Teenagers are being sold banned vaping devices containing up to 3,500 puffs, investigation shows

Mary O'connor ⋮⋮ 6/2/2023

- **It's illegal to sell vapes containing nicotine to under-18s, but some shops do**
- **Sold devices more than five times legal size giving young users up to 3,500 puffs**
- READ MORE: Top-selling vape stripped from shelves over illegal nicotine level

By Mary O'connor

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Schoolchildren are buying illegal supersize vapes over the counter from local corner shops, a Mail investigation has found.

It is illegal to sell vapes containing nicotine to under-18s, but in some parts of the country many shops sell the devices to youngsters for around £5 – with no questions asked.

Some stores sell devices that are more than five times the legal size, giving young users up to 3,500 puffs instead of the legal limit of between 600 and 800.

Authorities are trying to seize these products amid fears the craze could see children become addicted to nicotine and be at greater risk of chronic lung conditions.

The Mail visited 30 corner shops and phone stores with Trading Standards officers last month.

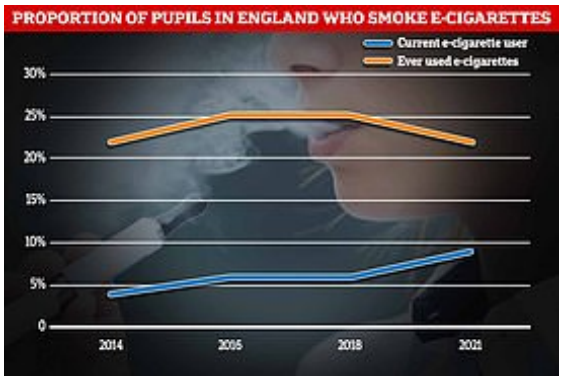
Schoolchildren are buying illegal supersize vapes over the counter from local corner shops, a Mail investigation has found

In Newcastle, for example, two male volunteers age 16 and 17 were sold vapes in ten of 15 shops visited.

Four shops sold the teens banned Elux Legend 3,500 puff vapes – the equivalent nicotine content of nearly 120 cigarettes.

The packaging of vapes sold during the undercover exercise had nicotine warnings and symbols showing they must not be sold to under-18s.

Vaping epidemic sees one in ten teenagers hooked - TRIPLE rate of kids who smoke tobacco: Surge in teen girls using e-cigs fuels 'deeply disturbing' rise as experts call for £5 gadgets to be sold in plain packaging - READ MORE



When one shop was raided by Trading Standards, officers found large packs of the Happy Vibes vapes on display as well as a black duffle bag containing illegal cigarettes and supersized vapes hidden beneath the counter.

The seller told officers he did not have the right to work in the UK and was an Iraqi migrant staying at a local asylum hotel.

A woman who claimed to be his girlfriend said she worked in the shop and had asked him to keep an eye on the counter while she went for a coffee.

The 10 shops in Newcastle that sold vapes to the children are not facing legal action but will be subject to monitoring by Trading Standards.

Paul Leighton, senior Trading Standards officer at Newcastle City Council, said reports of illegal vapes sales and underage sales had 'exploded' in the area.

'A lot of independent businesses seem to have recognised the popularity of these vapes among young people and others, and they are just cashing in.'

He said some shops selling banned vapes use stealth tactics to avoid detection, including concealing them in floors, fridges and even behind fake boiler covers.

Others hide them in cars outside and bring them in when customers request them.

A London-based teacher later told the Mail how increasing numbers of students are being excluded for vaping in school, and lambasted local shops for selling to children in school uniforms.

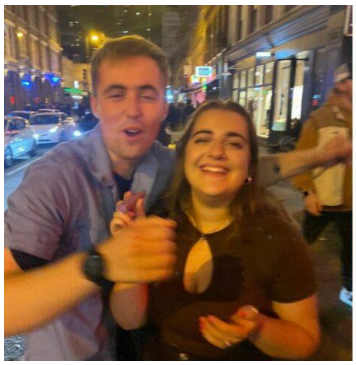
Meanwhile, one teenager told the Mail how their peers hide vapes in toilet tanks, underneath toilet brushes and in toilet block ceilings to conceal the habit.

John Herriman, chief executive of the Chartered Trading Standards Institute (CTSI), a membership body for Trading Standards officers, said: 'We very much welcome this investigation by the Daily Mail, particularly because this helps to highlight the mounting concerns our profession have about the sale and supply of illicit vapes and to those underage – this is something which Trading Standards teams across the country are now sadly finding on a regular basis.'

thetab.com /uk/2022/12/22/18000-of-you-took-part-these-are-the-uk-unis-that-are-most-hooked-to-elf-bars-287153

18,000 of you took part, these are the UK unis that are most hooked on Elf Bars

22/12/2022




Oxford Brookes students can't go more than five minutes without a hit of Blue Razz Lemonade

2 months ago | UPDATED 1 month ago


Pieter Snepvangers

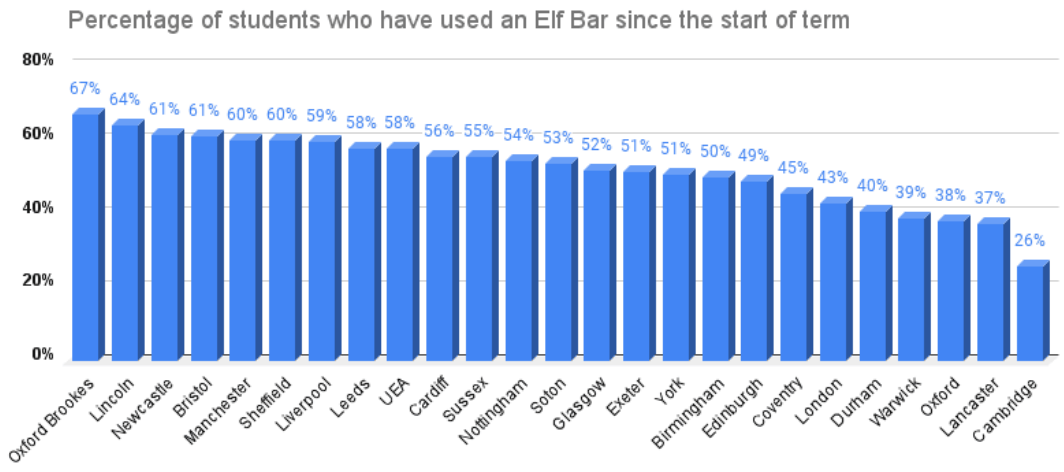
Over a quarter of UK university students say they are addicted to Elf Bars, an investigation by The Tab has found.

27 per cent of student admitted **being addicted to the disposable vapes** whilst **more than half of students (53 per cent) have used an Elf Bar since the start of term in September.**

The data also suggests the proportion of students using Elf Bars who have never previously smoked is far higher than previously thought among e-cigarette research.

The study, the first of its kind to measure the popularity of Elf Bars among university students, **surveyed more than 18,000 students across 25 universities via individual university Tab Instagram accounts**. **Figures were only recorded from a university if there were at least 100 respondents to the question asked.**

The findings present **the most up to date picture** of the extent the brightly coloured disposable vapes have taken over campuses across the country.



Oxford Brookes had the largest proportion of students **who have used an Elf Bar** this year. **67 per cent said they have used one since September**. This was followed by Lincoln (64 per cent), Newcastle (61 per cent), Bristol (61 per cent) and Manchester (60 per cent). Of the 25 universities surveyed, a majority of students had used an Elf Bar in 15 universities.

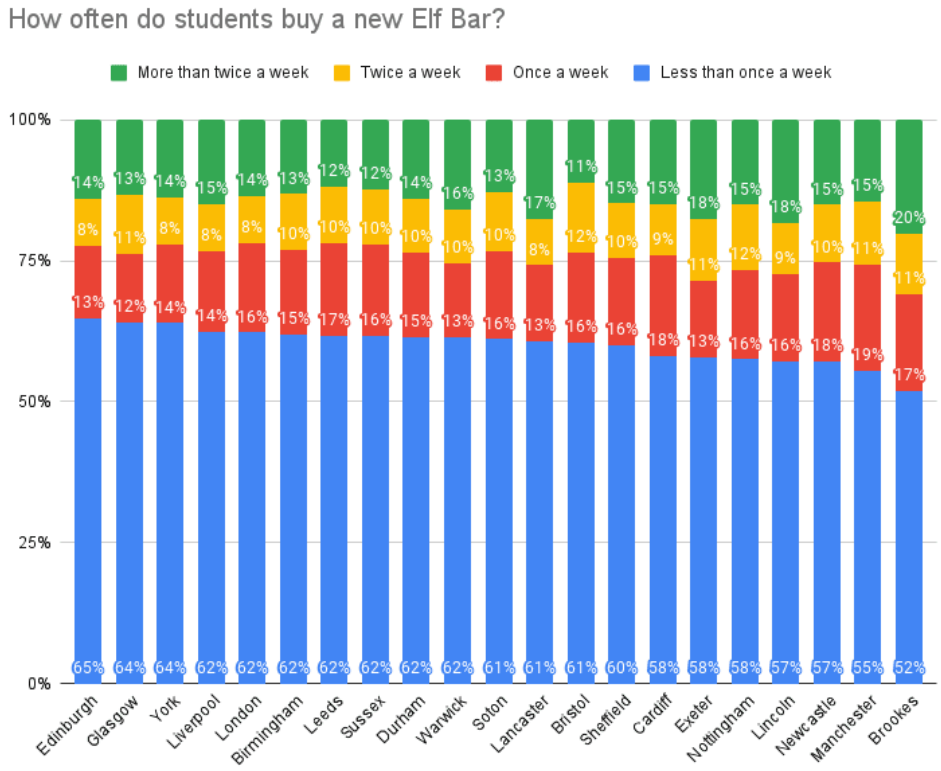
At the other end of the scale, Oxbridge students aren't convinced. A modest 38 per cent had used an Elf Bar in Oxford and it was even lower at 26 per cent in Cambridge. Clearly full of Oxbridge rejects, Durham equally scored low on Elf Bar usage, with a similar **40 per cent having used them.**

Elf Bars are the joint-strongest disposable vape you can buy in the UK, meeting the legal limit of 20mg/ml of high-strength nicotine salts e-liquid. Each bar contains the nicotine dosage of 48 cigarettes.

Well, read this:

https://www.dailymail.co.uk/news/article-11716721/Teenagers-sold-banned-vaping-devices-containing-3-500-puffs-investigation-shows.html

The Tab also surveyed just how quickly students are getting through their 48-cigarette nicotine dosage. For the majority of students, it appears they are casual users. 60 per cent said they bought a new Elf Bar "less than once a week". There was little variation in this figure between universities but was highest in Edinburgh, Glasgow, York, Liverpool and London (UCL).



15 per cent of students who use Elf Bars say they buy them weekly, 10 per cent buy them twice a week and 15 per cent buy more than two a week. This means a quarter of student users are buying a minimum of the nicotine dosage of 96 cigarettes each week.

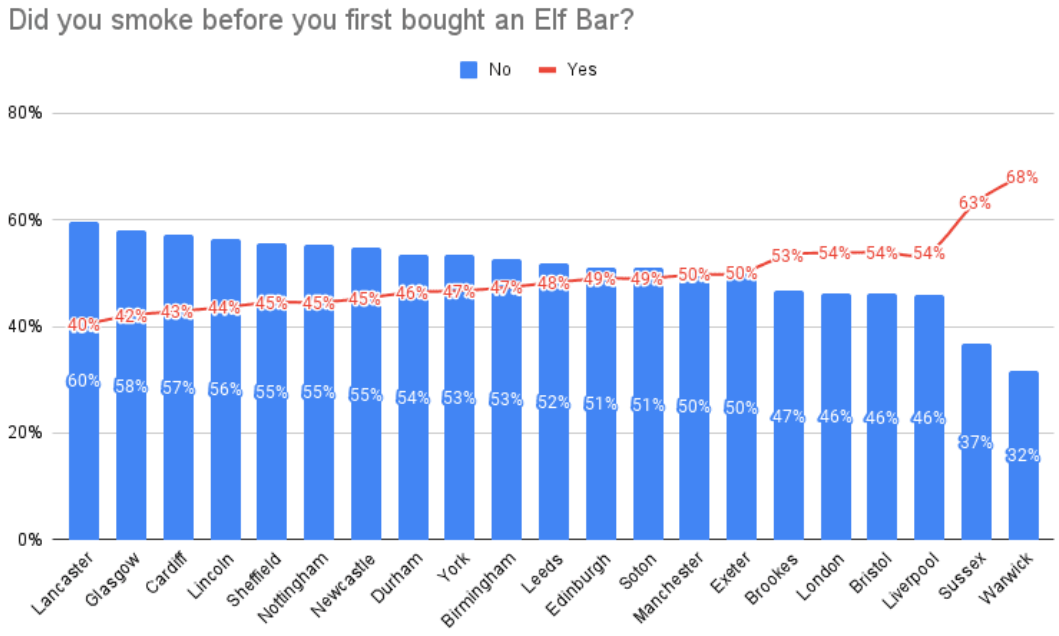
It is important to stress an Elf Bar does not cause the same damage as 48 cigarettes. Public Health England has found e-cigarettes to be 95 per cent less harmful for your health than smoking. (***this is piffle and disproved = UK whitecoats deliberately misled the public***)

https://tobacco.ucsf.edu/e-cig-emperor-naked-%E2%80%93-or-very-least-95-naked

However, when polling more than 8,500 students who say they use Elf Bars, The Tab found 51 per cent said they did not previously smoke cigarettes.

CHART:

DID YOU SMOKE BEFORE YOU FIRST BOUGHT AN ELF BAR?

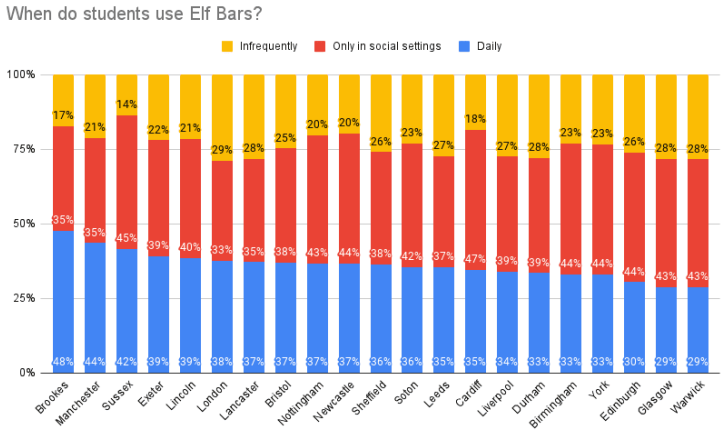


This was highest in Lancaster (60 per cent), Glasgow (58 per cent), Cardiff (57 per cent), Lincoln (56 per cent) and Sheffield (55 per cent).

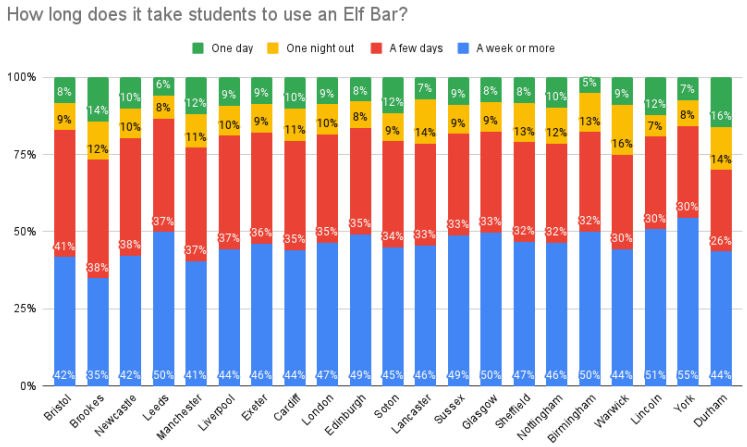
A previous **study by ASH (Action on Smoking and Health**) found whilst the proportion of never smokers now vaping is the highest it's ever been**, the public health charity found it to be only 8.1 per cent.**

Dr **Lion Shahab**, professor of health psychology at University College London and co-director of UCL's Tobacco and Alcohol Research Group told The Tab: "I would have assumed that something like 80 per cent would have been previously smokers and maybe 20 per cent who weren't. So that is something that jumped out at me and is ***somewhat concerning*** because as you can imagine the argument in the tobacco control community is that e-cigarettes are a harm reduction product and harm reduction for existing smokers."

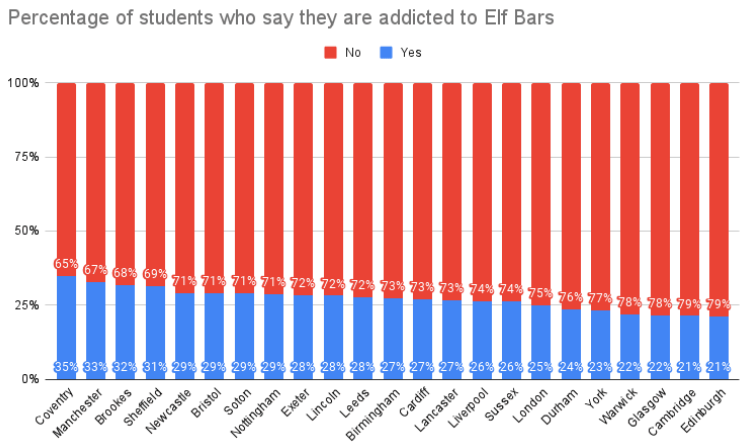
41 per cent of students said they only used their Elf Bar in social settings compared to 36 per cent who admitted to using theirs daily and 23 per cent who said infrequently.



There is a clear divide between the social users and the daily users. 45 per cent of students said an Elf Bar would last them for a week or longer. But an equally sizeable 35 per cent said they would finish and Elf Bar in a few days. A combined 20 per cent use an entire Elf Bar in a day or on one night out (10 per cent each respectively).



Despite the majority of students saying they've used an Elf Bar this term, the figure who admit to being addicted is far lower, measuring nationally at 27 per cent**. In Coventry and Manchester, over a third of students said they were addicted to Elf Bars but for Durham, York, Warwick, Glasgow, Cambridge and Edinburgh, this figure was below 25 per cent.**



Dr Shahab said: "To some degree, **it doesn't surprise me** that increasingly quite a lot of students might be using [Elf Bars] **but what does surprise me though, is that a lot of them obviously have never smoked.**

"Up until the introduction of these new disposable devices, I would have thought we were striking the right balance. Use was very low among young people and mainly restricted to smokers.

