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Nicotine and tobacco-specific nitrosamine exposure among youth in England who smoke cigarettes and/or vape

Eve Taylor [1,2] Debbie Robson,[1] Leonie S Brose [1] David Hammond,[3] Jessica L Reid [3] Ashleigh C Block [4] Maciej Lukasz Goniewicz [4] Maria Nikolaidou,[5] Ann McNeill [1]

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[1]Addictions Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[2]Behavioural Science and Health, UCL, London, UK
[3]School of Public Health Sciences, University of Waterloo, Waterloo, Ontario, Canada
[4]Department of Health Behavior, Roswell Park Comprehensive Cancer Center, Buffalo, New York, USA
[5]School of Sciences, Bath Spa University, Bath, UK

Correspondence to
Eve Taylor; eve.taylor@ucl.ac.uk

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ABSTRACT

Significance Compared with adults who smoke cigarettes, adults who vape nicotine are exposed to similar levels of nicotine and significantly lower levels of tobacco-specific nitrosamines (TSNAs). Little research outside the USA has included youth who vape, particularly those using newer disposable vapes. We investigated exposure to nicotine and the TSNA NNK (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol) among youth in England who vape, smoke, do both (dual) or do neither.

Methods In 2023, youth aged 16–19 years from England completed a survey and provided a urine sample (n=201). Linear regressions examined associations of creatinine-normalised urinary concentrations of total nicotine equivalents (TNE-2) and NNAL (a metabolite of NNK) with past 7-day smoking/vaping status and self-reported recency of vaping. All analyses were adjusted for age, sex at birth, ethnicity and any past 7-day cannabis use.

Findings Over three-quarters (77%) of those vaping were using the newer disposable vapes. Urinary TNE-2 concentrations among those who exclusively vaped in the past 7 days (n=83, geometric mean (GM)=5.09 nmol/mg creatinine (95% CI 3.19 to 8.12)) did not differ significantly from those who smoked (n=9, GM=1.74 nmol/mg creatinine (95% CI 0.64 to 4.72), p=0.426) or those who dual used (n=55, GM=5.60 nmol/mg creatinine (95% CI 3.32 to 9.43), p=0.953). Levels of NNAL among those who exclusively vaped (GM=1.87 pg/mg creatinine (95% CI 1.62 to 2.17)) were significantly lower than those who smoked (GM=4.87 pg/mg creatinine (95% CI 2.45 to 9.68), p=0.001) or those who dual used (GM=3.67 pg/mg creatinine (95% CI 2.76 to 4.86), p<0.001) and not significantly different from youth who neither vaped nor smoked (GM=1.84 pg/mg creatinine (95% CI 1.52 to 2.24), p=0.887).

Interpretation Youth who vape are exposed to similar levels of nicotine as those who smoke or who dual use. NNAL exposure among youth who vape is much lower than among those who smoke and indistinguishable from youth who do not vape or smoke.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ It is well established that vaping exposes adults to lower levels of tobacco-specific nitrosamines (TSNAs), some of which are highly carcinogenic to humans, and to similar levels of nicotine compared with smoking. However, there is limited evidence on nicotine or TSNAs among youth who vape, many of whom have never smoked. Moreover, there is no current research on toxicant exposure among youth who use new disposable devices.

WHAT THIS STUDY ADDS

⇒ This is the first exposure study using biomarkers among youth in England conducted after the rise of the disposable vaping device. We found that, although youth who vaped are exposed to levels of nicotine similar to cigarette smoking, they are exposed to substantially lower levels of the carcinogenic compound NNAL (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol), with levels similar to youth who have neither vaped nor smoked.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Due to the levels of nicotine that young people who vaped were exposed to, similar to smoking, vapes likely have the capacity to be addictive. However, based on NNAL exposure, vapes likely present substantially lower carcinogenic risks to youth compared with smoking, although they may expose users to other toxicants. Repeated biomarker monitoring among youth is needed to capture how market and product changes affect exposure levels and potential health effects.

BACKGROUND

The use of nicotine-containing vapes (e-cigarettes) varies globally among youth. The WHO estimates the highest prevalence of ever use among 13–15-year-olds is in European countries (34.5%), and the lowest is in African countries (8.8%).[1] Specifically in England, annual surveys of 11–17-year-olds found that current vaping had increased from 3.2% in 2021 to 7% in 2025 and a survey of 16–19-year-olds found that past 30-day vaping prevalence increased from 9% in 2018 to 25% in 2023.[2 3] Conversely, past 30-day smoking has stayed relatively stable in 16–19-year-olds at 17% in 2018 and 15% in 2023,[2] although there has been a substantial decrease in smoking rates among 11–15-year-olds in this time frame.[4] The rapid

increase in vaping has coincided with a changing marketplace, with new, affordable disposable products entering the market in 2020.[2] In England, use of these products among 11–17-year-olds increased from 8% in 2021 to 69% in 2023.[5 6]

Vapes contain a liquid composed of propylene glycol or vegetable glycerine, flavourings and nicotine, which is aerosolised by heating components and then inhaled. Vapes can help people who smoke to quit.[7] Nicotine is the major addictive component in vapes and tobacco, but the physical health harms from tobacco use are primarily from other constituents such as tobacco-specific nitrosamines (TSNAs), volatile organic compounds and carbon monoxide.[8] Nicotine is thought to have some effects on cardiovascular health, such as an increase in blood pressure, heart rate and vasoconstriction.[9] However, evidence does not suggest an association between nicotine and serious cardiovascular events.[10–12] Animal, but not human, research has also suggested an effect of nicotine on neurodevelopment.[13 14] When considering vapes as a smoking cessation tool, sufficient nicotine exposure can help alleviate cravings and withdrawal from tobacco.

