flavour and brand descriptions, together with retail display bans should be introduced to decrease youth interest in trying vaping.
- E-cigarette price and taxation strategies should reduce the affordability of the cheapest products most commonly used by youth vapers (ie disposable e-cigarettes), while ensuring that the products most likely to be used by adults who smoke/quitters (ie rechargeable and refillable products), which are also less damaging to the environment, remain affordable.
- A review of current advertising regulation of e-cigarettes, including social media and retail product placement, is required to ensure it adequately protects young people and never-smokers.
- Policies and regulations should be introduced to reduce access to e-cigarettes for young people, particularly in retail settings, including retail licensing schemes and age verification at the point of purchase.
- Research is needed to test school-based interventions for preventing e-cigarette uptake.

# 8.1 Introduction

As set out earlier in this report, there is good evidence to support the effectiveness of e-cigarettes for smoking cessation, although uptake of this treatment intervention is widely under-utilised and more needs to be done to promote its use for smoking cessation (chapter 7). However, this must be in parallel with the need to prevent vaping among non-smokers, particularly children, which has risen over the past decade (see chapter 3, Fig 3.10). Uptake of vaping among non-smokers is influenced by a number of factors, including risk perceptions, product appeal, price and promotion, and accessibility. Many of these aspects will also affect e-cigarette use among smokers, creating a challenge in balancing policy and regulation that promotes e-cigarette use for smoking cessation but discourages non-smokers from taking up vaping. This chapter describes the evidence on discouraging uptake among people who do not smoke, particularly children, and makes recommendations for discouraging e-cigarette use among people who do not smoke.

# 8.2 Public attitudes and perceptions

## 8.2.1 Risk perceptions

In contrast to chapter 7, section 7.2.1, this section aims to summarise the evidence on risk perceptions of vaping among youth and people who have never smoked. We first present data from national surveys and then summarise peer-reviewed literature with respect to a) how risk perceptions influence vaping uptake, and b) interventions that can change vaping risk perceptions, among youth and people who have never smoked. Here, we update the 2022 Nicotine vaping in England review to include articles published up to January 2023, resulting in a) 26 studies that examined how risk perceptions influence vaping uptake among youth and/or people who have never smoked (an increase from 14 identified in 2022),[1–12] and b) 31 studies that examined interventions that can change vaping risk perceptions among youth and/or people who have never smoked (an increase from 19 identified in 2022).[13–24]

As outlined in section 7.2, risk perceptions can include perceptions of the relative harms of vaping and smoking, perceptions of absolute harms of vaping (ie, relative to not using cigarettes), and perceived addictiveness. Relative risk perceptions were considered accurate if vaping was perceived to be lower risk than smoking, or inaccurate if vaping was perceived to be of equal, greater, or unknown harm than smoking.

### 8.2.1.1 How risk perceptions influence vaping uptake

#### 8.2.1.1.1 National survey data

Trends in vaping risk perceptions among youth are similar to among adults, such that misperceptions are pervasive. In 2023, among youth aged 11–17 in Great Britain (96% of whom do not smoke), a third (33%) accurately perceived that vaping is less harmful than smoking, down from 66% in 2014.[25] Over half of youth in Great Britain inaccurately perceive that vaping is equally or more harmful than smoking (54%), up from 20% in 2013.[25]

#### 8.2.1.1.2 Peer-reviewed literature

The 2022 Nicotine vaping in England evidence update included a systematic review which assessed whether vaping risk perceptions predicted changes in vaping or smoking behaviours.[26] A total of 14 studies that included populations of youth and/or people who have never smoked and assessed vaping uptake were identified,[26] and we have since identified an additional 12 studies published up to January 2023,[1–12] bringing the total to 26. The studies covering adults overlap with those discussed in section 7.2.1 because all interventions that included adults who did not smoke also included adults who smoke.

The 26 studies were all from the USA or Canada; none were from the UK. The literature suggests that overall, vaping risk perceptions predicted subsequent changes in vaping behaviours and smoking among youth and adults who did and did not smoke.[26] Specifically, numerous studies now suggest that accurately perceiving vaping as less harmful than smoking predicted subsequent increases in vaping (including starting vaping) among young people and young adults, as well as adults who did and did not smoke.[2] Conversely, perceiving vaping as harmful was associated with not starting vaping among young people and young adults.[26] As with section 7.2.1, there are fewer studies that examine smoking behaviours as an outcome; however, those that do assess smoking have found that, among youth and young adults, relative and absolute harm perceptions (sometimes including perceived risk of addiction) were not associated with starting smoking.

### 8.2.1.2 Interventions that can change vaping risk perceptions

The 2022 Nicotine vaping in England evidence update also included a systematic review which assessed interventions that have been effective in changing vaping risk perceptions.[26] A total of 19 studies that included populations of youth and/or people who have never smoked were identified, although we have since identified an additional 12 studies published up to January 2023,[13–24]

bringing the total to 31 studies. Several of the studies covering adults overlap with those discussed in section 7.2.1.2 because some interventions that included adults who did not smoke also included adults who smoke. The literature suggests that overall, interventions targeted at youth, and young adults who did not smoke, tended to communicate information about the harms of vaping specifically to deter youth vaping, typically via educational workshops, videos, video games, and mass media campaigns.[26] Interventions targeting youth typically communicated information about the absolute harms of vaping (vaping compared to non-use of tobacco or nicotine products) and generally increased the perception that vaping is harmful to health, can lead to developing diseases or other health issues, and the inaccurate relative perception that vaping is equally or more harmful than smoking.[26] All of these studies were from the USA.

As above, there were no studies identified that examined interventions to change vaping risk perceptions among adults who did not smoke only; all interventions that included adults who did not smoke also included adults who smoke and are described in section 7.2.1.2. Furthermore, of the 31 included studies, the vast majority were from the USA with only four that included the UK (one was from the UK as well as another country). Overall, perceiving vaping as less harmful than smoking predicted subsequent vaping uptake among youth and adults who did and did not smoke, while perceiving vaping as harmful was associated with not starting vaping. Fewer studies assessed whether vaping risk perceptions predicted subsequent changes in smoking behaviours, but the limited evidence suggests that perceiving vaping as equally or more harmful than smoking was not associated with starting smoking among youth or young adults. As with section 7.2.1, the findings were broadly consistent with people's normal expectations for approaching what they perceive to be lower harm and avoiding what they perceive to be greater harm. Moreover, providing information about the health harms of vaping to youth and never-smokers, with the aim of deterring them from trying vaping, can increase perceptions of the health harms of vaping including misperceptions that vaping is equally or more harmful than smoking; this could serve to reduce vaping among these populations. However, interventions on absolute harms of vaping need to be carefully designed so as not to misinform people about the relative harms of smoking and vaping and deter adults and people who smoke from vaping to quit or reduce their smoking.

### 8.2.2 Public health campaigns

In the USA and Canada, vaping campaigns and associated messages from public health organisations have focused predominantly on youth vaping prevention.[27–35] For example, in the USA in 2018, national campaigns aiming to prevent vaping among youth were launched (eg 'The Real Cost' in September 2018, and the 'Truth' campaign which ran from October–December 2018),[28,32,33,34] as well as several state and regional campaigns.[30,31,35] Similarly, in Canada, a national campaign aiming to prevent youth from vaping was launched in December 2018, followed by the national 'Consider the Consequences of Vaping' campaign in February 2019,[29] as well as provincial youth vaping prevention campaigns over the same period.[27] The national campaigns in the USA[31,33,35] and Canada[29] that have attempted to deter youth from vaping have predominantly disseminated information via television, online videos, social media, dedicated websites and schools.

There is a wealth of evidence suggesting that campaigns aiming to deter youth from trying vaping (eg school vaping prevention campaigns in the USA) have been found to increase perceptions of vaping as harmful (including misperceptions that vaping is equally or more harmful than smoking) among youth, including schoolchildren.[26,36,37]

## 8.3 Product characteristics

### 8.3.1 Product design

E-cigarette use among people who have never smoked, although still infrequent, increased in England between 2021 and 2022 (see chapter 3, Fig 3.14).[25,38,39] A similar trend was observed in the USA and Canada in 2018 (see chapter 3, section 3.9).[40] The increased uptake was associated with the introduction of disposable vape bars in the UK, and the earlier introduction of the Juul pod device in the USA and Canada. This suggests that certain aspects of the product (eg device type, nicotine concentration, alongside other factors covered in this chapter) may appeal to those who have never smoked. As most research on vaping in non-smokers is concentrated among adolescents and young adults, this section mainly focuses on these age groups.

Studies across a range of countries that have asked young non-smokers (usually college students) why they vape/have tried vaping, overwhelmingly point to 'curiosity' and 'friends using' as key reasons.[25,41–45]

Aspects of the product (that either encourage or deter use) are not often stated (see chapter 2, section 2.3) . Where these have been explored, the most commonly cited characteristic promoting appeal is the inconspicuous design (eg discreetness, concealability, easy to hide, covert use, stealth vaping)[46–49] and, to a lesser extent, vape-tricks (eg using the e-cigarette vapour to create shapes on exhalation),[50–52] both of which were associated with more frequent use and lower odds of quitting vaping in one study of US students.[47] However, studies do not always distinguish between those who smoke and those who do not, and these features seem to appeal to both groups.

Nicotine e-liquid concentration is another key product characteristic. In a systematic review of 66 studies exploring consumer preferences, it was concluded that non-smokers tended to prefer low or no-nicotine e-cigarettes.[53] Reduced appeal with nicotine versus no-nicotine e-liquids among never-smokers has also been reported in laboratory studies,[54,55] but the appeal-reducing effects of nicotine also interact with flavour and power output of the device.[55]

Despite these reported preferences for low or no nicotine, uptake among young non-smokers has been rapid in the USA where much higher nicotine concentrations (59 mg/mL) are available (even with the same device, eg Juul). It is likely that a higher nicotine concentration will contribute to continued use and dependency in some people, even if it is not identified as an influential factor by users. One survey that looked at adolescents and young adults who had used e-cigarettes in the past 30 days found that use of higher nicotine concentration was associated with greater dependency although this also depended on flavour.[56] Among US high school students who used Juul in the past month, the top reason for liking Juul was because 'it gives me a buzz', although reasons for disliking it included 'the nicotine is too high' and 'it gives me a headache'. 'Buzz', ability to concentrate, and nicotine level were associated with more days of use in the last month.[57] Hence, while other characteristics (discreet appearance, peers using) may entice young people to try e-cigarettes, high nicotine concentrations appear to be associated with continued use.

Discreet nature and high nicotine concentration may be key product features contributing to the increased prevalence of vaping in the USA and Canada between 2017 and 2018[40] (including for non-smokers and experimental smokers), following the launch of Juul in 2015. This increase was not seen when Juul was launched (with lower nicotine concentrations) in England in 2018.[39] However, vaping prevalence did increase rapidly between 2021 and 2022 following the introduction of disposable vape bars (see chapter 3). Among 11–17-year-old never-smokers, the proportion who had tried e-cigarettes at least once or twice increased from 3.3% to 5.6%[25,58] and current use in adult never-smokers increased from 4.9% to 8.1%.[38] Disposable devices became the most used e-cigarette types used among 11–17 year olds and 18–24 year olds in 2022,[25,38] with Elf Bar and Geek Bar being the most popular brands in the UK.[25] Prior to this, vaping rates among never-smokers had remained static.[25,38,39]

In the only published study to date exploring perceptions of disposable vape bars, researchers in Scotland conducted focus groups with 82 young people aged 11–16.[59] 76% were never-smokers and 39% had ever used an e-cigarette. Disposables were described as 'cool', 'fashionable' and a modern lifestyle 'accessory'. As well as the flavour, participants described design characteristics that appeared to be targeted to a younger audience including: the small, compact design; bright, colourful appearance; and resembling other objects such as highlighters or tins of mints. This contrasted with tank/mod devices which were described as 'bulky' and perceived as being used by older adults. Similarly, in a discreet choice experiment with US students (including smokers, non-smokers, vapers and non-vapers), mods (but also cig-a-likes) were also viewed as less easy to use and eliciting less curiosity compared to tank and pod-types.[60] This study, however, did not include disposable vape bars since it was conducted before these had become widely available.

## 8.3.2 Flavours

The appeal, availability and accessibility of a wide range of flavours is often cited as the main reason for taking up vaping among people who have never smoked, particularly young people.[61] A general overview of flavours in e-cigarettes is given in chapter 7, section 7.3.2; this section sets out the evidence on the appeal of flavours among young people.

### 8.3.2.1 The appeal of flavours among young people

People who have never smoked and currently vape appear to be less attracted to tobacco flavours than people who vape and also smoke or used to smoke. For example, in 2023 among 74 adult vapers in Great Britain who had never smoked, 43% vaped fruit flavours and no one reported using tobacco flavours.[38] Among 394 current smokers who vaped and 617 ex-smokers who vaped, 49% and 47% used fruit flavours respectively and 11% and 14% respectively used tobacco flavours.[38] In a similar survey including 187 young people (11–17 years of age) in Great Britain, 60% who currently vaped used fruit flavour, 17% used a dessert/sweet flavour and 2.3% used tobacco flavour.[25]

Surveys suggest the appeal of flavours is a reason, but not the *main* reason, why young people who have never smoked start vaping. In a 2023 survey of 215 people aged 11–17 in Great Britain who have tried an e-cigarette, when asked what their main reason for vaping was (from a choice of multiple responses), the most common reason for trying an e-cigarette was 'just to give it a try' (54%), followed by 'other people use them so I join in' (18%) and 'I like the flavours (12%).[62] The proportion of people who had never smoked reporting 'other people use them so I join in' has gone up significantly from 11% to 18%. 'I like the flavours' has not significantly changed from 10% in 2022. Survey findings are similar in other countries. For example, a nationally representative sample of current (past 30-day) e-cigarette users aged between 11–18 in January–March 2020, using the National Youth Tobacco Survey in the USA, found that overall, curiosity ('I was curious about them') was the top reason reported for vaping (42.1%), followed by peer influence ('A friend used them' – 35.4%), 'I used them for some other reasons' (25.7%), 'I can use them to do tricks' (24.5%), and 'They are available in flavours, such as mint, candy, fruit, or chocolate' (19.5%).[47] A factor analysis yielded four subscales related to reasons for use 1) replacing cigarettes, 2) product characteristics (eg flavours, concealability, and vape tricks), 3) family/friend use, and 4) curiosity. Authors were able to identify distinct patterns and user characteristics related to reasons for use. Curiosity was associated with lower odds of frequent e-cigarette use, and dual use of e-cigarettes and other tobacco products, but higher odds of intention to quit cigarettes and past year quit attempts. Vaping due to product characteristics (including flavours) was associated with higher odds of frequent e-cigarette use and lower odds of intention to quit and past year quit attempts. The development of tailored interventions or policy strategies may be needed depending on people's motivation for vaping.

### 8.3.2.2 Restricting flavours

There is evidence to suggest that flavours can encourage youth vaping in both the UK and USA, although no clear evidence that flavours encourage subsequent smoking.[63,64] The main strategy in several jurisdictions for trying to prevent or discourage people who have never smoked from taking up vaping is to ban or restrict access to flavours. The evidence for the impact of this on preventing uptake of vaping among youth and people who have never smoked is mixed and can have the unintended consequence of increasing cigarette smoking (see chapter 7, section 7.3.2.4).[65,66] In an attempt to prevent never-smokers and young people from taking up vaping, Pennings *et al* (2023) have proposed a restrictive list of 16 tobacco-related flavouring additives to Dutch regulators.[67] These include flavourings that have a tobacco flavour and are not sweet or fruity. It is not yet clear if Dutch regulators will adopt these proposals, but Pennings *et al* (2023) do acknowledge such a restrictive list may result in vaping becoming a less attractive alternative for people who want to quit smoking or that users may circumvent the restrictions and add their own flavourings.

Gibson *et al* (2023) developed a decision aid for policymakers to estimate the impact of an e-cigarette flavour ban in three populations.[68] For the UK general population, they estimated that 53,609 young people aged 11–17 who did not smoke were at risk of ever vaping due to the availability of e-liquid flavours, and 26,269 of those were at risk of ever smoking due to the availability of e-liquid flavours. Gibson *et al* (2023) also estimated that 33,000 potential quit attempts would be lost per year and 295,403 ex-smokers would relapse to smoking. For the UK low-socio-economic position population, they estimated that 30,484 young people aged 11–17 who did not smoke were at risk of ever vaping and 13,109 of those were at risk of ever smoking due to the availability of e-liquid flavours; 19,096 potential quit attempts would be lost per year and 171,299 ex-smokers would relapse to smoking. For the US general population, they estimated that 355,617 young people aged 11–17 who did not smoke were at risk of ever vaping, and 78,236 of those were at risk of ever smoking due to availability of flavours; 7,172,481 potential quit attempts would be lost per year and 1,369,341 ex-smokers would relapse to smoking. The authors concluded that, based on the available evidence, there would be a negative net population impact of a flavour ban on the UK general, UK low-socio-economic and US general population.

The names or 'descriptors' of flavours may be a factor in attracting young people who have never smoked to vaping and could be a potential target to address this concern. Experimental research among youth aged 11–18 in England has found that compared to branded and standardised packaging, youth interest in trying e-cigarettes is lowest when standardised packaging is combined with reduced flavour and brand descriptions (eg changing cherry lemonade to cherry and lemon, and changing 'Moreish Puff' to brand RT56).[69] Further research could be useful to distinguish the impact of flavour names separate from the flavours themselves, on the youth appeal of vaping.

Policy changes to reduce the uptake of vaping among people who have never smoked needs to be carefully balanced against potential impact on the uptake of vaping among adults for smoking cessation and one should not be sacrificed for the sake of the other.

### 8.3.3 Cartoons

Historically, the tobacco industry has used cartoons on packaging to promote its products. Exposure to these cartoons, such as 'Joe Camel' (a popular cartoon that was featured on Camel cigarettes packaging and advertising campaigns), was found to increase youths' recognition, appeal and use of brands.[70] The use of cartoons for company logos and branding is also common among vaping companies.[71,72] Cartoon recognition has been associated among adults with susceptibility to vape, expectations of taste, enjoyment, social facilitation, but not overall appeal,[73] and among youth current vaping or susceptibility to use e-cigarettes.[74] Viewing e-liquid packaging with cartoons has been found to not be associated with risk perceptions among youth, however some effects were reported when groups were separated by susceptibility to vape.[74]

The banning of child-friendly cartoon packaging has been recommended by the 2022 independent review of Smokefree 2030 in England.[75] Based on the findings discussed above, the removal of cartoons on e-cigarette packs may reduce youth appeal. Moreover, the removal of cartoon branding from packs would likely have little impact on the appeal of products to adults who smoke. Therefore, cartoon packaging bans should be part of policy to reduce youth appeal.

### 8.3.4 Health messages

Vaping prevention messages/health warnings displayed on packs may be one way to deter e-cigarette use among young non-smokers. These most commonly focus on nicotine addiction, harmful chemicals, health effects and industry involvement.[30]

A recent review of 12 experimental studies focused on messages designed to prevent vaping in people aged 25 or under.[76] Compared with control conditions, vaping prevention messages were associated with increased perceptions of risk and decreased intentions to vape (although the latter effect was very small). However, although the vaping status of participants in the studies was reported (with two-thirds of studies including e-cigarette users), smoking status was not. This makes it difficult to draw conclusions about the effects of prevention messages specifically on non-smokers. However, other studies with non-smokers also report increased perceptions of harm after viewing e-cigarette health warnings but no, or very little, effect on intention to use.[77–81] This does not appear to apply to smokers, where messages focusing on harmful chemicals can decrease intentions to use without influencing intentions in non-smokers.[82] Effects of the message can also depend on context, with one study reporting increased harm perceptions with a text-only warning but no effect when combined with a vaping advert,[83] suggesting that warnings on e-cigarette packs may have little effect on non-smokers.

## 8.4 Price

As outlined in section 7.4, the need to ensure affordable access to e-cigarettes for adults who want to quit smoking needs to be balanced against the risk that low prices make e-cigarettes appealing to non-smokers, particularly children.

As for adults, the evidence base on the impact of price on youth e-cigarette consumption is limited; however, existing studies are in line with the expectation that higher prices will lead to lower levels of youth vaping. For example, a US study of the effect of price on youth found that a $0.50 and $1.00 price increase led to a 4.1% and 8.2% decrease in past 30-day use and a 4.2% and 8.3% decrease in intensity (amount vaped).[84] Another study in the USA found that a 10% increase in e-cigarette disposable prices was associated with a reduction in the number of days vaping among school age e-cigarette users by approximately 9.7%.[85] Refillable e-cigarette prices were not statistically significant predictors of vaping.

No studies have investigated the impact of e-cigarette price among youth in the UK; however, the recent rapid increase in the use of low-cost disposable vapes among youth (see chapter 3) suggests that price is likely to be a significant factor in youth e-cigarette use.

To minimise youth e-cigarette use while avoiding the unintended consequence of deterring adults who wish to quit smoking/stay quit with the help of e-cigarettes, e-cigarette price and taxation strategies should target the cheapest products most commonly used by youth vapers (ie disposable e-cigarettes), while ensuring that the products most likely to be used by adult smokers/quitters (ie rechargeable and refillable products), which are also less damaging to the environment, remain affordable. E-cigarette tax recommendations are outlined in detail in chapter 6.

## 8.5 Promotion and advertising

### 8.5.1 Advertising by industry

A systematic review of the literature on responses to e-cigarette marketing and communications found 124 publications on this topic up to June 2017.[86] Twelve studies reported an association between e-cigarette advertising and intention to use, or use of e-cigarettes, including among never-users of both e-cigarettes and cigarettes. Seven studies suggested that the content and/or placement of adverts was accessible and appealing to youth. A more recent review of literature up to October 2020 on e-cigarette advertising exposure and disparities found that adolescents and young adults up to the age of 26, along with those with more than a high school diploma, men, sexual and gender minorities, people of White ethnicity, and urban residents were more likely to be exposed to e-cigarette advertising. The authors found evidence that US middle and high school students' exposure to advertising in all channels (point of sale, internet, TV/movies, newspapers/magazines) grew as school year increased.[87]

There are some limitations to the above reviews. Much of the research exploring associations between e-cigarette advertising and uptake/use is cross-sectional,[86] and most studies exploring advertising exposure originate in the USA.[87] Findings therefore need to be interpreted with caution given differences in the e-cigarette market and e-cigarette advertising regulations in the UK. The UK Advertising Standards Authority (ASA) Code of Advertising Practice (2019) includes five rules specifically targeting never-smokers and/or young people (see chapter 6).[88]

In the UK in 2019, overall expenditure on e-cigarette advertising was £32,239,052.[89] The greatest expenditure was on outdoor advertising (90%). A small amount of expenditure was on cinema advertising (5%), door drops (4%), direct mail (0.9%), press (0.1%) and the internet (0.002%). Of these channels, only press advertising is prohibited in the UK.

A content analysis of 130 UK e-cigarette adverts appearing in 2019 found overall good compliance with e-cigarette advertising regulation for traditional advertising channels (eg outdoor, cinema, direct mail), but all adverts in the social media sample were judged to be in breach of the rules.[90] In traditional channels, only 2% of adverts were judged to likely appeal to people under 18, and 1% were judged to include people who seemed to be under 25. The authors did not identify any adverts as being in breach of rule 22.8 related to the encouragement of non-smokers or non-nicotine users, but 25% were categorised as 'not sure', reflecting a broader issue with the clarity of the rules guidance and difficulties in assessing appeal to non-smokers/non-nicotine users.