"However, in this context, with the huge proliferation of use among never smoking students, I do think that that we may have to pivot a bit in terms of our approach to how we deal with this." *Elf Bar has been approached for comment.*

THE TAB INVESTIGATION TARGETTED THE UK UNIVERSITY STUDENT USE OF ELF BAR DISPOSABLE LITHIUM POWERED VAPES – HOW MANY UNI STUDENTS USED ANY FORM OF E-CIGARETTE , JUUL, VUSE OR WHATEVER? SHOULD BE THEIR NEXT PROJECT ADDRESSED TO THEIR TARGET AUDIENCE.

THE EVIDENCE TENDS TO SHOW THAT THE AUGUST 2022 REPORT PROVIDED BY ASH LONDON CONCERNING THE LEVEL OF YOUTH-ADULT USAGE OF ENDS PRODUCTS AND THE TYPE OF ENDS PRODUCT MOST USED IS PRIMA FACIE MASSIVELY FLAWED AND MISLEADING TO GOVERNMENT AND THE PUBLIC ALIKE.

THE GENIE IS OUT OF THE BOTTLE AND AN EPIDEMIC OF NICOTINE ADDICTION IS BEING INFLICTED ON UK YOUTH FOR PROFIT.

Use of e-cigarettes (vapes) among adults in Great Britain

August 2022

Summary of key findings

This factsheet analyses how behaviour and attitudes to e-cigarettes among adults aged 18 and over have changed over time. The data are taken from an annual survey, Smokefree GB, carried out for ASH by YouGov in Spring each year. The survey first started asking about e-cigarette use in 2010 and this update includes the results of the 2022 survey carried out in February and March 2022. The COVID-19 pandemic is likely to have affected e-cigarette use in 2021, but it is not yet clear whether any changes in attitudes or behaviour are permanent or substantial.

Note

Appendix 1 sets out the methodology in detail. Percentages in this report are given to the nearest whole number, or to one decimal place if under 10%. As a result, some sums may appear out by ±0.1 percentage points due to rounding error.

Set out below is a summary of the key findings.

USE AND AWARENESS OF E-CIGARETTES

- The proportion of the adult population using e-cigarettes has increased this year to 8.3%, the highest rate ever, amounting to 4.3 million people in Great Britain. (Table 1)
- Most current vapers are ex-smokers (57%). The proportion peaked in 2021 at 64%. (Figure 1)
- Only 1.3% of never smokers are current vapers, amounting to 8.1% of vapers. (Figure 1)
- The proportion of adult smokers who have never tried e-cigarettes is continuing to decline slowly, down to 28% in 2022.The proportion of smokers who are current vapers has increased from 2021 (17%) to 2022 (22%). (Figure 2).

ATTITUDES TOWARDS E-CIGARETTES

- As in previous years, the main reason given by ex-smokers for vaping is to help them quit (29%). The next most common reasons are to prevent relapse (19%), because they enjoy the experience (14%), and to save money (11%). (Figure 5)
- The main reason given by current smokers for vaping are to cut down on smoking (17%), to save money (16%), to try to help them quit (14%) and to prevent relapse (13%). (Figure 5)
- A third of smokers (32%) incorrectly believe vaping is more or equally as harmful as smoking. (Figure 9)

DEVICES AND PRODUCTS USED

- The most frequent type of e-cigarette device remains a refillable tank system, with 65% of current vapers reporting this type as their main device. (Figure 12). Vapes with replaceable cartridges and disposable vapes were the main type of device for 17% and 15% of vapers, respectively.
- However, use of disposable vapes has risen, particularly among younger adults. (Figure 13). Among 18-24

year olds, almost half of current e-cigarettes users (48%) use disposables as their main type in 2022, an increase from only 2.8% in 2021.

- For those who have tried vaping and used cartridges, JUUL has risen since 2021 to the most popular brand (19%), followed by Logic (17%), Vuse (16%), Vype (16%) and blu (14%).
- Only 0.9% of adults who vape nicotine use e-liquids over the legal limit of 20mg/ml. (Table 4)
- Among current vapers, 50% say that they use the same strength e-liquid as when they first started vaping, while 38% have decreased the strength and only 4.2% have increased the strength over time. (Figure 14). Ex-smokers are the most likely group of vapers to report currently using a lower strength of e-liquid than when they began (50%).

Use and awareness of e-cigarettes

In 2022, 94% of smokers and 92% of the general population had heard of e-cigarettes or vapes. This contrasts with 2012, when 49% of adults responding to the same question were aware of them. The number of e-cigarette users grew from around 700,000 in 2012 to 4.3 million in 2022. (Table 1).

There are differences in vaping behaviour by social class, with 9.5% of those classified as C2DE being current vapers compared to 7.3% of those classified as ABC1. This reflects the socio-economic distribution of smokers; in this survey 17% of C2DE are smokers compared to 10% of ABC1. The rate of growth of vaping has been similar across the social classes; in 2015 6.3% of C2DEs vaped and 4.6% of ABC1s.

The peak age group for current e-cigarette use in 2022 is 18-24 year olds (11%) followed by 25-34 year olds (11%), 35-44 year olds (11%) and 45-54 year olds (10%). People aged 55 and over had the lowest rate at 4.9%. The age distribution in 2022 has changed since 2021, where the 18-24 year old age group had the lowest vaping rate at 5.0%. A higher proportion of those identifying as male (9.3%) say that they currently use e-cigarettes than those identifying as female (7.4%).

Table 1: Number of e-cigarette users in Great Britain

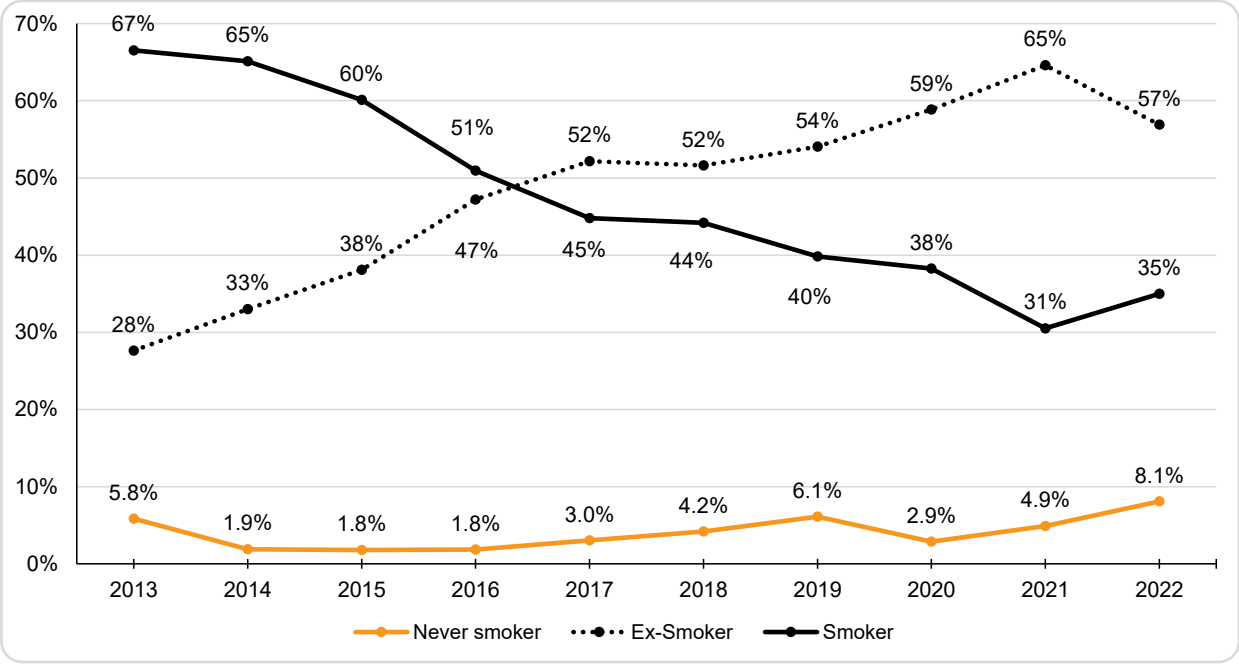
	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
% population current users	1.7%	2.7%	4.2%	5.4%	5.7%	5.8%	6.2%	7.1%	6.3%	7.1%	8.3%
Percentage point change (YoY)		+1.0pp	+1.6pp	+1.2pp	+0.3pp	+0.1pp	+0.4pp	+0.9pp	-0.8pp	+0.8pp	+1.2pp
Number of users (millions)	0.8	1.3	2.1	2.7	2.9	2.9	3.2	3.6	3.3	3.7	4.3
Rate of growth (YoY)		+62%	+60%	+29%	+7%	+3%	+7%	+16%	-11%	+12%	+17%

PROPORTION OF VAPERS BY SMOKING STATUS

Use of e-cigarettes is largely confined to current and ex-smokers. Use among never smokers remains low. Of the 4.3 million current vapers, around 2.4 million are ex-smokers, 1.5 million are current smokers and 350,000 are never smokers. Since 2013, the proportion of current electronic cigarette users who smoke tobacco has generally fallen, while the proportion who are ex-smokers has risen (Figure 1). However, this trend has slightly reversed in 2022. There is a significant decrease in the proportion of current e-cigarette users who are ex-smokers, from 65% in 2021 to 57% in 2022. The proportion of current e-cigarette users who are never smokers has increased, from 2021 (4.9%) to 2022 (8.1%). In 2022, 35% of current vapers also smoked (dual users). The proportion of NRT users who also smoke is 41%.

In every year since 2017, most e-cigarette users have been ex-smokers. However, there are more ex-smokers (33%) than current smokers (13%) in the whole adult population. As a result, only 14% of the whole group of ex-smokers vape compared to 22% of all current smokers.

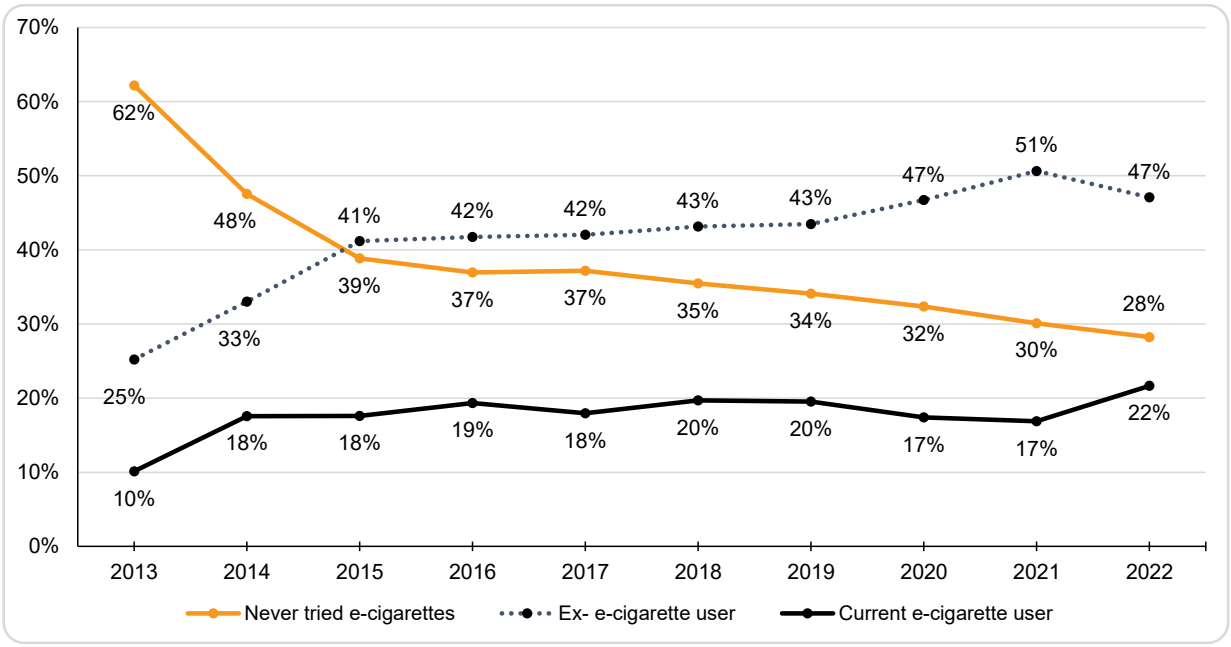
Figure 1 - Smoking status among current adult e-cigarette users, Great Britain (2013–2022)



Unweighted base: GB adult current vapers (2013=325 2014=498, 2015=614, 2016=667, 2017=669, 2018=738, 2019=854, 2020=787, 2021=826 2022=1089)

The proportion of adult smokers who have tried e-cigarettes has continued to grow. However, in 2022 28% of current smokers had never used e-cigarettes. (Figure 2).

Figure 2 - E-cigarette use among current adult cigarette smokers, Great Britain (2013-2022)



Unweighted base: GB adult current smokers (2013=1895 2014=1776, 2015=2037, 2016=1704, 2017=1632, 2018=1633, 2019=1777, 2020=1694, 2021=1512, 2022=1751)

VAPING BEHAVIOUR

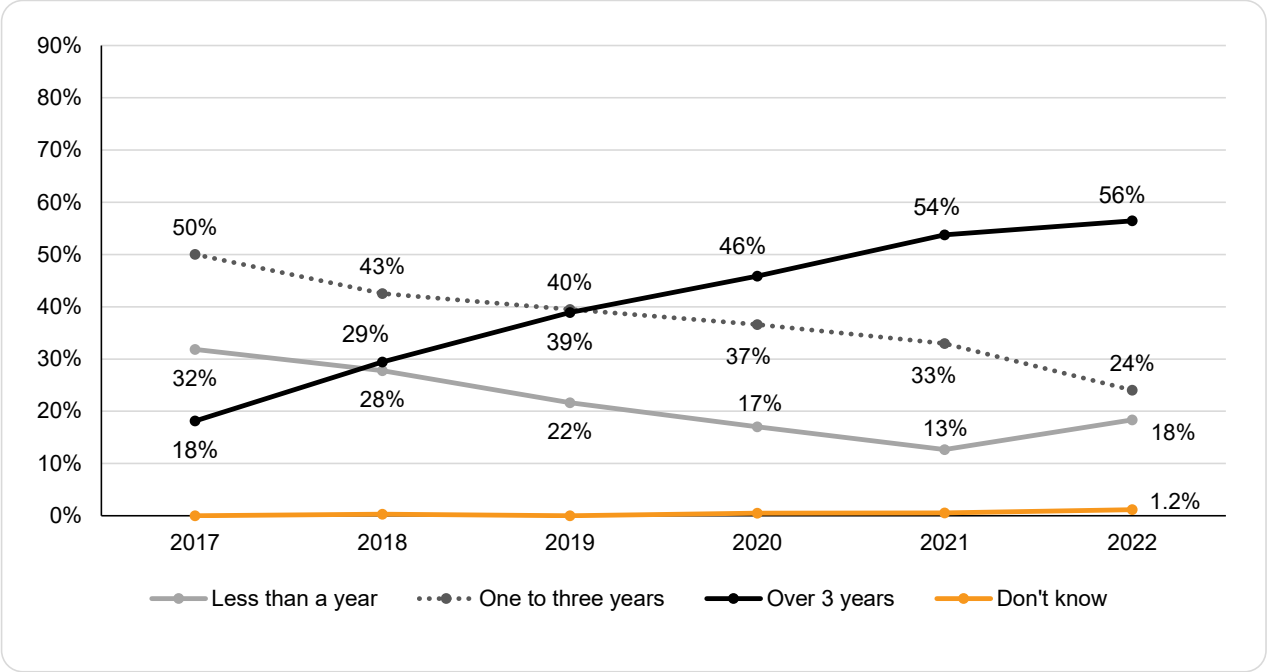
Vaping behaviour in ex-smokers

Among ex-smokers, 20% had used a vape in their most recent smoking quit attempt. Current use of e-cigarettes among ex-smokers is 14%, and a further 17% have tried vaping but no longer vape. This means there are 2.4 million ex-smokers who are current vapers compared to 2.9 million ex-smokers who have tried vaping but no longer do it.

More than half of current vapers who are ex-smokers in 2022 said they had been vaping for over 3 years (56%), compared with 18% in 2017 when we started asking this question. (Figure 3).

- 18% have vaped for under 1 year
- 24% have vaped for 1-3 years
- 56% have vaped for >3 years

Figure 3 - Length of e-cigarette use by adults who are ex-smokers and who currently vape, Great Britain (2017-2022)

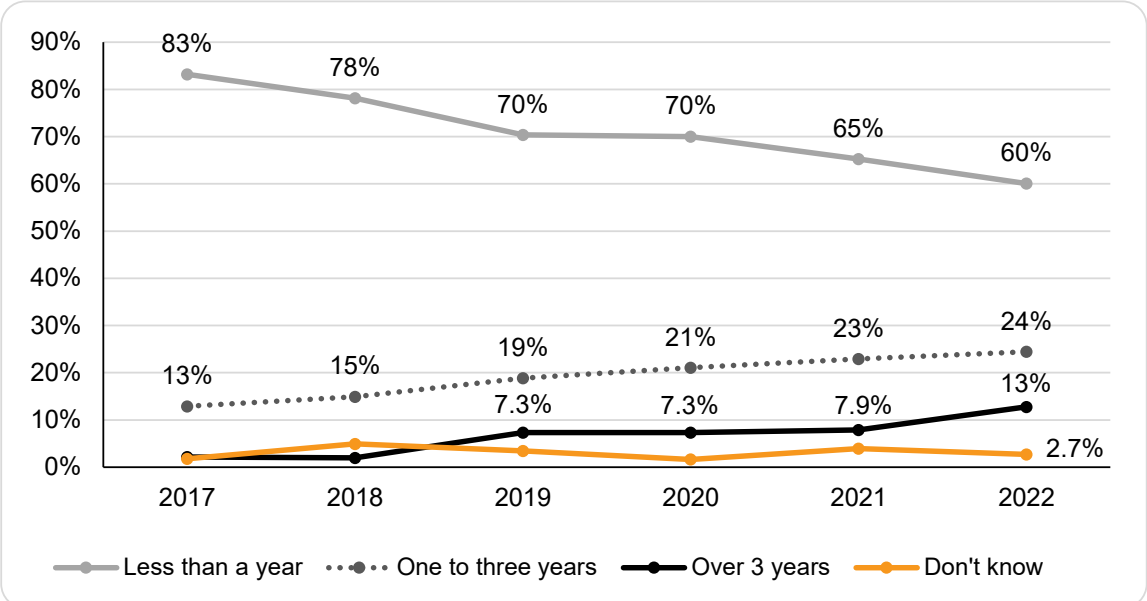


Unweighted base: GB adult ex-smokers who currently vape (2017=357, 2018=399, 2019=456, 2020=473, 2021=533 2022=586)

Most ex-smokers who currently use e-cigarettes vape daily (86%), with 96% vaping at least weekly. Many ex-smokers who used to vape did so regularly, with almost a third saying they vaped daily (33%) and 46% at least weekly. The remainder reported vaping less frequently, with slightly more than a third (36%) reporting they only tried vaping once or twice while 6.2% could not remember or didn't know.

