

# Comparison of nicotine emissions rate, 'nicotine flux', from heated, electronic and combustible tobacco products: data, trends and recommendations for regulation

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## ABSTRACT

**Introduction** Tobacco smoking is a major cause of disease and premature death worldwide. While nicotine is recognised as the main addictive component in tobacco smoke, the total nicotine amount emitted (nicotine yield) and the rate of nicotine emission per second ('nicotine flux') contribute to the abuse liability of a given product. These variables can be regulated for public health ends and conveniently so for electronic cigarettes or electronic nicotine delivery systems (ENDS).

**Methods** In this study we computed nicotine flux from previously reported values of yield and puff topography for a wide range of tobacco products.

**Results** We found that nicotine flux varied widely across tobacco products, from less than 0.1 µg/s to more than 100 µg/s, and that since 2015 the upper limit of the ENDS nicotine flux range has risen significantly and is now approaching that of combustible cigarettes. We also found that products that differ in nicotine flux may exhibit similar nicotine yields due to differences in user puffing behavior. Nicotine flux is a tool that can be used to regulate nicotine emissions of tobacco products, including ENDS.

## INTRODUCTION

Despite decades of tobacco control efforts, tobacco smoking remains one of the leading causes of premature death globally, estimated at 8 million deaths per year, and a major threat to public health.<sup>1</sup> The psychomotor stimulant nicotine is the main addictive agent in tobacco smoke and, without it, tobacco consumption would not be sustained.<sup>2,3</sup> As with other abused drugs, the dose and the speed at which nicotine reaches brain are critical to producing the addictive character of tobacco smoking.<sup>4</sup> In principle, more rapid delivery and greater dose result in greater reinforcement and greater abuse liability.<sup>5</sup> One reason combustible cigarettes are addictive is that inhaled tobacco smoke delivers nicotine to the brain in seconds, more rapidly even than intravenous nicotine delivery.<sup>6</sup> Historically, nicotine yield has served as the metric for characterising the amount of nicotine emitted by different combustible cigarette products.<sup>7</sup> Yield is defined as the mass of nicotine emitted through the mouth end of a tobacco product per unit of consumption (eg, milligrams of nicotine per cigarette; mg/cig). The rate at which nicotine is delivered, the yield per unit time, is referred to as the 'nicotine flux' (mg/s or

µg/s).<sup>8</sup> Because combustible cigarettes are made in a standard size and are consumed in roughly 5 min, nicotine yield and nicotine flux are closely coupled with combustible cigarettes—a cigarette with a high yield will also have a high flux.

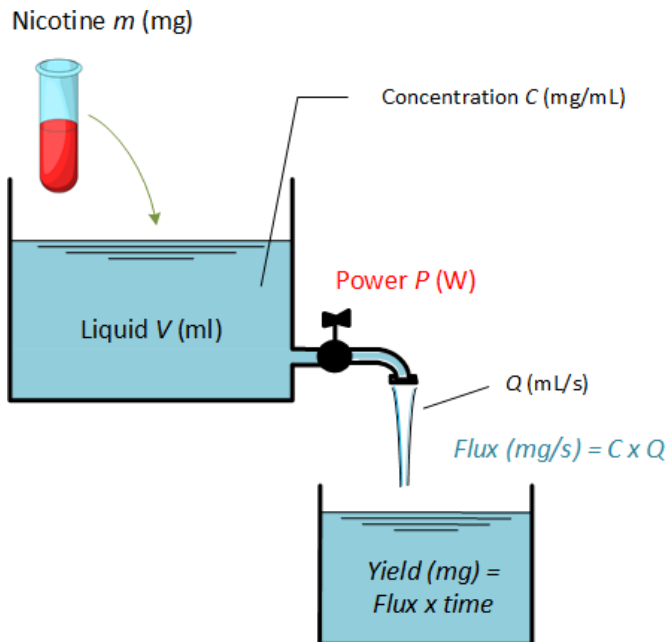
However, with electronic nicotine delivery systems (ENDS) and other products whose use patterns vary widely, the yield and the flux are not coupled closely. A product may have low yield and high flux (eg, the one-puff 'dokka'<sup>9</sup>) or vice versa (eg, nicotine patch). Typically, an ENDS product is consumed during multiple use sessions spanning a period of one to several days, depending on such factors as the size of the reservoir containing the nicotine solution and the electrical power of the device. Therefore, the nicotine yield of the product per unit sold may not be relevant to the yield obtained during a single use session. For example, a single JUUL pod emits roughly the same amount of nicotine as an entire pack of cigarettes but is unlikely to be consumed entirely in a single-use session.<sup>10</sup> Even the notion of a use session for an ENDS product may be difficult to define. Does taking a single puff just before entering an office building constitute a 'session'? Nicotine patches, too, can deliver a dose of nicotine over a day that is comparable with a pack of cigarettes. Clearly, a comparison of the yield of a JUUL pod, a nicotine patch and a cigarette stick has little value because the consumption patterns differ greatly; as a regulatory target, yield is not a useful construct. Nicotine flux, however, allows comparisons across products and product classes because it normalises nicotine emission by time. In doing so, flux also highlights the key factor of speed of delivery: nicotine flux is the theoretical upper limit of the rate at which nicotine can reach the brain. As we have discussed elsewhere,<sup>11</sup> to be enforceable a flux standard implies that only closed systems will be allowed on the market.

Figure 1 illustrates by analogy the relationship between nicotine flux, liquid nicotine concentration, device power, time and nicotine yield for ENDS products. The large tank can be thought of as the liquid reservoir of an ENDS product, while the small container can be considered the mouth of the user. The nicotine concentration of the liquid in the tank was prepared by dissolving a given mass,  $m$ , of nicotine (mg) in a given volume,  $V$ , of liquid (mL), resulting in a liquid nicotine concentration  $C=m/V$



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**Figure 1** Relationship between liquid nicotine concentration, device power, flux (nicotine emission rate) and yield for an ends device by analogy to a reservoir emptying into a container through a valve and tap assembly. In this analogy, the electrical power of the ENDS device determines the degree to which the tap is open during a puff; greater power means a more open valve. ENDS, electronic nicotine delivery systems.