Nicotine exposure from a vape is not just determined by the levels of nicotine in the vape liquid, but by individual differences, such as a person's nicotine metabolism,[15] vaping behaviour and device characteristics.[16] Device type and power settings[17] have been shown to influence nicotine levels. The chemical profile of nicotine in e-liquids can also influence exposure levels; nicotine salts have a lower pH, feel less irritating to the airways, taste sweeter than free-base nicotine[18] and may be associated with increased nicotine exposure. Although studies have shown lower nicotine exposure from vaping compared with smoking, adults who have vaped for some time showed similar exposure compared with smoking,[16] and the ability of vapes to deliver nicotine has improved over time. There has, however, been little research on nicotine exposure in youth. We previously examined nicotine biomarkers in a cross-sectional sample of 16–19-year-olds recruited between 2019 and 2022 (with three-quarters of the sample recruited by 2020), across the USA, Canada and England[19 20]; vaping was associated with similar nicotine exposure to smoking, and higher exposure was observed among those who reported using nicotine salt vapes.

When considering toxicant exposure from vapes, recent systematic reviews of biomarker studies, predominantly among adults but including a few studies among youth, concluded that vaping exposes people to a fraction of the toxicants compared with smoking,[12 16 21 22] but continued use is likely to incur some harms, so use among youth or people who would otherwise not smoke (or use nicotine-containing products) should be deterred.[12 16 21 22] In particular, levels of TSNAs, some of which are highly carcinogenic compounds in tobacco, have been reported to be over 90% lower among people who vape compared with people who smoke.[23] TSNAs are formed through the nitrosation of nicotine alkaloids during the tobacco curing and fermentation process and are thought to be specific to tobacco exposure.[24] The TSNA 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and its metabolite NNAL (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol) are considered known carcinogens.[25] TSNAs should not be present in vapes as they do not contain tobacco; however, their formation is possible if e-liquids contain impurities.[26] It is possible that tobacco-derived nicotine may contain higher levels of TSNAs from tobacco impurities than synthetic nicotine; however, the current evidence does not suggest a difference in TSNA levels between the two.[27] Exposure can also come from secondhand smoke (SHS).[28] Little is known about exposure to TSNAs in adolescents who vape, particularly outside the USA. Our recent study of 16–19-year-olds in England, the USA and Canada found that levels of NNAL were significantly lower among adolescents who vaped than smoked and not significantly different from those who neither vaped nor smoked.[19 20]

Due to differing regulations, such as limitations on tank/pod size, a maximum nicotine concentration of 20 mg/mL and a ban on certain constituents in England and the European Union (EU), products legally available in the USA differ from those in England and the EU.[29] These differences in products may lead to differences in toxicant exposure.[30 31] Moreover, the current disposable vaping products, used by 69% of youth who vaped in England in 2024,[5 6] often include nicotine salts at the highest legal concentrations (20 mg/mL), are available in a range of flavours and can contain synthetic coolants.[5 32] Therefore, these new products may expose consumers to different levels of nicotine and toxicants than other types of vaping devices, such as tanks.

Our previous study included only 30 16–19-year-olds in England who vaped (14 exclusively, 16 who also smoked), recruited mainly before the introduction of newer disposable products.[19 20] Here, we build on that study to assess the use of more recent vaping devices in England. Therefore, we aimed to investigate levels of urinary nicotine metabolites and NNAL among young people aged 16–19 years in England who exclusively vape, exclusively smoke cigarettes, smoke cigarettes and vape ('dual use') or neither vape nor smoke cigarettes.

METHODS

Design

In this cross-sectional observational study, data were obtained from young people aged 16–19 years from England between 11 September 2022 and 6 December 2023. The full protocol was preregistered, with the present study described under Community Biomarker Sub-Study https://fundingawards.nihr.ac.uk/award/NIHR130292.

Procedures

Purposive sampling methods were used, recruiting participants through online advertising and via schools, colleges and universities. Young people registered their interest in participating using an online survey or by email contact with the research team. Participants then provided consent and completed an online screening questionnaire (Questionnaire 1) to assess eligibility. Participants were eligible if they were aged 16–19 years and fulfilled the criteria for one of the following groups:

- Exclusively smoked: smoked cigarettes but did not vape in the past 7 days.
- Exclusively vaped: vaped but did not smoke cigarettes in the past 7 days.
- Dual use: smoked cigarettes and vaped in the past 7 days.
- Neither vaped nor smoked: did not smoke cigarettes or vape in the past 7 days.