The proportion of ex-smoker, ex-vapers who used e-cigarettes for less than a year has fallen over time from more than four in five in 2017 to three in five in 2022. (Figure 4) The proportion using for more than a year has more than doubled from 14% in 2017 to 37% in 2022, with 13% saying they vaped for more than three years.

Figure 4 - Length of e-cigarette use by adult ex-e-cigarette users who are also ex-smokers, Great Britain (2017-2022)



Unweighted base: GB Adult ex-smokers who have ever used e-cigarettes more than 'once or twice', who no longer use e-cigarettes (2017=233, 2018=242, 2019=272, 2020=321, 2021=402, 2022=418)

Vaping behaviour in smokers (dual use)

People who vape and smoke are known as dual users. Of smokers who vape, 45% do so daily and 51% less than daily, with the remaining 3.6% being unsure or having only tried e-cigarettes once or twice. Those who vape everyday smoke on average less than those who vape less frequently than daily. Table 2 gives a breakdown for the number of cigarettes smoked a day, by daily, non-daily and never vaping. Fewer than six cigarettes per day is considered low daily smoking, while 21 or more is considered heavy smoking. Just over half of all daily vapers can be defined as "light" smokers, smoking fewer than six a day compared to under a third of non-daily vapers (Table 2).

Table 2

Cigarettes smoked per day (ready-made or handrolled)	Never vaper	Non-daily vaper	Daily vaper
6 or fewer a day	34%	32%	38%
7-20 a day	55%	55%	52%
More than 20 a day	11%	13%	10%

Unweighted base: GB adult vapers; 2022, all current smokers except those who report not knowing how many cigarettes they smoke or who chose N/A. Daily vapers n=318; Non-daily vapers n=373; never vapers n=440.

Vaping behaviour in never-smokers

The proportion of current vapers who say they have never smoked has fluctuated over the years of the survey but is currently at an all-time high of 8.1% of current e-cigarette users. (Figure 1). However, never smokers make up most of the population so the proportion of never smokers who are current vapers is only 1.3%, with 5.2% having ever tried vaping.

ARE E-CIGARETTES CONTRIBUTING TO DECLINES IN SMOKING?

The Annual Population Survey found that smoking prevalence among adults aged 18 and over in England declined by 5.9 percentage points from 2011 to 2019. In 2011 20% of adults smoked, falling to 14% in 2019; equivalent to a drop from 7.7 million smokers in 2011 to 5.7 million in 2019.[1] Due to changes in survey methodology in 2020 (see COVID-19 section in the Methods section), we use 2019 as the comparison point, as 2021 is not yet available at the time of writing.

A comprehensive approach to tobacco control was implemented during this period, which has been associated with reductions in smoking prevalence.[2 3 4]This included a tobacco display ban, large graphic health warnings on the front of packs, plain packaging, increased tobacco taxes and minimum pack sizes. A number of factors are likely to have contributed to this decline in prevalence.

However, the Smoking Toolkit Study (an ongoing series of monthly surveys of the adult population of England) has shown a clear association between changes in population rates of quitting smoking and prevalence of e-cigarette use after adjusting statistically for a range of potential confounding factors.[5] If the association is causal, e-cigarettes were responsible for an estimated 69,930 additional ex-smokers in England in 2017.[6] Furthermore, evidence from a randomised controlled trial found that vaping was nearly twice as effective as NRT in helping smokers quit in a Stop Smoking Service setting in England,[7] and a Cochrane systematic review of the evidence has concluded that there is moderate-certainty evidence that ECs with nicotine increase quit rates compared to ECs without nicotine and compared to NRT.[8] This is now a living review which will be updated as further evidence is published.

Attitudes to vaping

REASONS FOR E-CIGARETTE USE

Among all e-cigarette users who vaped more than once or twice, the four main reasons for vaping are as an aid to quitting (22%) followed by preventing relapse (16%), because they enjoy the experience (13%) and to save money compared with smoking tobacco (13%). The majority of those who had only vaped once or twice (71%) said that their main reason was something other than the options provided in the survey.

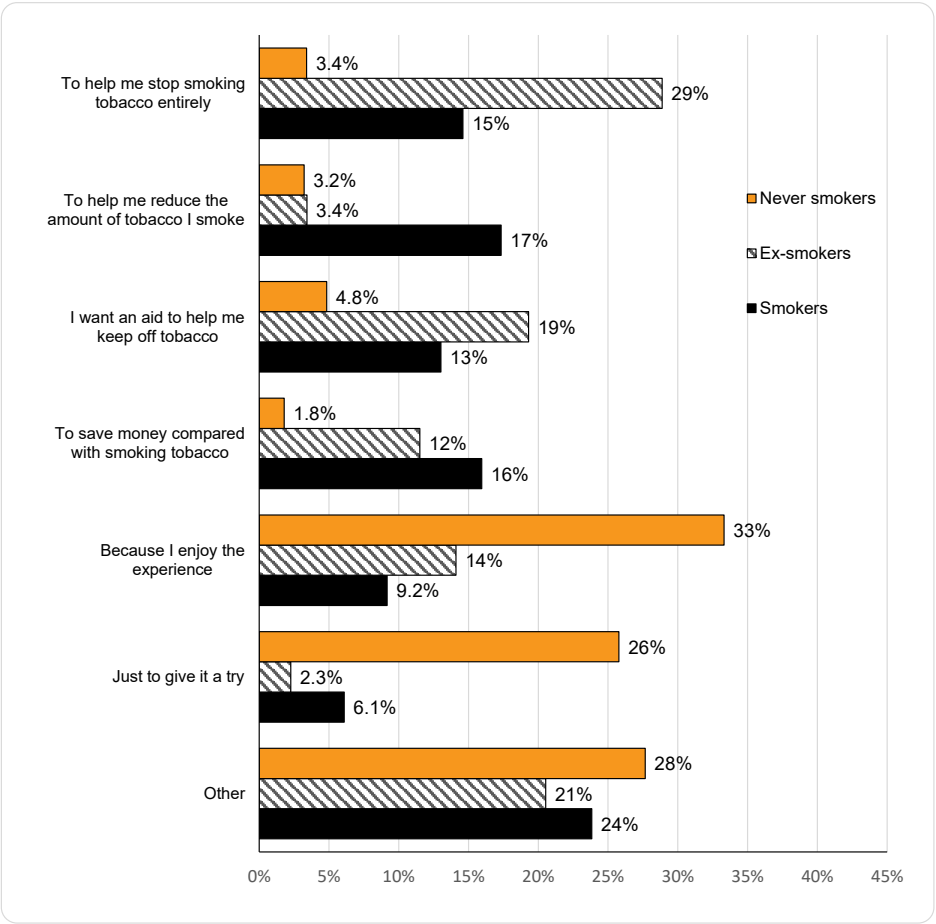
REASONS FOR E-CIGARETTE USE BY SMOKING STATUS

When current e-cigarette users who are ex-smokers are asked for their main reason for vaping, the most frequently cited reasons are: to help them quit (29%); as an aid to keep them off tobacco (19%); because they enjoy it (14%); and to save money (12%). (Figure 5)

The main reasons current e-cigarette users who also smoke (dual users) give for using e-cigarettes are to help them to help cut down the amount smoked (17%), to save money (16%), to try to help them quit (15%) and as an aid to keep them off tobacco (13%).

The main two reasons for vaping among never smokers are enjoying the experience (33%) and just to give it a try (26%).

Figure 5 - Main reason for vaping among adult smokers, ex-smokers and never smokers who vape, Great Britain (2022)



Unweighted base: GB adult current c-cigarette users excluding those who only vaped once or twice 2022; current vaper and current smoker n = 390, current vaper and ex-smoker n = 590, current vaper and never smoker n = 73. Other options to choose are grouped under 'Other'; 'To help deal with situations where I cannot smoke', 'To avoid putting those around me at risk', 'Because I feel I am addicted to smoking tobacco', 'It was advised by a health professional', 'It was suggested or recommended by a friend' and 'Other'. 'Other' was directly chosen by 20% of never smokers, apart from which each of the options were chosen by under 10% of each group.

In 2019 to explore vapers' views about their e-cigarette use, current vapers were asked whether they agreed or disagreed with a series of statements. For most e-cigarette users, improving their health is their number one reason for vaping. Among all vapers, 60% agree that "health is my number one reason for taking up e-cigarettes". (Table 3).

Table 3

How e-cigarette users view vaping	Strongly Agree or Agree	Strongly Disagree or Disagree
Health is my number one reason for taking up e-cigarettes	60%	14%
I get a great deal of pleasure out of vaping	51%	12%
E-cigarettes have improved my quality of life	51%	12%
Vaping is not a magic solution for stopping smoking	50%	26%
Vaping is a medicine that I use in order to address my smoking addiction	50%	20%
Lowering the levels of nicotine I consume through vaping is a priority for me	44%	22%
I am worried that I'm getting more nicotine now that I use an e-cigarette	13%	61%
I like to spend time discussing vaping online	7.8%	73%

Unweighted base: GB adult vapers; 2019, n=854. Options were on a five point 'Strongly agree/Agree/Neither agree nor disagree/ Disagree/Strongly disagree' scale, plus a 'Don't know' option.

SATISFACTION

Those who tried vaping were also asked how satisfying they found it.

Ex-smokers who currently vape

Around two thirds of e-cigarette users who no longer smoke find vaping more or equally satisfying as smoking (63%). The proportion finding it less satisfying is 32% (Figure 6). Although enjoyment of vaping is cited as the main motivation for use by only 13% of current e-cigarette users, our 2019 survey found that when asked if they get "a great deal of pleasure from vaping" and whether "e-cigarettes had improved my quality of life" 51% of e-cigarette users agreed (Table 3).

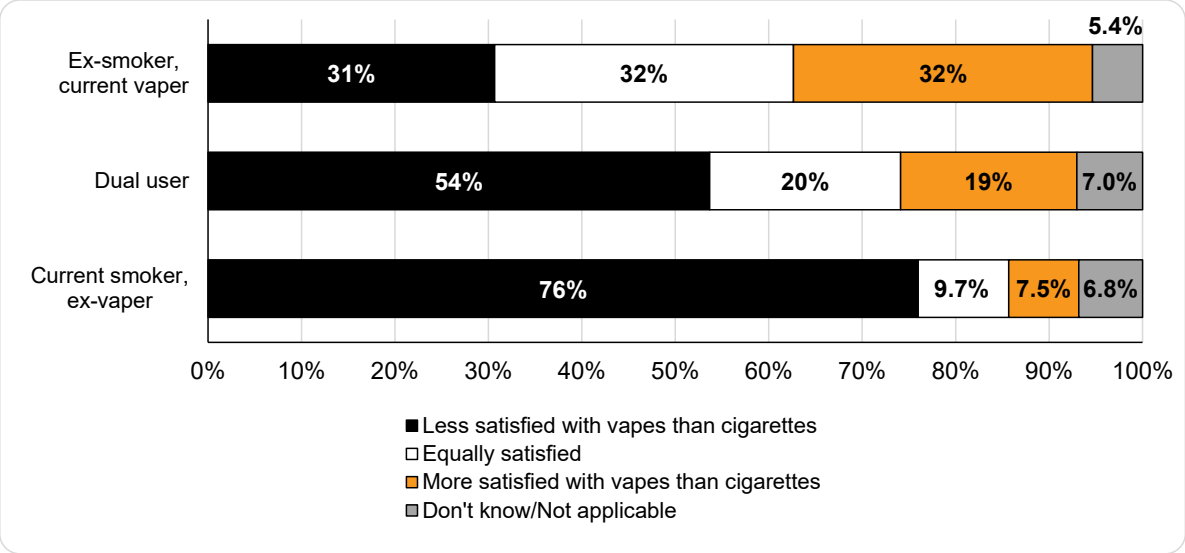
Smokers who currently vape

More than half of vapers (54%) who also smoke find it less satisfying than smoking, and 39% find it more than or equally as satisfying as smoking. These figures are very similar to 2021 (55% and 40%, respectively).

Smokers who are ex-vapers

Satisfaction levels are lowest of all for smokers who have tried but no longer use e-cigarettes, 76% of whom say they found vaping less satisfying than smoking, little changed from 79% in 2021. Products have improved over the years, and it could be worth encouraging ex-vapers who smoke to try vaping again to prompt further quit attempts.

Figure 6 - Satisfaction levels from e-cigarettes compared with smoking in adults, Great Britain 2022



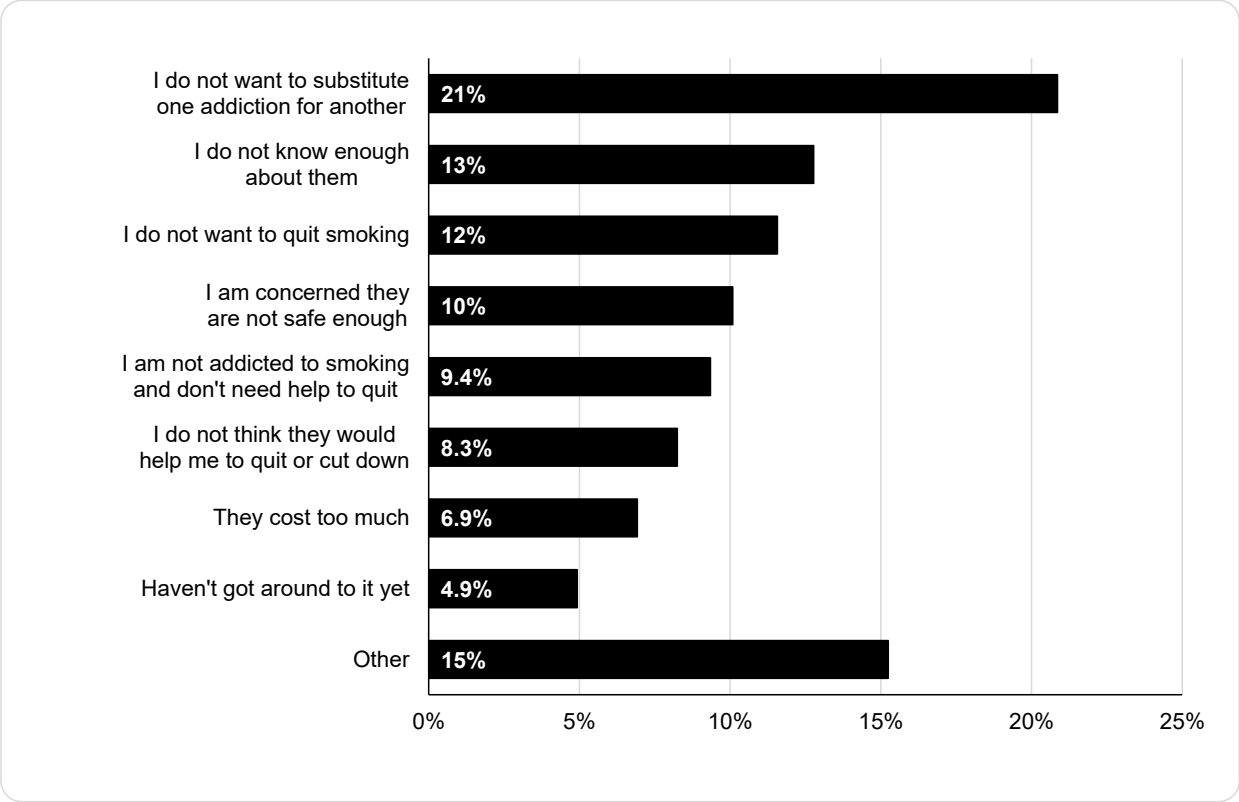
Unweighted base: GB Adults who have ever used e-cigarettes, excluding those that have tried e-cigarettes only once or twice. Current vaper & ex-smoker n= 590; Ex-vapers & current smokers n=442; Current vapers & current smokers n=390.

REASONS WHY SMOKERS HAVEN'T TRIED OR HAVE STOPPED USING E-CIGARETTES

Less than a third, 28%, of smokers have not yet tried e-cigarettes. Smokers' views on addiction were the most frequently cited main reason, with 21% saying they do not want to substitute one addiction for another, while conversely 9.4% say that they're not addicted to smoking and don't need help to quit. A further 12% say that they do not want to quit smoking, similar to 2021 (12%).

Not knowing enough about e-cigarettes is the main reason for 13% of smokers who hadn't tried them, and a further 10% say their main reason was concern for the safety of e-cigarettes. A further 8.2% say that they do not believe that e-cigarettes could help them quit or cut down, showing a lack of confidence in these products. (Figure 7).

Figure 7 - Main reason for not trying an e-cigarette among adult smokers, Great Britain 2022



All adult GB current smokers who have not tried e-cigarettes 2022. n=432. Other options to choose are grouped under 'Other'; 'There are too many products to choose from' (3.8%), 'I do not like the way they look' (3.7%), 'I'm using other things to help me quit smoking' (2.7%), 'I would be embarrassed to use them in public' (1.6%), 'They are too difficult to get hold of ' (0.3%) and 'Other' (3.2%).

Almost half, 47%, of smokers have tried but no longer use e-cigarettes. The main three reasons cited for stopping using e-cigarettes were the same as last year:

- 23%: that vaping did not feel like smoking a cigarette (23% in 2021)
- 17%: that vaping did not help them deal with cravings (14% in 2021)
- 14%: that they had only tried them to see what they were like (9.9% in 2021)

Negative experiences included feeling unwell (5.7%), not liking the taste (4.9%), and leaks (4.3%).