(mg/mL). When a puff is executed, the rate at which liquid is aerosolised by the ENDS device (ie, in the form of an inhalable aerosol) and delivered to the mouth of the user is represented by opening the tap, allowing the flow to commence at some rate  $Q$  (mL/s). The nicotine flux is the product of the nicotine concentration  $C$  and the volume flow rate  $Q$ . To a close first approximation,  $Q$  is directly proportional to the power ( $P$ , Watts); greater power translates to a more open tap in figure 1. As a result, nicotine flux is directly proportional to the product of  $C$  and  $P$ . Finally, the amount of nicotine collected from the tap while the valve was open is the yield, which is simply the product of the flux and time.

In this study, we sought to estimate nicotine flux for a wide range of tobacco products to provide a base against which a potential ENDS product regulation could be considered. To date, extant EU and proposed US regulations have focused exclusively on limiting liquid nicotine concentration,<sup>12 13</sup> an approach that, counter to the stated aims of those regulations, constrains neither yield nor flux and therefore does not constrain exposure (ie, nicotine dose inhaled by the user).

## METHODS

Nicotine flux can be computed from published reports on tobacco product yields as the ratio of the yield to the cumulative puffing time of an inhaled tobacco product (eg, a cigarette or pipe) or as the ratio of the yield to the cumulative time of use of a product that emits nicotine continuously (eg, a nicotine patch).

For inhaled products, we searched the Scopus database using the following Boolean expression: (“nicotine” OR “nicotine yield”) AND (“flow rate” OR “puff duration” OR “interpuff interval” OR “puff volume” OR “topography”). The search resulted in 651 documents, of which 39 reported values of

nicotine yield, puff duration, and number of puffs; these 39 documents were retained for analysis.

The nicotine flux was computed as:

$$\text{Nicotine flux } \left( \frac{\mu\text{g}}{\text{s}} \right) = 1000 * \frac{\text{Nicotine yield } \left( \frac{\text{mg}}{\text{unit}} \right)}{\text{Total puffnumber } \left( \frac{\text{puffs}}{\text{unit}} \right) * \text{puff duration } \left( \frac{\text{s}}{\text{puff}} \right)}$$

For patch and gum products, we computed the flux as:

$$\text{Nicotine flux } \left( \frac{\mu\text{g}}{\text{s}} \right) = 1000 * \frac{\text{Nicotine dose } \left( \frac{\text{mg}}{\text{unit}} \right)}{\text{Total time of consumption } \left( \frac{\text{s}}{\text{unit}} \right)}$$

where the time of consumption was taken as 24 hours for patches and 30 min for gum. The dose was taken as that provided by the manufacturer assuming complete release of nicotine during the time of product consumption.

Average (SD) of nicotine fluxes for each tobacco product were determined to compare different products. A simple linear regression was used to test the correlation between year of publication versus nicotine flux. Statistical significance was taken as  $p < 0.05$ .

## RESULTS

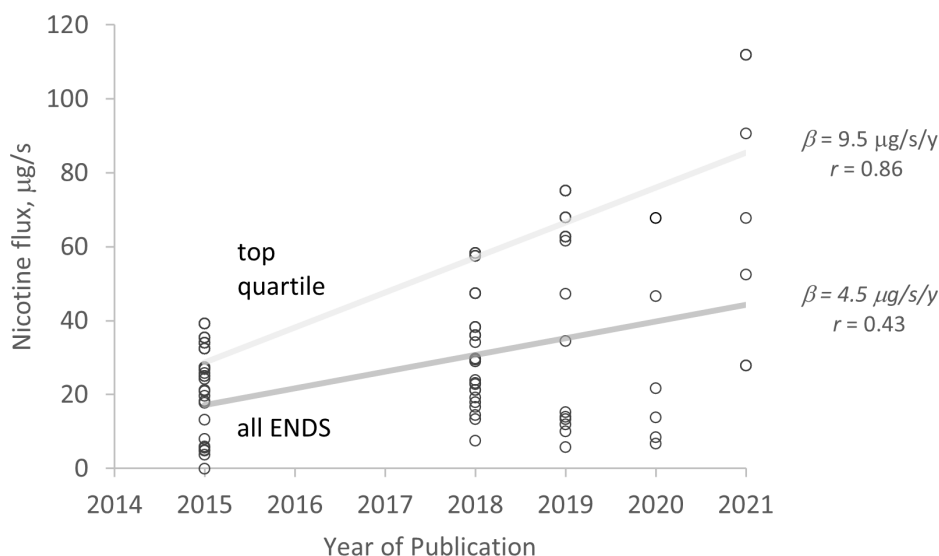
Published data were available to compute nicotine flux for approximately 90 products, spanning the categories of cigarettes, cigarillos, small cigars, waterpipes, ENDS, heated tobacco products, patches and nicotine gum. Online supplemental table S1 lists the results obtained for tobacco products that were machine smoked by mimicking human puffing patterns or by standard machine smoking regimens (eg, Canadian Intense, ISO). The nicotine flux across products ranged four orders of magnitude, from less than 0.1  $\mu\text{g/s}$  to more than 100  $\mu\text{g/s}$ , with the low end of the spectrum populated exclusively by nicotine patch and gum products and very low nicotine cigarettes and products above 100  $\mu\text{g/s}$  consisting exclusively of conventional combustible cigarettes. The results are summarised in table 1.

We also found a significant increase in reported flux over time (figure 2) for ENDS products (4.5  $\mu\text{g/s/year}$ ;  $p < 0.001$ ). Whereas prior to 2018, no publications reported products with a flux exceeding 40  $\mu\text{g/s}$ ; from 2019 onwards, nearly 40% of the tested products exceeded a flux of 60  $\mu\text{g/s}$ . The upper quartile flux for ENDS products in a given year also increased significantly at a mean rate of 9.5  $\mu\text{g/s/year}$  ( $p < 0.001$ ).