The International Tobacco Control (ITC) Youth Tobacco and Vaping Survey examines 16–19-year olds' responses across countries with different e-cigarette marketing regulations.[91] An analysis of three survey waves (2017, 2018, 2019) with young people from England, Canada and the USA, suggested that e-cigarette marketing restrictions in England may have limited English youth exposure to, or appeal of, marketing. Between 2017–19, self-reported frequent exposure to e-cigarette marketing increased in each of the three countries (including among never-smokers/vapers), but the increase in England was significantly smaller than in Canada or the USA. In the same period, there was a significant increase in youth reporting that e-cigarette adverts made vaping seem appealing in Canada and the USA, but not in England.[91] A further study exploring youth survey data from England and Wales before and after the introduction of the advertising restrictions found evidence that young people's experimentation with e-cigarettes had plateaued following introduction of the regulation.[92] Moreover, a content analysis of 10 popular brand websites reported that marketing elements that might appeal to youth were common, and that CAP code compliance was low. Authors perceived that brands had violated CAP codes by featuring medicinal claims (80%), including contents which may appeal to non-smokers (70%), associations with youth culture (60%), and depictions of youth using e-cigarettes (60%).[93]

Three studies have found mixed effects of e-cigarette advertising with UK non-smokers/non-nicotine users. A small survey with students aged 18+ found that after viewing e-cigarette adverts, non-smokers and non-vapers reported being more inclined to vape, while there was no effect for vapers.[94] An experimental study with non-smoking/non-vaping 11–16-year-olds in England explored exposure to glamorous e-cigarette adverts compared with adverts unrelated to smoking or vaping. No statistically significant differences between the experimental groups were found on the perceived harm of using e-cigarettes occasionally, regularly or in general, perceived susceptibility to using e-cigarettes, or prevalence estimates for using e-cigarettes.[95] Another

experimental study with non-smoking/non-vaping youth in England found that flavoured e-cigarette adverts were more appealing than non-flavoured adverts and elicited greater appeal and interest in buying/trying e-cigarettes.[96]

Observational studies of e-cigarette point-of-sale (POS) displays in England and Scotland have found high visibility of displays, with e-cigarettes being placed close to products of interest to children.[97,98] Few UK studies have explored the impact of e-cigarette POS displays on never smoking young people and adults. One experimental study, which showed images of e-cigarette retail displays from supermarkets and convenience stores to 11–17-year-olds across the UK, found that neither e-cigarette retail display visibility, nor the proportion of e-cigarette images displayed, appeared to influence susceptibility to using e-cigarettes.[99] An earlier study in Scotland found an association between e-cigarette POS recall and intention to use e-cigarettes in high school students.[100,101] When followed up longitudinally over 1 year, the study found that young never-users of e-cigarettes who recalled seeing e-cigarette displays in shops were more likely to have tried an e-cigarette within 1 year than those who did not.[101]

It is important to note that the research reported above was conducted prior to recent significant and rapid change in the e-cigarette market. The new type of disposable e-cigarettes, including brands such as 'Elf bar' and 'Geek bar', first emerged on the market in 2021 and have experienced growing popularity among young people. A recent UK qualitative study exploring 11–24-year-olds' responses to the whole marketing mix for e-cigarettes found that the marketing of disposable e-cigarettes, compared with other types of devices, is ideal for targeting young people, including young never-smokers.[102] The study found youth cues and messages within the advertising of disposable e-cigarettes, both in traditional channels and in social media content, compared with other types of devices.

Recent data from the annual ASH Smokefree GB Youth Survey[62] collected in March and April 2023, shows a significant increase in awareness of e-cigarette promotion among 11–17-year-olds between 2022–23. Fifty-three per cent reported awareness of e-cigarette promotion in shops, while 32% reported that they had seen e-cigarette promotion online. Fewer reported seeing promotion on billboards (14%), buses (11%), and TV (9%), and in newspapers/magazines (7.2%). Given the considerable shift in the e-cigarette market, a review of current advertising regulation is required to ensure it adequately protects young people and never-smokers.

## 8.5.2 Exposure to e-cigarettes in movies/TV and e-cigarette uptake

A systematic review assessing the exposure to e-cigarettes in movies or television and the uptake of e-cigarettes[103] was updated for this report to provide an estimate of the magnitude of the association. Briefly, a comprehensive search of three databases (Medline, EMBASE, PsycINFO) was conducted from inception to August 2023 to identify cross-sectional surveys or longitudinal studies that reported the association between exposure to e-cigarettes in movies or television and e-cigarette uptake in adolescence. Controlled vocabulary and text words relating to e-cigarettes and relevant media terms including advertisement, marketing, television and movies were used in addition to specific study design terms.[104] Reference lists of reviews were screened to identify further studies. Uptake was categorised as either initiation or ever use of an e-cigarette, and current use was categorised as regular or current use of an e-cigarette. Studies where the average age of the population was older than 19 years were excluded, as were those in which intention or susceptibility to e-cigarettes was the only outcome.

Twelve studies (Table 8.1) were included in the systematic review.[105–116] Eleven of the studies were conducted in US populations, with one study conducted in a German population.[107] Two of the included studies used data from the Texas Adolescent Tobacco and Marketing Surveillance System (TATAMS),[87,89] three studies used data from the 2014 National Youth Tobacco Survey,[110,112,113] and a further two studies used data from the 2016 Population Assessment of Tobacco and Health (PATH) study.[114,115] The methodological quality of the studies (assessed using the Newcastle-Ottawa Scale) was moderate, ranging from 4–7, with a median score of 5.5. Studies tended to have lower scores for either presenting crude estimates of effect which were not adjusted for potential confounders, including people who had a history of using e-cigarettes, and/or having a response/follow-up rate of less than 80%.

A random effects meta-analysis of eight studies found exposure to e-cigarette advertising in television or movies significantly increased the risk of the uptake of e-cigarette use (OR 1.36, 95% CI 1.22 to 1.53; Fig 8.1).[105–110,114,116] Inconsistency ($I^2$= 57%) was not explained by study design (cross-sectional studies OR 1.42, 95% CI 1.16 to 1.73; longitudinal studies OR 1.34, 95% CI 1.20 to 1.50; p value for subgroup differences=0.64). Similar findings were also seen between exposure to e-cigarette advertisements in TV/movies and current use of e-cigarettes (OR 1.51, 95% CI 1.15 to 1.99; Fig 8.2).[107,111,112,114]

This updated systematic review confirms that exposure to advertisements of e-cigarettes in TV and movies may increase uptake of e-cigarettes by 36% in adolescents. The evidence base for the association between exposure to e-cigarette in TV and movies has not grown substantially over the past three years, since we conducted the search of the previous systematic review; therefore, the findings from this review are similar to those from the previous review.[103] Additionally, the generalisability of the findings is limited by all except one of the studies[107] being conducted in the US and all studies focusing on exposure to advertisements or marketing, rather than occurrence in TV or movies. In contrast to the previous review, two of the included studies reported on the frequency of exposure to e-cigarette advertisements, finding evidence of dose response relationships suggesting that the risk of e-cigarette uptake was increased as exposure to e-cigarette advertisements increased.[108,113] However, both studies scored lower for methodological quality;[108,113] therefore, future higher quality studies should be conducted to address this.

**Table 8.1 Characteristics of included studies**

| Author, year | Study design and name, year of (baseline) data collection | Sample characteristics | Exposure | E-cigarette outcome | Quality |
|---|---|---|---|---|---|
| Camenga, 2018[105] | Longitudinal, 2013 | 1,742 participants, US, average age: 14 years | Advertisements of e-cigarettes on TV/radio | Experimentation, 6 months follow-up | 5 |
| Cruz, 2019[106] | Longitudinal, Children's Health Survey, 2014 | 2,097 participants US, ages: 16–18 years | Advertisements of e-cigarettes on TV/movies | Initiation, 2 years follow-up | 6 |
| Hansen, 2018[107] | Cross-sectional, 2016/2017 | 6,902 participants, Germany, average age: 13 years | Three advertisements of e-cigarettes (two on TV, 1 on internet) | Ever use, Current use | 5 |
| Leung, 2020[108] | Cross-sectional, National Youth Tobacco Survey, 2017 | 17,872 participants, US, ages: 9–19 years | Advertisements of e-cigarettes on TV | Ever use | 4 |
| Loukas, 2019[109] Nicksic, 2017[111] | Longitudinal, Texas Adolescent Tobacco and Marketing Surveillance System, 2014/2015 | 3,907 participants, US, ages: 11–16 years | Advertisement of e-cigarettes on TV | Initiation, Current use, 2.5 years follow-up | 7 |
| Mantey, 2016[110] Pu, 2017[112] Singh, 2016[113] | Cross-sectional, National Youth Tobacco Survey, 2014 | 22,007 participants, US, ages 9–19 years | Advertisement of e-cigarettes on TV/movies | Ever use, Current use | 5 |
| Pierce, 2018[116] | Longitudinal, Population Assessment of Tobacco and Health (PATH) study, 2013–2014 | 10,989 participants, US, 12–17 years | Receptivity to advertising, 20 out of 959 near-census collection of advertisements including TV | Ever use, one year follow-up | 7 |
| Stanton, 2022[114] Sun, 2023[115] | Longitudinal, Population Assessment of Tobacco and Health (PATH) study, 2016–18 | 16,671 participants, US, 12–17 years | Advertisement of e-cigarettes on TV | Ever use Current use, 1 year follow-up | 7 |

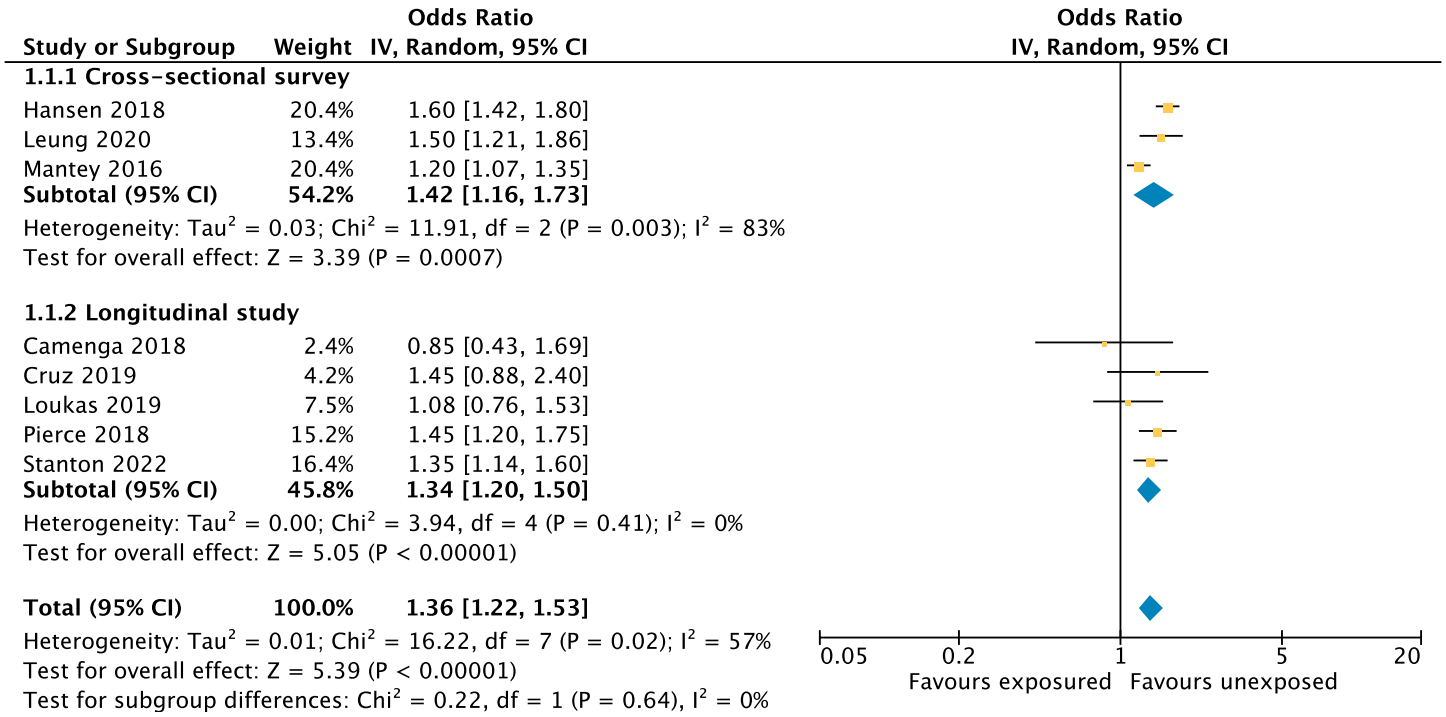


**Fig 8.1. Exposure to e-cigarette advertisements and uptake of e-cigarettes.**

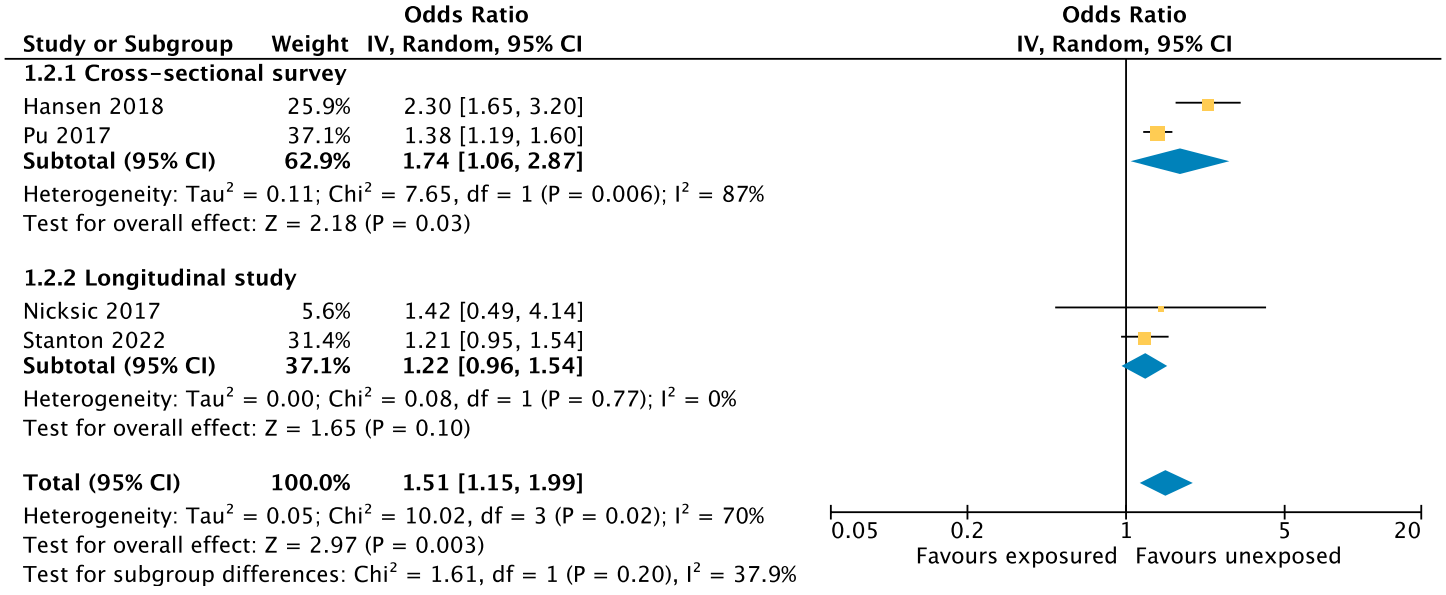


**Fig 8.2. Exposure to e-cigarette advertisement and current use of e-cigarettes.**

## 8.5.3 Exposure to e-cigarettes in social media and e-cigarette uptake

A systematic review was conducted to assess the impact of exposure to social media on uptake of e-cigarettes in adolescence. Briefly, a comprehensive search strategy of three databases (Medline, EMBASE, PsycINFO) was conducted from inception to August 2023 to identify cross-sectional surveys or longitudinal studies that reported the association between exposure to social media and e-cigarette uptake in adolescence. Controlled vocabulary and text words relating to e-cigarette and relevant social media terms were used in addition to specific study designs terms.[104] Reference lists of reviews were screened to identify further studies. We excluded studies where the average age of the population was older than 19 years, and those in which intention or susceptibility to e-cigarettes was the only outcome. Meta-analysis was conducted using random effects models. Ten studies were included in the review, comprising 42,198 participants (range 351 to 12,470).[105,117–125] A further two studies[126,127] were excluded due to using the same cohort of adolescents used in an included study.[119] Eight included studies were conducted in US populations and the remaining two studies were conducted in populations from either the UK or China.[123,124] E-cigarette use was reported as initiation in four studies, ever use in four studies, current use in one study,[120] or as use in one study.[123] A range of measures were used to define exposure to social media, which included daily/high frequency use of social media,[117,120–123] exposure to e-cigarette advertisement or posts on social media,[104,124,125] talking about e-cigarettes on social media,[118] or liking or following e-cigarette brands on social media.[119]

Overall, exposure to social media was significantly associated with a 62% increase in the uptake of e-cigarette use (OR 1.62, 95% CI 1.23 to 2.13, 10 studies; Fig 8.3). A stratified analysis found daily or high frequency use of social media did not significantly increase the risk of the uptake of e-cigarette use (OR 1.50, 95% CI 0.92 to 2.42; 5 studies); however exposure to daily or high frequency exposure to e-cigarettes via social media was significantly associated with a 70% increase in e-cigarette uptake (OR 1.70, 95% CI 1.30 to 2.23; five studies).

**Table 8.2 Characteristics of included studies**

| Author, year | Study design and name, year of (baseline) data collection | Sample characteristics | Social media exposure | E-cigarette outcome |
|---|---|---|---|---|
| Camenga, 2018[105] | Repeated survey, 2013 | Mean 14 years, USA, excluding ever e-cigarette users, 1,742 participants | Exposure to e-cigarette advertisements on social media | Initiation of e-cigarettes |
| Dai, 2022[124] | Cross sectional survey, 2019 | 13–18 years, China, excluding ever e-cigarette users, 12,470 participants | Exposure to e-cigarette advertisement on social media | Ever use of e-cigarettes |
| Hebert, 2017[125] | Cross sectional survey, Texas Adolescent Tobacco and Marketing Surveillance (TATAMS), 2014–15 | 11–18 years, USA, 3,887 participants | Exposure to e-cigarettes related posts on social media | Ever use of e-cigarettes |
| Kelleghan, 2020[121] | Longitudinal study, Happiness and Health Study, 2015 | 16–17 years, USA, 1,558 participants | High frequency of engagement with, or posting on, digital media sites | Initiation of e-cigarettes |
| Lee, 2021[120] | Cross sectional survey, Florida Youth Tobacco Survey, 2019 | 11–18 years, USA, 10,776 participants | Daily use of social media | Current use of e-cigarettes |
| Lin, 2021[122] | Cross sectional survey, Health Starts Here project, 2019–20 | 18–19 years, USA, 351 participants | Daily use of social media | Ever use of e-cigarettes |

| Author, year | Study design and name, year of (baseline) data collection | Sample characteristics | Social media exposure | E-cigarette outcome |
|---|---|---|---|---|
| Mamudu, 2022[118] | Cross sectional survey, 2019 | 12–14 years, USA, 399 participants | Talk about e-cigarettes on social media | Ever use of e-cigarettes |
| Purba, 2022[123] | Longitudinal study, Millennium Cohort, 2017–19 | 14 years, UK, 6,234 participants | 2 hours+ use of social media per day | Use of e-cigarettes |
| Shan, 2022[119] | Longitudinal study, Population Assessment of Tobacco and Health (PATH), 2013–14 | 12–14 years, USA, excludes ever e-cigarette users, 6,632 participants | Liked or followed e-cigarette brands on social media | Initiation of e-cigarettes |
| Vassey, 2022[117] | Longitudinal study, Trends in Tobacco Use Survey (TITUS), 2020–21 | 14–17 years, USA, excludes current e-cigarette users, 2,036 participants | Use of social media (at least several times per day vs less frequently used) | Initiation of e-cigarette use |

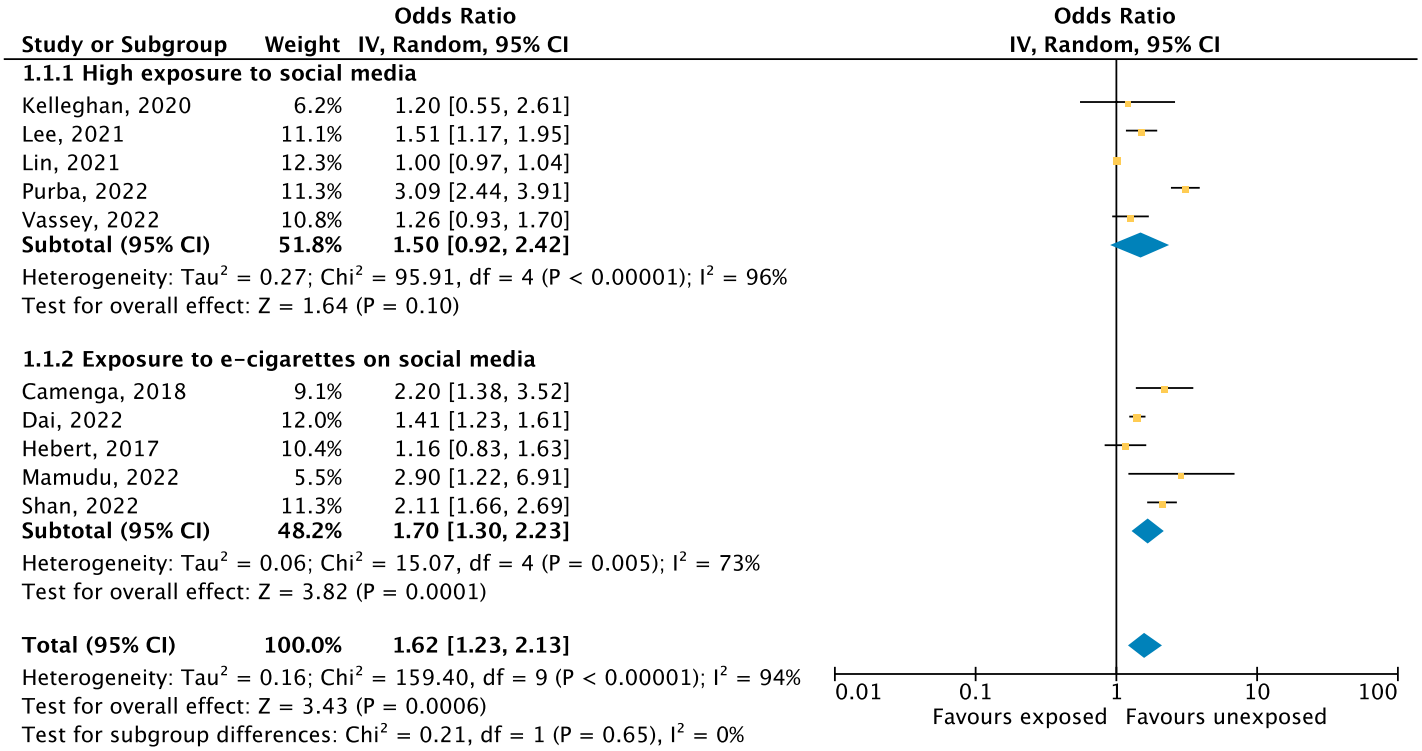


**Fig 8.3. Exposure to social media and uptake of e-cigarettes.**

## 8.6. Access and availability

Across the UK, a minimum age of sale for e-cigarettes is in place, including online, making it illegal to sell e-cigarettes containing nicotine to anyone under 18 years or to buy them on behalf of anyone under 18 years (a proxy purchase offence). These regulations commenced in England and Wales by October 2015 (The Nicotine Inhaling Products (Age of Sale and Proxy Purchasing) Regulations 2015),[129] in Scotland in April 2017 (Health (Tobacco, Nicotine etc and Care) (Scotland) Act 2016) and in Northern Ireland in 2022 (The Nicotine Inhaling Products (Age of Sale and Proxy Purchasing) Regulations (Northern Ireland) 2021).[131] In Scotland and Northern Ireland, e-cigarette sales by vending machine were prohibited from April[130] and June 2017[131] respectively. Retailers may only sell e-cigarettes (vapes) and nicotine-containing e-liquid products that have been notified to the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK government and that appear in the MHRA's published lists.[132] Products are required to meet technical and safety standards enforced by Trading Standards and the MHRA.

Currently, vapes are accessible from a large number of retail outlets and other places, as outlined in chapter 7 section 7.6. In addition to specialised vape stores (bricks and mortar and online) and some local authority stop smoking services, they are also available in supermarkets (stores and online), co-operatives, off-licences, forecourts, convenience store chains, market stalls, pharmacies and online marketplaces. Many retail outlets that have not traditionally sold age-restricted products such as mobile phone shops and boutiques are also selling vapes.[109] Vending machines with age-verification technology are being trialled in England.

Despite it being illegal to sell vapes to anyone under the age of 18 years, data from the annual ASH Smokefree GB Youth Survey collected in spring 2023, show that the most common place to purchase vapes reported by under-18s is from a newsagent, corner shop or off-licence (26%).[62] Fewer young people said they usually purchased vapes from garage forecourts (9%), supermarkets (7.2%), street markets (5.8%), machines (2.4%), or from some other type of shop (15%). In contrast to adult vapers in the survey, a smaller proportion of under-18s usually bought vapes online (7.6% vs 36%). Among under-18s who had ever tried vaping, few first used vapes that they had bought (16%); most were given them by somebody (73%). The usual source of vapes for under-18s who currently vape was to buy them from a formal or informal source (72%), although nearly half were still given them by somebody (46%). A very small proportion of those who had tried vaping selected 'They are easier to get hold of than tobacco' as the main reason for using a vape (2.2%).

In a recent qualitative study on perceptions of disposable vapes among 14- and 15-year-olds in Scotland with a range of vaping and tobacco use behaviours, ease of access by their age-group, principally from corner shops, and online was emphasised.[59] This appears to have moved on from a previous mixed methods study among the same age group in 2017 in Great Britain, which suggested that very few obtained their vapes from retailers and they were not buying from specialist vape shops.[92] Most were obtained via informal routes (peers or adults) and they reported that obtaining vapes was easier than obtaining tobacco cigarettes. This was reinforced by the survey element of the study with 13- and 15-year-olds in Wales (predominantly ever-smokers, (72%)), which found that most obtained vapes from peers (32%) or adults (17%), and fewer bought them from a shop (15%) or the internet (7%). Others reported 'taking them' (9%), obtaining them from siblings (4%) or accessing them in other ways (20%).