Availability and accessibility of vapes was rarely the main problem, with few people saying that they cost too much (3.0%), refills and replacements were not easily available (1.1%), they were embarrassing to use in public (0.6%) or the flavours they wanted were unavailable (0.6%).

Perceptions of harm

ADULT POPULATION MISPERCEPTIONS OF HARM

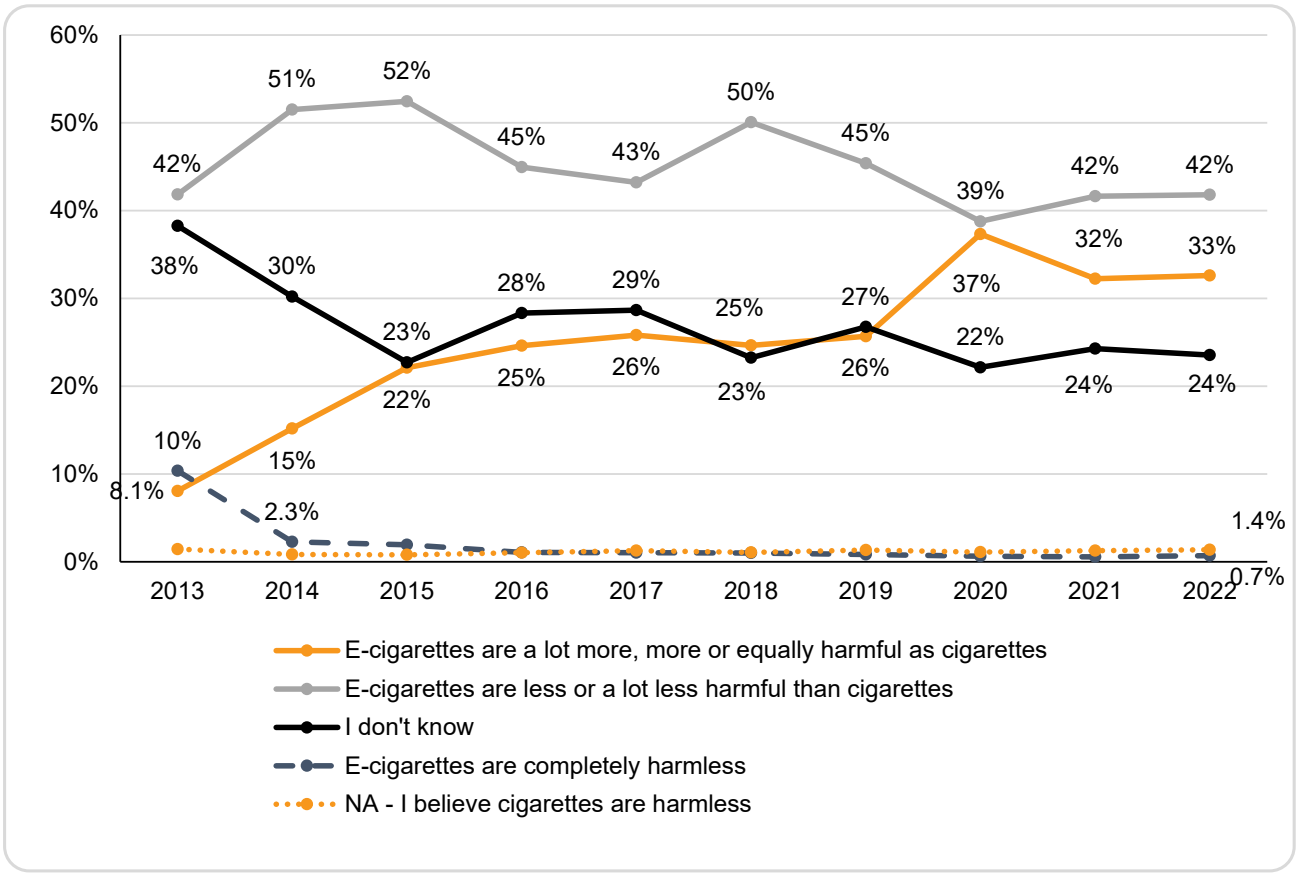
From 2016 to 2019 the proportion of adults who inaccurately believed that vaping is as, or more harmful than smoking hovered around one in four, with between 43% and 50% believing it was less harmful. However, in 2020 the proportion believing it was more or equally harmful rose significantly to 37% with the proportion believing it to be less harmful falling to 39%.

The likely driver for this change in public perception was the impact of the media coverage of an outbreak of serious lung injury to vapers in the US, called EVALI. The number of hospital admissions from EVALI peaked in September 2019 and by February 2020 the US had reported 2,807 hospitalised cases and 68 deaths.[9]

Since 20 May 2016, the MHRA reported that there have been three fatalities in the UK linked with vaping products, one of which appeared to meet the criteria for 'e-cigarette, or vaping product, use-associated lung inju' ('EVALI').[10] While the cause of this outbreak has since been identified as vitamin E acetate used to adulterate cannabis-containing e-liquids the media coverage of the initial outbreak was far more prominent than the subsequent explanation or the fact that both vitamin E acetate and THC containing liquids are banned under UK rules.

The proportion believing vaping was more or equally harmful fell back from 37% in 2020 to 32% in 2021 and 33% in 2022. Similarly, the proportion believing it to be less harmful than smoking rose slightly from 39% in 2020 to 42% in 2021 and 2022. Although the 2020 change has partly reversed, still only 12% of adults correctly state that e-cigarette use is a *lot* less harmful than smoking.

Figure 8 - Adults' perception of harm from e-cigarettes, Great Britain (2013-2022)

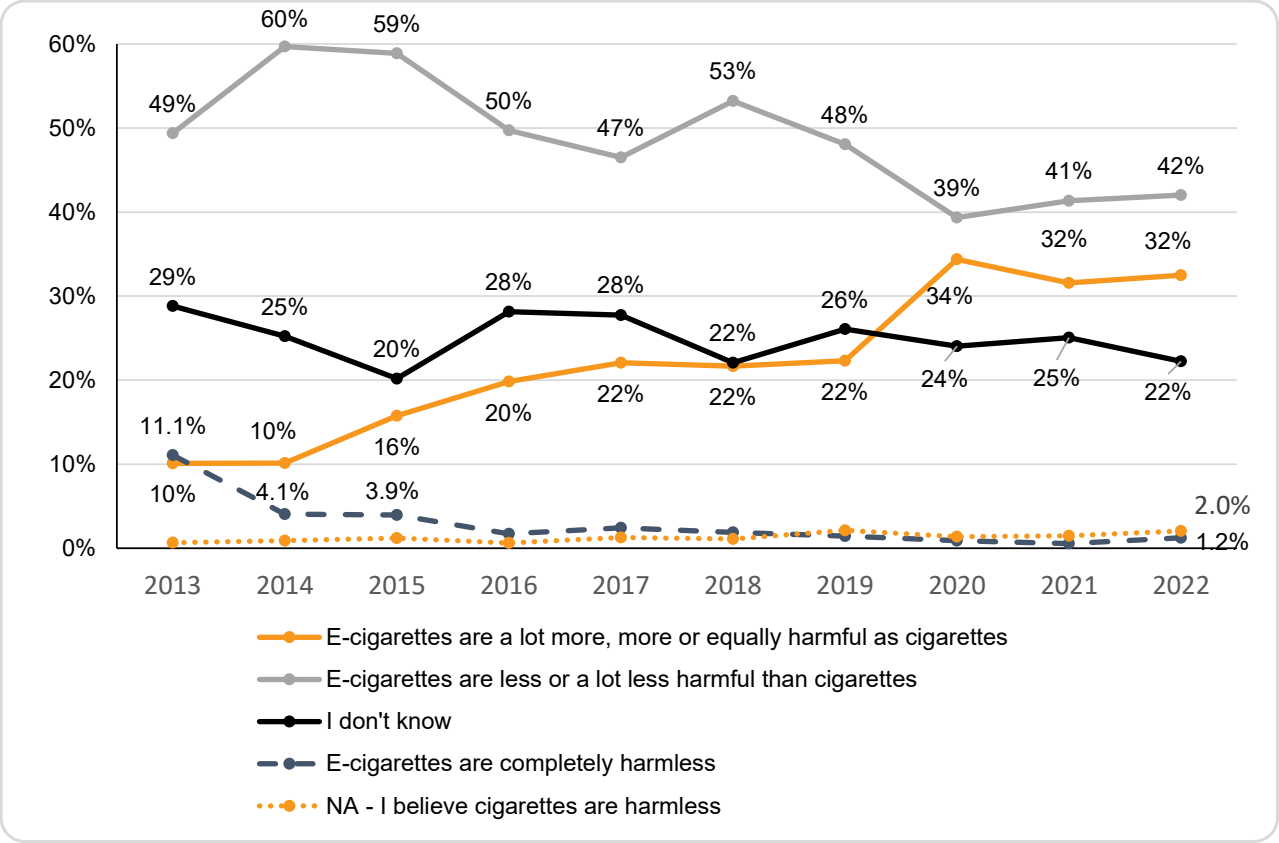


Unweighted base: All GB adults who have heard of e-cigarettes: 2013 n=8936; 2014 n=11,307; 2015 n=11,340; 2016 n=11,489; 2017 n=12,101; 2018 n=12,070; 2019 n=11,634; 2020 n=11,954; 2021 n=11,429; 2022 n=12,039)

SMOKERS' PERCEPTIONS OF HARM

A similar pattern can be seen among smokers' perceptions of harm in 2022 (Figure 9) with nearly a third (32%) believing vaping was more or equally harmful, and more than one in five (22%) saying they don't know. The proportion thinking that vaping is less harmful than smoking is similar to that among the general population (42% compared to 42%), but a higher proportion think e-cigarettes are a lot less harmful (14% compared to 12%).

Figure 9 – Smokers' perception of harm from e-cigarettes, Great Britain (2013-2022)

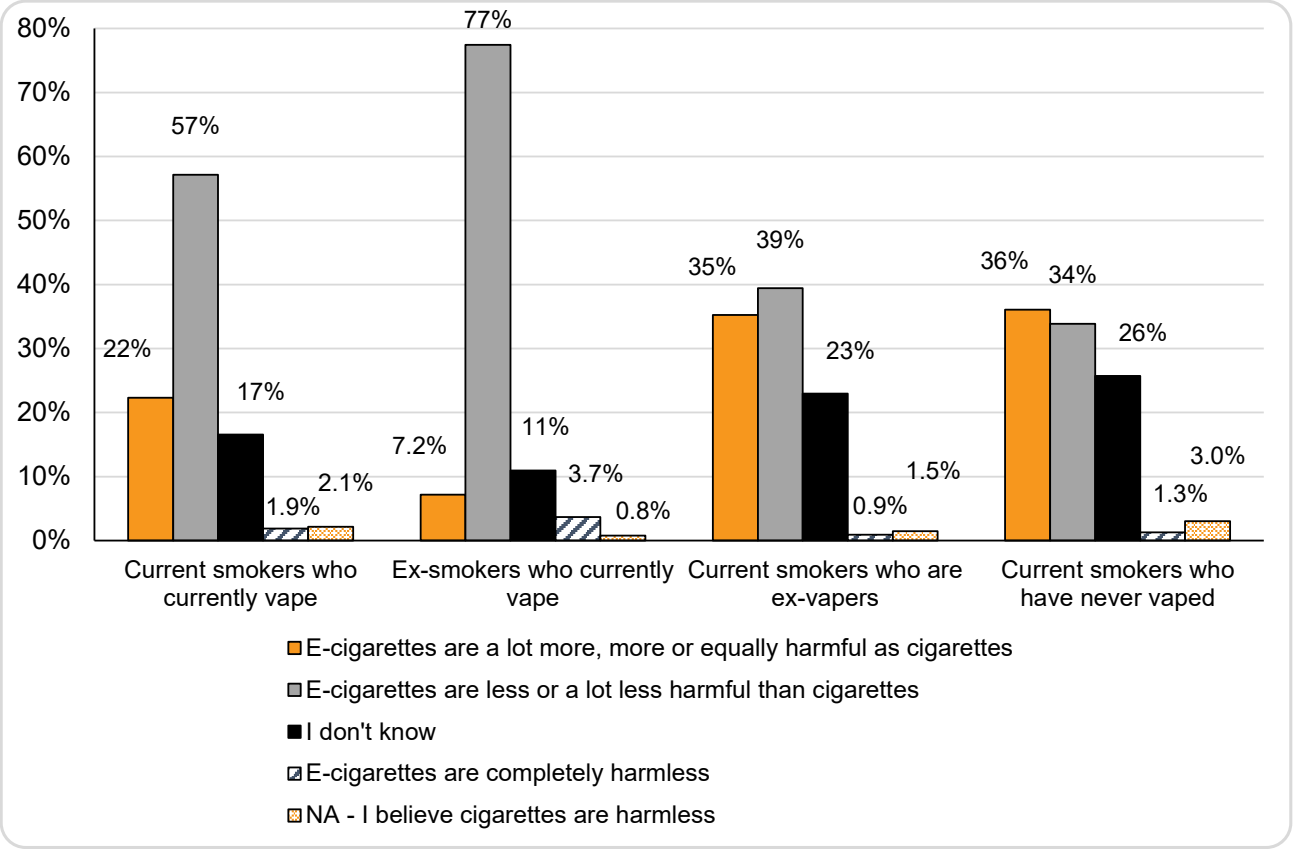


Unweighted base: GB adult smokers who have heard of e-cigarettes (2013, n=1720; 2014, n=1694; 2015, n=1945; 2016, n=1639; 2017, n=1569; 2018, n=1566; 2019 n = 1,679; 2020 n=1; 2021 n=1,438; 2022 n=1,641). The 'E-cigarettes are less harmful than cigarettes' response does not include those saying that e-cigarette use is 'completely harmless'.)

Smokers who currently use e-cigarettes have more accurate perceptions of their harm, with 57% thinking that e-cigarettes are less harmful (down from 71% in 2019) and 22% thinking that they are more or equally harmful (up from 9.2% in 2019). (Figure 10). The proportion of current smokers who have never tried e-cigarettes who believe they are more than or equally as harmful as cigarettes increased between 2019 and 2022 from 27% in 2019 to 36% in 2022.

Ex-smokers who currently use e-cigarettes have the most accurate perceptions of the harm of e-cigarettes. In 2022, 77% of them correctly thought e-cigarettes are less harmful than smoking. However, like the other groups, this is a lower proportion than in 2019 (83%). In 2022, 7.2% of ex-smokers who currently use e-cigarettes said that they are more or equally harmful (5.0% in 2019). (Figure 10).

Figure 10 - Adults' perception of harm from e-cigarettes by smoking and vaping status



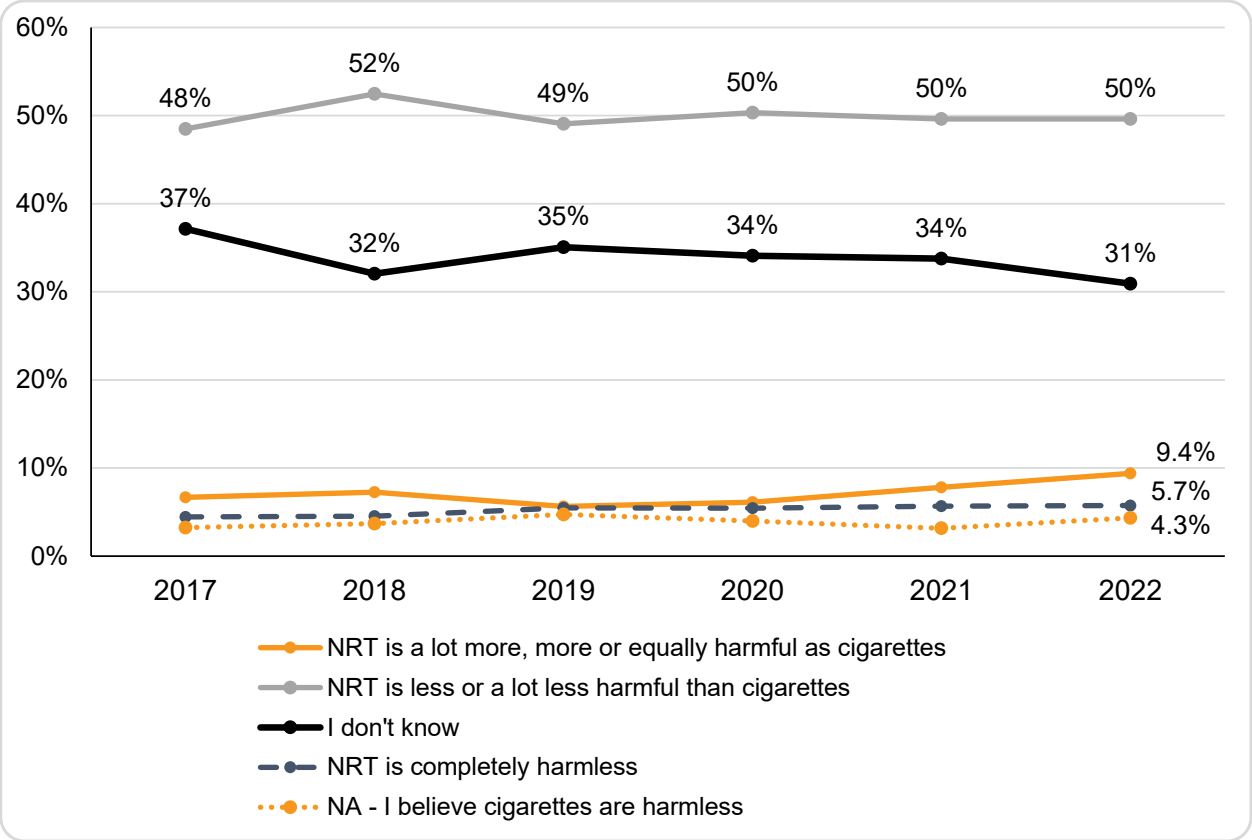
Unweighted base: GB adults who have heard of e-cigarettes. Current e-cigarette user & current smoker = 394; Current e-cigarette user & ex smoker= 594; Ex e-cigarette user & current smoker= 815; Never e-cigarette user & current smoker= 432. The 'E-cigarettes are less harmful than cigarettes' response does not include those saying that e-cigarette use is 'completely harmless'.