Eligible participants were invited to complete a video call with the research team to confirm their age and provide additional verbal consent. Participants were then sent a link to a second online questionnaire and, once they had completed it, they were sent an at-home urine sample collection kit. Participants who returned urine samples received a £50 shopping voucher in appreciation for their participation. For details of sample collection, see online supplemental file 1.

Participants

A total of 1468 youth registered interest in participating, 911 completed the screening questionnaire and 533 were eligible and

contacted for a video call. Recruitment of youth who neither vaped nor smoked was capped at 54, with those screened after this deemed ineligible. Of these, 252 completed the video call and online questionnaire and were sent sample kits, of whom 205 (81%) returned the kits. Four incomplete kits were removed, resulting in an analytical sample of n=201.

Outcomes

Primary outcome

Biomarkers of nicotine and TSNA exposure: urine samples were tested for cotinine, 3-hydroxycotinine (3-HC) and NNAL using established protocols at the NicoTAR lab (Roswell Park Comprehensive Cancer Centre, Buffalo, New York, USA).[33] See online supplemental file 1 for details.

Questionnaire measures

Data were collected using three questionnaires; Q1, an online screening questionnaire; Q2, an online questionnaire completed once participants had been screened, consented and deemed eligible and Q3, a pen-and-paper questionnaire completed at the same time as providing the urine sample.

For details, see online supplemental file 1; for full questionnaires, see https://osf.io/xuw3n.

Smoking/vaping

The primary definition of smoking/vaping was use within the past 7 days. However, as cotinine has a half-life of approximately 16 hours,[34] 3-HC 7 hours and NNAL 10 days,[35] we also measured use at 24 hours and 30 days to account for washout from previous nicotine and/or tobacco use.

Past 7-day smoking/vaping status: 'Exclusively smoked', 'Exclusively vaped', 'Dual used' or 'Neither vaped nor smoked', all defined as per the eligibility criteria.

Additionally, we measured use at 7 days using more conservative definitions to exclude any smoking history among the exclusive vapers and any smoking and vaping history in the non-use group: 'Exclusively smoked', 'Exclusively vaped but never smoked', 'Dual used' or 'Never vaped nor smoked'.

Past 24-hour smoking/vaping status: 'Exclusively smoked' (smoked in the past 24 hours but did not vape in the past 7 days), 'Exclusively vaped' (vaped in the past 24 hours but did not smoke in the past 7 days), 'Dual use' (both smoked and vaped in the past 24 hours) or 'Neither vaped nor smoked' (neither vaped nor smoked in the past 7 days).

Past 30-day smoking/vaping: 'Exclusively vaped' (vaped but did not smoke in the past 30 days), 'Exclusively smoked' (smoked but did not vape in the past 30 days), 'Dual use' (vaped and smoked in the past 30 days) or 'Never smoked/vaped' (never smoked or vaped).

Vaping recency (among those who vaped in the past 7 days): 'Less than 1 hour ago', '1–6 hours', '7–12 hours', '12–24 hours' or '1–7 days'.

Characteristics of the vaping product last used

Device type ('disposable', 'other'), flavour ('menthol', 'fruit', 'candy/chocolate/dessert', 'non-alcoholic drink', 'alcoholic drink', 'other/don't know/no response'), nicotine strength ('0 mg/mL', '1–10 mg/mL', '11–20 mg/mL', '21 mg/mL or above', 'don't know/no response') and nicotine salt use in the past 7 days ('yes', 'no'). Device type was derived by researchers based on brand information. As few participants knew whether they were using nicotine salt products, brand information was also used to derive salt use.

Potential confounders

Other exposures

Past 7-day exposure to: other tobacco smoking (cigars, cigarillos, bidis, shisha, etc); smokeless tobacco use (chew, pinch, snuff, snus); other nicotine product use (patches, gum, lozenges, nicotine pouches); cannabis (smoked and/or vaped cannabis/marijuana) and SHS exposure.

Cannabis ever-use: 'Never used cannabis', 'Used cannabis but not in the past 30 days' and 'Used cannabis in the past 30 days'. One 'Don't know' response was excluded from cannabis ever-use analyses.

Demographics: age (years), sex at birth (male, female), England region (North, Midlands, South), perceived financial status (not meeting basic expenses, just meeting basic expenses, meeting needs with a little left over, living comfortably, don't know/no response). Ethnicity/race (Asian/Asian British, Black/Black British, mixed ethnicity, White, other ethnicity, don't know/no response) was derived from questions using the census classifications.[36] Due to small cell counts, ethnicity was collapsed into 'White' and 'racialised minority' (including 'don't know/no response') for regression analyses.

Biomarker analysis

Concentration values below the limit of quantification (LOQ) for each biomarker were imputed as the LOQ divided by the square root of 2.[37] All biomarker values were 'normalised' for creatinine (metabolite/creatinine per dL)×100. For descriptive analysis, geometric means (GMs) were reported for biomarkers. For regression analysis, concentration values were log-transformed.[38] Total nicotine equivalents (TNE-2) were calculated by combining the molar sum for cotinine and 3-HC. TNE-2 is considered the gold standard for measuring nicotine intake.[39]

Statistical analysis

Analyses were preregistered in the Open Science Framework (https://osf.io/xuw3n).