Survey data collected the same year (2017) with older teens, 16- and 17-year-olds, in England who had purchased vaping products over the year, indicated a different pattern of using fewer informal routes. Most (58%) purchased from a vape shop, 26% online, 23% regular shop (eg newsagents or supermarket) and 8% purchased elsewhere, including from pharmacies or social sources.[134] In 2021, 70% of a sample of 16–19-year-olds in England perceived accessing vape devices, cartridges or e-liquids, if they wanted to, as very or fairly easy; a little higher than accessing cigarettes (67%).[135] A country comparison of perceived ease of accessing vapes over time by 16–19-year-olds in England versus those in Canada and the USA, found that access was perceived as harder in the USA compared with the other two countries, in line with minimum legal age policy which is higher in the USA (typically 21 years (mostly) versus 18 years in Canada and England).[135]

Earlier qualitative studies indicated that teenage school pupils were observing changes in the retail environment as the vaping market developed.[101,136] The widespread availability of vapes in retail environments and their point-of-sale displays were mentioned in qualitative research in Scotland. Some school pupils reported trying or being given family members' vapes.[101] Teenage school pupils, mostly non-smokers, interviewing each other about smoking and smoking cessation for an intervention evaluation study, saw vapes as cessation aids and noted they were cheaper than tobacco, but also described their noticeable availability from shops, newsagents, kiosks, market stalls, online and teleshopping, and highlighted display stands at point of sale.[136] Findings from a cross-sectional survey in secondary schools in Scotland

indicated that seeing vapes on display in small stores, such as corner shops, newsagents, convenience stores, petrol stations and off-licences, was associated with an increased probability that teenage school pupils would go on to try vaping.[100] At that time (2015), regular use of vapes was low in that age group.

Before the minimum legal age policy was enacted in the UK, a study of 14- to 17-year-olds reported that some participants, mostly those who did not use cigarettes or vapes, reasoned that a regulated, supervised, method could be used to make vapes available to people who smoked, whatever their age.[137] Many endorsed an age restriction, although it was also raised that if vapes were restricted to adults only, this could be a barrier to under-18s using them for quitting tobacco.

## 8.7 Retail licensing

E-cigarette retail licensing schemes require retailers to be licensed to sell e-cigarettes and e-liquids. Licences can be revoked, banning retailers from selling e-cigarettes, if they sell to underage customers. No country in the UK currently has a licensing system for the sale of e-cigarettes. The Scottish government introduced a registration scheme on 1 April 2017, requiring all retailers selling nicotine vapour products to be registered on the free Register of Tobacco and Nicotine Vapour Product Retailers.[138] In Scotland, a registration, rather than licensing, scheme was chosen to reduce the burden on local authorities and retailers. While a licensing scheme requires retailers to provide information to the relevant authority to determine whether they are allowed to sell a product, a registration scheme only requires retailers to notify authorities that they are selling a product, reducing administration and costs.[139]

For tobacco, it has been suggested that retail licensing may reduce smoking by 1) decreasing the number and/or density of tobacco outlets, reducing visibility and availability of tobacco products, 2) further denormalisation of tobacco, and 3) improved compliance/enforcement of age-of-sale policies.[140,141] A representative survey of 2,197 British adults in 2021 found strong support for retailer licensing for tobacco products, and for restrictions on the sale of cigarettes and tobacco near schools.[142] To our knowledge there are no equivalent studies exploring support for retailer licensing of e-cigarettes in the UK.

A review of e-cigarette retail licensing policies in 2020 found that 45 countries including Canada, the USA, the European Union (EU) countries, the UK and New Zealand have adopted various approaches of regulating sale of e-cigarettes, including minimum age of sale/purchase provisions, restricting/regulating cross-border sale and restricting venues of retailing.[143] In response to youth vaping rates in the USA, most states have enacted policies requiring retailers to have a licence for selling vaping products.[144] There is limited evidence evaluating such policies for their effectiveness in reducing or preventing vaping among youth or never-smokers. One study exploring the impact of a retail licensing policy in Pennsylvania found that past 30-day adolescent e-cigarette use significantly declined post policy, compared to neighbouring states without a policy.[145]

Retail licensing can provide an opportunity to manage the number of stores in a given area. Studies exploring tobacco outlet density have found associations with youth smoking.[146] For e-cigarettes, one study conducted in four Canadian provinces found that e-cigarette retailer proximity and density surrounding a school were not significantly associated with the likelihood of young people ever or currently using e-cigarettes. The authors note, however, that only one in 10 high schools in the sample had at least one e-cigarette retailer within walking distance (1,000 m) of the school and this was expected to increase over time.[147] A study in four counties in Texas found associations between the presence of retail outlets around some schools and e-cigarette use among students, but this association was not consistent across all the counties.[148]

In the UK, there is concern that under 18s who vape report that they most commonly make their purchases from a newsagent, corner shop or off-licence.[62] There is also evidence of poor compliance of age-of-sale restrictions in other types of premises, including market or car boot sales, discount stores and mobile phone shops.[149] The rapid growth of the e-cigarette retail market, along with the increasing range of types of retailers selling e-cigarettes, means that some retailers may have less awareness and understanding of age-of-sale regulation requirements.[133] A study exploring the views of trading standards officers in 13 UK local authorities highlighted that retailers who have never previously sold age-restricted products are now selling nicotine vaping products.[133] It has been suggested that licensing schemes may make retailers more invested to comply with regulations to avoid having their licence revoked, increase efficiency in compliance checks, and raise funds through licence fees to cover enforcement costs.[141] The UK Vaping Industry Association (UKVIA) is currently calling for new requirements on e-cigarette retailers, including an e-cigarette retail licensing scheme.[150]

## 8.8 Schools

As set out earlier in this chapter, interventions to improve understanding of the risks of vaping could influence e-cigarette use among non-smokers, particularly children. Schools may have a role to play, but there is uncertainty about what this should involve. For tobacco use, randomised controlled trials and other high-quality evaluations provide insights on preventing smoking uptake.[151] For example, interventions focused on diffusion of tobacco education through social networks via influential peers played a modest but important role in reducing smoking at its peak around the turn of the century.[152] More recently, approaches which focus on common causes of a range of adolescent risk behaviours, such as school connectedness, have shown good impacts on preventing smoking uptake.[153] However, the rapidly changing nature of e-cigarettes, the range of settings in which they are bought and sold, and young people's engagement with them, has meant the gradual and rigorous process via which school-based interventions to prevent smoking uptake have been developed and evaluated cannot as easily be applied to the problem of young people's use of e-cigarettes.

While avoiding treating these products as presenting equal harms, tailoring models which have worked for smoking prevention might be an effective approach. Mirroring longer standing approaches for tobacco prevention in schools, recruitment of peer leaders to dissuade peers from use of e-cigarettes has been found to be feasible in the USA,[154] although its effectiveness is not yet known. School policies appeared to play an important role in reducing between school differences in smoking uptake when implemented at times when smoking was relatively normalised behaviour.[155] Interviews with young people across Great Britain emphasised the role of informal playground supply networks in the distribution of e-cigarettes,[156] and these might be an important target for intervention within schools. Schools report vaping is commonly part of a cluster of antisocial behaviours among young people, whose identity and sense of group belonging is formed through counter-school cultures, much as has been the case for smoking.[157] Consistent with this hypothesis, approaches focused on enhancing school connectedness have been shown to reduce e-cigarette use, as well as smoking.[158]

School-based actions may, in the coming years, interact with a changing legislative context focused on reducing the appeal and availability of e-cigarettes, while maintaining their availability for smokers attempting to quit tobacco. There is, however, a need to further develop this evidence base, to better understand the drivers of young people's e-cigarette use which schools can influence, and to evaluate impacts of school-based approaches for reducing young people's use of e-cigarettes. Evaluating how schools approach the integration of education and policies on e-cigarettes into existing strategies that regulate unhealthy commodities within the school environment, and how this maps onto variability in young people's use of e-cigarettes may be informative. While it is important not to frame e-cigarettes as equal to tobacco, adapting models that have been effective for reducing tobacco use is likely to be an avenue for future research in this area.

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# 09

# Tobacco industry interests, recent conduct and claims around harm reduction

## Key points

- The premise of this chapter is that the ability of e-cigarettes (or any other 'reduced risk' product) to lower tobacco-related harm at population level depends not only on the product, but also on the conduct of the companies selling it.
- E-cigarettes first emerged in China in 2003 (in the UK and USA from 2007) and over the next few years became a significant threat to the major tobacco companies and their uniquely profitable primary product, the cigarette. This was a period when implementation of tobacco control policies was advancing rapidly, and global cigarette consumption was declining. From 2012, the profitability of cigarettes (as measured by their global retail value) also began to fall.
- From 2012, the major tobacco companies responded by starting to acquire existing e-cigarette brands and by launching their own. From 2013, they also began to launch new heated tobacco products (HTPs) and a variety of new oral tobacco and nicotine-only products.
- Although all four transnational tobacco companies (TTCs) now sell e-cigarettes, HTPs and tobacco and nicotine-only pouches for oral consumption, cigarettes remain their primary product. While TTCs dominate the global HTP market, they hold only 26% of the e-cigarette market.
- More recently, three TTCs have expanded beyond tobacco and nicotine products to pharmaceutical inhalers, vaccines and cannabis products. Ethical issues are raised when they sell medicines used to treat diseases caused by their primary tobacco products. Moreover, evidence of the impact of nicotine on brain neuroplasticity raises the possibility that companies may be able to exploit increases in youth e-cigarette use to encourage long-term multiple product use and addiction.
- Harm reduction involves reducing the health and social risks associated with addictive behaviour at both individual and population level. In the context of tobacco control, this would involve shifting current smokers to lower-risk products (if unable to quit) while not increasing harmful product use among others, notably new users. It is not, therefore, a sustainable business model for TTCs.
- This is something the tobacco industry's historical documents make explicit, indicating that TTC investments in e-cigarettes and other new products were driven by declining cigarette sales rather than a desire to reduce harm to consumers. Similarly, TTC presentations to investors emphasise that e-cigarettes and HTPs are intended to expand rather than substitute lost revenues from cigarette sales and that a significant proportion of sales growth is being driven by new users.
- Nevertheless, some TTCs have been using these investments to claim a commitment to what they label 'harm reduction' via 'transformation' away from cigarettes.
- Evidence shows that such claims are highly misleading and that, instead, TTCs have strategically co-opted harm reduction and used it against public health. They have used their power to shape media coverage and understanding of harm reduction and the role of the tobacco industry. Specifically, they have sought to use 'harm reduction' to:
  - rehabilitate their image, increase their policy access and influence
  - split and undermine the public health community
  - position themselves as the solution to the tobacco epidemic they created
  - push against population level tobacco control measures of proven effectiveness (which reduce their sales) in favour of harm reduction approaches (which increase their product sales), ultimately seeking to amplify their ability to undermine progress in tobacco control.
- Simultaneously, TTCs have continued to heavily market and increase the attractiveness of their cigarettes, buy up new cigarette companies and lobby against policies that would reduce smoking.
- TTC-funded research accounts for a significant proportion of the science on new products and harm reduction approaches; yet evidence indicates that they may be engaging in many of the problematic scientific practices of the past, raising concerns about the quality and veracity of that research.

- While e-cigarettes represent a potential opportunity for tobacco control, industry conduct makes it hard to realise this opportunity. This is the case even in countries like the UK with strong regulatory, enforcement and scientific capacity: worrying trends in youth use of e-cigarettes, including disposables, are being reported, impacts on youth cigarette uptake remain uncertain, and industry interference is increasing.
- In countries where institutional, regulatory and scientific capacity is more limited, the risks to tobacco control are likely greater. It is notable that some worrying patterns are emerging in global data, notably:
  - from 2015 the rate of decline in smoking prevalence has slowed in every region of the world
  - following nearly two decades of decline, since 2020 global cigarette consumption is no longer falling
  - global sales of e-cigarettes and HTPs are expanding more rapidly than cigarette sales were declining, suggesting that many of these sales are additional to, rather than replacements for, cigarettes or accounted for by dual use
  - increases in HTP sales are outstripping e-cigarette sales despite the lack of evidence that such products enable quitting.

## Recommendations

- If potential public health benefits from e-cigarettes are to be realised, it is essential to take account of the conduct of TTCs. This requires strong and well-enforced regulation to ensure that companies that profit from the manufacture and sale of tobacco play no role in policy development.
- The impacts of harm reduction approaches will be context specific, varying with regulatory and enforcement capacity such that what works in one jurisdiction may not work elsewhere. Protecting national policy space must therefore be respected.
- The need to de-normalise the tobacco industry and protect public policy from tobacco industry interference in line with Article 5.3 of the Framework Convention on Tobacco Control (FCTC) is more important than ever; the decline in the UK's position in the Global Tobacco Industry Interference Index indicates that this is a key issue in the UK.

## 9.1 Introduction

In 2007, electronic cigarettes (e-cigarettes) emerged on the global market, sold primarily online by manufacturers in China. E-cigarettes subsequently became a 'disruptive technology' that could threaten the world's largest transnational tobacco companies (TTCs), namely Philip Morris International (PMI), British American Tobacco (BAT), Japan Tobacco International (JTI) and Imperial Brands, and their uniquely profitable product: the cigarette.[1] These major tobacco industry players attempted to turn this threat into opportunity by working to stifle competition: they rapidly acquired independently owned e-cigarette brands and launched their own e-cigarette products, alongside a growing array of other products.[2] Simultaneously, TTCs made very public claims of commitment to what they called 'harm reduction',[3,4] despite continuing to heavily invest in and market their tobacco product lines.[5–7]

This conduct is the latest manifestation of a decades-long effort of seeking to rebuild credibility, secure policy influence and reverse declines in cigarette sales.[8] Since the 1950s, TTCs have repeatedly invested in new products while publicly claiming a commitment to reducing harm,[8–11] each time in response to ongoing threats to their highly profitable cigarette business.[9] When evidence on the harms of smoking first emerged, TTCs developed and marketed filter-tipped (1950s) and 'light' (1970s) cigarettes.[12,13] In the 2000s, when smoke-free legislation was driving declines in cigarette sales and smoking uptake, TTCs invested in smokeless tobacco options such as snus and nicotine pouches.[8] Internal industry documents reveal that, at each stage, TTCs' interest in 'new' products was never genuinely driven by harm reduction priorities, but rather by a desire to generate new users and sources of profit, to increase sales and to rehabilitate the tobacco industry's reputation (Table 9.1).[9,11,14]

Growing evidence indicates that the TTCs' latest behaviour mirrors these previous attempts to strategically misappropriate harm reduction.[5,8,17–19] However, there are a number of important differences from earlier iterations that make the current situation arguably more complex and threatening to public health. First, the global market in tobacco, nicotine and related products has become more complex, with TTCs diversifying into a wider range of products (tobacco, nicotine and other products) and numerous small-scale companies participating in the e-cigarette market (section 9.2). Second, unlike previous instances, these developments surfaced at a time when global cigarette sales were declining, particularly in the most profitable tobacco markets[17] and thus TTCs had more reason to feel threatened (section 9.3). Finally, TTCs both in the UK and globally, most notably PMI and BAT, are now making far greater public claims of a commitment not just to harm reduction but to 'transformation',[20–22] including by allegedly taking actions to achieve a 'smoke-free' future (see Box 9.1).[23–25]

**Table 9.1. Tobacco company (mis)use of the harm reduction agenda**

| Pathway to profit | Rehabilitates image | Weakens tobacco control | Gives impression of divided public health community |
|---|---|---|---|
| Uses emergent products to maintain nicotine addiction, undermine cessation, recruit novel users and eliminate competition[14] | Uses claims of transformation to position itself as part of the solution and public health as the problem, securing both political and reputational benefits[8] | Promotes harm reduction policies that focus on minimising harm at the individual level, rather than evidence-based, population-level measures[9,11] | Opportunistically exploits latent divisions within the tobacco control community so as to imply extreme polarisation on the issue of harm reduction[15,16] |

Adapted from Evan-Reeves and Gilmore (2020)[17]

**Box 9.1. Transformation claims made by PMI**

Since at least 2017, PMI has significantly increased and refocused its political activity, with vast investment in what is known as reputation management.[26] These efforts have focused on positioning PMI and its products as the solution to the tobacco epidemic and future of tobacco control, while attacking public health.[8,27] In September 2017, the tobacco giant set up the Foundation for a Smoke-Free World (FSFW), with almost $1 billion in funding.[28] The FSFW claims to be an independent scientific organisation,[17,29] despite evidence to the contrary.[30] In 2018, PMI launched a £2 million campaign 'Hold My Light' in the UK, where its share of the cigarette market is minimal.[31] The campaign encouraged smokers to shift to its heated tobacco product (HTP), IQOS. IQOS was also conflated with e-cigarettes on the campaign website,[17] despite the lack of evidence that HTPs aid cessation and greater uncertainty over their safety.[32–37] PMI offered the NHS £1 billion to help smokers switch to alternatives, under the condition that the UK relax regulation on e-cigarettes and HTPs following Brexit, an offer that the UK government rejected.[8,38] In January 2018, PMI took out a series of ads in UK newspapers claiming that it was 'giving up cigarettes'.[39] This was followed by, among other things, a vast global campaign[40,41] involving advertorials across international media claiming that it would 'unsmoke' the world, with funding to various media outlets including a new website by *Vice News* called Change Incorporated,[42] the *Economist*, *Financial Times* and *Foreign Policy*, all to help secure favourable coverage. PMI has also publicised its presence at important global events such as the World Economic Forum, G20 summit and UN General Assembly (many of which tobacco companies were officially excluded from) and sought to extensively promote its scientific credentials[43,44] in an attempt to convey respectability[8,17] and trust in the company.[45] Yet, in many ways, its current scientific conduct mirrors the industry's highly problematic practices of the past that played a key role in obfuscating tobacco's harms.[28,30,33,46,47]

The purpose of this chapter is threefold: to detail recent TTC investments and product launches (section 9.2); to understand the changing global market in tobacco and nicotine products that both underpinned and resulted from these investments (section 9.3); and to examine recent TTC conduct in this area (section 9.4).

Advancements in tobacco control have been largely contingent on understanding and addressing industry behaviour, including *inter alia* how TTCs obfuscate information to deceive the public and policymakers, and to influence and circumvent legislation.[48] Consequently, policy and practice in harm reduction, as in other areas of tobacco control, must be informed by knowledge of industry conduct. This approach,* enshrined in Article 5.3 of the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC), the first international health treaty negotiated under the auspices of the WHO,[49] helps to explain the greater advancements to date in tobacco control than in other areas of public health involving industry vectors,[50] including alcohol, gambling, obesity and climate change.[48]

* The recognition of a fundamental and irreconcilable conflict between public health objectives and tobacco industry interests, as enshrined in Article 5.3 of the FCTC, has increasingly led to major TTCs being politically marginalised and losing influence.[8] This underlying history and context are important to highlight, as TTC engagement in harm reduction amid their recent investments in e-cigarettes and other products offer the potential for TTCs to rehabilitate their tarnished image and re-engage in policymaking circles from which they have been excluded.[2]

**Table 9.2. TTC investments in a diverse range of recreational products and drug delivery devices (as of August 2023)**

| | E-cigarettes | Heated tobacco products (HTPs) | Oral tobacco and nicotine | Inhaler devices | Cannabis |
|---|---|---|---|---|---|
| **PMI** | **IQOS**<br>**VEEV**<br>**VEEBA** [IQOS Mesh]<br>**Vivid**<br>**Solaris** [Nicocigs] [Nicolites] | IQOS and HEETS tobacco sticks | AG snus and nicotine pouches Swedish Match | **Fertin Pharma**<br>**Vectura**[51] (75 % ownership)<br>**OtiTopic** | **Syqe Medical**[52,53] |
| **Altria** | **NJOY** [Greek Smoke] [MarkTen] | – | [Verve] (lozenge)<br>**On!** nicotine pouches<br>**Lexaria Nicotine** | – | **Cronos Group** (45 % ownership) |
| **BAT** | **Vuse** [Vype]<br>**Ten Motives**<br>**VIP**<br>**CHIC** (inc. Volish, Liqueen) [Twisp] | **Glo and NEO stiks**<br>**Neo Core –** carbon tip [Revo/Eclipse] | **Zonnic** (gum, pouch, spray)<br>**Revel lozenge**<br>**Lyft and Velo –** nicotine pouches | **KBio Holdings**(54) | **Organigram** (20 % ownership)<br>**VUSE CBD Zone** |
| **JTI** | **Logic** [E-Lites] | **Ploom** | **Nordic Spirit** | - | |
| **Imperial Brands** | **blu**<br>**Von Erl and My VonErl** [myblu] [JAI, Puritane] | **Pulze** | **Skurf**<br>**zoneX** | - | **Oxford Cannabinoid Technologies**[55] (10 % ownership)<br>**Auxly**[56] (20 % ownership) |

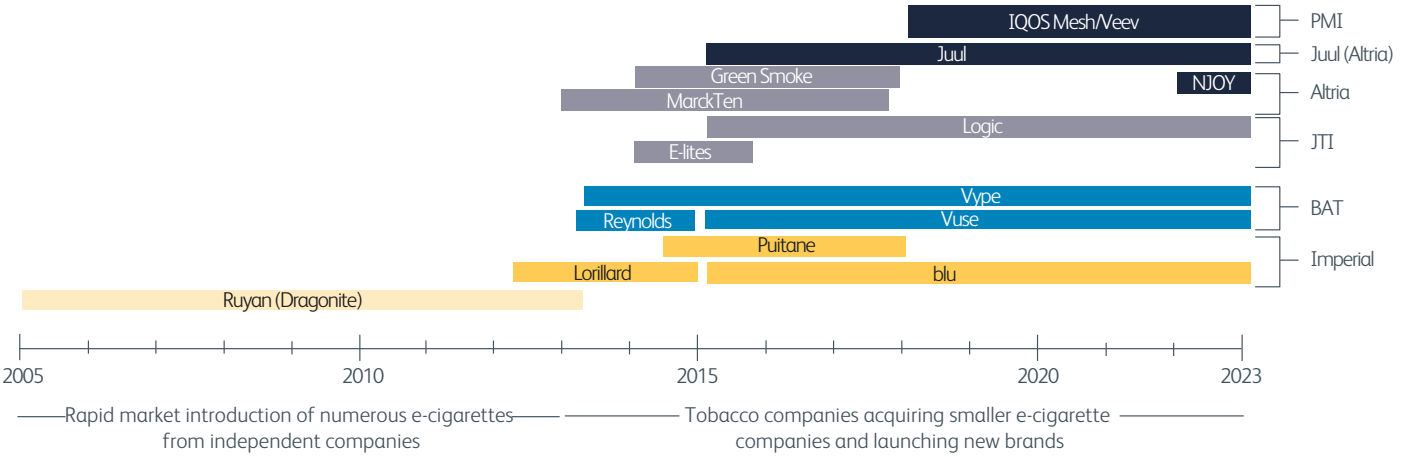
Adapted from the University of Bath's Tobacco Control Research Group Tobacco Tactics Table on Newer Nicotine and Tobacco Products: Tobacco Company Brands.[57] Note that, as of August 2023, this is a partial list that does not include nicotine salts, and that tobacco company investments and brand developments can change both rapidly and frequently. Such developments are regularly monitored and reported by Tobacco Tactics, and updates to information found in this table can be accessed at https://tobaccotactics.org/article/newer-nicotine-and-tobacco-products-tobacco-company-brands/

## 9.2 TTC investments in e-cigarettes, HTPs and other products

In recent years, all four TTCs have both acquired existing e-cigarette companies and developed their own brands of e-cigarettes, heated tobacco products (HTPs) and tobacco (snus) and nicotine pouches for oral consumption, while also investing in non-nicotine products, including cannabis, and pharmaceutical products, notably inhalers (Table 9.2).

### 9.2.1 E-cigarettes

The first commercially successful e-cigarette entered the Chinese market in 2003, and the UK and US markets in 2007.[58] Initially, the global e-cigarette market was dominated by independent companies (ie not wholly or partially owned by tobacco companies).[1] E-cigarettes rapidly gained in popularity and their market potential, particularly in Western markets, became apparent, as did their potential to disrupt the cigarette market.[1]




BAT = British American Tobacco; JTI = Japan Tobacco International; PMI = Philip Morris International

**Note:** In 2015, BAT obtained the Vuse brand, which was acquired as part of its takeover of RJ Reynolds. In 2014, RJ Reynolds sold blu e-cigarettes to Imperial to avoid any potential issues with anti-trust legislation.

