Exhalation of alternative tobacco product aerosols differs from cigarette smoke—and may lead to alternative health risks

Tobacco Use Insights
Volume 15: 1–6

DOI: 10.1177/1179173X221078200
SAGE

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ABSTRACT

BACKGROUND: Variation in alternative tobacco product (ATP) constituents, heating potential, and consumer behaviors have made it difficult to characterize their health risks. To date, most toxicity studies of ATPs have used established cigarette endpoints to inform study design. Furthermore, to assess where ATPs fall on the tobacco harm continuum, with cigarettes representing maximum potential risk, studies have tended to compare the relative biological responses to ATPs against those due to cigarettes.

OBJECTIVES: 1) To characterize the exhalation profiles of two popular ATPs: electronic cigarettes (e-cigarettes) and hookah waterpipes (hookah) and 2) to determine if ATP exhalation patterns were representative of cigarette exhalation patterns.

METHODS: Exhalation patterns were recorded (mouth only, nose only, or both mouth and nose) among individuals observed in the New York City tri-state area using a recognizable tobacco product (cigarette, e-cigarette, or hookah). Cigarette smokers and e-cigarette vapers were observed on city streets; water-pipe smokers were observed inside Manhattan hookah bars.

RESULTS: E-cigarette vapers practiced exclusive nasal exhalation at far higher rates than did cigarette smokers (19.5% vs 4.9%). Among vapers, e-cigarette device type was also significantly associated with exhalation profile. Overall, cigarette smokers exhaled from their nose approximately half to one-third as often as ATP users (hookah and e-cigarettes, respectively).

CONCLUSIONS: Nasal exhalation of tobacco emissions appears to be a shared characteristic across several types of ATPs. It is therefore plausible that ATP-specific consumer behaviors may foster unique upper respiratory health consequences that have not been observed in smokers. Thus, product-specific behaviors should inform the prioritization of biological endpoints used in studies evaluating ATP toxicity and health effects.

KEYWORDS: alternative tobacco products, electronic cigarettes, hookah, vaping

RECEIVED: March 26, 2021. **ACCEPTED:** January 16, 2022.

TYPE: Short Report

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

FUNDING: The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study is supported by NIH/NHLBI (R01 HL139239-03) and NIH/NIEHS (R21 ES026996-02; T32ES007324).

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Introduction

Since the introduction of electronic cigarettes (e-cigarettes) to the US market 15 years ago, vaping rates have surged exponentially,[1,2] with current usage rates among US adults exceeding 1 in 20.[3] Separately, waterpipe hookah tobacco (hookah) use continues to gain popularity in the U.S.,[4] with year-over-year ever use increasing by as much as 40%.[5] The toxicological research needed to characterize the potential health risks associated with alternative tobacco products (ATPs), including e-cigarettes and hookah, has not kept pace with their growing popularity and use.[6–8] Not only do ATP constituents and toxicity profiles tend to differ from those of combustible tobacco cigarettes,[9–11] but consumer demographics and puff topographies also can vary by tobacco product.[12–15] Importantly, product-specific behaviors can affect health risk: Inhalation depth (a measure of how deeply into the lungs tobacco smoke is inhaled) is greater among cigarette smokers than persons who smoke other combustible tobacco products.[16–18] In fact, physicians have attributed increased incidence of chronic bronchitis in cigarette smokers to this cigarette-specific behavior for more than a century.[19,20]

Several studies have implicated tobacco-smoke inhalation depth as an independent risk factor for lung and laryngeal cancers, independent of pack-years.[21–24] Separately, among combustible tobacco products, epidemiology studies have identified the strongest association between cigarettes and lung-cancer diagnoses.[16,25-27] Cigarette smokers who do not inhale tobacco smoke into their lungs, however, face a lower risk of lung cancer.[21,28] Hence, cigarette smoke inhaled more deeply may foster lung-cancer risk by increasing pulmonary exposure to—and deposition of—harmful tobacco-smoke toxicants.[29-31]

Further differences in product-specific puff topographies (e.g., puff duration, volume, and velocity) have been shown to affect the resultant tobacco emissions and potentially influence associated health risks.[32,33] However, despite the fact that most ATPs, including e-cigarettes and hookah, contain chemicals that have been added to enhance odor/flavor,[34] little is known about how ATP-specific features, such as flavor, might impact their use and subsequent health risks. Research shows that taste is strongly influenced by retronasal olfaction,[35] which has been found to improve odorant identification *and* strengthen perceived flavor intensity.[36] Furthermore, several internet forums and news outlets have ascribed "retrohaling"—the practice of intentionally exhaling tobacco emissions from the nose to increase flavor intensity—as a feature common among various ATP users including cigar and hookah smokers and e-cigarette vapers.[37,38] Separately, the lungs have been posited to serve as a "sink" for odorants that could reinforce retrohaling of inhaled tobacco product emissions.[39] Together, these data suggest that ATP-specific breathing patterns could differentially affect respiratory exposures and any health risks associated with these products.