Descriptive analyses and GMs were used to report biomarker levels by demographics and vaping and smoking variables.

Linear regressions were used to examine associations between the concentration of each biomarker and past 7-day, past 24-hour and past 30-day smoking/vaping status.

Among youth who exclusively vaped, linear regression models examined associations between the levels of each biomarker and the recency of vaping.

All analyses were adjusted for age, sex at birth, ethnicity/race and past 7-day cannabis use and conducted on Stata V.17.0.

Sensitivity analyses

As cannabis is often consumed in combination with tobacco in England,[40] its use may confound nicotine levels. To control for the effect of cannabis consumption, analyses were repeated excluding those who used cannabis in the past 30 days (n=66).

To investigate the effect of potential confounding variables, linear regression models explored biomarker levels by past 7-day smoking/vaping status and other tobacco smoking, other nicotine use and SHS exposure separately.

Deviation from the preregistration

In addition to the preregistered sensitivity analysis and due to the high prevalence of SHS exposure, analyses were repeated excluding those exposed to SHS in the past 7 days (n=108). We also repeated the past 7-day analysis using the more conservative definitions of smoking/vaping. In deviation from

Table 1 Participant characteristics by past 7-day smoking/vaping status (n=201)

	All participants	Exclusively vaped	Exclusively smoked	Dual use	Neither vaped nor smoked
	% (n)	% (n)	%(n)	% (n)	% (n)
Total	100 (201)	41.8 (83)	4.5 (9)	27.4 (55)	26.9 (54)
Age (years)					
16	18.9 (38)	28.9 (24)	0 (0)	10.9 (6)	14.8 (8)
17	42.8 (86)	41.0 (34)	11.1 (1)	43.6 (24)	50.0 (27)
18	29.9 (60)	25.3 (21)	33.3 (3)	38.2 (21)	27.8 (15)
19	8.4 (17)	4.8 (4)	55.6 (5)	7.3 (4)	7.4 (4)
Sex					
Female	59.2 (119)	42.2 (35)	22.2 (2)	38.2 (21)	55.6 (30)
Male	40.8 (82)	57.8 (48)	77.8 (7)	61.8 (34)	44.4 (24)
Ethnicity/race					
Asian/Asian British	11.4 (23)	14.5 (12)	11.1 (1)	7.3 (4)	11.1 (6)
Black/Black British	1.5 (3)	0 (0)	0 (0)	0 (0)	5.6 (3)
Mixed ethnicity	9.5 (19)	8.4 (7)	0 (0)	12.7 (7)	9.3 (5)
White	72.6 (147)	73.5 (61)	66.7 (6)	78.2 (43)	68.5 (37)
Other ethnicity	3.5 (7)	1.2 (1)	22.2 (2)	1.8 (1)	5.6 (3)
Don't know/no response	1.5 (2)	2.4 (2)	0 (0)	0 (0)	0 (0)
Region					
Midlands	7.0 (14)	8.4 (7)	0 (0)	12.7 (7)	0 (0)
North	67.7 (136)	73.7 (61)	11.1 (1)	52.7 (29)	83.3 (45)
South	22.3 (45)	14.4 (12)	88.9 (8)	30.9 (17)	14.8 (8)
Don't know/no response	3.0 (6)	3.6 (3)	0 (0)	3.6 (2)	1.9 (1)
Perceived family financial status					
Not meeting basic expenses	3.0 (6)	0 (0)	0 (0)	10.9 (6)	0 (0)
Just meeting basic expenses	17.4 (35)	16.9 (14)	0 (0)	18.2 (10)	20.4 (11)
Meeting needs with a little left over	31.8 (64)	28.9 (24)	33.3 (3)	32.7 (18)	35.2 (19)
Living comfortably	43.3 (87)	45.8 (38)	66.7 (6)	38.2 (21)	40.7 (22)
Don't know/no response	4.5 (9)	8.4 (7)	0 (0)	0 (0)	3.7 (2)
Past 7-day other tobacco use	2.0 (4)	0 (0)	0 (0)	7.3 (4)	0 (0)
Past 7-day other nicotine product use	1.4 (3)	2.4 (2)	0 (0)	1.8 (1)	0 (0)
Past 7-day SHS*	54 (108)	55.4 (46)	33.3 (3)	70.9 (39)	37.0 (20)

*Past 7-day SHS data were missing for n=1 participant.
SHS, secondhand smoke.

the preregistration, analyses were not conducted examining biomarker concentrations by vaping device characteristics, due to a lack of variation in reported characteristics.

RESULTS

Sample characteristics

Sample characteristics are outlined in table 1. The majority of participants were female (59.2%), identified as White (72.6%) and were from the north of England (67.7%). Most participants perceived that their family financial situation was 'living comfortably' (43.3%) or 'meeting needs with a little left over' (31.8%).