**Table 1** Computed nicotine flux by tobacco product category

Product	N	Year span	Flux ( $\mu\text{g/s}$ )	
			Mean (SD)	Range
Combustible cigarettes	27	1988–2020	79(32)	29–140
ENDS	52	2015–2021	29(23)	3.7–110
Heated tobacco products	14	2018–2020	31(18)	5.8–58
Waterpipe	8	2003–2019	11 (5.6)	5.8–20
Cigars/cigarillos	9	1976–2018	62(35)	12–110
Roll your own	3	1985–2014	69(28)	52–100
Bidi	2	1988–2003	60 (6.8)	55–64
Kretek	3	2014	47(16)	29–60
Nicotine patch and gum products	4	2018–2019	0.4 (0.48)	0.08–1.1
Very low nicotine cigarettes	1	2019	1.7(-)	–

N indicates the number of products reported, while year span indicates years of publication for the studies included.  
ENDS, electronic nicotine delivery systems.



**Figure 2** Reported nicotine flux of ENDS products by year of manuscript publication ( $p < 0.001$  for both regression lines). ENDS, electronic nicotine delivery systems.

## DISCUSSION

Nicotine flux is a performance metric that describes the acute nicotine throughput of a tobacco product, the net outcome of the interactions between numerous product design and operating variables. While nicotine flux represents the rate at which nicotine can enter the human body, and therefore the theoretical limit of the rate of delivery to the brain, the rate is mediated by other factors that influence the pharmacokinetics of nicotine delivery. For inhaled products, these factors include such things as the particle size distribution and freebase-to-protonated nicotine ratio of the aerosol. In this study, we sought to document nicotine flux from a range of tobacco products whose yields and puffing parameters had been reported in the literature. One limitation of this study is that products studied by previous researchers may not represent well the sales-weighted average of each category. A second limitation is that reported smoking machine studies may not have always used representative puffing parameters (eg, puff velocity, duration or inter-puff interval), biasing nicotine yield and, therefore, the computed flux. The most accurate analytical determinations of nicotine emissions are made using puffing conditions appropriate to the product in question; for example, users of large sub-Ohm ENDS devices typically draw up to an order of magnitude greater flow rate than a user of a small pod-based device.

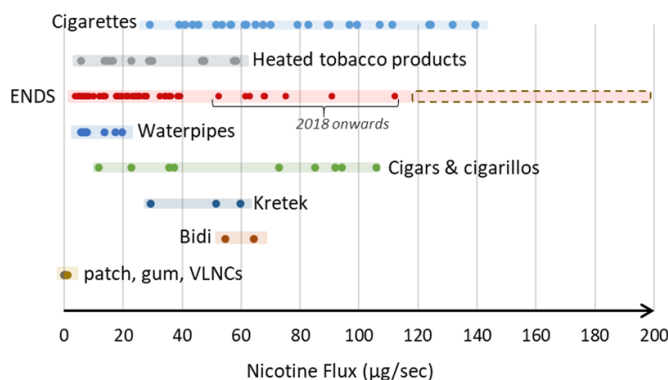
We found that for inhalable tobacco products, combustible cigarettes exhibited the greatest average nicotine flux, while waterpipes exhibited the greatest nicotine yield per session. Overall, nicotine patches had the greatest yields but also, owing to the long duration of use per unit, the lowest fluxes. These findings underscore the limitations of nicotine yield as a regulatory construct for tobacco products that vary widely; in these cases, greater yield was associated with *lower* abuse liability.

We also found significant variability in flux within and across product categories, as illustrated in figure 3. While ENDS generally exhibited nicotine fluxes lower than those of combustible cigarettes, reports from 2018 onwards began revealing ENDS products whose fluxes were equivalent to combustible cigarettes. Importantly, the 110 µg/s maximum flux reported to date for an ENDS product does not represent an intrinsic physical limit. With products available over the counter today, an ENDS user can readily access a liquid/device combination whose flux

exceeds any value yet reported. For example, based on the mathematical model of Talih *et al*,<sup>14</sup> a device operating at 60 W with an EU-compliant 20 mg/mL nicotine concentration liquid can produce a flux of approximately 240 µg/s, roughly double the maximum reported for any combustible cigarette.

The current regulatory environment therefore allows marketing ENDS products whose nicotine emission rate exceeds that of the high abuse liability combustible cigarette. Combined with emerging evidence that the convenience of ENDS use leads to far more frequent nicotine administration throughout the day than for combustible cigarettes,<sup>15–17</sup> the availability of high-flux ENDS products may portend greater population-wide nicotine dependence than was present prior to the advent of ENDS, if this outcome has not already been realised. Empirical data on the relationship between flux, acute delivery and dependence is too thin to evaluate this hypothesis at present; such data are urgently needed. Of note, Do *et al*<sup>18</sup> recently reported an association between nicotine flux and dependence scores in a pilot study of experienced users of pod-based devices.