Given that product-specific behaviors (e.g., puff topographies) are well documented among consumers of combustible tobacco, we sought to determine whether product-specific retrohaling behaviors could be identified. We evaluated real-world product-specific behaviors of subjects in their naturalistic environment using tobacco products of choice at their discretion ad libitum (i.e., without being prompted). Of particular interest were retronasal exhalation patterns associated with two of the most popular, and commonly flavored, ATPs: e-cigarettes and hookahs.[40,41]

Methods

From March 2018 through February 2019, researchers observed people using tobacco products. Exhalation patterns of cigarette smokers (n = 122) and e-cigarette vapers (n = 124) were observed on New York City streets. Water-pipe smoker (n = 96) exhalation patterns were observed inside Manhattan hookah bars. Binary categorization of e-cigarette devices as either pod-like or modular-tank formats (e.g., cig-a-like, vape-pen and clear-o-mizers vs box-mod, and sub-ohm atomizers, respectively) was assigned using commonly cited size and shape criteria.[42,43]

To characterize consumer behaviors associated with distinct tobacco products, a disguised naturalistic observational approach was used. These data were collected by a team of tobacco-product researchers with prior experience identifying unique tobacco products and exhalation patterns discretely and accurately. Additionally, avoiding direct interaction with the subjects offered several experimental advantages: This methodology qualifies for IRB exemption, subject anonymity is maintained,[44] and observations would not bias subject behaviors.[45]

Observations were limited to circumstances where product type and exhalation pattern could be visually confirmed; subjects were excluded from analysis when the facial source of exhaled smoke/aerosol was unclear or product type could not be verified. To limit risk of researchers being noticed or confronted, observation windows were limited to no more than 1 minute or 5 individual puffs; subjects commuting on foot were not followed for more than 1 block. To maintain discretion, researchers recorded observations on their phone; individual subject details were submitted to a centralized email for blinded quantification. The observational nature of this study precluded verification of a subject's age.

Tobacco-exhalation profiles were characterized by exclusive exhalation (mouth or nose only) or dual exhalation (both mouth and nose). Dual exhalation was defined as either combined oral and nasal exhalation during the same puff or exclusive exhalation from the mouth and nose during different puffs (but in the same individual). Relative product-specific exhalation patterns were determined by calculating the percentage of individuals observed exhaling exclusively from either their mouth or nose, vs exhaling from both their mouth and nose. Visual confirmation of e-cigarette device type was used to further dichotomize vapers into modular-tank users (n = 60) or pod-like users (n = 64).

Pearson's chi-squared tests[46] were run in STATA (StataCorp LLC, College Station, TX) to determine if overall exhalation patterns differed by gender (i.e., male vs female), tobacco product (i.e., cigarettes vs hookah vs e-cigarettes) or e-cigarette devices (i.e., modular vs pod-like). Significance was set at $P \leq .05$. To identify which tobacco products were associated with different exhalation patterns (e.g., mouth only, nose only, or both mouth and nose), a two-tailed Z-test for two proportions was run, where cigarettes were the reference group for tobacco-product pairwise comparisons and modular tanks were the reference group for pairwise e-cigarette device comparisons ($P \leq .05$). Analyses were conducted using the infrrr Difference in Proportions Hypothesis Test Calculator (https://www.infrrr.com/).

Results

A total of 341 people were observed using tobacco products: 122 cigarette smokers, 96 hookah smokers, and 123 e-cigarette vapers (Table 1). Subjects that outwardly presented as male accounted for at least two-thirds of all observed individuals, regardless of product used. Within e-cigarette users, roughly half used pod-like devices (52%). Irrespective of device style, females accounted for fewer than 25% of vapers.

Chi-squared analyses revealed that exhalation patterns did not differ significantly by gender (Table 1, statistics not shown).

Table 1. Sex-specific exhalation patterns by product type (cigarette, hookah, and e-cigarette).