**Fig 9.1. Timeline of acquisitions and product launches within the e-cigarette market (2004–23). Data source: University of Bath's Tobacco Control Research Group Tobacco Tactics.**

Consequently, major tobacco companies rapidly began to invest in the then-burgeoning e-cigarette market.[17] Fig 9.1 provides a timeline of key tobacco company investments and product launches in the e-cigarette market between 2005 and 2023. First was US-based cigarette manufacturer Lorillard, which acquired the e-cigarette brand blu™ in April 2012. This was followed by British American Tobacco (BAT), which in December 2012 purchased the UK e-cigarette company CN Creative, manufacturer of Intellicig. PMI was the last TTC to enter the e-cigarette market in 2014,[59] and, possibly as a reflection of this delayed entry, holds the smallest share of the market (see below). In 2015, Juul was launched by an independent producer as the first nicotine salt-based e-cigarette product, and rapidly acquired market share – particularly in the US market, where, by July 2018, it accounted for 70% of e-cigarette sales.* Subsequent to Juul's explosive growth in the USA, driven by its popularity particularly among youth,* all four TTCs began to launch their own nicotine salt products and Altria* acquired a 35% stake in Juul Labs in December 2018.[62]

While all major TTCs have now invested in e-cigarettes, collectively they still only account for 26.2% of the global e-cigarette market. Other than BAT (22%), the TTCs' market shares remain small – Imperial Brands (3%), Japan Tobacco International (JTI) (1%) and PMI (0.2%).

Juul holds 12% of the market. The market therefore still largely consists of non-TTC-linked e-cigarette companies,[63] with Chinese manufacturers RELX Technology and Shenzen Imiracle holding the largest share (Fig 9.2).

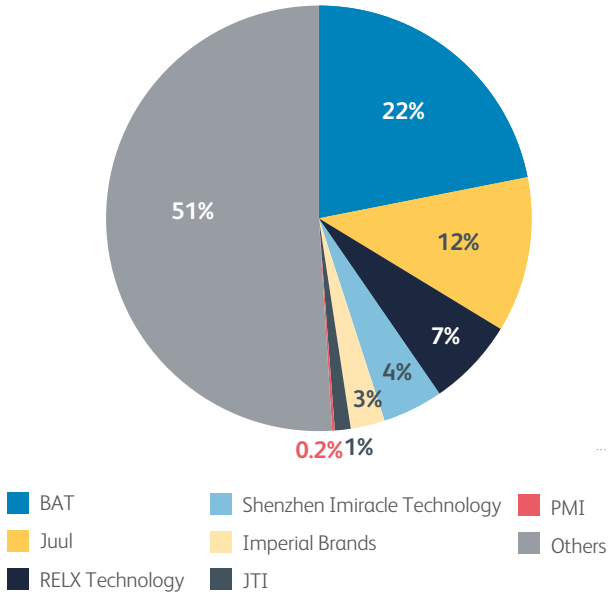



**Fig 9.2. Global e-cigarette market share by company 2022. Chart created by University of Bath using data from Euromonitor,†,# downloaded August 2023.[63]**

* In March 2023, Altria exchanged its non-voting stake in Juul labs for intellectual property rights related to its heated tobacco products.[62]

† Note that Euromonitor does not provide a definition of what constitutes 'other' companies, making it difficult to assess whether they are genuinely independent companies or whether they are partially owned by major TTCs.

# The data supporting this research are available from the following source: www.euromonitor.com. The University of Bath subscribes to Euromonitor Passport and the data were accessed through the University of Bath library portal.

## 9.2.2 HTPs

Shortly after their initial e-cigarette investments (from 2013), TTCs began to launch HTPs[#] (Fig 9.3). In contrast to e-cigarettes, TTCs dominate the global market for HTPs (Fig 9.4). Since 2014, when PMI launched its flagship HTP brand IQOS, it has been the market leader. However, PMI's 99% market share in 2016[17] has been challenged now that all major TTCs have launched their own HTP brands (Fig 9.4). Imperial Brands was the last to introduce a product in 2019, currently limited to a single market in Fukuoka, Japan.

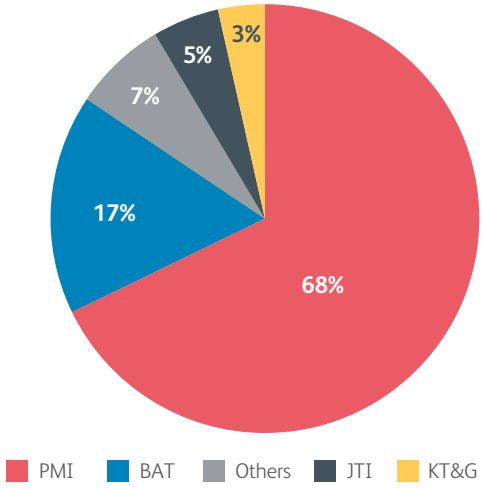



**Fig 9.4. Global HTP market shares by company 2022. Chart created by University of Bath using data from Euromonitor, downloaded August 2023.[65]**

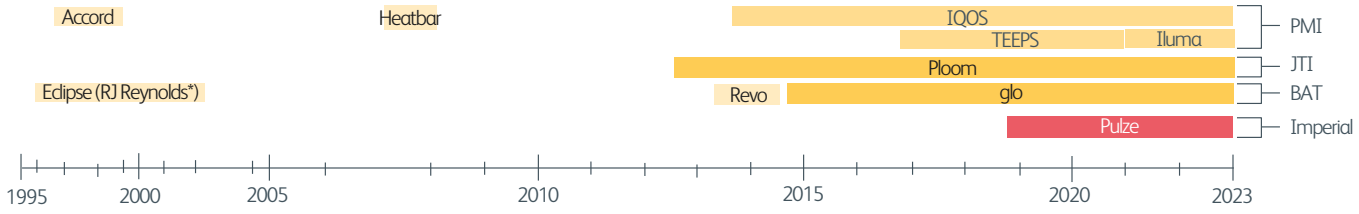
## 9.2.3 Tobacco and nicotine for oral use

TTCs have also been expanding their product portfolios to include tobacco and nicotine products for oral use, such as Swedish-style snus and nicotine pouches, the latter of which contain not tobacco leaf, but a form of dehydrated nicotine. TTC interest in snus is not new, however, with both PMI and BAT having explored opportunities to enter US and European markets in the 1970s and 1980s.[11]

Across all TTCs, PMI has had the lowest investment in the snus product category, though this seems to be changing after it acquired Swedish Match in 2022, giving the company access to the largest snus markets, in Europe and the USA.[66] Like HTPs, TTCs dominate the global market for nicotine pouches, with PMI and BAT accounting for 76% of the total market as of 2022 (60% and 16% respectively).[67]

## 9.2.4 Other products: cannabis, pharmaceutical inhalers and beyond

Recent developments indicate further diversification[21,68] to cannabis products, pharmaceutical inhalers (Table 9.2) and vaccines.[69,70] With most TTCs (except JTI) now invested in cannabis products and clear links between products (eg PMI's acquisition of Syqe Medical,[52] an Israeli company developing a medical cannabis inhaler, and BAT's pilot launch of its CBD eLiquid pods[71] under its global VUSE brand and for use in its VUSE e-cigarettes), a future in which the tobacco industry sells diverse recreational psychoactive, addictive products should be expected.[55,72,73]




BAT = British American Tobacco; JTI = Japan Tobacco International; PMI = Philip Morris International; TTCs = transnational tobacco companies.

**Fig 9.3. TTC investment in HTP market (1995–2023). Data source: University of Bath's Tobacco Control Research Group Tobacco Tactics**

[#] HTPs are not new, with TTCs first developing this technology in the 1980s and introducing HTP products in the 1990s in response to concerns around secondhand smoke exposure. In 1996, RJR (now owned by BAT) launched Eclipse and PMI introduced Accord 2 years later in 1998, which was subsequently rebranded as Heatbar in 2007. After failing to gain commercial success, PMI and RJR discontinued these early iterations of their HTP products in 2006 and 2014 respectively.[64]

Links across tobacco, cannabis and e-cigarettes have the potential to extend marketing and branding, and reinforce sales across the whole product portfolio.

A key concern in this area is evidence from clinical studies and animal models suggesting that nicotine use in adolescence, a developmental period characterised by heightened neuroplasticity, induces changes in critical circuitry including reward-related behaviours that may increase the risk of diverse addictions in the long term. [74] Given the TTCs' extensive knowledge of addiction,[12,75] it is therefore likely that TTCs will use their investments to further expand nicotine and cannabis use, including dual use, alongside existing product revenue streams. The fact that BAT has chosen to launch its VUSE CBD e-Liquid pods in Manchester, with plans for rollout across the UK,[71] suggests that it considers the UK a key market, perhaps because of its relatively liberal stance on e-cigarettes and because increasing rates of youth e-cigarette use (chapter 3) create a long-term market opportunity. A further trend is tobacco industry 'pharmaceuticalisation'.[76] While the decline in global cigarette sales provides clear incentive for diversification, expansion into pharmaceuticals has also been used to falsely signal transformation[5] and position tobacco companies as aligned with a public health mandate.[77,78] PMI has been most active in this area, acquiring three pharmaceutical companies (presented as part of the company's efforts to accelerate what it portrays as its 'beyond nicotine',[21] rather than 'beyond tobacco', vision). Critically, TTC acquisition of pharmaceutical companies raises important ethical issues when they profit from the sale of medicines used to treat diseases caused by their tobacco products.[79] Moreover, TTC investments in this area have presented significant reputational and financial risks to their pharmaceutical partners.[80–84] TTCs are also signalling further expansion into other areas, including 'health and wellness', 'functional products' and 'tech' for BAT,[70] and 'botanicals' such as 'sleep aid', 'calm and control' for PMI.[69]

# 9.3 State of global market in nicotine products

## 9.3.1 Cigarettes

The timing of TTC investments detailed above coincides with a period when the tobacco industry and its primary product – the cigarette – were arguably under greater threat than in previous decades. Implementation of tobacco control policies had been advancing around the world[83] and since at least 2000, smoking prevalence rates had been steadily declining.[84] More worryingly for the industry, the retail value of cigarettes (a proxy for profitability) had also begun to fall (Fig 9.5). Euromonitor data, covering 202 countries including all major tobacco markets except China, and available only from 2008, show that the total number of cigarettes sold globally fell markedly (Fig 9.5), declining by 20% over the 10-year period from 2009 to 2019 (Table 9.3). In the initial period of this decline, the retail value of cigarettes increased (Fig 9.5). This pattern occurs when TTCs are able to increase the price of their cigarettes (and thus profits) sufficiently to offset the negative impact of any declines in sales.[10,85]

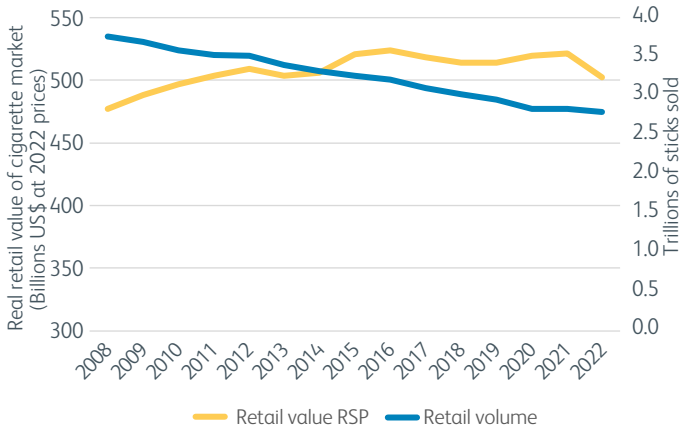



**Fig 9.5. Global real retail value (in US$ billions) and number of cigarettes sold (in trillions of sticks). Data source: Euromonitor, downloaded August 2023.[86,*]**

* Retail values are expressed in 2022 US$ prices ('real' value) to account for the effect of inflation when looking at data retrospectively from 2022. The drop in real value observed between 2021 and 2022 is almost entirely driven by inflation in the Western European and North American markets. These markets saw a combined increase in nominal value of US$ 2 billion in the cigarette retail market between 2021 and 2022, but inflation wiped this out to provide a US$ 20 billion drop in value in real terms.

Due to the addictiveness of cigarettes, increasing value (despite volume declines) had been a consistent pattern. Yet, in 2012 – the year that TTCs first invested in e-cigarettes – the retail value of global cigarette sales fell for the first time, wavering thereafter (Fig 9.5).

At this point, the situation did not appear positive for the tobacco industry: cigarette sales volumes were increasing in just one region – the Middle East and Africa – which accounted for just 8.2% of the global cigarette market by value. In all other regions, volumes were falling markedly (between 14% and 44%) and these regions collectively accounted for the remaining 91.8% of the global value of cigarettes. It is within this context that the major TTCs began investing in, developing and aggressively marketing e-cigarettes, HTPs and other products.

Subsequently, and worryingly for public health, since 2020 the previous marked and steady decline in global cigarette sales has slowed (Fig 9.5). In line with this, the Global Burden of Disease data from 1990 to 2019 indicate that, although smoking prevalence is still declining, the rate of decline has now stalled in every region of the world, particularly since 2015.[87,88] In the UK, survey findings differ somewhat and while adult smoking prevalence in all surveys remains at its lowest level, the most up-to-date survey, the Smoking Toolkit Study, suggests that the rate of decline in smoking prevalence in young adults in England has slowed from 2020 onwards, while e-cigarette use rates continue to rise. It also suggests that while more smokers are quitting and using e-cigarettes to do this, smoking uptake (ever-smoking in those 18–24 years) has increased, and current smoking in the youngest age groups (between 16–21 years) is non-significantly higher now than in 2020.[89] This may be a temporary phenomenon linked to COVID-related lockdown.[90] Youth use of e-cigarettes is also increasing rapidly.[89,91] (see chapter 3 for trend data.)

**Table 9.3. Number of cigarettes sold (in billions of sticks) by region. Data source: Euromonitor, downloaded August 2023.[92]**

| | % share of global cigarette value (2019) | Cigarette volumes (billions of sticks), 2009 | Cigarette volumes (billions of sticks), 2019 | % change in volume (2009 to 2019) |
|---|---|---|---|---|
| Australasia | 2.8% | 243 | 135 | –44% |
| Eastern Europe | 11.8% | 748 | 453 | –39% |
| North America | 23.4% | 352 | 268 | –24% |
| Latin America | 4.3% | 252 | 168 | –33% |
| Western Europe | 26.7% | 613 | 461 | –25% |
| Middle East and Africa | 8.2% | 461 | 504 | 9.3% |
| Asia Pacific (excl China) | 22.8% | 1,238 | 1,069 | –14% |
| Total | 100% | 3,690 | 2,960 | –20% |

## 9.3.2 E-cigarettes, HTPs and oral tobacco and nicotine products

### 9.3.2.1 E-cigarettes

Since their emergence, e-cigarette sales values have grown at an exceptionally rapid pace, both globally and in the UK. Accurate data on volume trends are not available through public datasets like Euromonitor, in part because of the diverse formats in which e-cigarettes are sold. Euromonitor is, however, able to provide data on retail value trends (Fig 9.6), which show very rapid growth, particularly from 2012 (the point at which TTCs first entered this emergent market).

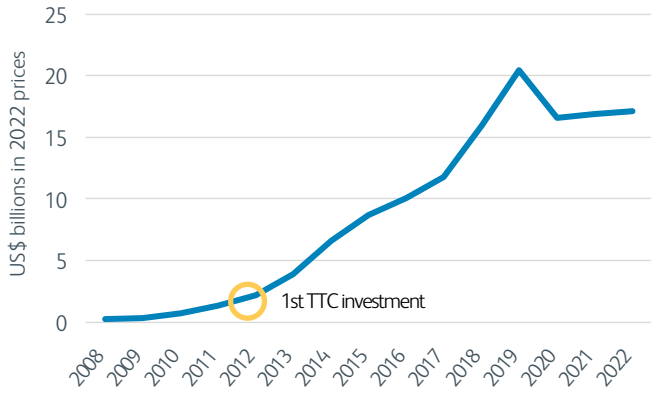



**Fig 9.6. Global retail value of e-cigarette sales (excluding China). Data source: Euromonitor, downloaded August 2023.[93]**

Global sales data do not indicate who is using such products, but a 2023 survey by Action on Smoking and Health (ASH) showed that, in Great Britain, regular youth use has trebled since 2021, trying e-cigarettes has increased by 50% since 2022 and 69% of young people who had tried them most frequently reported using disposable e-cigarettes (see chapter 3).[91] Compared with refillable e-cigarette devices, which experienced an 11% global value growth in 2021, demand for disposable products increased by 22%, with forecasters estimating that this will reach 30% by 2026.[94] In addition to concerns about youth use,[95,96] disposable e-cigarette products are a major environmental liability.[97]

## 9.3.3 HTPs

Unlike e-cigarettes, sales volume data do exist for the heat sticks used in HTPs (Fig 9.7). These data show that both the sales volume and retail value of heat sticks have increased exponentially from 2016. In recent years, the global e-cigarette market has slowed, particularly since 2019 (Fig 9.6), whereas the global HTP market has continued to grow (Fig 9.7). From a public health perspective, this trend is concerning because, while there is evidence that e-cigarettes can help smokers quit,[32,98,99] similar evidence does not exist for HTPs.[32] Moreover, while the evidence remains uncertain,[100–105] use of HTPs is likely to be more harmful to health than e-cigarette use.[100–104,106,107]

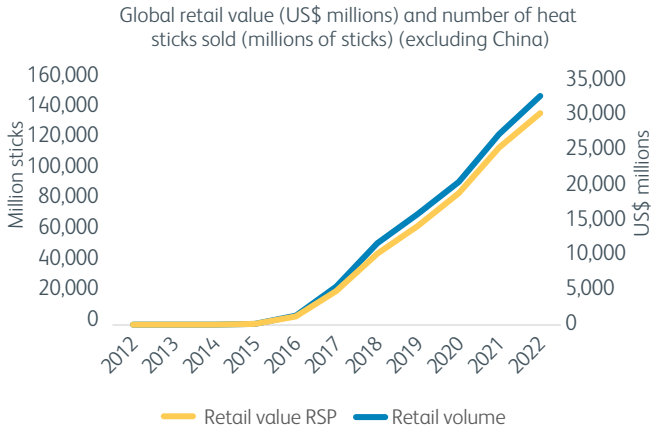



**Fig 9.7. Global retail value (in US$ millions) and number of heat sticks sold (in millions of sticks) (excluding China). Data source: Euromonitor, downloaded August 2023.[108]**

Because of the absence of volume data for e-cigarettes, trends in the tobacco and nicotine market as a whole can only be examined using retail value data (Fig 9.8). Despite the stagnation in cigarette value, the total value of the combined global tobacco and nicotine market (excluding pharmaceutical nicotine) has been steadily increasing, particularly since 2015, after all major TTCs had entered the e-cigarette and HTP markets.

Consistent with TTC reports to investors (section 9.4), Fig 9.8 shows that this value growth is largely due to newer nicotine and tobacco products. The close match between value and volume data for HTPs (Fig 9.7) suggests that these value data may act as a proxy for volumes,* indicating that these newer products are serving largely as additions, rather than alternatives, to cigarettes. Moreover, despite significant growth over the past decade, e-cigarettes, HTPs and new oral products still account for a small fraction of the global market in tobacco and nicotine products, with cigarettes remaining the dominant product category.[17]

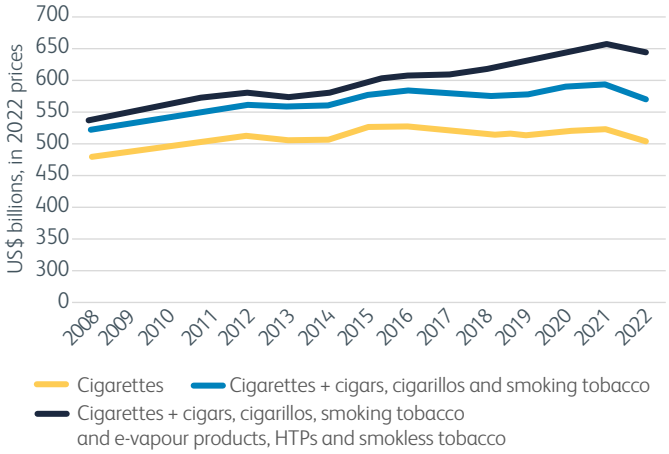



**Fig 9.8. Global retail value of tobacco and nicotine products (excluding China).† Data source: Euromonitor, downloaded August 2023.[109]**

# 9.4 Analysing TTCs' latest conduct and claims around harm reduction

## 9.4.1 Diversification as profit maximisation rather than harm reduction

In line with the worrying trends in product sales and the stalling rate of decline in global cigarette consumption and smoking prevalence,[84,87] detailed above, TTCs are now reporting to investors that e-cigarettes and HTPs represent significant growth opportunities, serving to expand, rather than substitute, revenue from declining cigarette sales.[17] This was epitomised in a July 2018 question and answer session when former Imperial Brands CEO Alison Cooper stated 'a lot of the time, it's actually also adding to the nicotine consumption in the market. It's not a question of shifting to NGP [next generation products] … because we are seeing nicotine market growth in the UK …'.[110] Critically, a March 2019 investor presentation by BAT indicated that poly-use was becoming the norm, and that between 58 % (e-cigarettes) and 11 % (HTPs) of the company's growth was driven by 'new entrants' to the market rather than former smokers.[111,112] It also highlighted the importance of poly-use to the TTCs' bottom line because it maximises their 'revenue per consumer'.[111,112] TTCs also sell e-cigarettes and HTPs in bundles,[113] thereby encouraging poly-use.[17]

Such patterns are consistent with evidence from tobacco industry documents that reveal the TTCs' real interests in potentially reduced risk products.[8,9,11,114] Dating back to the 1970s, industry documents explicitly state that such products could work as a viable long-term business strategy only if they were to enable TTCs to recruit new users rather than merely replace existing smokers.[11]

* We note that value and volume data for HTPs correlate closely (Fig 8.7). This is also the case for nicotine pouches (data not shown), although not for cigarettes (Fig 8.5). We hypothesise that the close correlation between value and volume is likely early in an epidemic when the industry is trying to expand the market and when products are taxed little. Thus, the value graph will likely represent a reasonable proxy for volumes for the newer products. Given that the volume of cigarettes has declined more than value, a volume graph of trends by product segment would likely show an even larger additive impact of e-cigarettes, HTPs and oral products.

† Smokeless tobacco includes both traditional smokeless tobacco products (chewing, snus, snuff) and nicotine pouches. See also footnote 1 on page xx for an explanation of the decline in real value from 2021 to 2021.

For example, in the 1970s and 1980s, BAT documents demonstrate that interest in new smokeless tobacco products was driven by a desire to attract new young users who otherwise would not have initiated smoking due to health-related concerns.[11] Similarly, PMI's documents from the 1990s reveal that its motivation behind developing a device that closely resembles the modern-day e-cigarette[115] was to maintain and possibly extend nicotine addiction in the context of 'a declining US market, the growth of smoking restrictions … and a marked decline in social acceptability of the smoking experience'.[116] Ultimately, however, PMI abandoned this research due to concerns that this development could lead to further regulation of smoked tobacco products.[115] Furthermore, leaked documents from PMI detailing its 10-year strategy to 2024 highlight the company's underlying motivations behind investing in 'reduced risk products' including to 'drive future growth', 'normalise' the company's image and allow it to shape regulation in its own interests.[15,16]

## 9.4.2 Tobacco industry capture of harm reduction

Such plans are, of course, inconsistent with genuine harm reduction – a public health concept that involves reducing harm from addictive behaviours by reducing harm for the individual user and for the community and society in which they live.[117] In tobacco control, harm reduction, as conceived by public health, would therefore involve shifting current smokers who were unable to quit to lower-risk products, but would not encompass using reduced-risk products to drive product use among nicotine-naïve consumers who would otherwise not have taken up smoking.* Genuine harm reduction is not, therefore, a long-term, sustainable business model for TTCs: once the current generation of smokers and former smokers dies, there are fewer and fewer potential new consumers.[118]

TTCs have strategically worked around this problem by misappropriating, misrepresenting and creating confusion about the concept of harm reduction.[8,17] For example, PMI's 'harm reduction equation' (Fig 9.9) misleadingly equates individual smokers switching to lower-risk products to population harm reduction, regardless of whether any smokers quit, the extent of dual use, or what happens in the wider population.[8,119] The latter, of course, includes the children who it targets with its new product marketing.[120–123] Similarly, TTCs have also misrepresented related terms such as 'smoke-free' and 'quitting'.[8] For example, PMI publishes misleading estimates of 'quitting' based on the number of people who have 'switched' to its HTP product, IQOS, even for a brief period, including dual users who continue smoking.[8]

Corporate capture of the concept of 'harm reduction' is not new and previously has been used by the alcohol industry to counter evidence-based alcohol policy development.[124] Internal tobacco industry documents show that tobacco companies strategically adopted the term 'harm reduction' (or 'tobacco harm reduction') from the public health community, which had become interested in the concept in the early 2000s. TTCs recognised that engagement with the harm reduction agenda would allow them to position themselves as part of the solution, affording the opportunity to secure both political and reputational benefits, notably to regain access to policymaking, scientific and public health circles.[9,11]

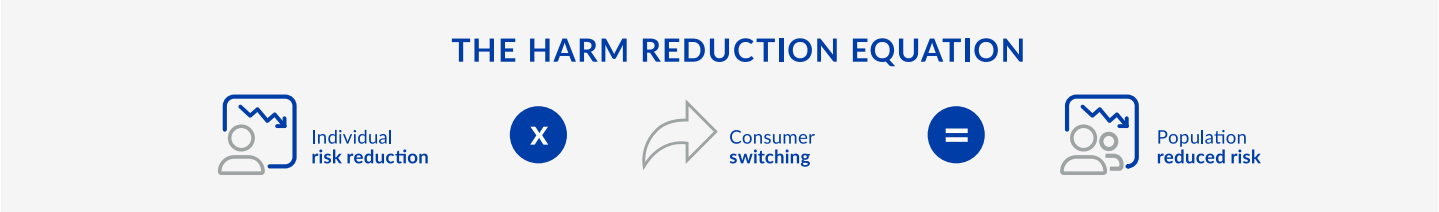



**Fig 9.9. Philip Morris International's harm reduction equation. Reproduced from PMI factsheet 'The importance of harm reduction and need for better alternatives'[125]**

* It is notable that, within the successful model of drug harm reduction, there are no glamorous high street stores selling flavoured methadone products, like there are for e-cigarettes and HTPs. Yet neither is heroin sold in retail outlets. While it makes little sense to make e-cigarettes less available and attractive to smokers than more harmful cigarettes, that does not require making e-cigarettes easily available and attractive to young people.