Given the approximate doubling of ENDS nicotine flux from 2015 to 2020, policy makers may not have the leeway to wait for a definitive evidence base to emerge and may find it prudent



**Figure 3** Nicotine flux ranges across tobacco products. The dashed line for ENDS represents the capacity of current over-the-counter products to exceed values reported to date. ENDS, electronic nicotine delivery systems.

to regulate flux in the interim. There is little reason to suspect that exceeding the nicotine flux of combustible cigarettes is necessary to improve public health. With this starting point, an upper limit on ENDS nicotine flux could be, at most, 140 µg/s (see table 1). However, given the greater convenience and greater use frequency observed in ENDS users, this upper limit, if applied to ENDS, may still lead to greater population-level nicotine dependence. For this reason, one potential approach is to use the mean observed for combustible cigarette flux (ie, approximately 80 mg/sec, see table 1) as a temporary ceiling for over-the-counter ENDS products, with further adjustments informed by empirical investigations aimed at understanding the abuse liability of ENDS products across populations of particular interest (eg, nicotine naïve individuals and former smokers at risk for relapse). Of course, if empirical work demonstrates that higher flux ENDS are safe and effective for smoking cessation, these products can be made available to cigarette smokers in a manner that does not risk the health of nicotine-naïve individuals (eg, restricted access rather than over-the-counter availability). An additional concern is that ENDS aerosols contain varying concentrations of toxicants such as carbonyl species. Thus, minimising the amount of inhaled aerosol may be desirable because it can reduce user exposure to harmful toxicants. From this perspective, to the extent that a user seeks to attain a given nicotine intake, too low a nicotine flux can, perversely, increase non-nicotine toxicant exposure because it may drive more prolonged puffing bouts.

Policymakers interested in reducing nicotine dependence at the population level would do well to address nicotine flux as a regulatory target and avoid the mistake of using inappropriate proxies (eg, liquid nicotine concentration) that cannot, by themselves, be used to control the nicotine dose inhaled by ENDS users.

### What this paper adds

- ⇒ To date, tobacco product regulation aimed at nicotine abuse liability has been hampered by reliance on metrics that are not relevant to many tobacco products.
- ⇒ Nicotine flux, the amount of nicotine emitted per unit time, is a metric of abuse liability that can be deployed across a diverse range of tobacco products, including those that are inhaled, chewed or applied to the skin.
- ⇒ Nicotine flux across products varies from less than 0.1 µg/s to more than 100 µg/s, and for electronic cigarettes has been rising at an average rate of 5 µg/s/year since 2015.

**Contributors** The idea for this report was developed at a meeting of the Center for the Study of Tobacco Products (CSTP) Nicotine Flux Work Group in Lisbon, Portugal, 25–27 October 2019, thus all CSTP Nicotine Flux Work Group members are listed as collaborators and the work group name is included in the author list. MH and AS prepared the first draft of the manuscript and performed data analysis and figure preparation. The manuscript was finalised with input from ST and TE. Study guarantor: AS.

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**Competing interests** TE and AS are paid consultants in litigation against the tobacco industry and also the electronic cigarette industry and are named on one patent for a device that measures the puffing behaviour of electronic cigarette

users. TE is also named on a patent for a smartphone app that determines electronic cigarette device and liquid characteristics.

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**Ethics approval** This study does not involve human participants.

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**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information.

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### REFERENCES

- 1 WHO. Tobacco Fact Sheet. WHO Newsroom, 2021. Available: <https://www.who.int/news-room/fact-sheets/detail/tobacco> [Accessed 3 Dec 2021].
- 2 Benowitz NL, Henningfield JE. Establishing a nicotine threshold for addiction. The implications for tobacco regulation. *N Engl J Med* 1994;331:123–5.
- 3 Henningfield JE, Benowitz NL, Slade J, et al. Reducing the addictiveness of cigarettes. Council on scientific Affairs, American Medical association. *Tob Control* 1998;7:281–93.
- 4 Carter LP, Stitzer ML, Henningfield JE, et al. Abuse liability assessment of tobacco products including potential reduced exposure products. *Cancer Epidemiol Biomarkers Prev* 2009;18:3241–62.
- 5 Allain F, Minogianis E-A, Roberts DCS, et al. How fast and how often: the pharmacokinetics of drug use are decisive in addiction. *Neurosci Biobehav Rev* 2015;56:166–79.
- 6 Henningfield JE, Stapleton JM, Benowitz NL, et al. Higher levels of nicotine in arterial than in venous blood after cigarette smoking. *Drug Alcohol Depend* 1993;33:23–9.
- 7 Djordjevic MV, Stellman SD, Zang E. Doses of nicotine and lung carcinogens delivered to cigarette smokers. *J Natl Cancer Inst* 2000;92:106–11.
- 8 Shihadeh A, Eissenberg T. Electronic cigarette effectiveness and abuse liability: predicting and regulating nicotine flux. *Nicotine Tob Res* 2015;17:158–62.
- 9 Samara F, Alam IA, ElSayed Y. Midwakh: assessment of levels of carcinogenic polycyclic aromatic hydrocarbons (PAHs) and nicotine in Dokha tobacco smoke. *J Anal Toxicol* 2021. doi:10.1093/jat/bkab012. [Epub ahead of print: 21 Jan 2021].
- 10 Trochaska JJ, Vogel EA, Benowitz N. Nicotine delivery and cigarette equivalents from vaping a JUULpod. *Tob Control* 2022;31:e88–93.
- 11 Eissenberg T, Soule E, Shihadeh A, et al. 'Open-System' electronic cigarettes cannot be regulated effectively. *Tob Control* 2021;30:234–5.
- 12 Nedelman M. New bill aims to cap nicotine levels in e-cigarettes. CNN, 2019. Available: <https://edition.cnn.com/2019/10/07/health/vaping-nicotine-cap-krishnamoorthi-bn/index.html> [Accessed 3 Dec 2021].
- 13 Directive 2014/40/EU of the European Parliament and of the Council of 3 April 2014 on the approximation of the laws, regulations and administrative provisions of the member states concerning the manufacture, presentation and sale of tobacco and related products and repealing directive 2001/37/EC. *OJEU* 2014;127:1–38 [https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ%3AJOL\\_2014\\_127\\_R\\_0001](https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ%3AJOL_2014_127_R_0001)
- 14 Talih S, Balhas Z, Eissenberg T, et al. Effects of user puff topography, device voltage, and liquid nicotine concentration on electronic cigarette nicotine yield: measurements and model predictions. *Nicotine Tob Res* 2015;17:150–7.
- 15 Cooper M, Harrell MB, Perry CL. A qualitative approach to understanding real-world electronic cigarette use: implications for measurement and regulation. *Prev Chronic Dis* 2016;13:E07.
- 16 Baweja R, Curci KM, Yingst J, et al. Views of experienced electronic cigarette users. *Addict Res Theory* 2016;24:80–8.
- 17 Paul K. Breaking up with my Juul: why quitting vaping is harder than quitting cigarettes. The guardian, 2019. Available: <https://www.theguardian.com/society/2019/oct/10/breaking-up-with-my-juul-why-quitting-vaping-is-harder-than-quitting-cigarettes> [Accessed 3 Dec 2021].
- 18 Do EK, O'Connor K, Perks SN, et al. E-Cigarette device and liquid characteristics and e-cigarette dependence: a pilot study of pod-based and disposable e-cigarette users. *Addict Behav* 2022;124:107117.