PERCEPTIONS OF HARM FROM NICOTINE REPLACEMENT THERAPIES (NRT)

Over the last seven years we also asked people for their views of the relative harms of NRT compared with tobacco smoking. NRT is a licensed medication with minor side effects.

Understanding of the relative risk of NRT compared to smoking among smokers remains poor. (Figure 11). However, it is considerably better than their understanding of the relative risk of vaping and smoking. (Figure 9). In 2022 nearly a third (31%) of smokers said that they did not know how harmful NRT is compared to smoking, 9.4% thought it was more than or equally as harmful as smoking, and only 32% correctly identified NRT as being *much* less harmful than smoking.

Figure 11 - Adult smokers' perception of NRT compared with regular cigarettes, Great Britain (2016-2022)



Unweighted base: GB adult smokers. 2016 n=1477; 2017 n=1632; 2018 n=1633; 2019 n=1777; 2020 n=1694, 2021 n=1512, 2022 n=1751

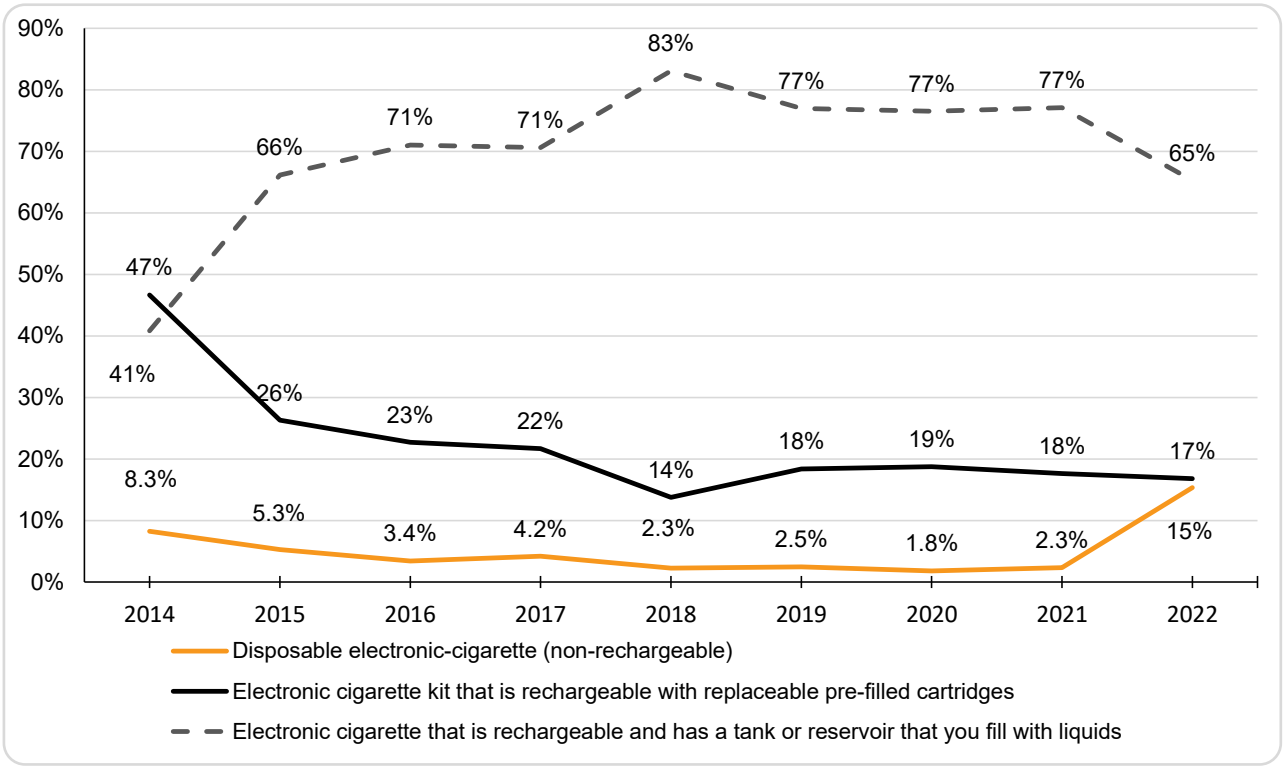
Types of device and e-liquids in use

E-CIGARETTE DEVICE USED

The most frequent type of e-cigarette device remains a refillable tank system, with 65% of current vapers reporting this type as their main device. (Figure 12). However, this decreased since last year when 77% of current vapers mainly used a tank-type e-cigarette. There has been a corresponding increase in the main use of disposable e-cigarettes, from 2.3% in 2021 to 15% in 2022. The proportion of current e-cigarette users who mainly use devices that are rechargeable with prefilled cartridges is 17%, which has been stable since 2019.

Of those who currently vape with a cartridge, the most popular types of rechargeable devices with pre-filled cartridges are JUUL (19%), Logic (17%), Vuse (16%), Vype (16%) and blu (14%).

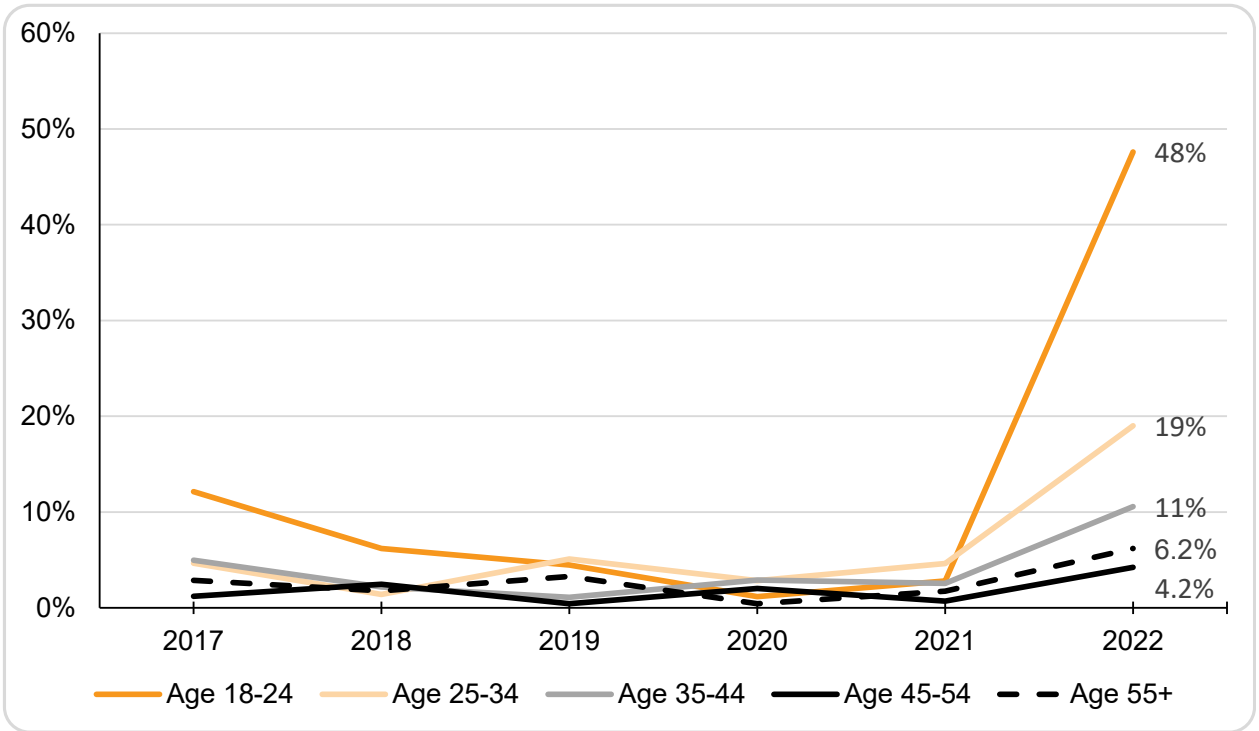
Figure 12 - Type of e-cigarette used by current e-cigarette users, Great Britain (2014 - 2022)



Unweighted base: All GB adults who currently use e-cigarettes, from 2017 onwards excluding those who only used them once or twice. 2014 n=498; 2015 n=614; 2016 n=667; 2017 n=657; 2018 n=715; 2019 n=800; 2020 n=767; 2021 n=790; 2022 n=1033

Younger adults are mostly driving the increase in 2022 in using disposable e-cigarettes as the main type of e-cigarette. (Figure 13). For 18-24 year olds, almost half of current e-cigarettes users (48%) use disposables as their main type in 2022, an increase from only 2.8% in 2021. In 2022, disposable e-cigarettes are also the most common main device type among 11-17 year old e-cigarette users (52%).[14]

Figure 13 - Use of disposable e-cigarettes by age group, Great Britain (2017-2022)



ASH Smokefree GB Adult Surveys 2022. Unweighted base: Adult current e-cigarette users, excluding only tried once or twice - see Table in Appendix for counts.

In 2021 nearly three quarters (73%) of all e-cigarette users said they only used one device. The most used additional device was a tank system, particularly for current vapers who are ex-smokers. This question was not asked in 2022.

In 2020 users were asked why they used the device they did. The most popular reasons for both tank and cartridge users was the hit of nicotine delivered (14% cartridge users 13% tank users) ease of use (11% for cartridge users 11% tank users) and price (10% cartridge users 12% tank users). However, there were also divergent reasons. For cartridge users, easy access to the device in local shops was more important (13% cartridge users, 4.9% tank users) while for tank users it was more important that the device was refillable (10% tank users, 0.9% cartridge users). This question was not asked in 2021 or 2022.

NICOTINE CONSUMPTION

Some stakeholders have expressed concerns that the cap on nicotine levels imposed by the Tobacco Products Directive (TPD)[11] could be discouraging use among smokers with the highest levels of addiction.[12] For example, in the US, where there is no cap on nicotine levels, the most popular product, Juul, sells in two strengths, 59 mg/ml and 35 mg/ml,[13] both much higher than the legal limit in the EU. In the UK only 18 mg/ml Juul products are available, below the legal maximum of 20 mg/ml.[14]

In 2016, before the legislation was introduced, more than three quarters of current or former e-cigarette users surveyed by ASH vaped liquids with concentrations of nicotine of 18 mg/ml or less (77%), with nearly half (49%) using e-liquid containing 12 mg/ml or less. One in ten (10%) used more than 18 mg/ml (20 mg/ml was only included as a specific break point from 2017 onwards). In 2017, at the time the sell through period was coming to an end, 5.9% of current vapers were using above the TPD limit, falling to 2.1% in 2018 and 1.0% in 2019. (Table 4).

The ASH survey suggests that the current nicotine cap of 20 mg/ml is not a problem for the majority of e-cig users who use e-liquid containing nicotine, as they are using strengths well under the legal limit. In 2022, 0.9% of current e-cigarette users said they use nicotine strengths above the legal limit, and a further 6.3% used nicotine strengths just under or at the legal limit (19-20mg/ml). 9.0% did not know what strength they used.

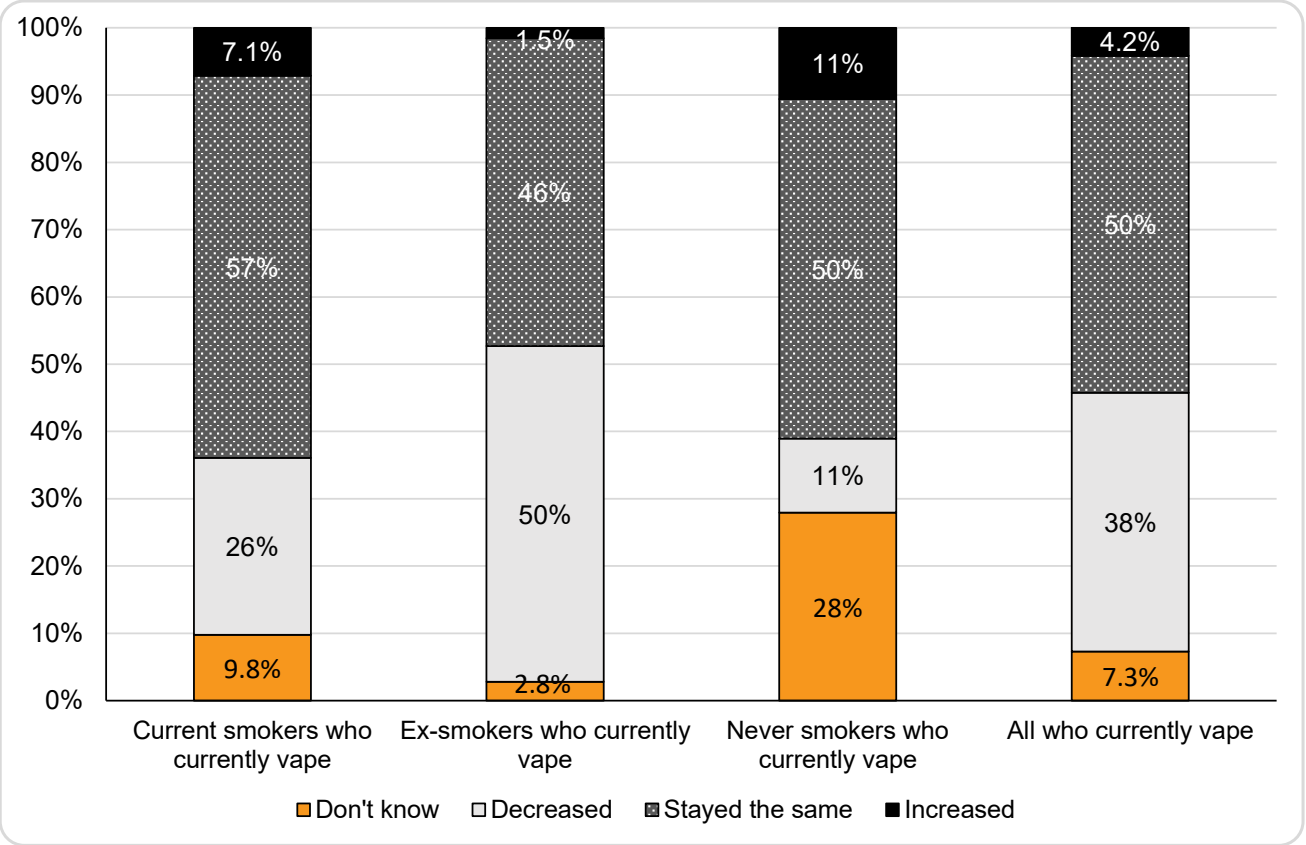
Table 4

Strength of nicotine used by current e-cigarette users						
Strength	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**
TPD level and lower	85%	90%	88%	91%	92%	90%
Higher than TPD	5.9%	2.1%	2.0%	2.1%	1.5%	0.9%
Don't know	9.5%	8.4%	9.8%	7.0%	6.5%	9.0%

Unweighted base: Current GB adult e-cigarette users who use nicotine. 2017 n=597; 2018 n=365; 2019 n=720; 2020 n=693; 2021 n=633; 2022 n=938

In 2022, 50% of current vapers say they use the same strength e-liquid as when they started, while 38% have decreased the strength. Only 4.2% have increased the strength over time. (Figure 14). E-cigarette users who have quit smoking are more likely than dual users to report using a lower nicotine strength over time (26% of current dual users compared with 50% of ex-smokers who vape).

Figure 14 - Change over time of e-liquid nicotine strength among current adult vapers, Great Britain 2022



Unweighted base: Current vapers excluding any current vapers who don't use nicotine-containing e-cigarettes. Current smokers n=394; Ex-smokers n=594; Never smokers n=101; All n=1089. Question asked e-cigarettes users about any change in nicotine strength comparing their first use to current use.

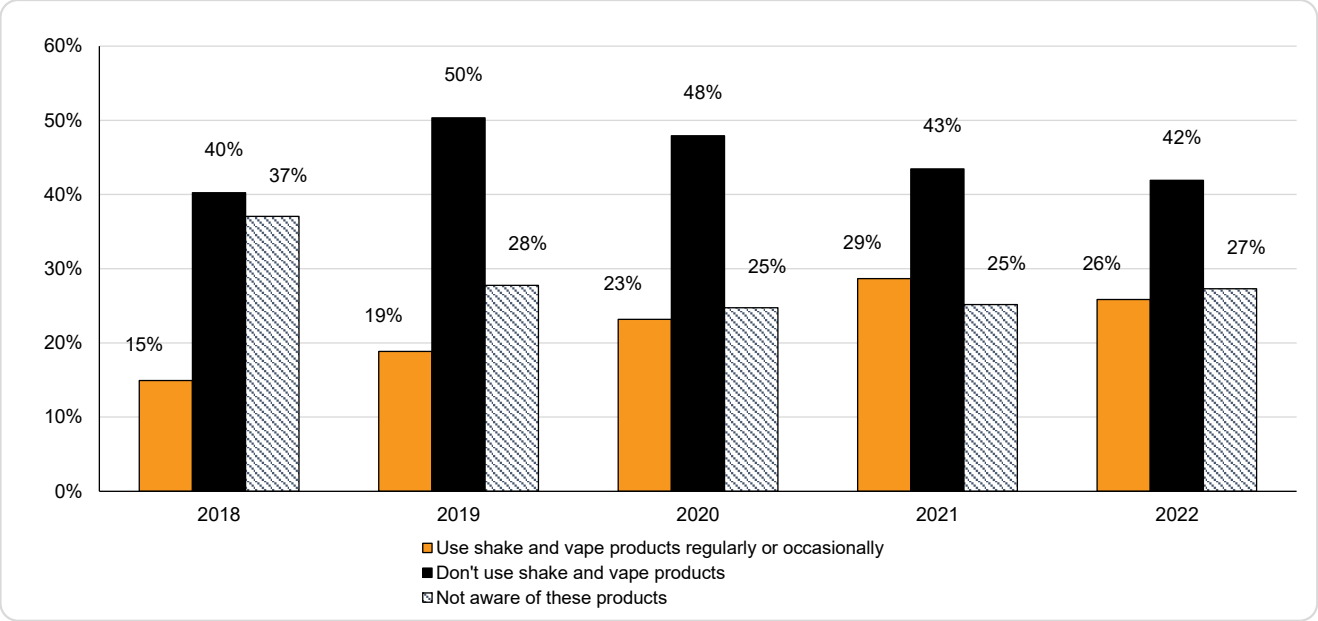
AMOUNT OF E-LIQUID USED IN TANK-TYPE E-CIGARETTES AND DEDICATED REFILL BOTTLES

Legislation limits the volume of e-liquid in an e-cigarette to less than 2ml and dedicated refill bottles for tank-type devices to 10ml.