## 9.4.3 False transformation

Some TTCs have now moved beyond misleading corporate narratives around a commitment to harm reduction[4] to claim that they are 'transforming' by allegedly taking actions to promote a 'smoke-free future'.[24] PMI has made the most prominent claims in this area (Box 9.1). However, in-depth analysis of its communications over an 8-year period shows that its public rhetoric – centred on reducing harm and delivering a 'smoke-free' future[3] – is highly misleading, contradicting its core business focus, with investors consistently reassured of PMI's commitment to maintaining leadership in the global cigarette category.[4] Its most recent 2022 annual report[126] informed investors that: 'For as long as a significant number of adult smokers continue to smoke, responsible leadership of the category is critical. We aim to maintain our competitive position in the cigarette market through selective investment.'

Similarly, in a 2021 investor presentation to the Consumer Analyst Group of New York (CAGNY), BAT chief executive Jack Bowles stressed the strength of its existing cigarette brand portfolios, reassuring investors of the profitability of '… our combustibles business'[127] and that it remains a key company priority.[128] A 2021 investor presentation by Imperial Brands was even more stark, highlighting that, for its 'combustible' product, the company's 'value creation model remains strong with reliable profit growth and high cash returns' while the 'transition to NGP [next generation products] is happening but at a modest pace'.[129]

Analysis of TTC transformation claims found no evidence of any substantial progress, suggesting rather that TTCs are engaging in 'pseudo-transformation'.[5,17] TTCs continue to invest in new cigarette companies and brands, heavily market cigarettes, and launch tobacco product and packaging innovations that increase the attractiveness and desirability of their tobacco product lines.[94,130] Evidence for this includes TTCs actively developing and aggressively marketing cigarette-flavour capsule cigarettes,[94,130] which are used to circumvent bans on the sale of flavoured and menthol cigarettes.[131] Critically, global evidence of ongoing TTC efforts to obstruct, delay and weaken implementation of effective tobacco control measures calls these commitments to 'smoke-free' futures into question.[18,26]

## 9.4.4 Misusing harm reduction and transformation claims to secure influence

Not only do TTCs wield their immense economic and political power in influencing policy,[26] but they now actively use their 'harm reduction' rhetoric to re-engage in policy circles from which they had been excluded.[8] On its UK website, for example, PMI underlines a role for harm reduction in (re)establishing dialogue with and access to policymakers by claiming a joint agenda with public health. Building on earlier efforts to use harm reduction to secure policy influence,[9] the company stresses the importance of a 'common-sense approach' and that 'the right mix of government leadership and commercial initiative will dramatically accelerate efforts to reduce the health burden of smoking'.[132] In line with this, Bialous found that TTCs have been using their investments in HTPs to rehabilitate their tarnished image so that they can more effectively influence governments to roll back existing tobacco control policies or create loopholes for HTPs.[18]

Furthermore, while companies like BAT and PMI advocate for 'freedom to innovate' and develop new products in the apparent interest of improving public health, they continue to advance narratives that place the responsibility for continued tobacco use squarely on the shoulders of consumers.[3] At the 2022 Global Forum on Nicotine, in a session on 'tobacco industry transformation: myth or reality?', Flora Okereke, head of BAT's global regulatory insights and foresights, indicated that the company's transformation strategy was shaped by the view that consumers were responsible for leading this change, suggesting that they must make 'a conscious effort on their side to stop smoking' and '[i]f people are not moving, there is no need for us to reduce it'.[133] By shifting blame to individual 'lifestyle choices', TTCs frame the health and environmental problems of tobacco use as one of individual failure to quit smoking or to choose 'better' products, thus downplaying industry's role in such harms. This limited focus also serves to preclude the need for population-based measures that target the upstream drivers of smoking (such as those relating to demand reduction via evidence-based denormalisation strategies).[3]

### 9.4.5 Exploiting tensions to further undermine tobacco control

As far back as 1995, PMI engaged in a political strategy known as 'Project Sunrise',[134] which intentionally sought to 'divide and conquer the tobacco control movement by forming relationships with [what it considered] "moderate" tobacco control individuals and organisations'.[135] Moreover, this strategy is not merely historical. Leaked 2014 PMI documents outline the company's corporate affairs strategy to 2024, which show that, in addition to its plans of exploiting harm reduction to normalise the company's image and re-engage with policymakers (as outlined above), PMI's corporate strategy sought to undermine the credibility and integrity of some tobacco control advocates.[8] The documents reveal the company's continued efforts to create fractures in the tobacco control community by 'amplify[ing] the voices of harm reduction supporters'.[15,16] Not only does this allow TTCs to assert that there is disagreement within the tobacco control community, but it also provides apparent legitimacy to promoting individual-level interventions as substitutes for, rather than complements to, effective population-based measures.[3]

### 9.4.6 Tobacco industry science as a further threat to tobacco control

Major TTCs have also sought to obfuscate information and create confusion[114] about the harms of their products, including HTPs.[33,47,136–138] A growing number of studies demonstrate that PMI's claims around the reduced-risk potential of IQOS are not entirely substantiated by its own scientific research.[123,139–143] PMI's published computational simulations of the potential impact of IQOS on public health have been shown to underestimate the health impacts of HTPs.[144] Recent research that critically appraised interventional clinical trials on HTPs also found that industry-affiliated studies were of poor quality and limited to investigating the impacts of their short-term use.[33] PMI has also misrepresented the science on smoke and aerosol, claiming that IQOS is smoke-free, safer than conventional cigarettes and even less harmful than e-cigarettes.[47,145] Simultaneously, TTCs have promoted the 'benefits' of nicotine while downplaying its addictiveness and health harms.[138]

Moreover, analysis of the activities of the Foundation for a Smoke-Free World[146] (FSFW, see Box 9.1) revealed that it produces PMI-favourable research and opinion[30] and effectively operates as a front group and public relations arm for the company, despite claiming independence. This mirrors the tobacco industry's historic scientific practices that served to obscure the harms of smoking.[28,30,46] FSFW funds numerous other third parties (both individuals and organisations) that champion and publicise PMI's version of harm reduction,[147,148] including the International Network of Nicotine Consumer Organisations (INNCO), an umbrella organisation with 40 listed members and affiliates (industry-linked and independent).[8] This is part of a broader shift in PMI's corporate political activities in which TTCs operate increasingly via third parties, making it difficult to determine individuals and organisations with industry links.[8,9,149]

## 9.5 Conclusions and ways forward

This chapter highlights the real and potential dangers of TTC interest in e-cigarettes, HTPs and other products (including cannabis) as part of their strategic engagement in what some TTCs claim is 'harm reduction'. E-cigarettes represent a potential opportunity for tobacco control. However, recognising and addressing how TTCs are attempting to (mis)use the concept of harm reduction, and the opportunities that it presents to them, are essential to ensuring the success of genuine approaches to harm reduction and tobacco control more broadly. This chapter reveals that TTCs are using and will continue to use their investments in tobacco and nicotine products to recruit new users who otherwise would not have initiated smoking,[113] promote poly-use,[17] create confusion around harm reduction, split the public health community, and secure influence and access to policy circles from which they have hitherto been excluded. TTC claims of commitment to harm reduction and 'transformation' are highly misleading and should instead be understood as public relations and policy influence strategies. Given their wealth and power (TTCs are some of the most profitable companies in the world)[150] and the resources that PMI, in particular, is committing to its public relations makeover and to 'science', there is a very real risk that such efforts will stymie progress in tobacco control.

Overall, our findings suggest that tobacco control may be under greater threat than ever before. The UK Tobacco Industry Interference Index, part of the Global Tobacco Industry Interference Index,* shows that industry attempts to influence policy here have been increasing over time[151,152] and the UK government has failed to address that interference, falling from third in global position in 2021 to 21st in 2023.[152] While this decline reflects increased activities by tobacco companies and their allies – much of it focused around harm reduction – it is also explained by the lack of a coordinated approach to managing conflicts of interest in tobacco policymaking, including implementation of measures to raise awareness of Article 5.3 of the WHO FCTC across different government departments and agencies beyond health.[153] This is particularly concerning as hitherto the UK has been seen as a global leader in tobacco control, including in implementation of Article 5.3. (For a full list of recommendations on how the UK can improve its performance in addressing tobacco industry interference, see Alebshehy *et al*'s 2023 UK Tobacco Industry Interference Index report.[152]

Government interest in using e-cigarettes to reduce the harms of smoking has been mainly limited to the UK and New Zealand.[150] Both have some of the strongest population-level tobacco control measures in the world, along with the required regulatory capacity and financial resources to ensure their effective compliance. Yet, as the UK data show, even in these favourable environments, implementing and enforcing regulation to both minimise youth uptake and maximise population-level benefit is difficult. This includes by minimising industry influence and circumvention of legislation,[150,153,154] highlighting the critical importance of ongoing vigilance and surveillance.

Each TTC's interest in promoting e-cigarettes, cigarettes and/or new products varies widely across jurisdictions,† as does the extent of its marketing and policy influence.[155] There is a need, therefore, to acknowledge that the potential role for harm reduction approaches using e-cigarettes will vary by locality and that approaches that may work in the UK may not work elsewhere, such as in low- and middle-income countries (LMICs). Accordingly, there must be respect for protecting national policy space, including decisions to ban importation of e-cigarettes and other products.

This is critically important given that TTCs, often via their allies[147,148,158–161] and front groups,[28] have been actively promoting the UK approach to harm reduction as an exemplar model that other governments should follow.

Our findings also highlight that the need to continue to protect the policymaking process from the commercial and other vested interests of the tobacco industry, as enshrined in Article 5.3 of the WHO FCTC, remains a priority. This situation may therefore require implementation of measures beyond those recommended in the original set of guidelines on Article 5.3 of the WHO FCTC,[162] as reflected in the COP 6(9) 2014, COP 7(9) 2016 and COP 8(22) 2018 decisions. The COP 6 and COP 7 decisions invited parties to consider:

- taking certain measures to protect tobacco control activities from all commercial and other vested interests related to ENDS/ENNDS (electronic nicotine delivery systems / electronic non-nicotine delivery systems), including interests of the tobacco industry
- ensuring that Article 5.3 (and its eight guideline recommendations) are respected when developing and implementing e-cigarette legislation and regulations.[163,164]

The COP 8 decision further reminded parties that 'their commitments under the WHO FCTC' extended beyond ENDS to 'emerging tobacco products such as heated tobacco products […]'.[165]

While these COP decisions do not explicitly account for the TTCs' latest investments in pharmaceutical and cannabis products, the pressing need to guard against conflicts of interest in policymaking and science more broadly is now widely recognised.[166,167] There is growing evidence that diverse industries behave similarly in terms of their corporate political activities (CPA)[168] and scientific conduct,[169] with e-cigarette,[170] pharmaceutical[171] and cannabis[172,173] companies without apparent links to TTCs all shown to influence science and public policy. TTCs will undoubtedly use these investments to advance their long-standing efforts to undermine the WHO FCTC and Article 5.3.[174,175] Such broad conflict of interest protections will be critical to ensuring that policy and science function in the interest of public health.

* The Global Tobacco Industry Interference Index rates countries on their performance in preventing tobacco industry interference in policy and legislation. Country ratings are based on data from survey questionnaires, which consist of 20 questions covering seven indicators of industry interference (developed from Article 5.3 guidelines). These include: 1) participation in policy development; 2) corporate social responsibility; 3) benefits to the tobacco industry; 4) unnecessary interaction; 5) measures for transparency; 6) conflict of interest; 7) preventive measures.

† This variation occurs in line with the stage of the tobacco epidemic (eg whether cigarette sales are falling), the tobacco control policies in place, and each TTC's market share (and thus its potential to secure gains relative to its competitors).

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# 10

# Ethics

## Key points

- E-cigarettes are not risk-free but from an ethical standpoint the significant issue is that they are demonstrably less harmful than smoked tobacco to user and bystander alike.
- The ethical arguments for e-cigarettes as a harm reduction tool in the context of a *comprehensive* tobacco control and smoking cessation strategy, as advanced in earlier RCP reports, are still sound.
- The imperative for collection of reliable evidence, including controlled trials, remains.
- The need for careful monitoring of the e-cigarette market and industry behaviour in that context continues to be paramount.
- The need for caution about the risks and unanticipated harms of interventions, such as e-cigarettes, which may assist in tackling the harms of smoking, is as strong as ever.

The ethical aspects of policy and regulation relating to alternative nicotine products were considered carefully in the RCP's 2007 report *Harm reduction in nicotine addiction*.[1] In that report, the RCP made a clear and robust case for thinking about the utility of alternative nicotine products in assisting smokers to quit smoking, and also to consume nicotine in a significantly less harmful form than smoked tobacco. At that time, the market in e-cigarettes was still relatively new, and the evidence base around patterns of usage and health effects was limited. It was thought unlikely that e-cigarettes would be taken up by individuals who had no history of tobacco smoking, or that users of e-cigarettes would progress to smoked tobacco. It was also thought that e-cigarettes would be seen by healthcare professionals and the public as a 'treatment' to assist quitting smoking rather than as consumer lifestyle products.

In its 2016 report, *Nicotine without smoke: tobacco harm reduction*,[2] the RCP continued to emphasise a harm reduction approach to *tobacco* use and addiction, evaluating the then available evidence on use and health impacts of e-cigarettes in the context of the known harms to health (including the impact on health inequalities) of tobacco smoking.

This 2024 report reviews the latest evidence, and it is clear that e-cigarettes continue to have an important part to play as part of a tobacco harm reduction strategy. However, this report also considers causes for concern about e-cigarettes in their own right, and it is timely to ask whether the ethical position has shifted.

If we consider e-cigarettes purely as an aid to smoking cessation, then it is clear from the evidence presented in chapters 4 and 7 that they have a valuable part to play, although there is much to do in terms of refining how smoking cessation programmes make use of these products. As the RCP has consistently argued since 2007, e-cigarettes are not risk-free (chapter 5), but from an ethical standpoint the significant issue is that they are demonstrably less harmful than smoked tobacco to user and bystander alike. It is unnecessary to rehearse the outline of the ethics of harm reduction here, as they are examined at length in the 2007 and 2016 reports.[3,4,5]

What has changed since 2007 is the nature of the market for e-cigarettes. On the supply side, the e-cigarette market has arguably been partly captured by the tobacco industry (chapter 9), and on the demand side there is evidence of e-cigarettes being taken up by a currently small but nevertheless significant number of individuals who have never smoked tobacco, including children and young people (chapters 3 and 8). This presents significant regulatory challenges (chapter 6), noting that e-cigarettes are not, considered on their own merits, risk-free products (chapter 5). With more to be learned about the health impacts of long-term nicotine use in non-smokers (chapter 2), delivery byproducts and device design (chapters 2 and 5), and addictiveness, the potential harms to these individuals pose ethical concerns to be considered. And while broadly the case for using e-cigarettes as part of a tobacco smoking cessation strategy is now well established, the case for widespread availability *outside* a tobacco control programme and a programme for smoking cessation in individuals is much more problematic.

The ethics literature on e-cigarettes has continued largely to focus on the older debate about harm reduction and the use of e-cigarettes as a potential tool in tobacco control and smoking cessation. Inasmuch as the literature does consider the harms of e-cigarettes, this has tended to frame them as a theoretical risk – what *might* happen as unintended consequences of allowing the regulated or unregulated sale or dispensing of e-cigarettes to consumers – rather than a considered evaluation of the actual effects of doing so.[6,7,8] This is because the evidence base of the longer-term health effects of e-cigarettes is currently sparse, and the social and epidemiological evidence around the uptake and use of e-cigarettes is only now starting to mature. Some of that older literature takes an essentially 'precautionary' approach to e-cigarettes (they might be harmful, at individual or population scale, so we should not introduce their use in the absence of evidence that they are not harmful). The RCP's position has been that a risk-based approach to harm reduction is ethically and scientifically more sound than a precautionary approach, especially given the known serious harms of tobacco and the known difficulties in driving tobacco smoking and its associated harms down further without new tools to assist. But where that precautionary approach may prove to have merit is in contexts where e-cigarettes are taken up by individuals who were previously non-smokers, many of whom may have been put off smoking by the associated health risks or by factors such as smell or social stigma, and may see e-cigarettes as safe 'enough' given their personal appetite for risk, and as socially acceptable in a way that cigarettes are not. Especially given the role of the tobacco industry in the e-cigarette market, there is reason for concern about marketing tactics from branding to product placement which 'normalise' e-cigarette use, particularly in consumer groups not previously exposed to tobacco products and tobacco marketing techniques.

In conclusion, we are now in a more complex situation where policy decisions may need to balance harms and benefits to different groups of individuals. The ethical arguments for e-cigarettes as a harm reduction tool in the context of a *comprehensive* tobacco control and smoking cessation strategy are still sound. But the imperative for collection of reliable evidence, including controlled trials, remains. The need for careful monitoring of the e-cigarette market and industry behaviour in that context continues to be paramount. And the need for caution about the risks and unanticipated harms of interventions, such as e-cigarettes, which may assist in tackling the harms of smoking, is as strong as ever.

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# Appendices to chapter 5

# Appendix 1: Methods for updated systematic review

We searched five databases from 1 July 2021 to 28 February 2023, as detailed in Fig A1.1. Search terms were adapted from McNeill *et al*[1] to identify relevant literature on e-cigarettes/vaping. We did not include cannabis vaping or vaping of other illicit substances. We included randomised controlled trials (RCT), non-randomised studies, cross-over studies, single group studies, longitudinal and cross-sectional studies.

Eligibility criteria included (words in italics reflect changes from the eligibility criteria used in McNeill *et al* report:[1]

- **Participants:** people (youth and adults) with and without pre-existing health conditions exposed to vaping products through direct use *(current daily use of a product was defined as using daily for at least the past 8 days*, as assessed through self-report or bio-verification), or second-hand exposure of any length. Studies where length of e-cigarette use was not provided but e-cigarettes were used at least weekly were also included.
- **Intervention(s)/exposure(s):** exposure to vaping products with or without nicotine over a specific time frame. This was defined as 1) acute (one-off exposure up to 7 days; *only for second-hand exposure*), *2) short term (8 days to <1 month), 3) medium-term (≥1 month to 12 months)*, and 4) long-term (more than 12 months).
- **Comparator(s)/controls:** we compared people who currently *exclusively* vape daily to people who 1) currently *exclusively* smoke tobacco daily for at least the past 8 days, 2) currently vape and smoke tobacco daily, 3) have quit smoking or vaping and have neither smoked nor vaped since quitting f*or at least the past 8 days and at most 6 months (ie short-term quitters)*, 4) *have quit smoking or vaping and have neither smoked nor vaped for longer than the past 6 months (ie long-term quitters)*, 5) have never smoked nor vaped.
- **Outcomes:** we extracted, compared, and reported levels of BoE, namely nicotine, cotinine, carbon monoxide (CO), and main toxicants or their metabolites related to smoking and vaping, identified as carcinogenic to humans or probably carcinogenic to humans by IARC[2] (group 1 and 2A) (see Table A1.1). We also extracted BoPH (surrogate endpoints) related to cancers, respiratory and cardiovascular health and those cutting across several diseases, such as oxidative stress, inflammation, and other health markers (see Table A1.1).

**Table A1.1. Biomarkers of exposure and potential harm included in the updated review**

| Biomarkers of exposure | |
|---|---|
| Nicotine | Nicotine, cotinine, total nicotine equivalents (TNE) |
| Carbon monoxide | Carboxyhaemoglobin (COHb) |
| Tobacco specific nitrosamines (TSNAs) | NNK (and its metabolite NNAL) |
| | NNN |
| Volatile organic compounds (VOCs) | 1,3-butadiene: dihydroxybutylmercapturic acid (DHBMA), monohydroxy-butenyl mercapturic acid (MHBMA) |
| | Acrolein:3-hydroxypropylmercapturic acid (3HPMA), N-acetyl-S-(carboxyethyl)-1-cysteine (CEMA) |
| | Acrylamide: N-acetyl-S-(3-amino-3-oxopropyl)-cysteine (AAMA), N-acetyl-S-(3-amino-2-hydroxy-3-oxopropyl)-cysteine (GAMA) |
| | Benzene: S-phenyl mercapturic acid (S-PMA) |
| | Ethylene oxide: N-Acetyl-S-(2-hydroxyethyl)-L-cysteine (HEMA) |
| Aromatic amines | 2-aminonaphthalene (2-AN) |
| | O-toluidine (o-tol) |
| Polycyclic aromatic hydrocarbons (PAHs) | Benzo[a]pyrene (3-hydroxybenzo[a]pyrene (Total-3 OHB[a]P)) |
| | Pyrene: 1-hydroxypyrene (1-HOP)* |
| Heavy metals | Cadmium |
| | Lead |
| | Arsenic |
| | Mercury |

| Biomarkers of potential harm | |
|---|---|
| Cutting across diseases | Oxidative stress (F2-isoprostanes) |
| | White blood cell count (WBC) |
| | Levels of C-reactive protein (CRP) |
| | High-density lipoprotein cholesterol-C (HDL-C) |
| | Fibrinogen |
| | Interleukins: IL-1b, IL-6, IL-8 |
| | Tumour necrosis factor alpha (TNF-α) |
| | Soluble intercellular adhesion molecule-1 (sICAM1) |
| Cancer-specific | DNA methylation |
| Respiratory diseases | Spirometry: forced expiratory volume (FEV1), forced vital capacity (FVC), FEV1/FVC ratio |
| Cardiovascular diseases | Heart rate (HR) |
| | Blood pressure, systolic and diastolic (SBP/DBP) |
| | Flow mediated dilation (FMD) |

* Pyrene is not classifiable as carcinogenic to humans but its metabolite 1-hydroxypyrene is often used as an indicator of exposure to other carcinogenic PAHs.