Based on past 7-day use, 41.8% of the sample had exclusively vaped (n=83), 4.5% exclusively smoked (n=9), 27.4% had dual used (n=55) and 26.9% had neither vaped nor smoked (n=54) (table 1). Of those who exclusively vaped, the majority had smoked (77.1%). Similarly, among those who exclusively smoked, all had tried vaping. Among participants who neither vaped nor smoked, most had never smoked (70.4%), and equal proportions had never vaped (44.4%) or had vaped but not in the past 30 days (44.4%). Ever cannabis use was common among participants who vaped (54.8%), smoked (88.9%) or dual used (88.9%), but less so for those who did not vape or smoke (22.2%) (online supplemental table S1). Past 7-day SHS exposure was high among participants who had vaped (55.4%), smoked (33.3%), dual used (70.9%) or neither vaped nor smoked (37.0%). Few participants smoked other tobacco products (2.0%), or used other nicotine products (1.4%) (online supplemental table S1).

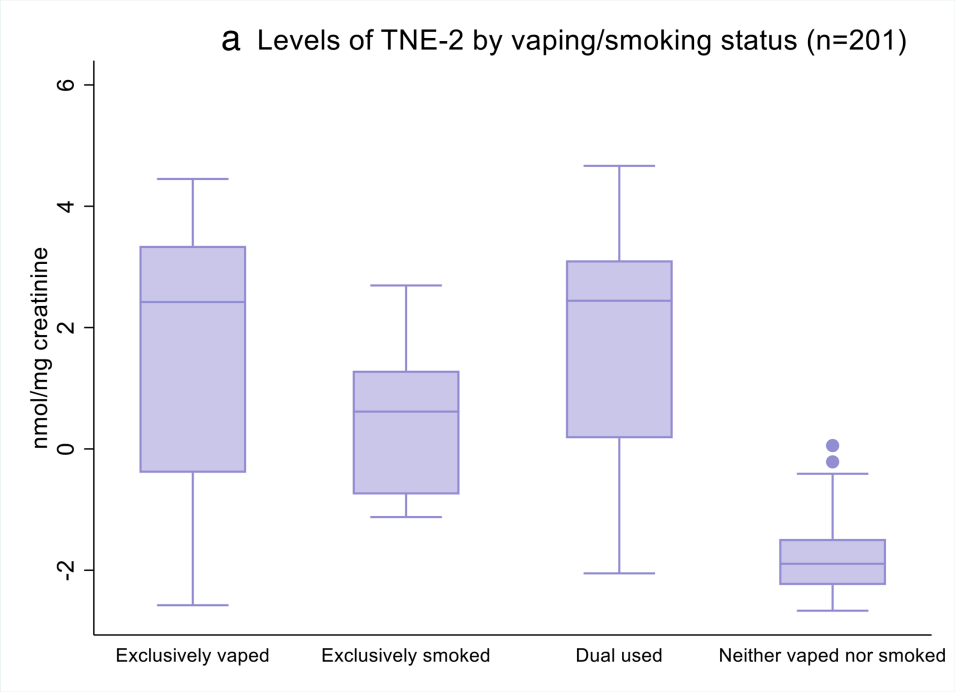
Among participants who had vaped, most used a disposable type (77% exclusive and 76% dual, respectively), nicotine strengths of 11–20 mg (78%, 76%), nicotine salts (94%, 88%) and fruit-flavoured e-liquids (76%, 58%) (online supplemental table S1).

Biomarkers

Nicotine metabolites

Overall, levels of cotinine and 3-HC were below the limit of detection for the majority of youth who neither vaped nor smoked (cotinine 81.5%; 3-HC 94.4%), around one-fifth of those who vaped (18.1%; 22.9%) and fewer youth who dual used (12.7%; 18.2%) or smoked (11.1%; 11.1%) (online supplemental table S2).

When comparing levels of nicotine metabolites (TNE-2) among participants who had vaped and/or smoked in the last 7 days descriptively, levels appeared highest among participants who had dual used (GM=5.60 nmol/mg creatinine (95% CI 3.32 to 9.43)), followed by those who had exclusively vaped (GM=5.09