In 2016, prior to this legislation coming into force, 44% of those vaping daily and using a tank device reported using 2ml or less a day with 0.2% reporting using more than 10ml of liquid a day. In 2022, the proportions were 28% of all daily e-cig users using 2ml or less a day and 2.4% more than 10 ml a day. We have not asked why vapers have increased the amount of liquid they use, but the most likely reasons are either the cap on nicotine strengths and/or changes in the types of products being used.

To get around the limits, larger bottles of zero-strength liquid are on sale alongside smaller bottles with the highest legal limit nicotine strength liquid, sold to be mixed together. This is sometimes marketed as 'shake and vape'. The product is only used with open or tank systems, as disposable and cartridge-type devices do not have refillable liquid. The ASH YouGov survey finds that 26% of current vapers who use tank devices with nicotine report using 'shake and vape' products. The proportion not aware of 'shake and vape' has been steady at 24%-28% between 2019 and 2022, declining from 37% in 2018. (Figure 15). Rates of awareness of shake and vape products are lower in current smokers (66%), than in ex-smokers (77%) and never-smokers (80%).

Figure 15 - Change in awareness and use of 'shake and vape' products, Great Britain (2018 and 2022)



Unweighted base: Current GB e-cigarette user using tank as main device and using nicotine. 2018 n=696; 2019 n=775; 2020 n=744; 2021 n=769; 2022 n=993

OTHER E-CIGARETTE PRODUCTS

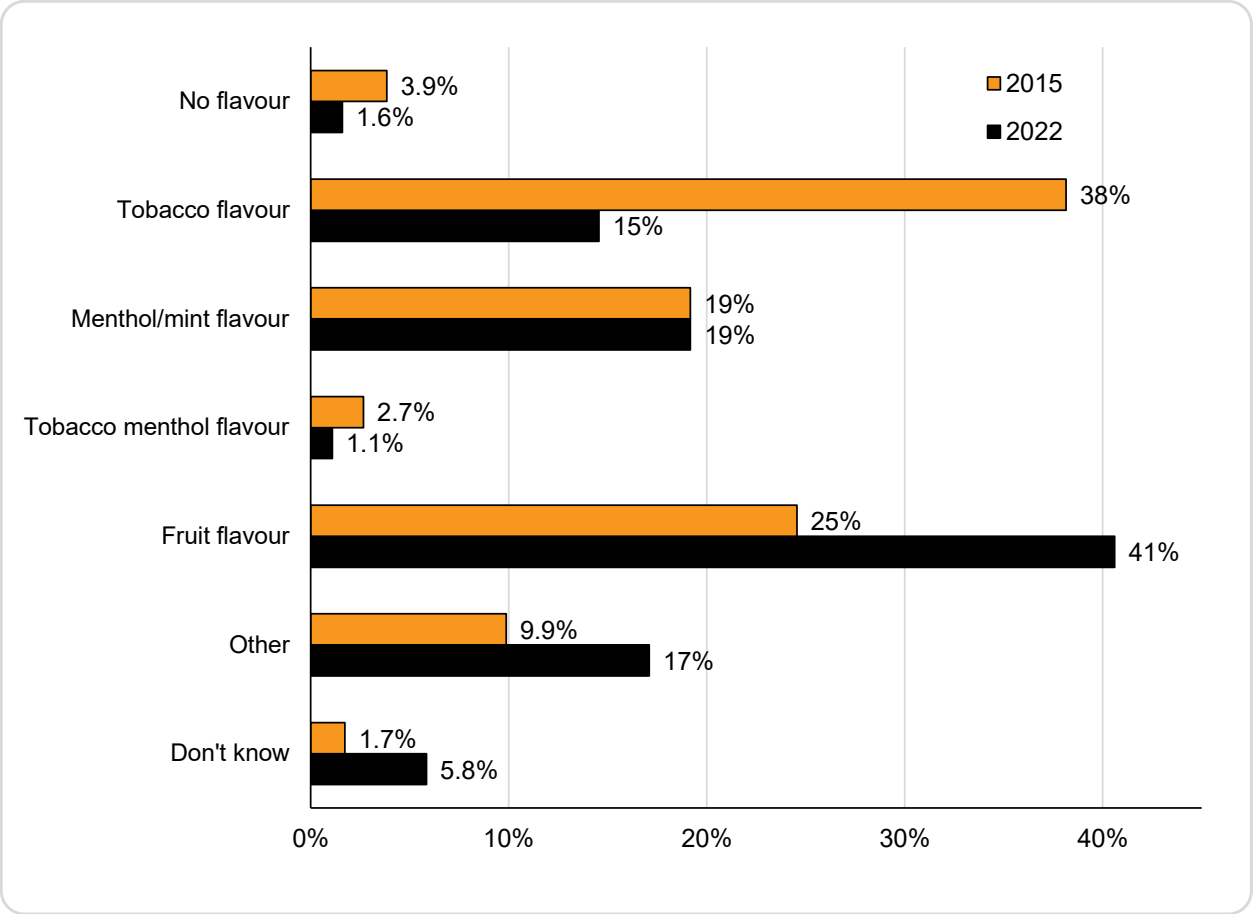
From 2017, after the launch of the Philip Morris International (PMI) product IQOS, the ASH Smokefree GB survey has asked about knowledge and use of heated tobacco products (also known as heat not burn). However, population level of knowledge and use was low to start with and has not grown significantly, so no detailed analysis can be carried out to date. In 2021, 14% of the public had heard of heated tobacco products and 1.7% had ever tried them. This finding is consistent with both the Smoking Toolkit Study and the ONS, which also find very low levels of knowledge and use of these products. In 2022 we did not ask about heat not burn products.

In 2020 we also included questions about other novel nicotine products to assess public awareness. Voke, a medicinally licenced inhalator which resembles an e-cigarette had ever been tried by 0.9% of the population with 9.0% aware of the product. Nicotine pouches (which includes brands such as Zin and Nordic Spirit) appear to have greater public awareness with 44% of people reporting they have heard of these products in 2022. However, ever use is still low at 3.9%.

USE OF FLAVOURS

In 2015, we started asking e-cigarette users what flavour they used most often. (Figure 16). In 2015 tobacco was most popular at 38% followed by fruit flavour at 24.6% and menthol 19%. This has changed over time with fruit flavours now the most popular at 41%, followed by menthol at 19%. Tobacco flavour has fallen to third most popular at 15%. Very few report using products with no flavours.

Figure 16 - Flavours used by adult vapers, Great Britain (2015 and 2022)



Unweighted base: All GB adults who currently use e-cigarettes 2015 n=614; 2022 n=1089; Other options to choose are grouped under 'Other'; in 2022 they were 'Coffee', 'Vanilla', 'Chocolate, desserts, sweet or candy flavour', 'Energy drink of soft drink' 'An alcoholic flavour' and 'Other'. In 2015, 'Mix of flavours' and 'Other' were options. All were under 2% of replies, except 'Chocolate, desserts, sweet or candy flavour' in 2022 at 6.3%.

Patterns of behaviour are similar for ex-smokers who vape and for dual users, although tobacco and menthol are more popular with ex-smokers and fruit flavours are more popular with current smokers. (Table 5). Never smokers are much more likely than other groups to not know what flavour e-cigarettes they use (31%), with very few choosing menthol or tobacco flavours (3.1% and 1.1%).

Table 5

Vape liquid flavour most often used (current e-cigarette users)			
	Current smokers (dual users)	**Ex-smokers**	**Never smokers**
Fruit flavour	44%	39%	41%
Menthol/mint flavour	15%	24%	3.1%
Tobacco flavour	14%	17%	0.0%

Unweighted base: All GB adults who currently use e-cigarettes 2022. Current smokers n=394; ex-smokers n=594; never smokers=101

In 2020, we asked vapers to describe their use of flavours and a higher proportion of ex-smokers who currently vape (74%) said they stick to the same flavours compared to dual users (61%).

Appendix 1

METHODS

This briefing reports the results of the ASH Smokefree GB surveys on the use of e-cigarettes among adults in Great Britain. All figures, unless otherwise stated, are from YouGov Plc. ASH included questions on e-cigarette use in this annual survey starting in 2010 with questions addressed only to smokers. ASH updated its annual survey with questions on e-cigarettes addressed to all respondents from 2012 onwards. (Appendix Table 1). These surveys have all been carried out online once a year in Spring by YouGov. All figures have been weighted and are representative of GB adults (aged 18+). Not all questions are asked every year, especially where answers have proven stable in the past. A few new questions are also introduced each year. ASH has also carried out a survey of youth e-cigarette use (11-18-year olds) since 2013. Analysis of e-cigarette use among youth is published separately.[14]

Calculations of the total number of vapers in Great Britain set out in Table 1 are by ASH. In each of the years we applied the proportions of e-cigarette use in the YouGov survey to the most recent available ONS mid-year GB population estimates at the time the YouGov data was gathered. In 2021 and 2022 the ONS mid-year GB population estimate for 2020 has been used.[15]

Table 1 - History of ASH Smokefree GB Surveys

Year	Sample Size	Dates
2008	3,329	20th – 25th February
2009	13,075	25th – 30th March
2010	12,597	17th – 22nd March
2012	12,436	27th February – 16th March
2013	12,171	1st – 19th February
2014	12,269	5th – 14th March
2015	12,055	26th February – 12th March
2016	12,157	2nd – 23rd March
2017	12,696	16th February – 19th March
2018	12,767	8th February – 6th March
2019	12,393	12th February – 10th March
2020	12,809	17th February – 11th March
2021	12,247	18th February – 18th March
2022	13,088	16th February – 21st March

Since the ASH-commissioned Smokefree GB survey first started, there have been a number of other surveys which have gathered data on e-cigarette use. The Smoking Toolkit Study is probably the most extensive of these and tracks both smoking and e-cigarette use throughout the year.[16] The study started in England in January 2007 and expanded to Scotland and Wales in December 2020. The countries' surveys are reported separately rather than together as Great Britain, and only the England data are discussed here. The trends are similar in both surveys,[17] but the ASH Smokefree GB survey consistently estimates a slightly lower figure for the proportion of e-cigarette users who are current smokers. The difference results from the assessment of smoking status: there are fewer ex-smokers and more current smokers in the Smoking Toolkit Study

than in the ASH Smokefree GB survey. Within the different categories of smoking status, the prevalence of e-cigarette use is similar between the surveys. For further information see the Smoking Toolkit.

COVID-19

The YouGov data collection for the ASH Smokefree surveys occurs in February and March, so we do not expect that the 2020 data was significantly affected by the COVID-19 pandemic. The data in subsequent years may capture changes in smoking and vaping attitudes and behaviours that are causally related to the pandemic or lockdown. In 2020, data collection for both the Annual Population Survey[18] and the Smoking Toolkit Study[19] had to be changed from face-to-face to telephone interviews. This means it is difficult to determine how far the changes in vaping patterns in these surveys were due to changes in the mode of data collection and how far they were directly due to COVID-19. The ASH Smokefree survey has always been online, so did not have a discontinuity in method during the pandemic.

Table 2 - Sample sizes for Figure 13

		Year					
		2017	2018	2019	2020	2021	2022
Age	18-24	52	50	56	55	52	217
	25-34	53	68	101	104	129	181
	35-44	127	129	159	168	177	217
	45-54	190	199	223	176	156	188
	55+	235	269	261	264	276	230

Appendix 2

E-CIGARETTE REGULATIONS

In 2015 a minimum age of sale for e-cigarettes of 18 was introduced, making it illegal to sell e-cigarettes containing nicotine to under 18s or to purchase them on behalf of under 18s.[20] From 20th May 2016, a regulatory framework for e-cigarettes was introduced in the UK under the EU Tobacco Products Directive (TPD) Article 20.[14] From that date, the advertising or promotion, directly or indirectly, of electronic cigarettes and re-fill containers on a number of media platforms, including on television, radio, newspapers and magazines, was prohibited. The only advertising still allowed is at point of sale and other local advertising such as billboards.

The new product rules under the TPD for electronic cigarettes introduced a notification process for manufacturers and importers in May 2016.[21] Non-compliant stock was allowed on sale for a further year until 20th May 2017.[22] See below for a summary of the key product standards:

Nicotine strength of e-liquid

- Electronic cigarettes which contain up to 20 mg per ml of nicotine are regulated as consumer products.
- Products containing over 20mg per ml of nicotine cannot be sold unless they have a medicinal licence.[23]
- Zero nicotine products are not included in the TPD and do not require a medicinal licence.

Quantity of e-liquid

- Disposable electronic cigarettes, cartridges and tanks can contain a maximum of 2ml of e-liquid, while dedicated refill containers can contain up to 10ml.

Safety

- Products must be child-resistant and tamper evident.

Health warnings

- The pack must carry a health warning covering 30% of the surfaces of the unit packet and any outside packaging stating '*This product contains nicotine which is a highly addictive substance*.'

The Medicines and Healthcare products Regulatory Agency (MHRA) is the competent authority for the notification scheme for e-cigarettes and refill containers in the UK.[24] Consumers and healthcare professionals can report side effects and safety concerns with e-cigarettes or refill containers to the MHRA through the Yellow Card reporting system.[25] They can also report products suspected to be defective or non-compliant to their local Trading Standards service or to TPDsafety@mhra.gov.uk.

The Yellow Card Scheme was put in place for e-cigarettes on 20 May 2016. Between then and February 2021, MHRA received 231 Yellow Card adverse reaction reports.[26] MHRA assess all reports received in associated with nicotine-containing e-cigarettes and should any potential safety concerns be identified regulatory action would be taken and communicated as appropriate. The MHRA also receives reports of potential safety concerns and works with local Trading Standards teams to investigate as needed.

There was a legal requirement to review the regulations within five years of implementation and publish a report by 20 May 2021.[27] The Department for Health and Social Care carried out a post-implementation review consultation January to March 2021.[28] The review found that the regulations were fit for purpose and to be retained in their current format.[29] ASH asks e-cigarette users questions about the type of product they use to inform our understanding of the impact of the current regulations and how the market for e-cigarettes is evolving.

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Molecular Imaging of Pulmonary Inflammation in Electronic and Combustible Cigarette Users: A Pilot Study

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ABSTRACT

Electronic cigarette (EC) use has increased dramatically, particularly among adolescents and young adults, which, like cigarette use, can cause pulmonary inflammation and increase the risk of lung disease. **Methods:** This preliminary study used positron emission tomography with ^{18}F-6-(1/2)(2-fluoro-propyl)-4-methylpyridin-2-amine (^{18}F-NOS) to quantify inducible nitric oxide synthase (iNOS) expression to characterize oxidative stress and inflammation in the lungs *in vivo* in three age- and sex-matched groups: (1) 5 EC users, (2) 5 cigarette smokers, and (3) 5 never smoke/vape controls. **Results:** EC users showed greater ^{18}F-NOS non-displaceable binding potential (BP_{ND}) than cigarette smokers (p= 0.03) and never smoke/vape controls (p= 0.01); whereas BP_{ND} in cigarette smokers did not differ from controls (p> 0.1). ^{18}F-NOS lung tissue delivery and iNOS distribution volume did not significantly differ between groups. Although there were no group differences in peripheral inflammatory biomarker concentrations, ^{18}F-NOS BP_{ND} correlated with the pro-inflammatory cytokine tumor necrosis factor-α concentrations (r_s= 0.87, p= 0.05) in EC users. Additionally, when EC users and cigarette smokers were pooled together, vaping episodes/cigarettes per day correlated with interleukin-6 levels (r_s= 0.86, p= 0.006). **Conclusion:** This is the first PET imaging study to compare lung inflammation between EC and cigarette users *in vivo*. We found preliminary evidence EC users had greater pulmonary inflammation than cigarette smokers and never smoke/vape controls, with a positive association between pulmonary and peripheral measures of inflammation.

Keywords: Electronic cigarettes, cigarettes, PET, ^{18}F-NOS, inflammation

INTRODUCTION

Tobacco use is the world's leading preventable cause of morbidity and mortality, accounting for more than 8 million deaths annually (*1*). Although public awareness of smoking-related risks has increased and tobacco smoking has declined, electronic cigarette (EC) use has increased dramatically, particularly among youth and young adults (*1*–*3*). The increase in EC use is partially driven by the assumption that ECs are safer than conventional cigarettes. Although ECs are often advertised as an alternative smoking cessation tool (*4*,*5*), their long-term effectiveness and safety have not been rigorously evaluated (*6*,*7*). Given the emergence of the EC or Vaping Product-Associated Lung Injury epidemic (*8*), EC use has become a major public health concern, and the adverse pulmonary effects of EC use remain unclear.

ECs deliver nicotine by heating e-liquids containing nicotine in a vegetable glycerin/propylene glycol vehicle with flavorings that are vaporized and inhaled, thus delivering nicotine without combusting tobacco. Although the propylene glycol and vegetable glycerin found in e-liquids are regarded as "safe" by the United States Food and Drug Administration, e-aerosols contain tobacco-specific nitrosamines, metals, polycyclic aromatic hydrocarbons, and volatile organic compounds that are known toxicants and carcinogens (*9*). As with smoking, several EC-related compounds are associated with inflammation, altered innate immune response, oxidative stress, and cytotoxicity (*9*–*11*). However, the existing human literature on the pulmonary effects of EC use is limited and comprised mainly of studies that use invasive approaches (e.g., induced sputum, bronchoalveolar lavage) that do not adequately assess the impact of EC use on the lungs.

Positron emission tomography (PET) imaging has been used to quantify and track inflammatory responses associated with smoking and EC use *in vivo* without the need for invasive diagnostic studies (*12*,*13*). PET with ^{18}F-fluorodeoxyglucose (^{18}F-FDG) has been used

extensively to detect enhanced glucose metabolic activity of activated immune cells in inflammatory diseases, including pneumonia (*14*), cystic fibrosis (*14*), and chronic obstructive pulmonary disease (COPD) (*15*). Although associations between ^{18}F-FDG quantification and inflammation have been observed, biological processes, including fibrosis and neoplasia, utilize glucose and limit the specificity of ^{18}F-FDG (*16*). PET radiotracers targeting the 18 kDa translocator protein, also known as the peripheral benzodiazepine receptor, have also been used to measure pulmonary inflammation (*17*,*18*). These radiotracers were initially considered putative markers of neuroinflammation; however, their specificity for inflammation is limited (*19*). Thus, recent efforts have focused on imaging specific aspects of immune regulation and response, such as nitric oxide synthase (NOS) enzymes, with promising results (*16*,*20*).