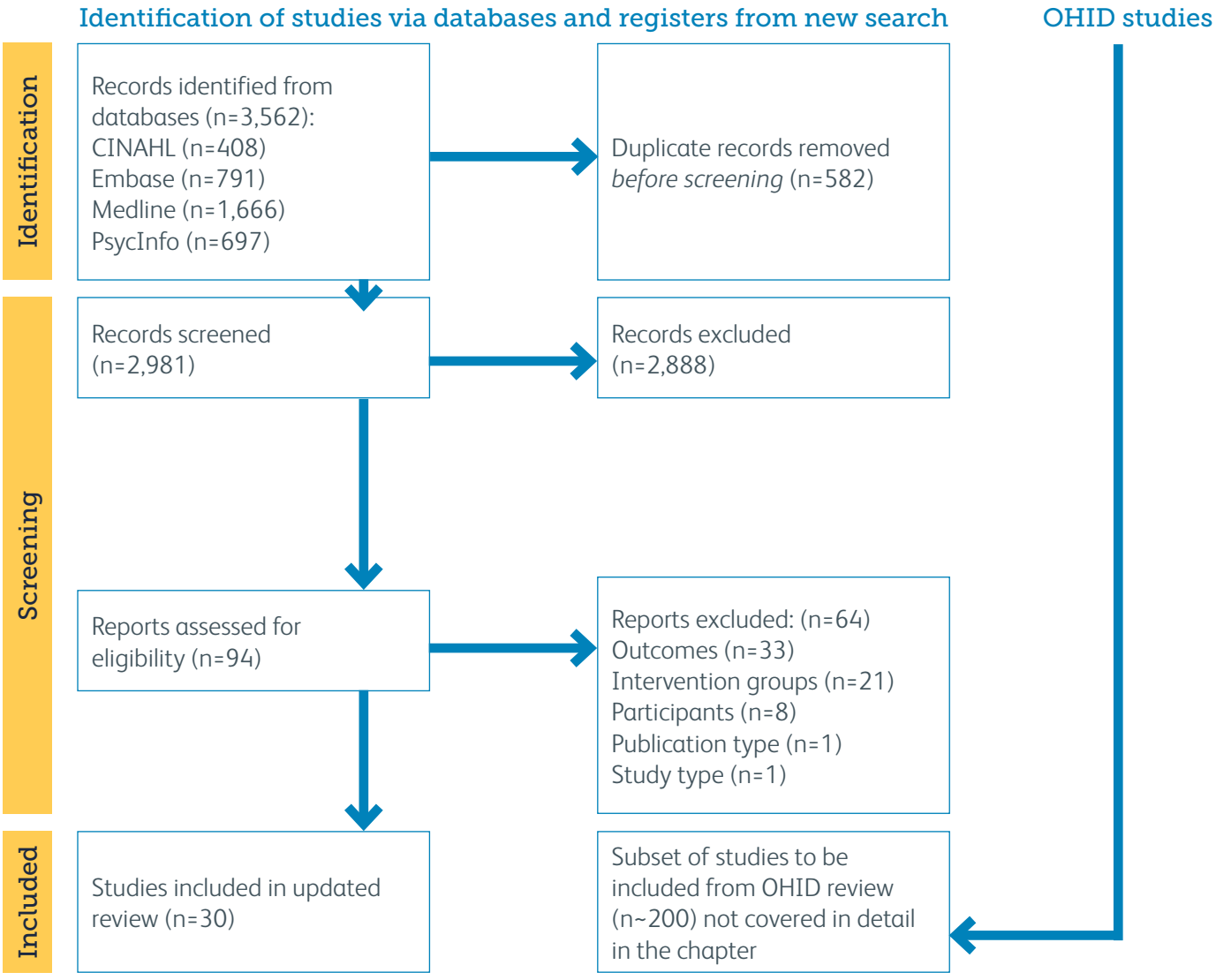


**Fig A1.1 Prisma flowchart.**

OHID = Officer for Health Improvement and Disparities

Titles, abstracts, and reports were independently reviewed by at least two researchers. Data were extracted by one researcher with all studies checked by a second researcher.

## Meta-analyses

In McNeill *et al*,[1] due to methodological heterogeneity of the included studies, we developed an algorithm to assess whether we were able to conduct meta-analyses. In this review, we have adapted the algorithm to meet the revised eligibility criteria (Table A1.2).

**Table A1.2. Steps for selecting studies for meta-analysis comparing between-group differences in vapers, smokers and non-users**

| Filter step | Description |
|---|---|
| **1. Study design** | > Meta-analyse four different types of studies (RCTs, non-randomised longitudinal studies, cross-over, and cross-sectional studies) separately if there are at least two studies of the same study design reporting on a biomarker. |
| **2. Population samples** | > We pool together studies reporting on biomarker levels in similar population samples (eg adults, youth, pregnant women, people with COPD etc) |
| **3. Clear definition of baseline sample (or a sample if study is cross-sectional)** | > Exclude studies that only define vapers' groups as vaping less than weekly – less frequent vaping might underestimate exposure to most toxicants that have shorter half-life characteristics.<br>> Initial sample characteristics can serve as a comparison group – eg smokers at baseline who switch to vaping only as a cross-over condition. |
| **4. Clear definition of follow-up groups (for RCTs, cross-over studies and non-randomised longitudinal studies)** | > Exclude studies that only define vapers' groups as vaping less than weekly – less frequent vaping might underestimate exposure to most toxicants that have shorter half-life characteristics.<br>> The step is not relevant for cross-sectional studies. |
| **5. Adherence to study groups** | > For RCT, cross-over and non-randomised longitudinal ad libitum use studies, analysis of vapers or non-users' group at follow-ups should consider the possibility of them continuing to smoke. A study analysing follow-up outcomes should state that participants in vapers or non-users' groups were not smoking, either by self-report or by bio-verification.<br>> If some participants in vapers or non-users' groups are nonadherent at follow-up (ie were smoking), exclude studies that analyse vapers or non-users' follow-up results as uniform groups (similar to intention-to-treat analysis) and include studies that account for participant smoking and analyse follow-up groups as adherent and non-adherent participants (similar to per-protocol analysis).<br>> The step is not relevant for cross-sectional studies. |
| **6. Biomarker samples** | > Include biomarkers from the same biosamples only (eg saliva) and when using the same analysis methodology (eg ELISA). Biomarkers collected in urine must be creatinine-adjusted. |
| **7. Data provided for baseline and follow-ups in geometric or arithmetic means and 95% CI, SE, SEM or SD.** | > For meta-analysis, only data that can be log-transformed are required.[3] Exclude if data are reported in graphs, as a difference from baseline or as median values.<br>> If a study reported mean difference between groups in log scale, these results can be used in meta-analysis without log-transformation. |
| **8. Data source** | > Where multiple studies have been published using the same data set (eg PATH), the study with the largest sample size will be selected for meta-analysis. |

# References

1 McNeill A, Simonavičius S, Brose L *et al. Nicotine vaping in England: an evidence update including health risks and perceptions.* A report commissioned by the Office for Health Improvement and Disparities, 2022. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1107701/Nicotine-vaping-in-England-2022-report.pdf [Accessed 5 January 2024].
2 Agents classified by the IARC Monographs, Volumes 1–134. 2023. https://monographs.iarc.who.int/list-of-classifications [Accessed 5 January 2024].
3 Higgins JP, White IR, Anzures Cabrera J. Meta analysis of skewed data: combining results reported on log transformed or raw scales. *Stat Med* 2008;27:6072–92.

# Appendix 2: Tables to support the systematic review

**Table A2.2. Algorithm for selecting studies for meta-analysis comparing differences between vaping, smoking, dual use and non-use groups**

| Filter step | Description |
|---|---|
| 1. Study design | > Meta-analyse four different types of studies (RCTs, non-randomised longitudinal studies, cross-over and cross-sectional studies) separately if there are at least two studies of the same study design reporting on a biomarker. |
| 2. Population samples | > We pool together studies reporting on biomarker levels in similar population samples (eg adults, youth, pregnant women, people with COPD etc) |
| 3. Clear definition of baseline sample (or a sample if study is cross-sectional) | > Exclude studies that only define vapers' groups as vaping less than weekly—less frequent vaping might underestimate exposure to most toxicants that have shorter half-life characteristics. Initial sample characteristics can serve as a comparison group – eg smokers at baseline who switch to vaping only as a cross-over condition. |
| 4. Clear definition of follow-up groups (for RCTs, cross-over studies and non-randomised longitudinal studies) | > Exclude studies that only define vapers' groups as vaping less than weekly – less frequent vaping might underestimate exposure to most toxicants that have shorter half-life characteristics.<br>> The step is not relevant for cross-sectional studies. |
| 5. Adherence to study groups | > For RCT, cross-over and non-randomised longitudinal ad libitum use studies, analysis of vapers or non-users' group at follow-ups should consider the possibility of them continuing to smoke. A study analysing follow-up outcomes should state that participants in vapers or non-users' groups were not smoking, either by self-report or by bio-verification.<br>> If some participants in vapers or non-users' groups are non adherent at follow-up (ie were smoking), exclude studies that analyse vapers or non-users' follow-up results as uniform groups (similar to intention-to-treat analysis) and include studies that account for participant smoking and analyse follow-up groups as adherent and non-adherent participants (similar to per-protocol analysis).<br>> The step is not relevant for cross-sectional studies. |
| 6. Biomarker samples | > Include biomarkers from the same biosamples only (eg saliva) and when using the same analysis methodology (eg ELISA). Biomarkers collected in urine must be creatinine-adjusted. |
| 7. Data provided for baseline and follow-ups in geometric or arithmetic means and 95 % CI, SE, SEM or SD | > For meta-analysis, only data that can be log-transformed are required.[1] Exclude if data are reported in graphs, as a difference from baseline or as median values.<br>> If a study reported mean difference between groups in log scale, these results can be used in meta-analysis without log-transformation. |
| 8. Data source | > Where multiple studies have been published using the same dataset (eg PATH), the study with the largest sample size will be selected for meta-analysis. |

**Table A2.3. Longitudinal studies reporting on nicotine exposure**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Group at baseline (n) | Biosample | % change at last follow-up (n) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Smoking | Vaping | Dual use | Non-use |
| Anic 2022,[2] USA[X] | PATH cohort 2013–15 | 12 months follow up Current use every day or some days | Smokers (n=1,899) | Urine | ↑5.9% (1479) | **↑72.1%*** (28) | ↑11.2% (204) | **↓85.7%*** (188) |
| | | | Dual users (n=576) | Urine | **↓19.8%*** (273) | ↑9.1% (30) | ↑10.9% (242) | ↓68.9% (31) |
| Dai 2022,[3] USA[X] | PATH cohort 2013–15 | 12 months follow up Current use every day or some days | Smokers (n=2,356) | Urine | ↑9% (1820) | ↑68% (32) | ↑13% (257) | ↓68% (247) |
| | | | Dual users (n=645) | Urine | ↓14% (315) | ↑3% (36) | ↑3% (252) | ↓54% (42) |
| | | | Vapers (n=210) | Urine | ↓6% (14) | ↑40% (121) | ↑69% (31) | ↓44% (44) |

**Note:** Statistically significant change from baseline noted with * for p<0.05.
[X] Although both studies assessed PATH cohort data from waves 1 and 2 (2013–15), we included both as they explored different user groups at baseline.

**Table A2.4. Cross-sectional studies reporting on nicotine exposure**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Biosample | Geometric means (95% CI), unless specified | | | |
|---|---|---|---|---|---|---|---|
| | | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Addicott 2022,[4] USA | Cross-sectional; Dates NR | 18–35-year-olds At least once/week past 30 days (n=24 daily) Vaping (n=16) Dual use (n=14) | Urine | | Mean (SD) 6.7 (6.7) | Mean (SD) 7.6 (13.4) | |
| | | | Blood plasma | | Mean (SD) 2 (2.8) | Mean (SD) 2.7 (4.1) | |
| Amalia 2023,[5] Australia | June-September 2019 | Adults Daily vaping ≥1 month Never use or non-use for >1 month | Urine | | 67.52 (10.82-421.3)[bd] (n=12, 1<LOQ) | | 0.63 (0.48-0.82)[bd] (n=11, 3<LOQ) |
| | | | Saliva | | 63.76 (15.28-266.01)[bd] (n=29, 1<LOQ) | | 0.28 (0.14-0.59)[bd] (n=21,19<LOQ) |
| Feng 2022,[6] USA | PATH cohort; cross-sectional data from wave 1 (2013-2014) | Daily vapers (no duration given) (n=148) Daily cigarette smokers (>100 lifetime cigs) (n=2021) Dual users (current daily user of combustibles, SLT, and/or vapes & intermittent use of >=1 other category) (n=1963) | Urine | 1451 (1325–1590) | 785 (620–993) | 1230 (1151–1314) | Not reported |
| Mohammadi 2022,[7] USA | Dates NR | Vaping (n=42, >5 times/ week for mean 1.7±0.7 years)) Cigarettes -exclusive (n=28, smoking >5 times a week for a mean of 10.2±10.4 years) Non-users (n=50, < 1 pack year and never users or quit 5+ years ago) | Urine | 1659 (2408.9)[ad] | 1135.1 (1314.8)[bd] | | 7 (7.71)[abd] |

**Note:** LOQ: limit of quantification; NR: not reported. Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.5. Longitudinal studies reporting on cotinine levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Group at baseline | Biosample | % change at follow-up (n) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Smoking | Vaping | Dual use | Non-use |
| Anic 2022,[2] USA[X] | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | Smokers (n=1,899) | Urine | ↓1.90% (1479) | **↓66.90%**** (28) | ↓12.10% (204) | **↓97.10%***** (188) |
| | | | Dual users (n=576) | | ↓3.80% (273) | ↓44.30% (30) | ↑8.80% (242) | **↓98.8%***** (31) |
| Dai 2022,[3] USA[X] | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | Smokers (n=2356) | Urine | 0% (1820) | **↓61.11%*** (32) | ↓17.81% (257) | **↓96.97%**** (247) |
| | | | Dual users (n=645) | | ↓2.31% (315) | **↓57.29%*** (36) | ↑6.13% (252) | **↓97.32%**** (42) |
| | | | Vapers (n=210) | | **↑286.87%**** (14) | ↓35.39% (121) | **↑164.37%*** (31) | ↓84.91% (44) |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.
[X] Although both studies assessed PATH cohort data from waves 1 and 2 (2013–15), we included both as they explored different user groups at baseline.

**Table A2.6. Repeated cross-sectional studies reporting on cotinine levels**

| Repeat cross-sectional waves and trend data | | | Comparison groups | Biosample | Smoking group[a] | Vaping group[b] | Dual use groups | Non-use group |
|---|---|---|---|---|---|---|---|---|
| Dai 2022,[8] USA | Cohort (PATH) 2013–19 | Current use every day or some days (vaping products with nicotine) Linear trend data | 2013/14 (W1) 2014/15 (W2) 2015/16 (W3) 2016/18 (W4) 2018/19 (W5) | Urine | ↑14.39% (4077 W1[ab] 3295 W2[ab] 3291 W3[ab] 3067 W4 2663 W5) | **↑99.8%**** (238 W1[ab] 235 W2[ab] 237 W3[ab] 232 W4 298 W5) | - | - |

**Note:** Statistically significant differences noted with * for p<0.05, ** for p<0.01, *** for p<0.001 (linear trend findings). Superscript letters ([a,b]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.7. Cross-sectional studies reporting on cotinine levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Biosample | Geometric means (95% CI), unless specified | | | |
|---|---|---|---|---|---|---|---|
| | | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Amalia 2023,[5] Spain | 2019 | Adults Daily vaping ≥1 month Never use or non-use for >1 month Vaping (n=12 urine, n=28 saliva), Non-use (n=11 urine, n=21 saliva) | Urine | - | 96.93 (12.49–752.07)[d] | - | 0.33 (0.19–0.57)[b] |
| | | | Saliva | - | 33.54 (10.01–112.34)[d] | - | 0 (0.00–0.12)[b] |
| Feng 2022,[6] USA | PATH wave 1, 2013–2014 | Daily vaping (no duration given, n=152); Daily smoking (>100 lifetime cigs, n=2,037); Dual use (current daily use of combustibles, SLT, and/or vapes, and intermittent use of ≥1 other category, n=1,987); Never use (n=1,541) | Urine | 3063 (2876–3263) | 1691 (1217–2351) | 2894 (2729–3070) | 0.42 (0.36–0.49) |

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Biosample | Geometric means (95% CI), unless specified | | | |
|---|---|---|---|---|---|---|---|
| | | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Melero-Ollenarte 2023,[9] Spain | 2013-14 (smokers)-2017–18 (vapers) | Vaping with nicotine (n=158), Smoking (n=154), Dual use (n=92), Non-use (n=409) | Saliva (ng/mL) | 150.61 (GSD 9.3) | 13.15 (GSD 50.2) | 137.1 (GSD 6.13) | 0.12 (GSD 2.45) |
| Payton 2022,[10] USA | 2014–17 | Healthy adults 18–50 yrs Vaping (n=17), Smoking (n=13), Non-use (n=14) | Blood (pg/mL) | 181.4 (range 57.2 –593.6)[b,d] | 129 (range 0–288.8)[a,d] | - | 0 (range 0)[a,b] |
| Sosnoff 2022,[11] USA | PATH wave 1, 2013–14 | Vaping (n=104), Smoking (n=1,380), Non-use (n=1271) | Blood (ng/mL) | 198 (181–218)[b] | 102 (70–149)[a] | - | 0.033 (0.028–0.037) |
| | | | | | Mean (SD) | | |
| Addicott 2022,[4] USA | Dates NR | 18–35-year-olds At least once/week past 30 days (n=24 daily) Vaping (n=16) Dual use (n=14) | Urine | - | 25.7 (18.2) | 22.7 (17.6) | - |
| | | | Blood (plasma) | - | 189.3 (134.2) | 182.5 (92.5) | - |
| Amraotkar 2023,[12] USA | Dates NR | Vaping (n=19), Dual (n=28), Smoking (n=212) | Urine (mg/dL) | 854 (763) | 826 (994) | 910 (777) | 3 (3) |
| Chaffee 2022, [13] USA | 2019–20 | HS students (mean age 15.2) Exclusive past 30-day vaping (n=234), Exclusive other tobacco use (n=26), Non-use (n=1078) | Saliva | 5.57 (19.65) | 13.15 (50.24) | - | 0.51 (7.71) |
| Hickman 2022,[14] USA | Dates NR | Daily vaping (no tobacco in 3+ months), 3rd gen. vapes (n=25)[1] or 4th gen. vapes (n=12)[2]. Smoking (n=20), Non-use (n=21) | Blood (ng/ml) | 188 (87.5)[d] | 1) 143 (82.2)[d] 2) 110 (90.5)[d] | - | 0 (0)[a,b1,b2] |
| Mohammadi 2022,[7] USA | Dates NR | Vaping (n=42, >5 times/week for mean 1.7±0.7 years), Smoking (n=28, >5 times a week for a mean of 10.2±10.4 years), Non-use (n=50, <1 pack year and never-users or quit 5+ years ago) | Urine | 1735 (1367)[d] | 923 (965)[d] | - | 2 (0.84)[a,b] |
| | | | | | Median (IQR), *unless specified* | | |
| Lee 2022,[15] South Korea | 2014–18 | 2014: current vaping (n=8), daily smoking (n=747), dual use(n=47), non-use (n=2,714) | Urine | 1291.4 (779.7–1870.8) | 760.4 (57.7–11750) | 1473.9 (973.3–2015.6) | 1.03 (0.62–1.82) |
| | | 2018: current vaping (n=13), daily smoking (n=782), dual use (n=124), non-use (n=4,223) | | 1422 (820.0–1948.0) | 712 (0.43–1528.0) | 1540 (870.0–2176.0) | 0.46 (0.78–1.08) |
| Pamungkasningsih 2021,[16] Indonesia | April–October 2018 | Vaping (n=34), Non-use (n=37) | Urine | - | 276.11 (range: 58.01–284.15[d] | - | 5.21 (range: 4.65–23.72)[b] |
| Tommasi 2021,[17] USA | Dates NR | Vaping (n=37), Smoking (n=22), Non-use (n=23) | Blood (plasma, ng/mL) | 121 (SE=11.2)[d] | 115 (SE=9.1)[d] | - | 2.5 (SE=0.1)[a,b] |

**Note.** Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.8. Longitudinal studies reporting on total nicotine equivalent (TNE) levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Group at baseline | Biosample and type of TNE | % change at follow-up (n) | | | |
|---|---|---|---|---|---|---|---|---|
| **Randomised controlled trials** | | | | | **Smoking** | **Vaping** | **Dual use** | **Non-use** |
| Edmiston 2022,[18] USA | RCT, January 2017–July 2018 | 24 weeks | Smoking | Urine; TNE6 mg/g creatinine | ↓11.61% (52) | ↑12.77% (98) | – | – |
| **Longitudinal studies** | | | | | | | | |
| Anic 2022,[2] USA[X] | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | Smoking | Urine; TNE2 µmol/g creatinine | ↓1.1% (1479) | **↓63.9%*** (28) | ↓8.9% (204) | **↓97%*** (188) |
| | | | Dual use | | ↓2.7% (273) | ↓43.1% (30) | ↑7.9% (242) | **↓98.6%*** (31) |
| Dai 2022,[3] USA[X] | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | Smoking | Urine; TNE2 nmol/mg creatinine | 0% (1820) | **↓59%**** (32) | ↓15% (257) | **↓97%***** (247) |
| | | | Dual use | | ↓3% (315) | **↓58%*** (36) | ↑7% (252) | **↓97%**** (42) |
| | | | Vaping | | **↑323%***** (14) | ↓34% (121) | **↑160%***** (31) | ↓84% (44) |
| Morris 2022,[19] USA | Open-label, two-part longitudinal study in confinement November 2019 – January 2020 | Healthy adults smoking ≥10 CPD for at ≥12 past months (urine cotinine ≥ 200 ng/mL, exhaled CO> 10 ppm). Switched to vaping exclusively for 14 days. | Site 1: smoking | Urine; TNE unspecified, mg/24 hours | – | 16.17% (14) | – | – |
| | | | Site 2: smoking | | – | 22.11% (11) | – | – |

**Note:** Statistically significant change from baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.
[X] Although both studies assessed PATH cohort data from waves 1 and 2 (2013–2015), we included both as they explored different user groups at baseline.

**Table A2.9. Repeated cross-sectional studies reporting on tobacco nicotine equivalent (TNE) levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Comparison groups | Biosample and type of TNE | Smoking | Vaping |
|---|---|---|---|---|---|---|
| Dai 2022,[8] USA | Cohort (PATH) 2013–19 | Current use every day or some days (vaping products with nicotine) Linear trend data | 2013/14 (W1)<br>2014/15 (W2)<br>2015/16 (W3)<br>2016/18 (W4)<br>2018/19 (W5) | Urine; TNE2 | ↑12.82% (44077 W1[ab]<br>3295 W2[ab]<br>3291 W3[ab]<br>3067 W4<br>2663 W5) | **↑98.18%**** (238 W1[ab]<br>235 W2[ab]<br>237 W3[ab]<br>232 W4<br>298 W5) |

**Note:** Statistically significant differences noted with * for p<0.05, ** for p<0.01 and *** for p<0.001 (linear trend findings). Superscript letters ([a,b]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.10. Cross-sectional studies reporting on tobacco nicotine equivalent (TNE) levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Biosample and type of TNE | Geometric mean (95% CI), unless specified | | | |
|---|---|---|---|---|---|---|---|
| | | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Mori 2022,[20] USA | 2015–19 | Healthy young adults (aged 21–30) 26 smoking (daily, >10 cpd for >6 months, no vaping for >1 year), 15 vaping (daily, for >1 year, no smoking for >6 months), 43 never-smokers (<100 lifetime cigarettes) | Urine; TNE2 nmol/mg creatinine | 19.5 (6.6–43.5)[d] | 15.2 (2.7–39.6)[d] | - | 0.003 (0.001–0.006) [ab] |
| Lizhnyak 2022,[21] USA | PATH wave 1, 2013–14 | Daily vaping, daily smoking, daily smoking and vaping, never-use | Urine; TNE7 | 10.66 (9,96,11.42) (n=2,411) | 5.68 (4.53,7.11) [bc] (n=164) | 10.98 (8.99, 13.41) [bc] (n=169) | 0.35 (0.15–0.78) (n=91) (>40% cases <LOQ) |
| Feng 2022,[6] USA | PATH wave 1, 2013–14 | Daily vaping (no duration given, n=152); Daily smoking (>100 lifetime cigs, n=2,037); Dual use (current daily use of combustibles, SLT, and/or vapes, and intermittent use of ≥1 other category, n=1,987); Never-use (n=1,541) | Urine; TNE2 µmol/g creatinine | 46.9 (43.8–50.3) (n=2,037) | 26.3 (19.2–36.1) (n=152) | 43.4 (40.9–46.1) (n=1,987) | 0.007 (0.006–0.008) (n=2,098) |
| | | | Urine; TNE3 µmol/g creatinine | 61.5 (58.2–65.0) (n=2,021) | 37.0 (30.2–45.3) (n=148) | 57.3 (54.4–60.4) (n=1,963) | - |

**Table A2.11. Longitudinal studies reporting on tobacco-specific nitrosamine (TSNA) levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Group at baseline | Biosample | NNAL % change at follow-up (n) | | | | NNN % change at follow-up (n) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Smoking | Vaping | Dual use | Non-use | Smoking | Vaping | Dual use | Non-use |
| Edmiston 2022,[18] USA | RCT, January 2017 – July 2018 | 24 weeks follow-up | Smoking | Urine | ↓25.4% (52) | ↓77.5%*** (98) | | | | | | |
| Morris 2022, [19] USA | Open-label, two-part longitudinal study in confinement November 2019 – January 2020 | 14 days follow-up | Site 1: smoking | Urine | | ↓71.8%*** (14) | | | | ↓92.0%*** (14) | | |
| | | | Site 2: smoking | Urine | | ↓75.7%*** (11) | | | | ↓89.2%*** (11) | | |
| Anic 2022,[2] USA[X] | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | Smoking | Urine | ↑0.5% (1479) | **↓92.8%***** (28) | **↓14.8%*** (204) | **↓85.0%***** (188) | ↓1.9% (1479) | **↓83.3%***** (28) | ↓13.4% (204) | **↓44.4%***** (188) |
| | | | Dual use | | ↓1.2% (273) | **↓95.4%***** (30) | ↓6.40% (242) | **↓90.5%***** (31) | ↓8.3% (273) | ↓25.1% (30) | 0.0% (242) | **↓60.5%***** (31) |
| Dai 2022,[3] USA[X] | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | Smoking | Urine | ↓1% (1820) | **↓92%**** (32) | ↓15% (257) | **↓84%**** (247) | ↓1% (1820) | ↓82% (32) | ↓14% (257) | ↓44% (247) |
| | | | Dual use | | ↓4% (315) | **↓96%**** (36) | ↓10% (252) | **↓89%**** (42) | ↓6% (315) | ↓28% (36) | 0.0% (252) | ↓52% (42) |
| | | | Vaping | | **↑367%**** (14) | ↓28% (121) | **↑327%**** (31) | ↓35% (44) | **↑42%**** (14) | ↑4% (121) | ↑42% (31) | ↓25% (44) |

**Note:** Statistically significant change from baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.
[X] Although both studies assessed PATH cohort data from waves 1 and 2 (2013–15), we included both as they explored different user groups at baseline.