**COMPARISON OF NICOTINE EMISSIONS RATE, “NICOTINE FLUX”, FROM HEATED, ELECTRONIC, AND COMBUSTIBLE TOBACCO PRODUCTS: DATA, TRENDS, AND RECOMMENDATIONS FOR REGULATION**

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## SUPPLEMENTAL MATERIAL

**Table S1.** Summary of the nicotine yield and flux of various tobacco products and the corresponding puffing topography parameters.

\* Average puff number under ISO smoking regime was used.

Tobacco Product	Brand	Puff Number	Puff duration (s)	Nicotine Yield (mg/unit)	Nicotine Flux ( $\mu\text{g/s}$ )	Reference	Year of Publication
Cigarettes	Maintained nicotine cigarette	15	2	2.7	90.0	[1]	1988
	Middle tar cigarette	15	2	2.9	96.7		
	Low tar cigarette	14	2.5	1.8	51.4		
	Regular-yield brands (9-15 mg ISO tar)	11.5	1.4	2	124.2	[2]	2006
	Matinee extra mild (4 mg ISO tar)	13.4	1.6	1.5	70.0		
	Own brand (female smokers)	13.5	1.33	1.92	106.9	[3]	2007
	Own brand (male smokers)	12	1.48	2.2	123.9		
	Kent (non-menthol cigarette)	14.4	1.17	0.9	53.4	[4]	2017
	Benson & Hedges Light (menthol cigarette)	15.1	1.23	1.05	56.5		
	Marlboro red	12.2	1.68	2.54	123.9	[5]	2020
	Lucky Strike	10.7	1.8	1.3	67.5	[6]	2018
	Lucky Strike Menthol	10	2	1.3	65.0		
	Lucky Strike	16.6	1.6	1.5	56.5	[7]	2020
	Low-yield cigarettes ( $\leq 0.8$ mg of nicotine/cigarette)	12.7	1.5	1.7	89.2	[8]	2000
	Medium-yield cigarettes (0.9–1.2 mg of nicotine/cigarette)	12.1	1.5	2.39	131.7		
	2R4F	9.5	2	0.829	43.6	[9]	2014
	1R6F	8.0	2	0.73	45.6	[10]	2018
	1R6F	8.4	2	2.34	139.3		
	3R4F	9.0	2	0.74	41.1		
	3R4F	10.7	2	2.38	111.2		
	Regular-yield brands (9-15 mg ISO tar)	9	2	1.1	61.1	[2]	2006
		12.1	2	2.4	99.2		
	Low-yield cigarettes ( $\leq 0.8$ mg of nicotine/cigarette)	9	2	0.7	38.9	[8]	2000
Medium-yield cigarettes (0.9–1.2 mg of nicotine/cigarette)	9	2	1.11	61.7			
Marlboro Ultra Smooth	7.2	2	0.42	29.2	[11]	2006	
	6.9	2	1.09	79.0			
Marlboro Regular	12	2	1.99	82.9	[12]	2018	
VLNC	VLN King	9*	2	0.03	1.7	[13]	2019
Roll Your Own Cigarettes	Average of 13 brands	12.4	2	1.3	52.4	[14]	1985
	Average of 11 brands	9.42	2	1.90	100.8	[15]	2014
	Average of 517 cigarettes made by 26 regular users	12.3	2	1.30	52.8	[16]	1998
Tobacco Heating Products	glo with Bright Tobacco Kent Neostiks	11.6	1.8	0.3	14.4	[6]	2018
	glo with mentholated Intensely Fresh Kent Neostiks	10	1.8	0.3	16.7		
	iQOS with Essence tobacco HeatStick	10.55	1.8	0.9	47.4		
	glo with Bright Tobacco Kent Neostiks	15.4	1.6	0.34	13.8	[7]	2020
	iQOS with Essence tobacco HeatStick	15	1.4	0.98	46.7		