Nitric oxide (NO) plays an important role in immune regulation and is produced by three NOS enzymes: neuronal NOS, endothelial NOS, and inducible NOS (iNOS) (*21*). iNOS is associated with acute and chronic inflammatory diseases, including asthma and COPD (*22*,*23*), and is expressed in normal lung epithelium (*24*). Convergent evidence indicates that iNOS plays a central role in mediating inflammation in combustible cigarette smokers, thereby contributing to smoking-related lung diseases. Preclinical models show that chronic exposure to cigarette smoke increases iNOS expression (*25*), whereas pharmacological inhibition of iNOS reverses tobacco-induced lung disease (*26*). Additionally, preclinical research has provided a mechanistic link between iNOS expression in the lung and inflammatory lung diseases (*26*,*27*). These findings strongly support iNOS as a mechanistically relevant target for molecular imaging of lung inflammation and inflammatory lung diseases.

The PET radiotracer ^{18}F-6-(1/2)(2-fluoro-propyl)-4-methylpyridin-2-amine (^{18}F-NOS) permits the visualization and measurement of *in vivo* iNOS expression (*16*,*28*). ^{18}F-NOS is a radiolabeled version of a reversible iNOS inhibitor with better selectivity than other NOS enzymes

(*28*). ^{18}F-NOS has been validated in an animal model of lipopolysaccharide-induced lung injury (*29*) and was used successfully to image iNOS expression in humans to characterize oxidative stress and inflammation in the heart and lungs (*16*,*28*). This study uses ^{18}F-NOS PET lung imaging to quantify differences in iNOS expression among EC users, cigarette smokers, and never smoke/vape controls. Based on preclinical research showing that exposure to e-liquid vapor and cigarette smoke increases iNOS expression (*25*,*30*), we hypothesized that EC users and cigarette smokers would show greater pulmonary iNOS uptake than never smoke/vape controls. We also assessed blood/plasma inflammatory biomarker concentrations (tumor necrosis factor-alpha (TNF-α), interleukin (IL)-6, C-reactive protein (CRP)) and examined their association with ^{18}F-NOS PET lung imaging parameters.

MATERIALS AND METHODS

Participants

The study protocol was approved by the University of Pennsylvania Institutional Review Board and conducted in compliance with the Health Insurance Portability and Accountability Act under exploratory Investigational New Drug #140,976 for ^{18}F-NOS. Participants were recruited via local print media, social media, and previous research studies. Interested individuals completed a brief telephone screen and, if eligible, completed an in-person intake session during which they provided written informed consent and were screened for eligibility. Twenty-four participants underwent screening, including a physical examination, medical history, routine clinical laboratory tests, and toxicologic urine analysis. Briefly, exclusion criteria included history or evidence of significant medical disorders, a lifetime DSM-5 diagnosis of a psychiatric or substance use disorder (except tobacco use disorder for EC users and cigarette smokers), a positive urine drug screen, use of inhaled or oral corticosteroids or anti-inflammatory medications,

and a past-month history of lung trauma or active lung infection that could impact the uptake of ^{18}F-NOS. All female participants had a negative pregnancy test on the scanning day before receiving the radiotracer. EC users vaped nicotine, and cigarette smokers smoked daily for the past six months. Current smoking status was confirmed by carbon monoxide levels greater than 10 parts per million (ppm) and urine cotinine levels greater than 150 ng/mL. Fifteen age- and sex-matched participants (5 exclusive EC users [mean age=27 ± 7], 5 cigarette smokers [mean age 35± 9], and 5 never smoke/vape controls [mean age=28 ± 7]), comprising 2 women and 3 men in each group, met eligibility criteria and completed the study (Supplementary Figure 1).

Before scanning, participants completed the Hospital Depression and Anxiety Scale (*31*) to assess symptoms of depression and anxiety. EC users completed measures of vaping behavior, including the Penn State Electronic Cigarette Dependence Index (*32*), and cigarette smokers completed measures of tobacco smoking behavior, including the Fagerström Test for Cigarette Dependence (*33*). A blood sample was obtained to measure blood/plasma cytokine concentrations (TNF-α, IL-6, and CRP). Participants underwent ^{18}F-NOS dynamic PET/CT thorax imaging with venous blood sampling.

Data Acquisition

The PET radiotracer ^{18}F-NOS was synthesized as previously described (*28*). Participants were scanned with a Philips Ingenuity PET/CT scanner (Philips Healthcare, Cleveland, OH, USA), which has a 5-mm full-width at half maximum PET spatial resolution and an 18-cm axial field of view (*34*). For each scan, thoracic scanning field of view to best include the heart and lungs was determined by a Nuclear Medicine physician. After a low-dose attenuation-correction CT scan, a 1-h PET dynamic acquisition was started at the time of an intravenous bolus injection of ^{18}F-NOS (199 ± 27 MBq) with the following framing schedule: 24×5-s, 6×10-s, 3x20-s, 2x30-s, 5x60-s, and 10×5-min frames. Based on published effective dose estimates of 15.9 μSv/MBq for ^{18}F-NOS,

199 MBq delivers an effective dose of 3.16 mSv with maximum critical dose to the urinary bladder wall of 19.0 mSv (*28*). The attenuation-correction CT images were reconstructed into PET images using a previously described list-mode, blob-based, ordered-subsets, maximum-likelihood, expectation-maximization algorithm, including flight-time and physical-data corrections (*34*). The radiologist who reviewed the images and the data analyst were blind to participant group status.

Metabolite Analysis

Venous blood was sampled at approximately 2, 5, 10, 15, 30, 45, and 60 min after injection to measure radiometabolites. The whole-blood and plasma activity concentrations were counted using a WIZARD^2 2480 gamma counter (Perkin Elmer, Waltham, MA). Acetonitrile-treated plasma supernatant was analyzed in a 1260 Infinity Series (Agilent Technologies, Santa Clara, CA) high-performance liquid chromatology system using an Agilent ZORBAX StableBond C18 column via a mobile phase of 73% 0.1 M ammonium formate buffer and 27% methanol. The resulting plasma-to-whole blood ratio as a function of time was used to convert the image-derived whole blood input function into a plasma input function. The resulting parent PET radiotracer fraction as a function of time and the plasma input function were inputted for subsequent kinetic analysis.

Volumes of Interest

Whole-blood pool time activity curves (TACs) were measured using 1 cm^3 peak volumes of interest (VOIs) within 2-cm diameter spherical search VOIs within the pulmonary artery, as this blood pool is sufficiently large to minimize partial volume effects and located immediately before blood enters the lungs (Figure 1). Lung uptake TACs were extracted from all lung tissue in the PET field of view (Figure 1).

Kinetic Analysis

Three models of kinetic analysis were compared for estimating the total volume of distribution (V_T) from the observed reversible tracer binding: graphical Logan plot (*35*), 1-tissue compartment (1TC), and 2-tissue compartment (2TC). The 2TC model, with an average whole lung Akaike information criterion (AIC) (*36*,*37*) of 184 ± 31, was selected over the 1TC, with a corresponding AIC of 295 ± 24, based on the 2TC having the lower, and therefore better, AIC score. V_T values estimated via the Logan and 2TC models were similar (R^2 = 0.99). As expected, V_T values from Logan plots were biased lower than when using the 2TC model, with the magnitude of the Logan plot V_T bias decreasing with increases in the duration of the PET acquisition. Thus, we used the 2TC model to quantify tracer uptake to avoid having metrics dependent on the PET scan duration.

Two approaches for blood volume fraction (vB) were examined for each model: fixed at 0.15 and floating between 0.05 and 0.3. Floating vB resulted in the least model variability. Kinetic analyses using a 2TC model with a floated lung blood volume fraction (vB) were performed to estimate V_T, transport into the first tissue compartment (K_1), distribution volume of the first tissue compartment (K_1/k_2), and non-displaceable binding potential (BP_{ND}) via Pmod image analysis software (Pmod v3.7, PMOD Technologies Ltd., Zurich, Switzerland) using the combined lung TAC and PET image-derived plasma input function from the pulmonary artery blood pool (see Figure 1) (*38*). Kinetic analyses were based on the first 40 min of PET acquisition to allow a consistent analysis of all participants' data after one participant's excessive motion resulted in unevaluable PET images after 40 minutes.

Statistical Analysis

All statistical tests were two-sided. Non-parametric Mann-Whitney and Kruskal-Wallis tests were used to assess group differences. Spearman rank-order correlations measured the

strength and direction of associations between inflammatory biomarkers, nicotine use behaviors (cigarettes per day for cigarette smokers; vaping episodes per day for EC users), and imaging parameters.

RESULTS

On average, EC users reported 7 ± 4 vaping episodes/day, with Penn State Electronic Cigarette Dependence Index scores of 6 ± 4, indicating moderate-to-high levels of EC dependence. Cigarette smokers reported smoking 8 ± 4 cigarettes/day, with Fagerström Test for Cigarette Dependence scores of 5 ± 2, indicating moderate levels of cigarette dependence. There were no significant group differences in age, depression and anxiety scores, injected mass radioactivity dose or plasma-free fraction.

Selection of the pulmonary artery to measure the blood input function is supported by the example fused PET/CT images in Figure 1, where the distribution of ^{18}F-NOS before entry into the lungs indicates ^{18}F-NOS entering the right atrium followed by the pulmonary artery before lung entry and subsequent transport to lungs followed by the left ventricle. Figure 2 shows average lung ^{18}F-NOS uptake for all participants as a function of time. Table 1 presents kinetic analysis results, where the average estimate of lung blood volume fraction (vB) of 0.15 ± 0.02 is consistent with the reported normal lung vB range of 0.14 to 0.19 from ^{18}F-FDG PET/CT scans (*39*).

^{18}F-NOS BP_{ND} values differed significantly between groups, $H(2) = 7.50$, $p = 0.02$ (Figure 3). Post-hoc comparisons revealed that EC users had higher BP_{ND} values than cigarette smokers ($p = 0.03$) and healthy never smoke/vape controls ($p = 0.01$). ^{18}F-NOS V_T and K_1 values did not differ between groups (p's> 0.09).

Peripheral inflammatory biomarker concentrations did not differ between groups (*p*'s> 0.16). Spearman's rank-order correlations examined the associations between daily smoking/vaping behavior, inflammatory biomarker concentrations, and imaging parameters. There was a positive correlation among EC users between ^{18}F-NOS BP_{ND} and TNF-α concentration (r_s= 0.87, *p*= 0.05; Supplementary Figure 2). Among EC users and cigarette smokers, cigarettes per day and vaping episodes per day correlated with IL-6 levels (r_s= 0.89, *p*= 0.001; Supplementary Figure 3). No other correlations were statistically significant.

DISCUSSION

EC use has increased dramatically, particularly among adolescents and young adults. Consequently, well-controlled studies are urgently needed to examine and compare the effects of EC use and cigarette smoking. The existing literature mainly comprises cell culture studies or *in vivo* animal studies. A few studies examine the effects of EC use on the human lung based on invasive approaches that do not assess the global burden of EC use on the lungs. This preliminary study addresses these gaps by using non-invasive, ^{18}F-NOS PET lung imaging to quantify and compare lung inflammation in exclusive EC users, exclusive cigarette smokers, and never smoke/vape controls. Our preliminary ^{18}F-NOS PET findings show that EC users have similar delivery of ^{18}F-NOS to the lung tissue and iNOS availability similar to that of cigarette smokers and never smoke/vape controls. However, ^{18}F-NOS BP_{ND} was significantly higher in the EC group than in cigarette smokers and controls. Moreover, ^{18}F-NOS BP_{ND} in EC users was associated with the pro-inflammatory cytokine TNF-α. Cigarettes and vaping episodes per day correlated with IL-6 levels among cigarette smokers and EC users. This is the first PET lung imaging study demonstrating that EC users show a unique PET lung phenotype associated with known inflammatory biomarkers.

Although we did not see the expected increase in ^{18}F-NOS uptake in cigarette smokers, findings are consistent with recent work that used bronchoscopy to isolate alveolar macrophages from bronchoalveolar lavage samples in smokers, EC users, and never-smokers and found that EC users showed greater iNOS expression in alveolar macrophages than in smokers or never-smokers (*40*). Animal and human studies show that iNOS expression is induced in most cell types upon exposure to inflammatory stimuli (*41*) and is associated with increased pulmonary NO (*42*). NO mediates neutrophil and macrophage actions that are thought to contribute to pulmonary oxidant stress and acute lung injury (*43*). Thus, our findings suggest that EC use may alter pulmonary oxidative stress responses and predispose them to acute lung injury.

Although groups showed similar levels of inflammatory biomarkers, EC users showed positive associations between ^{18}F-NOS PET imaging parameters and TNF-α concentration. TNF-α is a pro-inflammatory cytokine produced by macrophages and secreted by neutrophil granulocytes at sites of injury (*44*) and is involved in the inflammatory cascade of acute lung injury (*45*). Indeed, studies show that pro-inflammatory cytokines induce iNOS expression in human alveolar cells in response to exposure to fine particulate matter (*46*). As such, our findings provide additional evidence of the altered immune responses in the lungs of EC users.

Several limitations should be considered. First, we did not account for vaping topography (i.e., how an EC is used, including puff duration, puff volume, and EC device and power settings). These factors are important in differential exposure to nicotine and toxicants among EC users (*47*). While we used individually measured PET radiotracer parent fractions as a function of time to correct for the presence of radiolabelled metabolites in the blood, we could not separate lung ^{18}F-NOS uptake due to binding of parent ^{18}F-NOS from any binding of radiolabelled metabolites. Huang et al. asserted, “because of [the metabolite’s] polarity, this metabolite is most likely excluded by the lung endothelium from entering the lung parenchyma” (*16*). Impacts of any lung

binding of radiolabelled metabolites on estimates of ^{18}F-NOS BP_{ND} will likely be inversely related to the validity of the assumption that polar ^{18}F-NOS metabolites cannot penetrate lung endothelium. To date, no studies provide information on the reproducibility of the ^{18}F-NOS PET assay; however, previous research showed consistent findings in left and right lung ^{18}F-NOS parameters (*16*). In addition, the sample sizes are small, so additional larger studies are needed to replicate these findings and provide greater statistical power for secondary analyses.

CONCLUSION

Using rigorous quantitative methods and a global technique to examine pulmonary oxidative stress, we find evidence that EC use causes a unique inflammatory response in the lungs, reflected by PET measures of iNOS expression and correlations with inflammatory biomarker concentrations. Future work is needed to elucidate the effect of EC use on respiratory health, especially the effects of chronic EC use.

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DISCLOSURES

Dr. Kranzler is a member of advisory boards for Dicerna Pharmaceuticals, Sophrosyne Pharmaceuticals, and Enthion Pharmaceuticals; a consultant to Sobrera Pharmaceuticals; recipient of grant funds and medication supplies from Alkermes for an investigator-initiated study; a member of the American Society of Clinical Psychopharmacology's Alcohol Clinical Trials Initiative, which was supported by Alkermes, Dicerna, Ethypharm, Lundbeck, Mitsubishi, and Otsuka; and a holder of U.S. patent 10,900,082 titled: "Genotype-guided dosing of opioid agonists," issued 26 January 2021. Drs. Dubroff, Doot, and Mach have received support from the Michael J. Fox Foundation. All other authors do not have disclosures to report.

KEY POINTS

QUESTION: What are the effects of e-cigarette use on pulmonary inflammation compared to combustible cigarette use and never smoking/vaping, as measured with ^{18}F-NOS PET imaging?

PERTINENT FINDINGS: In this preliminary PET imaging study, e-cigarette users showed greater ^{18}F-NOS non-displaceable binding potential (BP_{ND}) than cigarette smokers and never smoke/vape controls. ^{18}F-NOS BP_{ND} significantly correlated with the pro-inflammatory cytokine TNF-α in e-cigarette users. Additionally, when e-cigarette users and cigarette smokers were pooled together, vaping episodes/cigarettes per day correlated with IL-6 levels.

IMPLICATIONS FOR PATIENT CARE: Preliminary data indicate that e-cigarette users show a unique PET lung imaging phenotype associated with known pro-inflammatory cytokines, suggesting that e-cigarette use may increase pulmonary inflammation.

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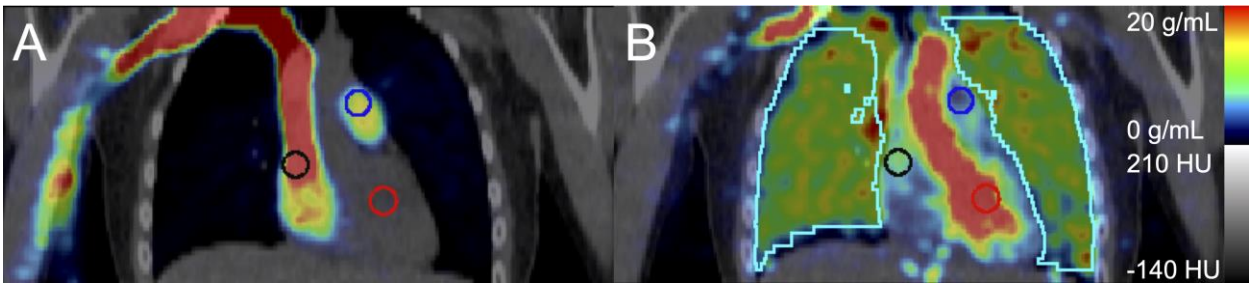


FIGURE 1. Representative fused coronal PET/CT images after injecting 207 MBq ^{18}F-NOS with 2-cm diameter spherical blood pool search volumes of interest in the right atrium (black), pulmonary artery (blue), and left ventricle (red) with (A) PET summed uptake 0-15 s post-injection and (B) PET summed 37 to 42 seconds post-injection with lung volume of interest (cyan).