**Table A2.12 Repeated cross-sectional studies reporting on tobacco-specific nitrosamine (TSNA) levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Comparison groups | Biosample | Smoking | Vaping |
|---|---|---|---|---|---|---|
| Dai 2022,[8] USA | Cohort (PATH) 2013–18 | Current use every day or some days (vaping products with nicotine) Linear trend data | 2013–14 (W1)<br>2014–15 (W2)<br>2015–16 (W3)<br>2016–18 (W4) | Urine<br>NNAL | ↑10.58 %<br>(4077 W1[ab]<br>3295 W2[ab]<br>3291 W3[ab]<br>3067 W4[ab]) | ↓19.05 %<br>(238 W1[ab]<br>235 W2[ab]<br>237 W3[ab]<br>232 W4[ab]) |

**Note.** Statistically significant differences noted with * for p<0.05, ** for p<0.01 and *** for p<0.001 (linear trend findings). Superscript letters ([a,b]) indicate user groups that were statistically significantly different from one another, p <0.05.

**Table A2.13 Cross-sectional studies reporting on tobacco-specific nitrosamine (TSNA) levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Biosample | NNAL geometric means (95%CI), unless specified | | | | NNN geometric means (95% CI), unless specified | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Amalia 2023,[5] Spain | June-September 2019 | Adults Daily vaping ≥1 month Never-use or non-use for >1 month | Urine | | 0.13 (0.01–1.76) (n=12; 9<LOQ) | | 0.23 (0.04–1.42) (n=11; 10<LOQ) | | 0.7 (0.31–1.59) (n=12; 11<LOQ) | | 0.65 (0.23–1.80) (n=11; 10<LOQ) |
| | | | Saliva | | 0 (0.0–0.68) (n=29; 26<LOQ) | | <LOQ (n=21) | | 0.39 (0.09–1.69) (n=29; 21 <LOQ) | | <LOQ (n=21) |
| Lizhnyak 2022,[21] USA | PATH wave 1, 2013–14 | Daily vaping, daily smoking, daily smoking and vaping, never use | Urine | 261.32 (240.16–284.34) (n=2437) | 6.5 (5.16–8.21)[bc] (n=169) | 270.27 (215.87–338.4)[bc] (n=169) | 0.96 (0.86–1.08) (n=1697) (>40 % cases <LOQ) | 14.79 (13.78–15.88) (n=2316) | 4.71 (3.95–5.6)[bc] (n=163) (>40 % cases <LOQ) | 12.74 (9.48–17.11)[bc] (n=161) | 1.98 (1.87–2.09) (n=1692) (>40 % cases <LOQ) |
| Melero-Ollenarte 2023,[9] Spain | 2013-14 (smokers) 2017–18 (vapers) | Vaping with nicotine (n=158), Smoking (n=154), Dual use (n=92), Non-use (n=409) | Saliva (ng/mL) | Mean (SD) = 1.09 (3.38) (n=140) | Mean (SD) = 0.29 (1.54) (n=157) | Mean (SD) = 0.44 (2.85) (n=91) | Mean (SD) = 0.26 (1.17) (n=400) | Mean (SD) = 7.31 (9.9) (n=153) | Mean (SD) = 1.38 (2.01) (n=158) | Mean (SD) = 3.15 (4.69) (n=92) | Mean (SD) = 0.61 (1.73) (n=420) |

**Note:** in Lizhnyak 2022, comparisons were only tested between the dual user group and other groups.

**Table A2.14 Longitudinal studies reporting on acrolein levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Group at baseline | % change (N) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Smoking | Vaping | Dual use | Non-use | Smoking | Vaping | Dual use | Non-use |
| | | | | 3HPMA (HPMA)* | | | | CEMA | | | |
| Anic 2022,[2] USA | Cohort, (PATH) 2013–15 | 12 months follow-up Current use every day or some days | Smoking | **↑15.5**%*** (1479) | **↓71.7**%*** (28) | ↑8.60% (204) | **↓44.9**%*** (188) | 0% (1479) | **↓55.8**%** (28) | ↑4.6% (204) | **↓36.5**%*** (188) |
| | | | Dual use | ↑2.3% (273) | **↓66.5**%*** (30) | **↑11.8%*** (242) | **↓45.2**%* (31) | ↓7.8% (273) | **↓57.3**%*** (30) | ↑1.4% (242) | **↓35.9**%** (31) |
| Dai 2022,[3] USA | Cohort, (PATH) 2013–15 | 12 months follow-up Current use every day or some days | Smoking | ↑18% (1820) | ↓73% (32) | ↑8% (257) | ↓46% (247) | ↑1% (1820) | **↓57%**** (32) | ↑1% (257) | ↓38% (247) |
| | | | Dual use | ↑1% (315) | ↓67% (36) | ↑13% (252) | ↓41% (42) | ↓8% (315) | **↓62%**** (36) | 0% (252) | ↓44% (42) |
| | | | Vaping | ↑175% (14) | ↓4% (121) | ↑163% (31) | ↑9% (44) | ↑61% (14) | ↓6% (121) | **↑83**%* (31) | ↓10% (44) |
| Morris *et al* 2022,[19] USA | Open-label, two-part longitudinal study in confinement November 2019 – January 2020 | Healthy adults smoking ≥10 CPD for at ≥12 past months (urine cotinine ≥ 200 ng/mL, exhaled CO> 10 ppm). Switched to vaping exclusively for 14 days. | Site 1 – Smoking | - | **↓85.92%***** (14) | - | - | - | **↓86.28%***** (14) | - | - |
| | | | Site 2 – Smoking | - | **↓68.73%***** (11) | - | - | - | **↓85.44%***** (11) | - | - |

**Note:** Dai 2022 reports HPMA levels, no comparisons provided.

**Table A2.15. Cross-sectional studies reporting on acrolein levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Acrolein metabolite | Geometric means (95% CI) | | | |
|---|---|---|---|---|---|---|---|
| | | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Lizhnyak 2022,[21] USA | Daily smoking, daily vaping, never use | Adults, Vaping (n=138), dual use (n=160), smoking (n=2,322), non-use (n=1,613) | 3-HPMA | 1353.71 (1268–1445.22) | 351.71 (301.86-409.79)[c] | 1223.92 (1058.14-1415.68)[b] | 275.23 (259.89-291.47) |
| | | Vaping (n=130), dual use (n=153), smoking (n=2,207), non-use (n=1,557) | CEMA | 308.54 (292.23–325.76) | 117.93 (102.63–135.51)[c] | 274.96 (238.85–316.54)[b] | 99.76 (95.35–104.37) |

**Note:** In Lizhnyak 2022, comparisons were only tested between the dual user group and other groups. Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.16. Longitudinal studies reporting on 1,3-butadiene levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Group at baseline | % change (n) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Smoking | Vaping | Dual use | Non-use | Smoking | Vaping | Dual use | Non-use |
| | | | | DHBMA | | | | MHBMA3 | | | |
| Anic 2022,[2] USA | Cohort, (PATH) 2013–15 | 12 months follow-up Current use every day or some days | Smoking | ↑0.1% (1479) | ↓9% (28) | ↑6.2% (204) | **↓17.4%**** (188) | **↑11.7%**** (1479) | **↓77.4% **** (28) | ↑4.8% (204) | **↓53.7%*** (188) |
| | | | Dual use | ↓4.9% (273) | **↓25.1%***** (30) | ↑0.8% (242) | ↓9.7% (31) | ↓4.3% (273) | **↓85.0%*** (30) | ↑6.2% (242) | **↓57.2%** (31) |
| Dai 2022,[3] USA | Cohort, (PATH) 2013–15 | 12 months follow-up Current use every day or some days | Smoking | ↑1% (1820) | ↓6% (32) | ↑4% (257) | ↓17% (247) | ↑10% (1820) | ↓80% (32) | ↑3% (257) | ↓56% (247) |
| | | | Dual use | ↓7% (315) | ↓25% (36) | ↑1% (252) | ↓10% (42) | ↓3% (315) | ↓84% (36) | ↑8% (252) | ↓47% (42) |
| | | | Vaping | ↑11% (14) | ↓4% (121) | ↑14% (31) | ↑3% (44) | ↑235% (14) | ↓2% (121) | ↑151% (31) | ↑7% (44) |
| Morris *et al* 2022,[19] USA | RCT Days 0–14 | Site 1 – Smoking at BL | | - | - | - | - | - | **↓84.63%*** (14) | - | - |
| | | Site 2 – Smoking at BL | | - | - | - | - | - | **↓60.44%** (11) | - | - |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.
Dai 2022 reports DHBM and MHB3 levels, no comparisons provided.

**Table A2.17. Cross-sectional studies reporting on 1,3-butadiene levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | 1,3-butadiene metabolite | Geometric means (95% CI) | | | |
|---|---|---|---|---|---|---|---|
| | | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Lizhnyak 2022,[21] USA | Daily smoking, daily vaping, never use | Adults, Vaping (n=142), dual use (n=160), smoking (n=2,357), non-use (n=1,509) | MHB3 (MHBMA3) | 33.36 (31.61, 35.21) | 4.35 (3.87, 4.9)[c] | 27.65 (23.73, 32.22)[b] | 4.62 (4.41, 4.83) |

**Note:** In Lizhnyak 2022, comparisons were only tested between the dual user group and other groups. Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.18. Longitudinal studies reporting on acrylamide levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Group at baseline | % change (n) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Smoking | Vaping | Dual use | Non-use | Smoking | Vaping | Dual use | Non-use |
| | | | | AAMA | | | | GAMA | | | |
| Anic 2022,[2] USA | Cohort, (PATH) 2013-2015 | 12 months follow-up Current use every day or some days | Smoking | ↓1% (1479) | **↓48.4%**** (28) | ↓6.2% (204) | **↓32.9%**** (188) | ↑3.1% (1479) | **↓41.3%**** (28) | ↑3% (204) | **↓15.6%**** (188) |
| | | | Dual use | ↓4.9% (273) | **↓25.1%**** (30) | ↓0.8% (242) | ↓9.7% (31) | **↓9.7%*** (273) | **↓64.6%**** (30) | ↓4.9% (242) | **↓36.0%**** (31) |
| Dai 2022,[3] USA | Cohort, (PATH) 2013-2015 | 12 months follow-up Current use every day or some days | Smoking | 0% (1820) | **↓46%**** (32) | ↓8% (257) | ↓34% (247) | ↑3% (1820) | ↓39% (32) | ↑3% (257) | ↓15% (247) |
| | | | Dual use | ↓8% (315) | **↓63%**** (36) | ↓4% (252) | ↓26% (42) | 0% (315) | ↓26% (36) | ↑3% (252) | 0% (42) |
| | | | Vaping | **↑51%**** (14) | ↓9% (121) | **↑96%**** (31) | ↓18% (44) | ↑26% (14) | ↑5% (121) | ↑23% (31) | ↑9% (44) |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.
Dai 2022 did not provide comparisons for GAMA levels.

**Table A2.19. Cross-sectional studies reporting on acrylamide levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Acrylamide metabolites | Geometric means (95% CI) | | | |
|---|---|---|---|---|---|---|---|
| | | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Lizhnyak 2022,[21] USA | Daily smoking, daily vaping, never use | Adults, vaping (n=142), dual use (n=158), smoking (n=2,334), non-use (n=1,605) | AAMA | 148.72 (143.12–154.53) | 58.65[c] (51.18–67.21) | 137.14[b] (123.16–152.73) | 48.57 (46.17–51.1) |

**Note:** In Lizhnyak 2022, comparisons were only tested between the dual user group and other groups. Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.20. Longitudinal studies reporting on benzene levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Benzene metabolite | Group at baseline | % change (n) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Smoking | Vaping | Dual use | Non-use |
| Anic 2022,[2] USA | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | PhMA | Smokers | ↓10.9% (1479) | ↓21.9% (28) | ↓18.2% (204) | **↓7.3%*** (188) |
| | | | | Dual users | ↓13.2% (273) | ↓10.8% (30) | 0% (242) | ↓9.2% (31) |
| Dai 2022,[3] USA | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | S-PMA | Smokers | ↓9% (1820) | ↓15% (32) | ↓15% (257) | ↓1% (247) |
| | | | | Dual users | ↓11% (315) | ↑8% (36) | ↓1% (252) | ↓1% (42) |
| | | | | Vapers | ↓55% (14) | ↓8% (121) | ↑19% (31) | ↓36% (44) |
| Morris 2022,[19] USA | Open-label, two-part study in confinement November 2019 – January 2020 | 14 days | S-PMA | Site 1 | - | **↓94.74***** (14) | - | - |
| | | | | Site 2 | - | **↓92.32***** (11) | - | - |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.

**Table A2.21. Longitudinal studies reporting on ethylene oxide levels**

| Study | Design, data collection dates | Participants, exposure length, frequency of use | Ethylene oxide | Group at baseline | % change (n) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Smoking | Vaping | Dual use | Non-use |
| Anic 2022,[2] USA | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | 2HEMA | Smokers | ↑4.3% (1479) | **↓65.7%***** (28) | ↓10.8% (204) | **↓45.7%***** (188) |
| | | | | Dual users | ↓0.6% (273) | **↓57.1%***** (30) | ↑1.4% (242) | **↓42.6%**** (31) |
| Dai 2022,[3] USA | Cohort (PATH) 2013–15 | 12 months follow up Current use every day or some days | HEMA | Smokers | ↑5% (1820) | ↓66% (32) | ↓12% (257) | ↓38% (247) |
| | | | | Dual users | ↓3% (315) | ↓60% (36) | ↑4% (252) | ↓32% (42) |
| | | | | Vapers | ↑74% (14) | ↑4% (121) | ↑101% (31) | ↓29% (44) |
| Morris 2022,[19] USA | Open-label, two-part study in confinementNovember 2019 – January 2020 | 14 days | HEMA | Site 1 | - | **↓70.47***** (14) | - | - |
| | | | | Site 2 | - | **↓46.00**** (11) | - | - |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.

**Table A2.22. Longitudinal studies reporting on cadmium exposure**

| Study | Follow-up and frequency of use | Participants' group at baseline | Participants' group and % (*n*) change at follow-up | | | |
|---|---|---|---|---|---|---|
| | | | Smoking | Vaping | Dual use | Non-use |
| Anic 2022,[2] USA | 12 months; use every day or some days | Smoking at baseline | ↑6.7% (1479) | 0% (28) | 0% (204) | 0% (188) |
| | | Dual use at baseline | **↑10.7%*** (273) | ↑20.7% (30) | ↑10.7% (242) | 0% (31) |
| Dai 2022,[3] USA | 12 months; use every day or some days | Smoking at baseline | ↑6% (1820) | ↑3% (32) | **↓1%*** (257) | **↑5%*** (247) |
| | | Dual use at baseline | ↑9% (315) | ↑19% (36) | ↓13% (252) | ↑6% (42) |
| | | Vaping at baseline | **↑15%*** (14) | ↑2% (121) | 0% (31) | ↑15% (44) |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.

**Table A2.23. Cross-sectional studies reporting on cadmium levels**

| Study | Use definitions | Participants and groups | Geometric means (95% CI) | | | |
|---|---|---|---|---|---|---|
| | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Amalia 2023,[5] Spain | Daily vaping ≥1 month, never use or non-use for >1 month | Adults; Vaping (n=12), Not vaping/smoking (n=11) | - | 0.05 (0.00–2.19) | - | 0.28 (0.12–0.66) |
| Lizhnyak 2022,[21] USA | Daily smoking, daily vaping, never use | Adults (PATH); Vaping (n=169), Dual use (n=169), Smoking (n=2,432), Non-use (n=1,697) | 0.31 (0.30–0.33) | 0.28 (0.25–0.30)[c] | 0.33 (0.29–0.37)[b] | 0.15 (0.14–0.16) |

**Note:** in Lizhnyak 2022, comparisons were only tested between the dual user group and other groups. Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.24. Longitudinal studies reporting on lead levels**

| Study | Follow-up and frequency of use | Participants' group at baseline | Participants' group and % (n) change at follow-up | | | |
|---|---|---|---|---|---|---|
| | | | Smoking | Vaping | Dual use | Non-use |
| Anic 2022,[2] USA | 12 months; use every day or some days | Smoking at baseline | 0% (1479) | ↑6.1% (28) | ↓7% (204) | ↓9.5% (188) |
| | | Dual use at baseline | ↓8% (273) | **↓24.6%* (30)** | ↑2% (242) | ↓10.2% (31) |
| Dai 2022,[3] USA | 12 months; use every day or some days | Smoking at baseline | 0% (1820) | ↑7% (107) | ↓7% (257) | ↓6% (247) |
| | | Dual use at baseline | ↓4% (315) | ↓6% (36) | ↑6% (252) | ↑3% (42) |
| | | Vaping at baseline | **↓24%**** (14) | ↓9% (121) | ↑6% (31) | 0% (44) |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.

**Table A2.25. Cross-sectional studies reporting on lead levels**

| Study | Use definitions | Participants and groups | Geometric means (95% CI) | | | |
|---|---|---|---|---|---|---|
| | | | Smoking[a] | Vaping[b] | Dual use[c] | Non-use[d] |
| Amalia 2023,[5] Spain | Daily vaping ≥1 month, never use or non-use for >1 month | Adults Vaping (n=12), Not vaping/smoking (n=11) | - | 0.48 (0.31–0.74) | - | 0.40 (0.13–1.20) |
| Lizhnyak 2022,[21] USA | Daily smoking, daily vaping, never use | Adults (PATH) Vaping (n=169), Dual use (n=169), Smoking (n=2,432), Non-use (n=1,697) | 0.50 (0.48–0.52) | 0.54 (0.47–0.62) | 0.57 (0.49–0.67) | 0.35 (0.33–0.37) |

**Note:** In Lizhnyak 2022, comparisons were only tested between the dual user group and other groups. Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.26. Longitudinal studies reporting on arsenic levels**

| Study | Follow-up and frequency of use | Participants' group at baseline | Participants' group and % (*n*) change at follow-up | | | |
|---|---|---|---|---|---|---|
| | | | Smoking | Vaping | Dual use | Non-use |
| Dai 2022,[3] USA | 12 months; use every day or some days | Smoking at baseline | ↓7% (1820) | ↓14% (32) | ↓14% (257) | ↓10% (247) |
| | | Dual use at baseline | ↓13% (315) | ↓6% (36) | ↓1% (252) | ↑4% (42) |
| | | Vaping at baseline | ↓27% (14) | ↓15% (121) | ↓11% (31) | ↓28% (44) |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.

**Table A2.27. Cross-sectional studies reporting on arsenic levels**

| Study | Use definitions | Participants and groups | Geometric means (95% CI) | | | |
|---|---|---|---|---|---|---|
| | | | Smoking | Vaping | Dual use | Non-use |
| Amalia 2023,[5] Spain | Daily vaping ≥1 month, never use or non-use for >1 month | Adults; Vaping (n=12), Not vaping/smoking (n=11) | - | 44.75 (28.13–71.18) | - | 48.95 (24.54–97.65) |

**Note:** Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.28. Cross-sectional studies reporting on lead levels**

| Study | Use definitions | Participants and groups | Geometric means (95% CI) | | | |
|---|---|---|---|---|---|---|
| | | | Smoking | Vaping | Dual use | Non-use |
| Amalia 2023,[5] Spain | Daily vaping ≥1 month, never use or non-use for >1 month | Adults; Vaping (n=12), Not vaping/smoking (n=11) | - | 0.92 (0.45–1.87) | - | 2.07 (1.23–3.49) |

**Note:** Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.29. Longitudinal study reporting on benzo[a]pyrene (BaP) levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Group at baseline | Biosample | % change at last follow-up (n) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Smoking | Vaping | Dual use | Non-use |
| Morris 2022,[19] USA | Open-label, two-part study in confinement November 2019 – January 2020 | 14-day follow up | Site 1 – Smoking | Urine | | **↓87%**** (14) | | |
| | | | Site 2 – Smoking | Urine | | **↓79.8%***** (11) | | |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.

**Table A2.30. Longitudinal studies reporting on hydroxypyrene levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Group at baseline | Biosample | % change at last follow-up (n) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | Smoking | Vaping | Dual use | Non-use |
| Anic 2022,[2] USA | PATH cohort 2013–15 | 12 months follow-up Current use every day or some days | Smokers | Urine | ↑3.5% (1479) | **↓55.2%*** ** (28) | ↓4.7% (204) | **↓15.2%** ** (188) |
| | | | Dual users | Urine | ↓5.2% (273) | **↓48.6%*** ** (30) | ↑1.3% (242) | **↓33.9%** * (31) |
| Dai 2022,[3] USA | PATH cohort 2013–15 | 12 months follow-up Current use every day or some days | Smokers | Urine | ↑5% (1820) | **↓53%** ** (32) | ↓5% (257) | **↓10%*** ** (247) |
| | | | Dual users | Urine | ↓6% (315) | **↓51%** ** (36) | ↑3% (252) | ↓31% (42) |
| | | | Vapers | Urine | ↑63% (14) | ↓7% (121) | **↑47%** ** (31) | ↓20% (44) |
| Morris 2022 [19], USA | Open-label, two-part study in confinement November 2019–January 2020 | 14 day follow up | Site 1 – Smoking | Urine | | **↓84%*** ** (14) | | |
| | | | Site 2 – Smoking | Urine | | **↓69.2%*** ** (11) | | |

**Note:** Statistically significant change compared with baseline noted with * for p<0.05, ** for p<0.01 and *** for p<0.001.

**Table A2.31. Cross-sectional study reporting on hydroxypyrene levels**

| Study, year, country | Design, data collection dates | Participants, exposure length, frequency of use | Biosample | Geometric means (95%CI) | | | |
|---|---|---|---|---|---|---|---|
| | | | | Smoking[a] | Vaping[b] | Dual use[c] | Non use[d] |
| Lizhnyak 2022,[21] USA | Daily smoking, daily vaping, never use | Adults, vaping (n=169), dual use (n=169), smoking (n=2440), non-use (n=1700) | Urine | 331.76 (315.89–348.43) | 164.24 (141.91–190.09)[c] | 319.79 (284.51–359. 44)[b] | 129.84 (122.06–138.11) |

**Note:** In Lizhnyak 2022, comparisons were only tested between the dual user group and other groups. Superscript letters ([a,b,c,d]) indicate user groups that were statistically significantly different from one another, p<0.05.