	carbon-based Eclipse	25	2	2.36	47.2	[17]	2019
	Glo with Bright Tobacco Kent Neostiks	8	2	0.462	28.9	[18]	2018
	Glo with mentholated Intensely Fresh Kent Neostiks	8	2	0.365	22.8		
	Unspecified Heat not Burn Device	12	2	1.4	58.3	[12]	2018
	Unspecified Heat not Burn Device with Mentholated flavor	12	2	1.38	57.5		
	Unspecified Heat not Burn Device	12	4	1.41	29.4		
	Unspecified Heat not Burn Device with Mentholated flavor	12	4	1.43	29.8		
	Carbon-based Eclipse	12	2	0.14	5.8	[17]	2019
Carbon-based Eclipse	18.3	2	0.56	15.3			
<b>Electronic Nicotine Delivery Systems</b>	<i>Volish, eGo-3 (nicotine concentration 18 mg/ml; liquid composition: Propylene glycol, nicotine, vanillin, linalool, flavorings)</i>	15	2.8	1.06	25.2	[19]	2015
	<i>Volish, eGo-3 (nicotine concentration 18 mg/ml; liquid composition: Propylene glycol, glycerin, nicotine, ethanol, flavorings)</i>	15	2.8	1.15	27.4		
	<i>Volish, eGo-3 (nicotine concentration 24 mg/ml; liquid composition: Glycerin, nicotine, propylene glycol, linalool, vanillin, flavorings)</i>	15	2.8	1.05	25.0		
	<i>Volish, eGo-3 (nicotine concentration 22 mg/ml; liquid composition: Glycerin, propylene glycol, nicotine, flavorings)</i>	15	2.8	1.43	34.0		
	<i>Volish, eGo-3 (nicotine concentration 12 mg/ml; liquid composition: Glycerin, propylene glycol, nicotine, flavorings)</i>	15	2.8	0.88	21.0		
	<i>Volish, eGo-3 (nicotine concentration 16 mg/ml; liquid composition: Glycerin, propylene glycol, nicotine, flavorings)</i>	15	2.8	1.02	24.3		
	<i>Volish, eGo-3 (nicotine concentration 25 mg/ml; liquid composition: Glycerin, propylene glycol, nicotine, ethanol, flavorings)</i>	15	2.8	1.36	32.4		
	<i>Volish, eGo-3 (nicotine concentration 28 mg/ml; liquid composition: Glycerin, propylene glycol, nicotine, ethanol, malic acid, flavorings)</i>	15	2.8	1.49	35.5		
	<i>Volish, eGo-3 (nicotine concentration 11 mg/ml; liquid composition: Glycerin, nicotine, menthol, vanillin, aromatic oils, vanilla)</i>	15	2.8	0.77	18.3		
	<i>Blu Cigs (Tobacco-flavored cartomizers with nicotine concentration of 16 mg/ml)</i>	33	2.75	1.2	13.2	[20]	2015
	<i>V2 Cigs (Tobacco-flavored cartomizers with nicotine concentration of 18 mg/ml)</i>	31	2.54	1.4	17.8		
	<i>Lab Assembled ECIG 6 W (E-liquid concentration range 6-18 mg/ml)</i>	57	4.6	3.5	13.3	[21]	2018
	<i>Lab Assembled ECIG 10 W (E-liquid concentration range 6-18 mg/ml)</i>	46	3.8	4.2	24.0		
	<i>KangerTech Mini ProTank with own flavor (E-liquid nicotine concentration range 1.6-16.7 mg/ml and PG/VG ratio range of 69/31-5/95)</i>	106	4.3	3.4	7.5	[22]	2018
	<i>KangerTech Mini ProTank with strawberry flavored e-liquid (E-liquid nicotine concentration 19.9 mg/ml and PG/VG ratio of 40/60)</i>	73	3.2	5.4	23.1		
	<i>KangerTech Mini ProTank with Tobacco flavored e-liquid (E-liquid nicotine concentration 19.3 mg/ml and PG/VG ratio of 44/56)</i>	69	2.8	4.1	21.2		
	<i>Vype with 'Twilight Tobacco' flavored e-liquid (E-liquid nicotine concentration 5 mg/ml and PG/VG ratio of 40/60)</i>	61.1	1.45	0.75	8.5	[7]	2020
	Vapour 2 cigs (E-liquid nicotine concentration 20 mg/ml and PG/VG ratio of 50/50)	12	2	0.46	19.2	[12]	2018
		12	4	0.86	17.9		
	eGo style, Epsilon (E-liquid nicotine concentration 20 mg/ml and PG/VG ratio of 50/50)	12	2	0.51	21.3		
	12	4	1.73	36.0			

	EVIC VTC Mini battery with Nautilus Mini atomizer (E-liquid nicotine concentration 20 mg/ml and PG/VG ratio of 50/50)	12	2	0.82	34.2			
		12	4	1.84	38.3			
<b>Electronic Nicotine Delivery Systems</b>	Vype Disposable Regular	1	3	0.04	13.3	[17]	2019	
		1	5	0.06	12.0			
	Intellicig XL	1	3	0.03	10.0	[23]	2015	
		1	5	0.07	14.0			
	V4L CoolCart cartomizers (8.53 mg/ml nicotine concentration)	2	15	0.11	3.7	[23]		2015
		4	15	0.30	5.0			
		4	15	0.29	4.8			
		8	15	0.72	6.0			
		8	15	0.68	5.7			
		2	15	0.64	21.3			
		4	15	1.18	19.7			
		4	15	1.50	25.0			
		8	15	3.23	26.9			
		8	15	3.09	25.8			
	V4L CoolCart cartomizers (15.73 mg/ml nicotine concentration)	4	15	0.48	8.0	[23]	2015	
		8	15	4.7	39.2			
	JUUL US - Tobacco flavor ( 65 mg/ml nicotine concentration)	15	4	1.3	21.7	[24]	2020	
	JUUL UK - Tobacco flavor (19 mg/ml nicotine concentration)	15	4	0.4	6.7			
	JUUL US - Tobacco flavor ( 69 mg/ml nicotine concentration)	15	4	2.07	34.5	[25]	2019	
	JUUL US - Tobacco flavor	1	2.5	0.157	62.8	[26]	2019	
	JUUL US – Crème brulee flavor	1	2.5	0.170	68.0			
	JUUL US – Fruit punch flavor	1	2.5	0.154	61.6			
	JUUL US - Mint flavor	1	2.5	0.188	75.2			
	JUUL US – Tobacco flavor ( 69.8 mg/ml nicotine concentration)	15	4	1.67	27.8			
	Ezzy Oval – Berry Cool flavor (53.8 mg/m nicotine concentration)	15	4	4.07	67.8	[27]	2021	
	Ezzy Oval – Mango Lychee flavor (75.4 mg/m nicotine concentration)	15	4	5.44	90.7			
	Hyde – Cherry lemonade flavor (86.9 mg/m nicotine concentration)	15	4	3.15	52.5			
Puff Bar – Banana ice flavor (83.4 mg/m nicotine concentration)	15	4	6.72	112.0				
SEA – Mint flavor (54.3 mg/m nicotine concentration)	15	4	1.67	27.8				
<b>Waterpipes</b>	-	77.7	3.6	1.6	5.8	[28]	2016	
	-	290	2.9	5	5.9	[29]	2018	
	-	220	2.8	4.8	7.8	[30]	2010	
	-	105	2.6	5.4	19.8	[31]	2019	
	-	171	2.6	2.96	6.7	[32]	2005	
	-	100	3.0	2.25	7.5	[33]	2003	
	-	171	2.6	6.06	13.6	[34]	2008	
	-	171	2.6	7.75	17.4	[35]	2011	
<b>Cigarillos</b>	<i>Black &amp; Mild</i>	23.1	2.8	2.3	35.6	[36]	2018	
	<i>Winchester</i>	9.8	2	1.8	91.8	[36]	2018	
<b>Small Cigars</b>	Average values of 8 commercially available small cigars in the US	16.6	2	1.24	37.3	[10]	2018	
		16.5	2	3.49	105.8			