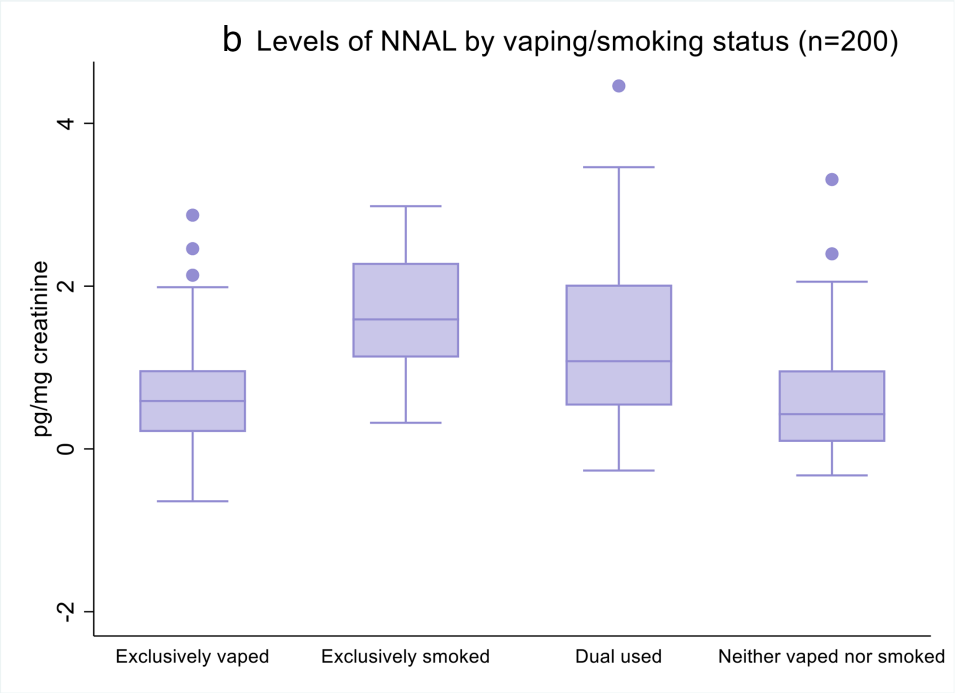


Figure 1 Box and whisker graphs of log-adjusted total nicotine equivalents (TNE-2) and NNAL (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol) concentrations among participants by past 7 day vaping and smoking status. Bars represent 95% CIs. In (b), the n=1 participant who vaped was removed due to improbable NNAL levels (433.84 pg/mg creatinine, 6.07 SD from the mean).

(95% CI 3.19 to 8.12)) and then those who had exclusively smoked (GM=1.74 (95% CI 0.64 to 4.72)); these differences were, however, non-significant (p>0.05) (figure 1a, table 2). Levels of TNE-2 were all significantly higher among youth who had vaped (GM=5.09 (95% CI 3.19 to 8.12)) compared with those who had neither vaped nor smoked (GM=0.17 (95% CI 0.14 to 0.20); B=−3.21 (95% CI −3.82 to −2.61), p<0.001) (figure 1a, table 2). Findings were similar for levels of cotinine and 3-HC and when participants who had vaped and/or smoked in the last 30 days and 24 hours were compared (online supplemental tables S3 and S4, figure S1 and S2). Findings were also similar when youth who exclusively vaped in the past 7 days but had never smoked were compared with youth who exclusively smoked, dual used or had never vaped nor smoked (online supplemental table S5).

Excluding participants who had used cannabis in the past 30 days or been exposed to SHS in the past 7 days did not change the interpretation of the findings (online supplemental table S6).

There were significant effects of other nicotine product use on 3-HC levels (B=−2.11 (95% CI −4.10 to −0.12), p=0.037),

Table 2 Associations between levels of nicotine metabolites and NNAL and smoking/vaping status (n=201)

	Cotinine			3-HC			TNE-2			NNAL*		
	nmol/mg creatinine			nmol/mg creatinine			nmol/mg creatinine			pg/mg creatinine		
	GM (95% CI)	Beta (95% CI)	P value	GM (95% CI)	Beta (95% CI)	P value	GM (95% CI)	Beta (95% CI)	P value	GM (95% CI)	Beta (95% CI)	P value
Past 7-day smoking/vaping												
Exclusively vaped	184.00 (108.14 to 313.06)	0	Ref.	735.98 (464.73 to 1165.54)	0	Ref.	5.09 (3.19 to 8.12)	0	Ref.	1.87 (1.62 to 2.17)†	0	Ref.
Exclusively smoked	70.30 (24 to 205.93)	−0.35 (−1.78 to 1.08)	0.631	246.56 (90.24 to 673.67)	−0.52 (−1.79 to 0.75)	0.422	1.74 (0.64 to 4.72)	−0.52 (−1.79 to 0.76)	0.426	4.87 (2.45 to 9.68)	1.06 (0.46 to 1.65)	0.001
Dual used	206.31 (118.01 to 360.67)	−0.03 (−0.76 to 0.70)	0.930	781.64 (459.34 to 1330.09)	−0.02 (−0.67 to 0.63)	0.949	5.60 (3.32 to 9.43)	−0.02 (−0.67 to 0.63)	0.953	3.67 (2.76 to 4.86)	0.65 (0.35 to 0.95)	<0.001
Neither vaped nor smoked	3.46 (2.79-4.30)†	−3.76 (−4.44 to −3.08)	<0.001	27.93 (23.76 to 32.83) †	−3.08 (−3.68 to −2.47)	<0.001	0.17 (0.14 to 0.20)†	−3.21 (−3.82 to −2.61)	<0.001	1.84 (1.52 to 2.24)†	0.02 (−0.27 to 0.31)	0.887
Age (years)		−0.36 (−0.7 to −0.03)	0.033		−0.35 (−0.64 to −0.05)	0.022		−0.5 (−1.05 to 0.04)	0.027		−0.09 (−0.23 to 0.05)	0.216
Sex												
Male	70.5 (39.04 to 127.33)	0	Ref.	314.66 (192.60 to 514.07)	0	Ref.	2.12 (1.28 to 3.53)	0	Ref.	2.16 (1.77 to 2.65)	0	Ref.
Female	57.07 (35.44 to 91.88)	−0.27 (−0.83 to 0.29)	0.340	279.36 (184.00 to 424.13)	−0.17 (−0.67 to 0.33)	0.507	1.88 (1.23 to 2.87)	−0.17 (−0.67 to 0.33)	0.509	2.47 (2.12 to 2.88)	0.10 (−0.14 to 0.33)	0.412
Ethnicity/race												
White	357.02 (245.29 to 519.63)	0	Ref.	77.07 (49.80 to 119.29)	0	Ref.	2.41 (1.64 to 3.53)	0	Ref.	2.34 (2.05 to 2.68)	0	Ref.
Racialised minority‡	181.97 (102.41 to 323.33)	−0.53 (−1.14 to 0.08)	0.088	36.50 (18.62 to 71.56)	−0.51 (−1.05 to 0.04)	0.067	1.22 (0.68 to 2.19)	−0.50 (−1.05 to 0.04)	0.070	2.34 (1.78 to 3.08)	0.04 (−0.22 to 0.29)	0.779
Past 7-day cannabis use												
Yes	8.05 (4.47 to 14.51)	0	Ref.	324.11 (176.24 to 596.05)	0	ref	1075.23 (578.20 to 1999.51)	0	Ref.	3.28 (2.20 to 4.89)	0	Ref.
No	1.48 (1.04 to 2.11)	−0.83 (−1.64 to −0.02)	0.046	44.06 (29.28 to 66.32)	−0.63 (−1.35 to 0.09)	0.087	224.84 (158.91 to 318.13)	−0.71 (−1.43 to 0.01)	0.055	2.18 (1.93 to 2.45)	−0.15 (−0.49 to 0.19)	0.387