**Table A2.32. Studies reporting on biomarkers of potential harm levels**

| Author, year of publication, country | Study characteristics | Participants' characteristics | Study findings |
|---|---|---|---|
| **Randomised controlled trials (RCT)** | | | |
| Edmiston *et al* 2022,[18] USA | RCT of adult smokers (n=450) randomised to:<br>1) Smoking (n=150 for 12 weeks; n=52 for 24 weeks);<br>2) Vaping cartridge-type e-cigarette (tobacco flavoured, 4% nicotine; n=150 for 12 weeks; n=50 for 24 weeks)<br>3) Vaping cartridge-type e-cigarette (menthol flavoured, 4% nicotine; n=150 for 12 weeks; n=50 for 24 weeks)<br>Follow-ups: 12 and 24-weeks<br>Biosample: blood plasma, blood serum. | n=450; smokers of >10 cigarettes per day for ≥10 years; compliance to vaping confirmed biochemically by exhaled CO<8ppm and <10% of baseline CPD at follow-up. | **High-density lipoprotein cholesterol (HDL)**<br>Week 12: ↑5.6% (tobacco), ↑6.1% (menthol), NS diff.<br>Week 24: ↑9.3% (tobacco), ↑7.3% (menthol), NS diff.<br><br>**sICAM1**<br>Week 12: ↓11.4%** (tobacco), ↓11.3%*** (menthol).<br>Week 24: ↓10.7%*** (tobacco), ↓9.9%** (menthol).<br><br>**White blood cells (WBC)**<br>Week 12: ↓9.1%*** (tobacco), ↓5.2%* (menthol).<br>Week 24: ↓8.8%*** (tobacco), ↓10.2%*** (menthol). |

| Author, year of publication, country | Study characteristics | Participants' characteristics | Study findings |
|---|---|---|---|
| Kim *et al* 2022,[22] USA | RCT of adult veteran smokers (n=21) randomised to:<br>1) Smoking (n=7) 2) Vaping 2nd generation e-cigarette (eVic Supreme; flavour-free, 12 mg/mL freebase nicotine; n=7);<br>3) Quitting smoking/non-use with NRT/varenicline (n=7)<br>Follow-up: 12 weeks.<br>Biosample: nasal epithelial cells and nasal epithelial lining fluid. | n=21 current active smokers with ≥5 pack-years smoking history; compliance to vaping confirmed biochemically by exhaled CO <6ppm and venous COHb<1.6% at follow-up. | **Tumour necrosis factor alpha (TNF-α)**<br>Week 12: NS change within vapers and smokers' groups (ps>0.05), stat sig reduction in quitting smoking/non-use group (p<0.05). |
| **Cross-sectional studies** | | | |
| Hickman *et al* 2022[14] and Payton *et al* 2022,[10] USA | Healthy adults (n=103) between 18 and 50 years old recruited in 2014–18.<br>Biosamples: nasal lavage fluid, epithelial lining fluid, induced sputum and blood serum. | Groups:<br>1) Smoking (n=21): self-reported active smokers.<br>2) Vaping (n=54): self-reported current daily vaping (10-20 puffs per day) for >6 past months without other use of tobacco, and <10 pack-year smoking history. In Hickman *et al*[14] split into<br>2.1) 3rd generation e-cigarette users (n=27; primary use of vape pens or box mods with freebase nicotine);<br>2.2) 4th generation e-cigarette users (n=27; primary use of Juul or other low-powered e-cigarettes that contain nicotine salts).<br>3) Non-users (n=28): not regularly exposed to second-hand smoke. | **Interleukin 1 beta (IL-1b)**<br>NS diff (p=0.18) between smoking, vaping (both subgroups) and non-use.<br><br>**Interleukin 6 (IL-6)**<br>Stat sig higher in smokers than non-users (p<0.01). NS diff between vaping (both subgroups) compared with smoking or non-use.<br><br>**Interleukin 8 (IL-8)**<br>NS diff (p=0.45) between smoking, vaping (both subgroups) and non-use.<br><br>**C-reactive protein (CRP)**<br>Stat sig lower in 4th generation e-cigarette users than non-users (p<0.05) or 3rd generation e-cigarette users (p<0.01).<br>NS diff between smokers, 3rd generation e-cigarette users and non-users.<br><br>**sICAM1**<br>Stat sig lower in 4th generation e-cigarette users than non-users (p<0.05) or 3rd generation e-cigarette users (p<0.0001).<br>NS diff. between smokers, 3rd generation e-cigarette users and non-users.<br><br>**Tumour necrosis factor alpha (TNF-α)**<br>NS diff between vaping and non-use, and smoking and non-use across all four biosamples. |

| Author, year of publication, country | Study characteristics | Participants' characteristics | Study findings |
|---|---|---|---|
| Christensen *et al*, 2021[23] and Lizhnyak *et al*, 2022,[21] USA | Healthy youth and adults (ages 12+ years) from a longitudinal PATH cohort wave 1 recruited in 2013–14.<br>Biosamples: urine (n=11,522) and blood (n=7,159).<br>Sample sizes: Christensen *et al*, 2021 (n=3,712); Lizhnyak *et al*, 2022 (n=8,628). | Christensen et al., 2021 groups:<br>1) Smoking (n=1891): daily or non-daily smoking and smoked >100 cigarettes in lifetime<br>2) Vaping (n=145): daily or non-daily exclusive vaping; (people who formerly smoked)<br>3) Dual use (n=596); daily or non-daily vaping and smoking<br>4) Never users (n=982) of any tobacco/ nicotine product<br>5) Former smokers (n=98): quit smoking >30 days but <4 years ago. (no current use of e-cigarettes or other 'tobacco' products)<br><br>Lizhnyak et al., 2022 groups:<br>1) Smoking ($n_{urine}$=2442, $n_{blood}$=1608): daily exclusive smoking;<br>2) Frequent dual use ($n_{urine}$=169, $n_{blood}$=117): smoking and vaping on ≥20 days per month;<br>3) Vaping ($n_{urine}$=169, $n_{blood}$=115): exclusive daily vaping;<br>4) Non-use ($n_{urine}$=1700, $n_{blood}$=986): never used tobacco or nicotine product. | **Interleukin 6 (IL-6)**<br>Stat sig ↓16% in vaping compared with smoking. NS diff. between vaping and never-use.<br>Stat sig ↑15% in dual use compared with never-use. NS diff between dual use and smoking. NS diff between frequent dual use and vaping.<br><br>**C-reactive protein (CRP)**<br>Stat sig ↓27% in vaping compared with smoking. NS diff between vaping and never use.<br>NS diff in frequent dual use compared with vaping. NS diff between dual use and smoking or never use.<br><br>**sICAM1**<br>Stat sig ↓18% in vaping compared with smoking. NS diff. between vaping and never use.<br>Stat sig ↑30% in dual use compared with vaping (p<0.003).<br>Stat sig ↑29% in frequent dual use compared with never use. NS diff. between dual use and smoking.<br><br>**Fibrinogen**<br>NS diff between vaping and smoking or never use.<br>NS diff in vaping compared with frequent dual use.<br>Stat sig ↑5% in dual use compared with never-use. NS diff between dual use and smoking.<br><br>**F2 isoprostane**<br>Stat sig ↓25% in vaping compared with smoking. NS diff between vaping and never use.<br>Stat sig ↑57% in dual use compared with never-use, and ↑9% in dual use compared with smoking. |
| Kamal *et al* 2022,[24] Egypt | Healthy student volunteers (n=150; mean age 28–29) recruited in 2020–21.<br>Biosample: unstimulated whole saliva. | Groups:<br>1) Smoking (n=50): self-reported daily smoking of ≥5 cigarettes a day for >1 year.<br>2) Vaping (n=50): self-reported exclusive vaping for >1 year and never smoked.<br>3) Non-use (n=50): never smoked. | **Interleukin 1 beta (IL-1b)**<br>Stat sig higher in smoking compared with vaping (p<0.001) or non-use (p<0.001).<br>Stat sig higher in vaping compared with non-use (p<0.001). |
| Wang *et al* 2022,[25] USA | Repeated cross-sectional survey (NHANES) of about 10,000 participants every 2 years. Participants for this study (N=17180) were recruited in 2013-2018.<br>Biosample: blood. | Groups:<br>1) Smoking (n=6792): smoked ≥100 cigarettes in life and was not vaping in the last 5 days.<br>2) Vaping (n=52): did not smoke ≥100 cigarettes in life and was vaping in the last 5 days.<br>3) Dual use (n=249): smoked ≥100 cigarettes in life and was vaping in the last 5 days.<br>4) Not smoking (n=10,087): did not smoke ≥100 cigarettes in life. | **White blood cells (WBC)**<br>Stat sig lower WBC level in not smoking compared with vaping (p<0.001). NS diff between vaping and dual use or smoking. |

| Author, year of publication, country | Study characteristics | Participants' characteristics | Study findings |
|---|---|---|---|
| Podzolkov *et al* 2021,[26] Russia | Healthy young adults (n=369; median age =21). Biosample: blood serum. | Groups:<br>1) Smoking (n=83): self-reported daily smoking for >12 months and no vaping history.<br>2) Vaping (n=90): self-reported vaping for >12 months and no smoking history.<br>3) Non-use (n=196): never-user of tobacco or nicotine products. | **C-reactive protein (CRP)**<br>Stat sig lower in non-use compared with smoking ($p<0.001$) or vaping ($p<0.001$). NS diff between smoking and vaping. |
| **Second-hand exposure** | | | |
| AlMubarak *et al* 2022,[27] Saudi Arabia | Young healthy adults (n=48; mean age 23–25 years) who did not use tobacco or nicotine products. Biosample: unstimulated whole saliva. | Groups:<br>1) Self-reported daily exposure of >5 minutes for >12 past months to vapour from e-cigarettes (n=24).<br>2) Never tobacco users who self-reported no exposure to tobacco or e-cigarette second-hand emissions (n=24). | **Interleukin 1 beta (IL-1b)**<br>Stat sig higher levels in those exposed compared with unexposed participants (26.2 (6.4) pg/mL vs 0.12 (0.005) pg/mL, $p<0.001$). IL-1b levels were also positively associated with the duration of exposure and daily frequency of exposure to second-hand e-cigarette aerosol. |

**Table A2.33. All suspected adverse reactions associated with e-cigarettes reported in the UK from January 2020 to August 2023**

| Reaction name | Number of reactions |
|---|---|
| Blood disorders | 1 |
| Cardiac disorders | 31 |
| Ear disorders | 4 |
| Endocrine disorders | 1 |
| Eye disorders | 9 |
| Gastrointestinal disorders | 122 |
| General disorders | 115 |
| Hepatic disorders | 1 |
| Immune system disorders | 24 |
| Infections | 20 |
| Injuries | 18 |
| Investigations | 9 |
| Metabolic disorders | 4 |
| Muscle and tissue disorders | 19 |
| Neoplasms | 1 |
| Nervous system disorders | 82 |
| Pregnancy conditions | 1 |
| Product label/physical/quality issues | 31 |
| Psychiatric disorders | 18 |
| Respiratory disorders | 411 |
| Skin disorders | 31 |
| Vascular disorders | 5 |
| Total reactions for drug | 958 |
| Total reports* | 347 |
| **Total fatal outcome reports** | **5 (2 cardiac, 3 respiratory)** |

**Note:** *The number of reports is lower than the total reactions because each report constitutes an individual for whom more than one adverse reaction could have been reported.

**Table A2.34. Summary of meta-analyses results from McNeill et al report[28] and the updated literature review**

| Biomarkers | Vaping vs smoking (relative risk) | Vaping vs non-use (absolute risk) | Vaping vs dual use |
|---|---|---|---|
| ↓ significantly lower, ↑ significantly higher, = no significant difference | | | |
| **Nicotine** | | | |
| *Nicotine* | = | ↑ | |
| *Cotinine* | = (urine)<br>↓ (blood) | ↑ | = |
| *Total nicotine equivalents* | = | ↑ | |
| 3-hydroxycotinine | = | ↑ | |
| Tobacco-specific nitrosamines | | | |
| *NNAL* | =<br>↓ | ↑ | |
| NAB | ↓ | ↑ | |
| NAT | ↓ | ↑ | |
| *NNN* | ↓ | | |
| **Volatile organic compounds** | | | |
| *Acrylamide* | = (longitudinal)<br>↓ (cross-sectional) | = | |
| *Acrolein* | ↓ (longitudinal)<br>= (cross-sectional) | | |
| Acrylonitrile | ↓ | ↑ | |
| *Benzene* | = | = | |
| *1,3-butadiene* | ↓ | = | |
| Crotonaldehyde | ↓ | = | |
| Toluene | = | = | |
| **Carbon monoxide (CO)** | | | |
| Expired air CO | ↓ | | |
| *COHb* | ↓ | | |
| *Metals* | | | |
| *Cadmium* | | ↑ | |
| *Lead* | | ↑ | |
| *Arsenic* | | = | |
| **Oxidative stress** | | | |
| *Low-density lipoprotein (LDL)* | | = | |
| *High-density lipoprotein (HDL)* | = | = | |
| **Inflammation** | | | |
| *C-reactive protein* | ↓ | = | |
| *Soluble intercellular adhesion molecule 1 (sI-CAM-1)* | ↓ | | |

**Note:** ↓ significantly lower, ↑ significantly higher, = no significant difference. Symbols in black note results from meta-analyses reported in the McNeill *et al* report[28] and symbols in colour note results from the current updated review with stricter inclusion criteria and added comparisons with people who both smoke and vape (dual use). Biomarkers in *italics* note biomarkers included in the updated review.

The updated literature review included studies published since July 2021, applied stricter inclusion criteria for definition of vaping (ie daily use for at least the past 8 days) and explored vaping-associated exposure to a narrower set of toxicants (Table A1.1) than in the McNeill *et al* report.[28] Following the algorithm for selecting studies for meta-analysis (Table A2.2), new data were used to update meta-analyses in the McNeill *et al* report[28] for biomarkers of nicotine, tobacco-specific nitrosamines and metals. Also, a new meta-analysis comparing exposure to cotinine between people who vaped exclusively and people who both vaped and smoked was conducted.

Results from the updated meta-analyses for exposure to nicotine and its metabolites did not differ from findings by McNeill *et al.*[28] Exposure to nicotine and its metabolites did not differ between people who vaped and people who smoked with one exception. Blood cotinine levels were found to be significantly lower in vaping than smoking groups while urinary cotinine levels did not differ between the two groups. Levels of blood cotinine better reflect recent exposure to nicotine while levels of urinary cotinine better reflect exposure over a longer period. These differences suggest that exposure to nicotine is lower from vaping than smoking over a short period and similar over a longer exposure. As expected, levels of nicotine and other metabolites were significantly higher among vaping than non-use groups. A comparison of urinary cotinine levels between vaping and dual use groups from five cross-sectional studies showed that cotinine levels were approximately 25% lower among people who vaped than those who vaped and smoked, but the difference was not statistically significant.

Regarding tobacco-specific nitrosamines, the updated meta-analysis included findings from two RCTs with longer follow-up periods which were not conducted in confinement. Results of the updated meta-analysis showed non-significantly lower levels of NNAL among people who vaped compared with people who smoked, which differ from the earlier finding that vaping groups were exposed to significantly lower NNAL levels than smoking groups. Nevertheless, the direction of both meta-analyses were similar, and the difference might be due to fewer participants in the updated meta-analysis (238 *vs* 313) and due to increased likelihood that participants in vaping groups could have been exposed to tobacco smoke over the longer follow-up periods.

Three new meta-analyses summarised data for absolute differences in exposure to cadmium, lead and arsenic between vaping and non-use groups. Data were mostly from wave 1 PATH survey (collected in 2013–14), indicating statistically lower urinary cadmium and lead levels in non-use than vaping groups, and similar urinary arsenic levels between the two groups. These findings were consistent with results of 10 studies that reported on exposure to metals in McNeill *et al* report.[28]

Other relative and absolute exposure comparisons from meta-analyses conducted in McNeill *et al*[28] are provided in Table A2.34.

**Table A2.35. Funding statements for studies included in the systematic review**

See Table 5.1 in chapter 5 for full reference information.

| Author/study | Funding, as reported in publications |
|---|---|
| Addicott *et al. Exp Clin Psychopharmacol* 2023;31:715–23. Epub 2022 Sep 15. | Medical Research Endowment Fund from University of Arkansas for Medical Sciences. National Institute of Health (NIH) Grant P30DA012393 |
| AlMubarak *et al. Oral Health Prev Dent* 2022;20:127–32. | Vice Deanship of Scientific Research Chairs, Research Chair for biological Research in Dental Health |
| Amalia *et al. Sci Total Environ* 2023;854:158668. | European Union's Horizon 2020 research and innovation programme under grant agreement No 681040. BA received the support of a fellowship from "La Caixa" Foundation (ID 100010434; Fellowship code: LCF/BQ/IN17/11620013). The Tobacco Control Research Group at ICO-IDIBELL (BA, EF, MF, OT, MB, YC) is partly supported by the Ministry of Universities and Research, Government of Catalonia (2017SGR319) and thanks CERCA Programme Generalitat de Catalunya for the institutional support to IDIBELL. The work of SG is partially supported by an Investigation Grant from the Foundation AIRC for the Research on Cancer (AIRC IG 2021, ID 25987). The Laboratory of Toxicology University of Granada (FG, PO) is funded by the Spanish National Research Agency and the European Regional Development Fund (FEDER; Project UNGR15-CE-3380) |
| Amraotkar *et al. Vasc Med* 2023;28:18–27. | In-part by the National Heart, Lung, and Blood Institute of the National Institutes of Health under Award Numbers U54HL120163 and P50HL120163 |
| Anic *et al. Int J Environ Res Public Health*2022;19:27. | Federal funds from the National Institute on Drug Abuse, National Institutes of Health, and the Center for Tobacco Products, Food and Drug Administration (FDA), Department of Health and Human Services, under contract to Westat (Contract Nos. HHSN271201100027C and HHSN271201600001C) and through an interagency agreement between the FDA Center for Tobacco Products and the Centers for Disease Control and Prevention |
| Chaffee *et al. Addict Behav* 2022;128:107235. | US National Institutes of Health (Grants U54HL147127, P30DA012393 and S10RR026437) |
| Christensen *et al. Cancer Epidemiol Biomarkers Pre* 2021;30:1947–55. | Federal funds from the National Institute on Drug Abuse, National Institutes of Health, and the Center for Tobacco Products, Food and Drug Administration, Department of Health and Human Services, under contract to Westat (Contract Nos. HHSN271201100027C and HHSN271201600001C), under contract to GenWay Biotech Inc. (Contract No. HHSF223201510013C), and through an interagency agreement between the FDA Center for Tobacco Products and the Centers for Disease Control and Prevention. Other authors are employed by the Food and Drug Administration, the Centers for Disease Control and Prevention, or the National Institutes of Health and have no other funding sources to report |
| Dai *et al. JAMA Netw Open* 2022;5:e2147891. | National Institute on Drug Abuse under Award Number 1R21DA054818 |
| Dai *et al. JAMA* 2022;328:1864–6. | 1R21DA054818 from the National Institute on Drug Abuse and award U54CA180905 from the National Cancer Institute |
| Edmiston *et al. Nicotine Tob Res* 2022;24:1047–54. | Altria Client Services LLC |
| Feng *et al. Nicotine Tob Res* 2022;24:768–77. | Federal funds from the National Institute on Drug Abuse, National Institutes of Health, and the Center for Tobacco Products, Food and Drug Administration, Department of Health and Human Services, under contracts to Westat (Contract Nos. HHSN271201100027C and HHSN271201600001C) and through an interagency agreement between the FDA Center for Tobacco Products and the Centers for Disease Control and Prevention |
| Hickman *et al. Am J Respir Crit Care Med* 2022;206(10):1248-58. | National Heart, Lung, and Blood Institute (F31 HL154758) and National Institute of Environmental Health Sciences (T32 ES007126) of the National Institutes of Health (NIH) (grants R01 HL139369 and P50 HL120100). This research was in part supported by the NIH and the U.S. Food and Drug Administration (FDA) Center for Tobacco Products (CTP). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or the FDA. Additional support was provided by the Institute for Environmental Health Solutions at the Gillings School of Global Public Health |
| Higham *et al. Eur Respir J* 2022;59:05. | A. Beech and D. Singh are supported by the National Institute for Health Research (NIHR) Manchester Biomedical Research Centre (BRC). This research was supported by the North West Lung Centre Charity, Manchester |
| Kamal & Shams. *Saudi Dent J* 2022;34:404-9. | Department of Oral Pathology, Faculty of Oral and Dental Medicine, Ahram Canadian University, Egypt |

| Author/study | Funding, as reported in publications |
|---|---|
| Kim et al. *ERJ Open Res* 2022;8:00117-2022. | NIH/NHLBI (R01 HL139365 to M. Salathe), the James and Esther King Florida Biomedical Research Program (grant number 5JK02 to M. Salathe and M. Campos), and the Flight Attendant Medical Research Institute (CIA 160011 to M. Salathe). A portion of this work was also supported by the NIH/NIDA (R01 DA046576 to N. Nollen), Frontiers: The Heartland Institute for Clinical and Translational Research which is supported by a CTSA grant to the University of Kansas Medical Center from the NIH National Center for Advancing Translational Science (grant number UL1TR000001), and by the National Cancer Institute Cancer Center Support Grant P30 CA168524 and used the Clinical Pharmacology and Biospecimen Repository Shared Resources. J.S. Ahluwalia was supported in part by P20GM130414, a NIH-funded Center of Biomedical Research Excellence |
| Lee *et al. Intern J Environ Res Public Health* 2022;19:29. | Wonkwang University, Korea |
| Lizhnyak *et al. Harm Reduct J* 2022;19:90. | Altria Client Services LLC |
| Melero-Ollonarte *et al. Addict Behav* 2023;140:107616. | Partially funded by the Instituto de Salud Carlos III, Subdireccion ´ General de Evaluacion, ´ Government of Spain (PI12/ 01114, PI12/01119, PI15/0029, PI15/00434), co-funded by ISCIIISubdireccion ´ General de Evaluacion ´ and by FEDER funds/European Regional Development Fund (ERDF) –a way to build Europe-. The Group of Evaluation of Health Determinants and Health Policies (HPM, CLM, AGM, JCMS, JMMS) receives support from the Ministry of Universities and Research, Government of Catalonia (grant 2021SGR00186). The Tobacco Control Research Group (MF, MB, JMMS, EF) receives support from the Ministry of Universities and Research, Government of Catalonia (grant 2021SGR00906) from the Government of Catalonia. EF is partly supported by the Instituto de Salud Carlos III, Government of Spain, co-funded by the European Regional Development Fund (FEDER; INT16/00211 and INT17/00103) |
| Mohammadi *et al. ArteriosclerThromb Vasc Biol* 2022;42:1333–50. | Grants U54HL147127, P50HL120163, and R01HL120062 from the National Heart, Lung, and Blood Institute at the National Institutes of Health (NIH/NHLBI) and the US Food and Drug Administration Center for Tobacco Products (FDA CTP); and grant P50CA180890 from the National Cancer Institute at the NIH and FDA CTP. L. Mohammadi was supported by a postdoctoral fellowship from the American Heart Association (19POST34380462) and by a generous gift from the Elfenworks Foundation in memory of Deb O'Keefe. The UCSF Flow Core facility (RRID:SCR_018206) is supported in part by the DRC Center Grant NIH P30DK063720 |
| Mori *et al. E BioMedicine* 2022;85:104301. | The National Cancer Institute, the National Heart, Lung, and Blood Institute, the Food and Drug Administration Center for Tobacco Products, the National Center For Advancing Translational Sciences, and Pelotonia Intramural Research Funds |
| Morris *et al. Intern Emerg Med* 2022; 17:397–410. | Fontem US LLC, a subsidiary of Imperial Brands PLC |
| Payton *et al. Am J Physiol Lung Cell Mol Physiol* 2022;322:L722–36. | National Institutes of Health (NIH) Grants T32 ES007126, P50 HL120100, and P30ES010126. This work was funded by NIH Grant P50 HL120100. Research reported in this publication was in part supported by NIH and US Food and Drug Administration Center for Tobacco Products (CTP). Support was also provided through the University of North Carolina (UNC) Institute for Environmental Health Solutions (IEHS) |
| Podzolkov *et al.* Ration Pharmacother Cardiol 2021;17:521–27. | Sechenov University, Russia |
| Reeve *et al. J Oral Maxillofac Surg* 2021;79:e95. | National Institute of Dental and Craniofacial Research |
| Richmond *et al. Clin Epigenetics* 2021;13:183. | Cancer Research UK Population Research Committee project grant (C57854/A22171). Further support was provided by the UK Medical Research Council (MC_UU_00011/5 and MC_ UU_00011/7), which funds a Unit at the University of Bristol where R.C.R., C.S.R., J.K., C.P., G.S., M.S., C.L.R and M.M. work, and the CRUK-funded Integrative Cancer Epidemiology Programme (C18281/A19169). R.C.R is a de Pass Vice Chancellor's Research Fellow at the University of Bristol. C.S.R's time is supported by the National Institute for Health Research Applied Research Collaboration West (NIHR ARC West) at University Hospitals Bristol NHS Foundation Trust. C.P. is supported by a Wellcome Trust PhD studentship in Molecular, Genetic and Lifecourse Epidemiology (108902/B/15/Z). The UK Medical Research Council and Wellcome (Grant ref: 102215/2/13/2) and the University of Bristol provide core support for ALSPAC |

| Author/study | Funding, as reported in publications |
|---|---|
| Pamungkasningsih *et al. Eurasian J Med* 2021;53:68–73. | The authors declared that this study has received no financial support. Authors affiliations - Department of Pulmonolgy and Respiratory Medicine, Universitas Indonesia School of Medicine, Jakarta, Indonesia; Persahabatan Central General Hospital, Jakarta, Indonesia 2 Dr. H.A. Rotinsulu Lung Hospital, Bandung, Indonesia |
| Sosnoff *et al. Nicotine Tob Res* 2022;24: 736–44. | National Institute on Drug Abuse at the National Institutes of Health and the Center for Tobacco Products at the U.S. Food and Drug Administration (FDA), under a contract to Westat (Contract No. HHSN271201100027C and HHSN271201600001C) and through an interagency agreement between the FDA Center for Tobacco Products and the CDC |
| Tommasi *et al. Sci Rep* 2021;11:22773. | National Cancer Institute of the National Institutes of Health (1R21CA268197) and the University of California Tobacco-Related Disease Research Program (28IR-0060 and T31IR1839) to AB. The bioinformatics sofware and computing resources used in the analysis are funded by the USC Office of Research and the Norris Medical Library |
| Tommasi *et al. Nicotine Tob Res* 2023;25:1145–54. | National Cancer Institute and National Institute of Dental and Craniofacial Research of the National Institutes of Health (1R21CA268197 and 1R01DE026043, resp.), and the University of California Tobacco-Related Disease Research Program (T31IR1839, and T32IR5144) |
| Wang *et al. Environ Sci Pollut Res Int* 2022;29:88531–9. | Not reported |

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