	Little cigars with cigar wrapper (average of 5 brands)	8.5	2	1.60	94.1	[37]	1976
	Little cigars with paper wrapper (average of 5 brands)	9.4	2	1.60	85.1		
	Average of 10 brands	14.4	2	2.1	72.9	[14]	1985
<b>Large Cigars</b>	Average of 5 brands	70.3	1.5	2.4	22.8	[37]	1976
	Average of 6 brands	108	1.5	1.9	11.7	[14]	1985
<b>Kretek</b>	Sampoerna	12.6	2	0.74	29.4	[9]	2014
	Garam	17.3	2	1.78	51.4		
	Kretek-R	14.4	2	1.72	59.7		
<b>Bidi</b>	Average of 21 brands	21	2	2.70	64.3	[38]	2003
	Average of 24 brands	17	2	1.86	54.7	[39]	1998
<b>Nicotine Patch</b>	NiQuitin Clear 7 mg	-	24 hrs	7	0.08	[40]	2019
	NiQuitin Clear 14 mg		24 hrs	14	0.16		
	NiQuitin Clear 21 mg		24 hrs	21	0.24		
<b>Nicotine Gum</b>	Zonnic 2mg	-	30 min	2	1.11	[41, 42]	2018/2020

## REFERENCES

- [1] Armitage AK, Alexander J, Hopkins R, *et al.* Evaluation of a low to middle tar/medium nicotine cigarette designed to maintain nicotine delivery to the smoker. *Psychopharmacology* 1988;96(4):447-453.
- [2] Hammond D, Fong GT, Cummings KM, *et al.* Cigarette yields and human exposure: a comparison of alternative testing regimens. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 2006;15(8):1495-1501.
- [3] Melikian A, Djordjevic M, Hosey J, *et al.* Gender Differences Relative to Smoking Behavior and Emissions of Toxins From Mainstream Cigarette Smoke. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco* 2007;9:377-387.
- [4] Watson CV, Richter P, de Castro BR, *et al.* Smoking Behavior and Exposure: Results of a Menthol Cigarette Cross-over Study. *American journal of health behavior* 2017;41(3):309-319.
- [5] Pauwels CGGM, Boots AW, Visser WF, *et al.* Characteristic Human Individual Puffing Profiles Can Generate More TNCO than ISO and Health Canada Regimes on Smoking Machine When the Same Brand Is Smoked. *Int J Environ Res Public Health* 2020;17(9):3225.
- [6] Gee J, Prasad K, Slayford S, *et al.* Assessment of tobacco heating product THP1.0. Part 8: Study to determine puffing topography, mouth level exposure and consumption among Japanese users. *Regulatory Toxicology and Pharmacology* 2018;93:84-91.
- [7] Jones J, Slayford S, Gray A, *et al.* A cross-category puffing topography, mouth level exposure and consumption study among Italian users of tobacco and nicotine products. *Scientific Reports* 2020;10(1):12.
- [8] Djordjevic MV, Stellman SD, Zang E. Doses of Nicotine and Lung Carcinogens Delivered to Cigarette Smokers. *JNCI: Journal of the National Cancer Institute* 2000;92(2):106-111.
- [9] Piadé JJ, Roemer E, Dempsey R, *et al.* Toxicological assessment of kretek cigarettes: Part 2: Kretek and American-blended cigarettes, smoke chemistry and in vitro toxicity. *Regulatory Toxicology and Pharmacology* 2014;70:S15-S25.
- [10] Goel R, Trushin N, Reilly SM, *et al.* A Survey of Nicotine Yields in Small Cigar Smoke: Influence of Cigar Design and Smoking Regimens. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco* 2018;20(10):1250-1257.
- [11] Laugesen M, Fowles J. Marlboro UltraSmooth: a potentially reduced exposure cigarette? *Tobacco control* 2006;15(6):430-435.
- [12] Farsalinos KE, Yannovits N, Sarri T, *et al.* Nicotine Delivery to the Aerosol of a Heat-Not-Burn Tobacco Product: Comparison With a Tobacco Cigarette and E-Cigarettes. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco* 2018;20(8):1004-1009.
- [13] Carmines E, Gillman I. Comparison of the Yield of Very Low Nicotine Content Cigarettes to the Top 100 United States Brand Styles. *Beiträge zur Tabakforschung International/Contributions to Tobacco Research* 2019;28:253-266.
- [14] Rickert WS, Robinson JC, Bray DF, *et al.* Characterization of tobacco products: A comparative study of the tar, nicotine, and carbon monoxide yields of cigars, manufactured cigarettes, and cigarettes made from fine-cut tobacco. *Preventive Medicine* 1985;14(2):226-233.
- [15] Marcilla A, Beltran MI, Gómez-Siurana A, *et al.* Comparison between the mainstream smoke of eleven RYO tobacco brands and the reference tobacco 3R4F. *Toxicol Rep* 2014;1:122-136.
- [16] Darrall KG, Figgins JA. Roll-your-own smoke yields: theoretical and practical aspects. *Tobacco control* 1998;7(2):168-175.