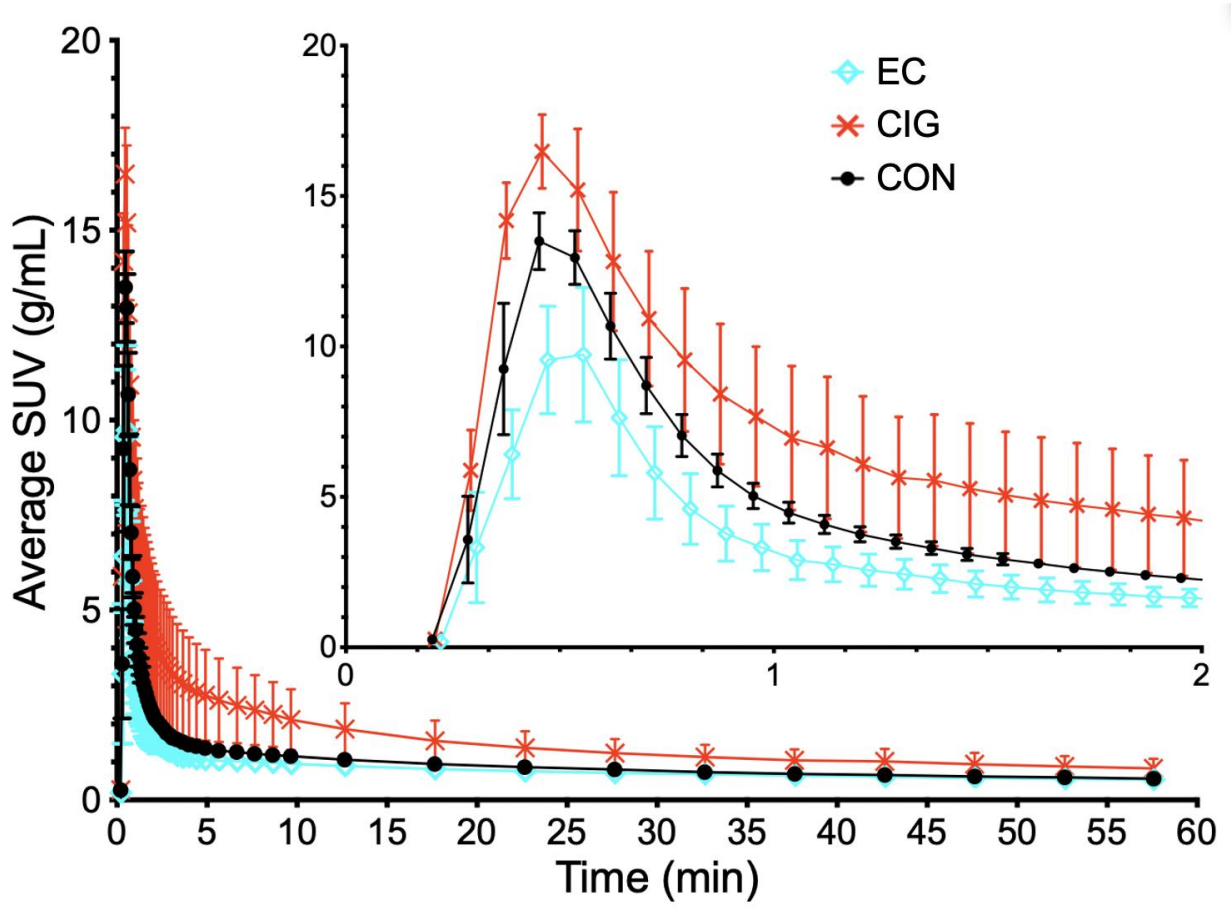


FIGURE 2. Average lung ^{18}F-NOS uptake for each group as functions of time with standard deviation error bars. EC = E-Cigarette Users, CIG = Cigarette Smokers, CON = Never Smoke/Vape Controls, SUV = standard uptake value.

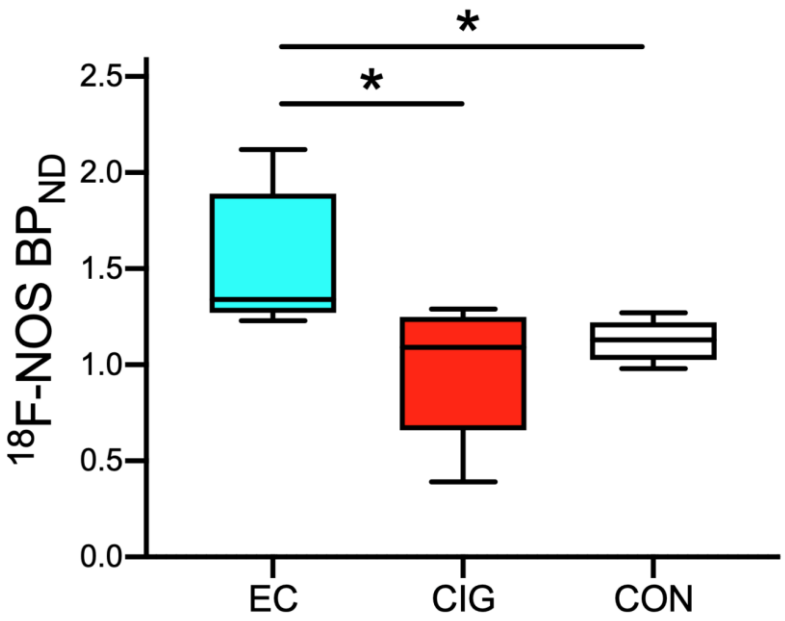


FIGURE 3. Boxplot of ^{18}F-NOS BP_{ND} by Group. EC Users show higher ^{18}F-NOS BP_{ND} than never smoke/vape controls ($p = 0.01$) and cigarette smokers ($p = 0.03$). BP_{ND} = non-displaceable binding potential. EC = E-Cigarette Users, CIG = Cigarette Smokers, CON = Never Smoke/Vape Controls. *$p < 0.05$

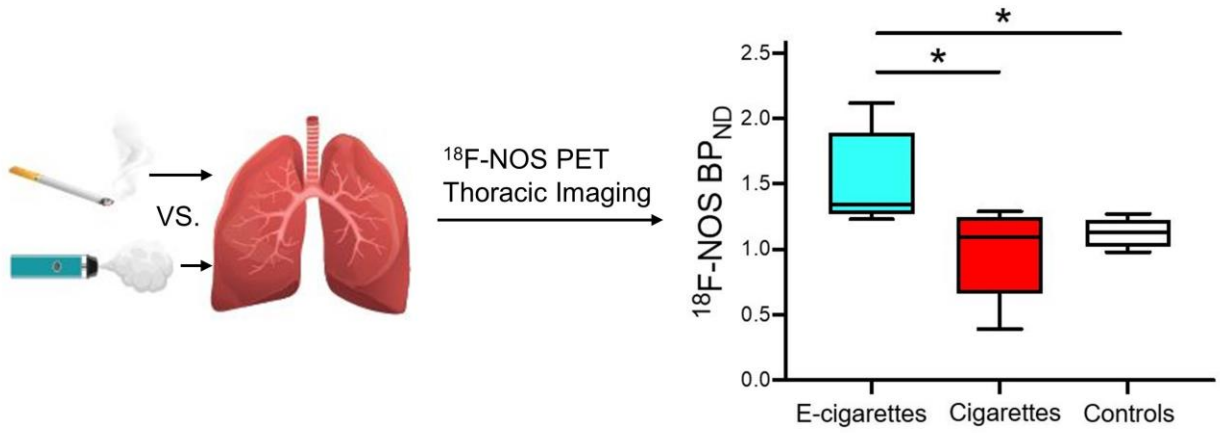
TABLE 1

Individual and cohort gender and ^{18}F-NOS kinetic measures

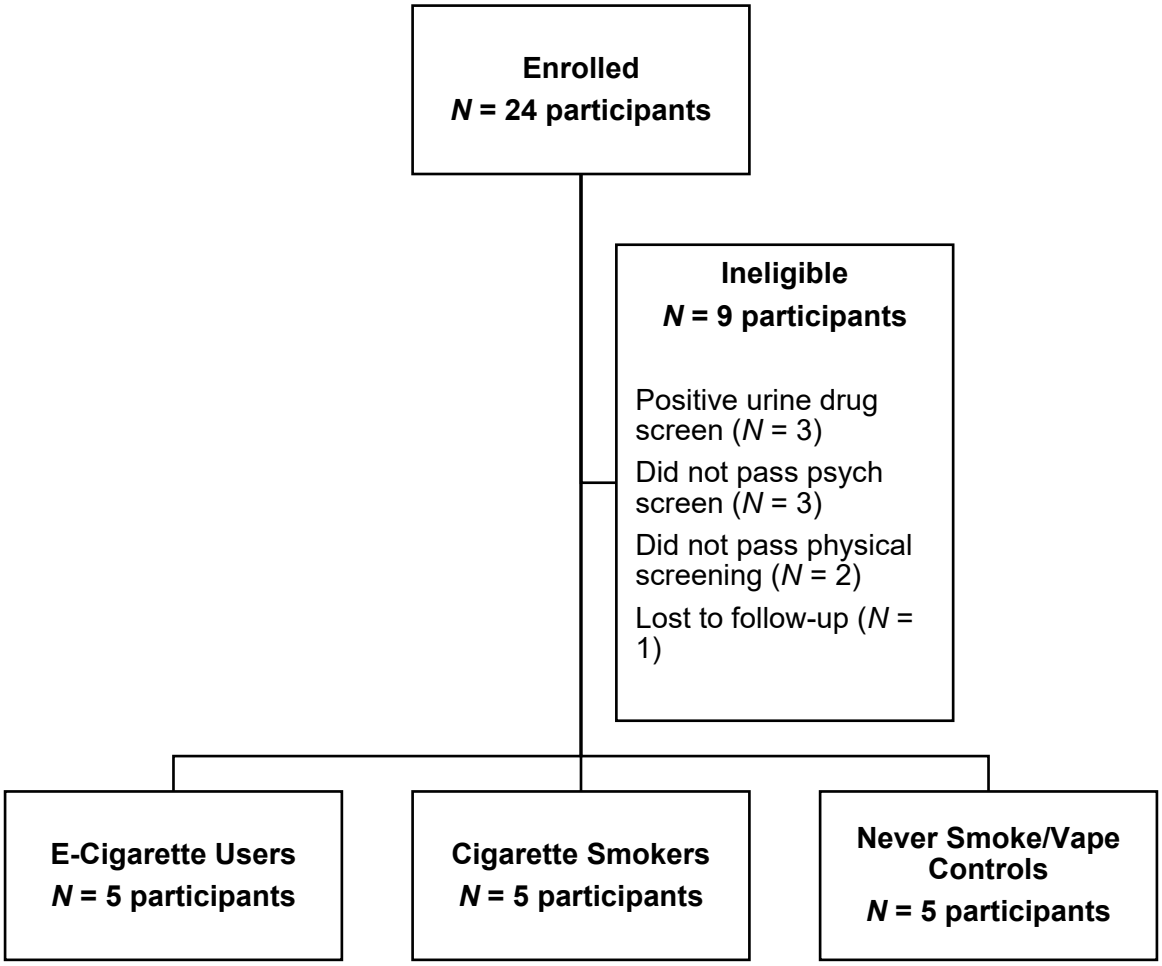
ID	M/F	V_T	K_1	K_1/k_2	BP_{ND}	vB
			Electronic cigarette users (EC)			
EC-07	F	1.17	1.62	0.51	1.31	0.15
EC-10	M	0.63	1.42	0.28	1.23	0.16
EC-13	F	0.99	1.58	0.42	1.34	0.18
EC-20	M	1.20	2.67	0.39	2.12	0.18
EC-23	M	0.83	1.26	0.31	1.66	0.13
			Combustible cigarette users (CIG)			
CIG-12	M	1.10	2.71	0.57	0.93	0.14
CIG-14	M	4.74	2.29	3.42	0.39	0.14
CIG-17	M	1.14	3.24	0.52	1.21	0.16
CIG-22	F	1.45	2.70	0.66	1.29	0.11
CIG-24	F	1.06	1.62	0.51	1.09	0.15
			Never users (NU)			
NU-01	F	1.15	1.95	0.58	0.98	0.18
NU-03	M	1.04	1.85	0.48	1.17	0.15
NU-05	M	0.91	1.37	0.40	1.27	0.15
NU-06	F	1.53	3.19	0.74	1.07	0.17
NU-09	M	1.18	1.62	0.56	1.13	0.13
	EC (n=5):	0.97 ± 0.24	1.71 ± 0.56	0.38 ± 0.09*	1.53 ± 0.37*	0.16 ± 0.02
	CIG (n=5):	1.90 ± 1.60	2.51 ± 0.60	1.13 ± 1.28	0.98 ± 0.36	0.14 ± 0.02
	NEVER USERS (n=5):	1.16 ± 0.23	1.99 ± 0.70	0.55 ± 0.13	1.12 ± 0.11	0.16 ± 0.02
	All (n=15):	1.34 ± 0.97	2.07 ± 0.67	0.69 ± 0.77	1.21 ± 0.37	0.15 ± 0.02
	p-value	0.36	0.09	0.03	0.02	0.31

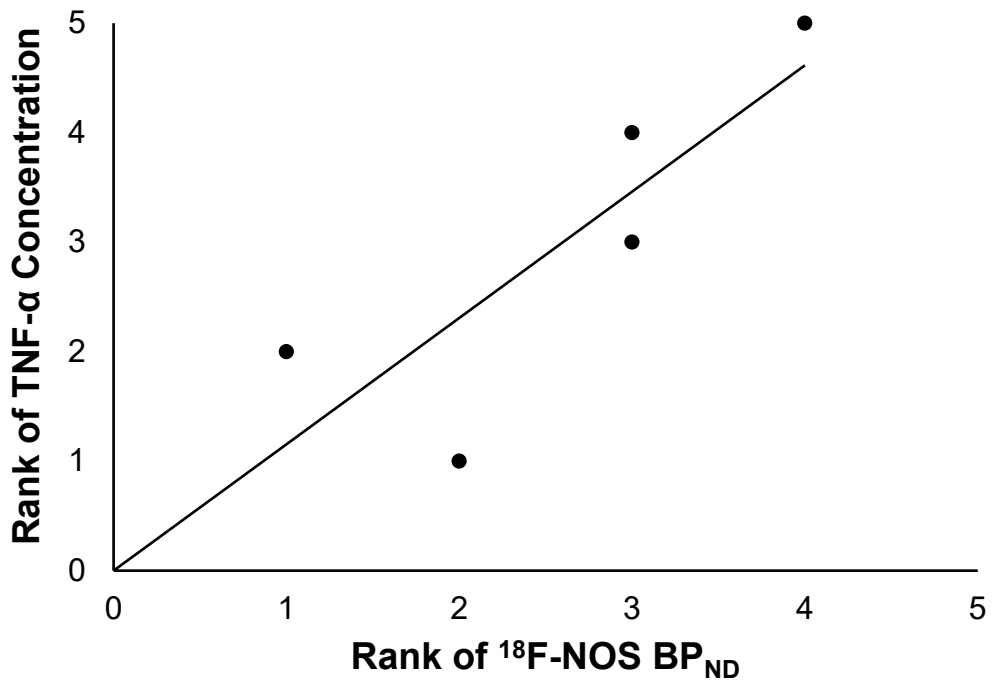
ID = participant study identification number; M/F = male/female biological sex; V_T = total volume of distribution; K_1 = delivery rate constant; K_1/k_2 = distribution volume of the first tissue compartment; BP_{ND} = non-displaceable binding potential; vB = blood volume fraction. Data are mean values and mean ± standard deviation. *p*-value from Kruskal-Wallis test comparing the three groups. *p<0.05 on comparison between EC and Never users.

Graphical Abstract

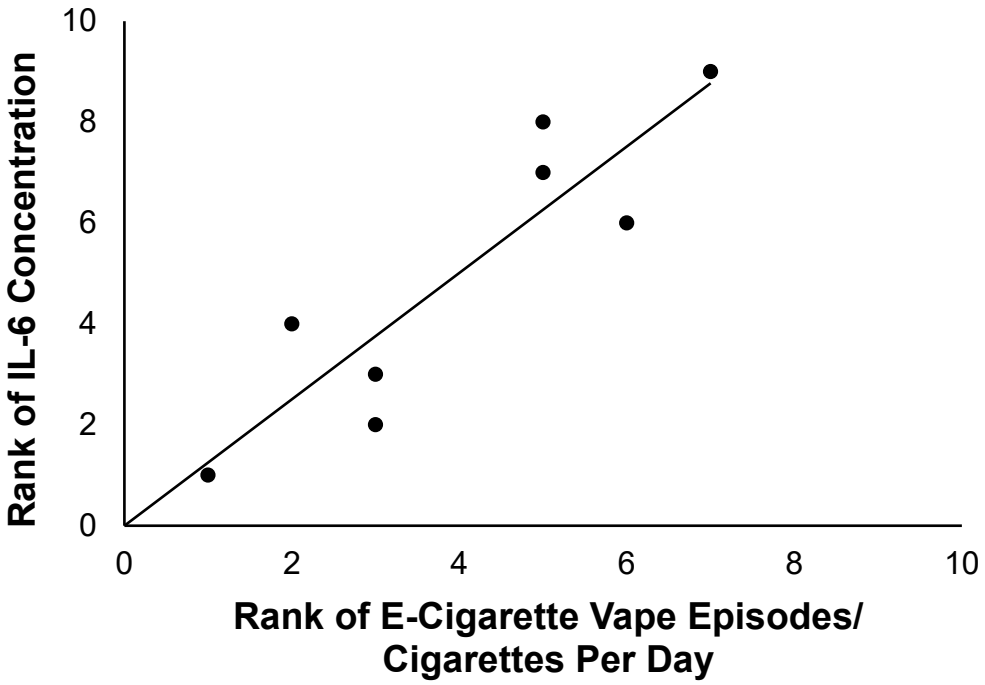


Supplementary Figure 1: STARD flow diagram





Supplementary Figure 2. Scatterplot demonstrating the rank-order correlation between ^{18}F-NOS non-displaceable binding potential and tumor necrosis factor-α concentration in e-cigarette users (r_s = 0.87, p = 0.05).



Supplementary Figure 3. Scatterplot demonstrating the rank-order correlation between e-cigarette vape episodes/cigarettes per day and interleukin (IL)-6 concentration in e-cigarette and combustible cigarette users (r_s = 0.89, p = 0.001).