*n=1 participant who vaped was removed due to improbable NNAL levels (433.84 pg/mg creatinine, 6.07 SD from the mean).
†Indicates levels are significantly different (p<0.05) from levels among those who exclusively smoked.
‡Includes those who identified as Asian/Asian British, Black/Black British, mixed ethnicity or other ethnicity.
GM, geometric mean; 3-HC, 3-hydroxycotinine; NNAL, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; TNE-2, total nicotine equivalents.

but not cotinine or TNE-2. As very few participants reported using other nicotine products (n=3) (online supplemental table S1), this measure was not adjusted for in sensitivity analyses. There were no significant effects of smoking other tobacco products on levels of nicotine metabolites.

Among youth who had exclusively vaped in the past 7 days, vaping recency was associated with nicotine metabolite levels, with greater concentrations observed among participants who had vaped in the hour prior to sample collection compared with 7–12 hours, 12–24 hours or 1–7 days prior. There were no significant differences between participants who had vaped in the past hour and those who had vaped in the past 1–6 hours (online supplemental figure S3 and table S7).

NNAL (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol)

NNAL was below the limit of detection for the majority of youth who had neither vaped nor smoked (88.9%), those who had exclusively vaped (86.7%), just over half of those who had exclusively smoked (55.6%) and two-fifths of youth who had smoked and vaped (40.0%) in the past 7 days (online supplemental table S3).

Compared with youth who had exclusively vaped (GM=1.87 pg/mg creatinine (95% CI 1.62 to 2.17)), levels of NNAL were significantly higher among youth who had smoked (GM=4.87 (95% CI 2.45 to 9.68), B=1.06 (95% CI 0.46 to 1.65), p=0.001) or dual used (GM=3.67 (95% CI 2.76 to 4.86), B=0.65 (95% CI 0.35 to 0.95), p<0.001) in the past 7 days (figure 1b, table 2). There was no significant difference in NNAL concentration between youth who vaped (GM=1.87 (95% CI 1.62 to 2.17)) and youth who neither vaped nor smoked (GM=1.84 (95% CI 1.52 to 2.24), B=0.02 (95% CI −0.27 to 0.31), p=0.887) (figure 1b, table 2). Findings were similar for past 24-hour and past 30-day smoking/vaping status (online supplemental tables S3 and S4, figure S4 and S5). Findings were also similar when youth who exclusively vaped in the past 7 days but had never smoked were compared with youth who exclusively smoked, dual used or had never vaped nor smoked (online supplemental table S5).

When people who had used cannabis in the past 30 days were excluded (n=66), or when people who had been exposed to SHS in the past 7 days were excluded (n=108), the interpretation of findings did not change (online supplemental table S6).

There were no significant effects of the use of other nicotine or tobacco on levels of NNAL.

Among youth who had exclusively vaped in the past 7 days (n=83), there were no significant differences in NNAL levels by vaping recency (online supplemental table S7).

DISCUSSION

Youth who had vaped in the past 7 days were exposed to similar levels of nicotine, but significantly lower levels of NNAL, than youth who smoked or both smoked and vaped. For youth who vaped in the past 7 days, NNAL levels were not significantly different from those who did not vape or smoke. Findings were not affected by recent cannabis use or SHS exposure. Among youth who vaped, nicotine exposure, but not NNAL, was associated with vaping recency.