- [17] McAdam K, Davis P, Ashmore L, *et al.* Influence of machine-based puffing parameters on aerosol and smoke emissions from next generation nicotine inhalation products. *Regulatory toxicology and pharmacology : RTP* 2019;101:156-165.
- [18] Forster M, Fiebelkorn S, Yurteri C, *et al.* Assessment of novel tobacco heating product THP1.0. Part 3: Comprehensive chemical characterisation of harmful and potentially harmful aerosol emissions. *Regulatory toxicology and pharmacology : RTP* 2018;93:14-33.
- [19] Kosmider L, Sobczak A, Szołtysek-Bońdys I, *et al.* Assessment of nicotine concentration in electronic nicotine delivery system (ENDS) liquids and precision of dosing to aerosol. *Przegląd lekarski* 2015;72(10):500-504.
- [20] Behar RZ, Hua M, Talbot P. Puffing topography and nicotine intake of electronic cigarette users. *PLoS One* 2015;10(2):e0117222.
- [21] Farsalinos K, Poulas K, Voudris V. Changes in Puffing Topography and Nicotine Consumption Depending on the Power Setting of Electronic Cigarettes. *Nicotine & Tobacco Research* 2018;20(8):993-997.
- [22] St Helen G, Shahid M, Chu S, *et al.* Impact of e-liquid flavors on e-cigarette vaping behavior. *Drug and alcohol dependence* 2018;189:42-48.
- [23] Talih S, Balhas Z, Eissenberg T, *et al.* Effects of user puff topography, device voltage, and liquid nicotine concentration on electronic cigarette nicotine yield: measurements and model predictions. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco* 2015;17(2):150-157.
- [24] Talih S, Salman R, El-Hage R, *et al.* A comparison of the electrical characteristics, liquid composition, and toxicant emissions of JUUL USA and JUUL UK e-cigarettes. *Sci Rep* 2020;10(1):7322.
- [25] Talih S, Salman R, El-Hage R, *et al.* Characteristics and toxicant emissions of JUUL electronic cigarettes. *Tobacco control* 2019;28(6):678.
- [26] Reilly SM, Bitzer ZT, Goel R, *et al.* Free Radical, Carbonyl, and Nicotine Levels Produced by Juul Electronic Cigarettes. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco* 2019;21(9):1274-1278.
- [27] Soha Talih RS, Eric Soule, Racehl El Hage, Ebrahim Karam, Nareg Karaoghlanian, Ahmad El-Hellani, Najat Saliba, Alan Shihadeh. Electrical features, liquid composition and toxicant emissions from 'pod-mod'-like disposable electronic cigarettes (Under Review). 2021.
- [28] Ramôa CP, Shihadeh A, Salman R, *et al.* Group Waterpipe Tobacco Smoking Increases Smoke Toxicant Concentration. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco* 2016;18(5):770-776.
- [29] Jawad M, Eissenberg T, Salman R, *et al.* Toxicant inhalation among singleton waterpipe tobacco users in natural settings. *Tob Control* 2019;28(2):181-188.
- [30] Katurji M, Daher N, Sheheitli H, *et al.* Direct measurement of toxicants inhaled by water pipe users in the natural environment using a real-time in situ sampling technique. *Inhalation toxicology* 2010;22(13):1101-1109.
- [31] El Hourani M, Talih S, Salman R, *et al.* Comparison of CO, PAH, Nicotine, and Aldehyde Emissions in Waterpipe Tobacco Smoke Generated Using Electrical and Charcoal Heating Methods. *Chemical research in toxicology* 2019;32(6):1235-1240.
- [32] Shihadeh A, Saleh R. Polycyclic aromatic hydrocarbons, carbon monoxide, "tar", and nicotine in the mainstream smoke aerosol of the narghile water pipe. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 2005;43(5):655-661.
- [33] Shihadeh A. Investigation of mainstream smoke aerosol of the argileh water pipe. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 2003;41(1):143-152.

- [34] Saleh R, Shihadeh A. Elevated toxicant yields with narghile waterpipes smoked using a plastic hose. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 2008;46(5):1461-1466.
- [35] Schubert J, Hahn J, Dettbarn G, *et al.* Mainstream smoke of the waterpipe: does this environmental matrix reveal as significant source of toxic compounds? *Toxicology letters* 2011;205(3):279-284.
- [36] Pickworth WB, Rosenberry ZR, Yi D, *et al.* Cigarillo and Little Cigar Mainstream Smoke Constituents from Replicated Human Smoking. *Chemical research in toxicology* 2018;31(4):251-258.
- [37] Irwin S, Klaus DB, Dietrich H, *et al.* On the Chemistry of Cigar Smoke: Comparisons between Experimental Little and Large Cigars. *Beiträge zur Tabakforschung International/Contributions to Tobacco Research* 1976;8(6):367-377.
- [38] Watson CH, Polzin GM, Calafat AM, *et al.* Determination of tar, nicotine, and carbon monoxide yields in the smoke of bidi cigarettes. *Nicotine & Tobacco Research* 2003;5(5):747-753.
- [39] Pakhale SS, Maru GB. Distribution of major and minor alkaloids in tobacco, mainstream and sidestream smoke of popular Indian smoking products. *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association* 1998;36(12):1131-1138.
- [40] Omega Pharma Ltd. NiQuitin Pre-Quit Clear 21mg Patch. *Electronic Medicines Compendium* 2019; <https://www.medicines.org.uk/emc/product/2938/smpc> (accessed 3 December 2021).
- [41] Shiffman S, Scholl SM, Mao J, *et al.* Using Nicotine Gum to Assist Nondaily Smokers in Quitting: A Randomized Clinical Trial. *Nicotine Tob Res* 2020;22(3):390-397.
- [42] Lande RG. What is the role of nicotine gum in the treatment of nicotine addiction? *Medscape* 2018; <https://www.medscape.com/answers/287555-158527/what-is-the-role-of-nicotine-gum-in-the-treatment-of-nicotine-addiction> (accessed 3 December 2021).