Findings that nicotine levels are similar between vaping and smoking are consistent with our systematic review of nicotine exposure among adults who had vaped for a period of time.[16] Levels of TNE-2 among participants who had exclusively vaped in our sample (GM=5.09 nmol) were greater than among samples from youth in England (GM=1.60 nmol), the USA (GM=3.88 nmol) and Canada (GM=3.96 nmol), collected in our earlier study from 2019 to 2022.[19] These differences may be due to changes in the devices and e-liquids that youth used, as the use of disposable products, which contain high concentrations of nicotine (20 mg/mL), and the use of salt-based e-liquids increased substantially among youth in England between the two study periods (10% in 2021, 83% in 2023).[41] Previous research has indicated that salt products are associated with higher nicotine exposure.[42] We were unable to compare nicotine types or other device characteristics in this study due to a lack of variation, but most of the sample used disposable vapes, 20 mg/mL nicotine concentrations and nicotine salt e-liquids. Differences in nicotine levels between samples collected in 2023 and those in 2019–2022 indicate the need for repeated biomarker monitoring among youth to capture how market changes affect exposure levels and monitor potential health effects.

There has been a substantial increase in vaping dependence across a range of measures among youth since 2017,[43] which may be linked to the new disposable nicotine salt products being more efficient at delivering higher levels of nicotine. The current study indicates that nicotine exposure from the newer disposable devices, mostly sold at the highest permissible nicotine concentration and used by around 76% of our sample who vaped, is at least at levels similar to smoking. For the first time, we also demonstrated this finding in a sample of youth who vaped but had never smoked. Moreover, we found that youth who had vaped in the past 24 hours had higher levels of TNE-2 and 3-HC metabolites than those who smoked in the past 24 hours. However, this may be because 3-HC has a half-life of 7 hours,[44] and 40% of youth who vaped, but no youth who smoked, had done so in the 6 hours before sample collection.

Findings for NNAL are in line with previous research among adults,[23] showing that NNAL levels among youth who vaped were often (86.7%) below the limit of detection, and similar to those who have never vaped or smoked. These findings are also similar to a previous study among youth.[45] NNAL levels were similar among youth who smoked and dual used, indicating that young people who dual use should be supported to stop smoking to reduce exposure to carcinogenic compounds. In addition to TSNAs, there are many other toxicant exposures from smoking and vaping that can increase the risk of disease. However, as NNAL exposure strongly predicts lung cancers among those who smoke,[46] it is likely that the reduced exposure to TSNAs from vaping relative to smoking substantially reduces the risk of cancer for youth who vape compared with those who smoke.

In this study, we found it difficult to recruit youth who exclusively smoked (n=9) compared with youth who exclusively vaped (n=82) or dual used (n=55), which limited our power to make comparisons with youth who exclusively smoked. Recruitment issues probably reflect the increasing popularity of vaping and decrease in smoking in England over time.[4 6] However, based on past 7-day use, our findings are consistent with our earlier research based on urine samples of youth who smoked, largely collected a few years earlier with a larger sample size (33 in England, 16 in Canada and 19 in the USA who were exclusively smoking). A further limitation was the use of self-report, whereby participants' smoking or vaping status was not bioverified. We were, however, able to assess biomarkers among a sample of youth who had never smoked or vaped, a group that is necessary to provide accurate absolute exposure comparisons.[16] Our study only focused on one type of carcinogen and found reduced exposure. This aligns with other evidence among youth and adults.[16 19 20] However, use among youth or people

who would otherwise not smoke (or use nicotine-containing products) should be deterred.

CONCLUSIONS

Overall, youth who vape are exposed to similar levels of nicotine compared with those who smoke or who both smoke and vape, and exposure is associated with vaping recency. NNAL exposure in youth who vape is much lower and indistinguishable from youth who do not vape or smoke. Thus, depending on frequency of use, vaping is likely exposing youth to levels of nicotine that could form dependence. It is, however, exposing them to far lower levels of the carcinogen NNAL, similar to youth who have never smoked or vaped.

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Contributors EVT (guarantor): data curation, formal analysis, investigation and writing—original draft. DR: conceptualisation, funding acquisition, methodology and writing—original draft. LSB: conceptualisation, funding acquisition, methodology and writing—original draft. DH: conceptualisation, funding acquisition, methodology and writing—review and editing. JLR: conceptualisation and writing—review and editing. MLG: conceptualisation, funding acquisition, methodology and writing—review and editing. ACB: data curation, formal analysis and writing—review and editing. MN: data curation, project administration, investigation and writing—review and editing. AM: conceptualisation, funding acquisition, methodology and writing—original draft.

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Competing interests DH has served as a paid expert witness on behalf of public health authorities in response to legal challenges from tobacco, vaping and cannabis companies. MLG received a research grant from Pfizer and serves as a member of the scientific advisory board to Johnson & Johnson. The other authors declare no potential conflicts of interest.

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ORCID iDs
Eve Taylor https://orcid.org/0000-0003-3987-4760
Leonie S Brose https://orcid.org/0000-0001-6503-6854
Jessica L Reid https://orcid.org/0000-0001-9909-6265
Ashleigh C Block https://orcid.org/0000-0001-9849-4421
Maciej Lukasz Goniewicz https://orcid.org/0000-0001-6748-3068
Ann McNeill https://orcid.org/0000-0002-6223-4000

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Correction: *Nicotine and tobacco-specific nitrosamine exposure among youth in England who smoke cigarettes and/or vape*

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This article has been corrected since it was published online. In the originally published version, the co-author's name was misspelled as Maria Nicolaidu. The author's name has now been corrected to Maria Nikolaidou.

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