TOBACCO PRODUCT/SUBJECT DETAILS			EXHALATION PATTERN		
PRODUCT (N)	SUBJECT GENDER[A]	N (%)	DUAL[B] N (%)	ORAL[C] N (%)	NASAL[C] N (%)
Cigarette[d] (122)	M	80 (65.6)	17 (21.2)	59 (73.8)	4 (5.0)
	F	42 (34.4)	4 (9.5)	36 (85.7)	2 (4.8)
Hookah[e] (96)	M	65 (67.7)	34 (52.3)	31 (47.7)	0 (.0)
	F	31 (32.3)	14 (45.2)	17 (54.8)	0 (.0)
E-cigarette[d,f] (124)	M	97 (78.2)	40 (41.3)	35 (36.1)	22 (22.6)
	F	27 (21.8)	13 (48.1)	12 (44.4)	2 (7.4)
Modular-Tank (60)	M	46 (76.7)	29 (63.0)	11 (24.0)	6 (13.0)
	F	14 (23.3)	8 (57.1)	5 (35.7)	1 (7.1)
Pod-like (64)	M	51 (79.7)	12 (23.5)	23 (45.1)	16 (31.4)
	F	13 (20.3)	5 (38.5)	7 (53.8)	1 (7.7)

[a]Determined by researcher (not verified by subject). M = male//F = female.
[b]Individual was observed exhaling from two facial orifices (oral *and* nasal).
[c]Individual was observed exhaling from a single orifice (oral *or* nasal).
[d]Observations took place in public spaces (outdoors).
[e]Observations took place in multiple hookah bars (indoors).
[f]E-cigarettes include both modular-tank and pod-like devices.

Table 2. Two-sample exhalation proportion Z-scores by tobacco product type and e-cigarette device type.

EXHALATION PATTERN	VS. CIGARETTE SMOKING	
Hookah Smoking	**Z-Score**	*P-value*
Mouth only	4.42	*.001*
Nose only	2.51	*.012*
Dual (mouth + nose)	−5.38	*<.001*
Ever nose (dual + nose only)	−4.42	*.001*
E-Cigarette Vaping	*Z-Score*	*P-value*
Mouth only	7.15	*<.001*
Nose only	−3.50	*.005*
Dual (mouth + nose)	−4.82	*<.001*
Ever nose (dual + nose only)	−6.96	*<.001*
E-Cigarette Modular-Tank Device	*vs. E-Cigarette pod-like device*	
	Z-Score	*P-value*
Mouth only	−2.91	*.004*
Nose Only[a]	—	—
Dual (mouth + nose)	4.41	*.001*
Ever nose (dual + nose only)	2.74	*<.001*

P-values are bold when z-score was determined to be statistically different.
[a]insufficient sample size for test to run.

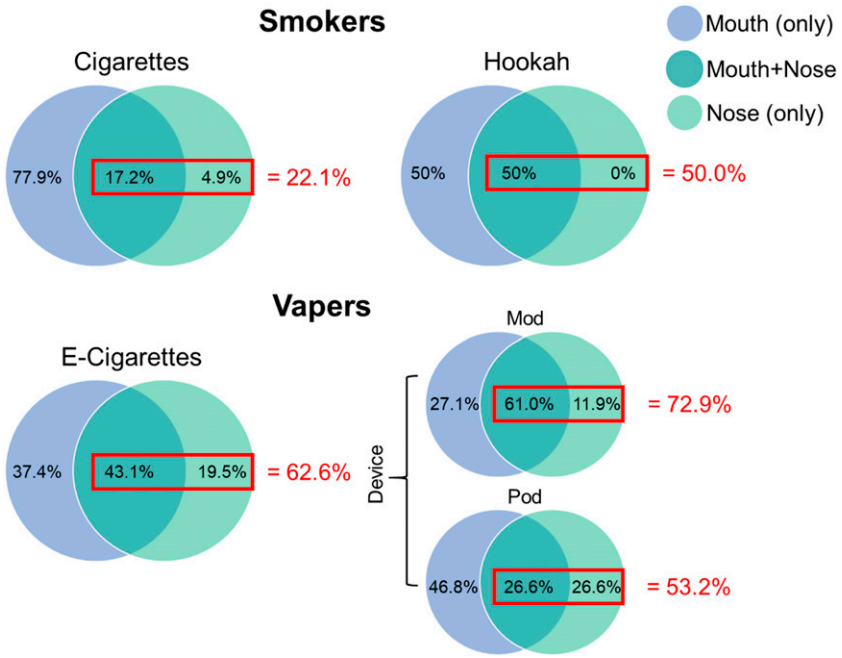

Figure 1. Product-specific exhalation patterns. Venn diagrams of exhalation patterns of smokers (cigarette, n = 122, and hookah, n = 96) and vapers (e-cigarette, n = 123) observed in New York City. E-cigarette users were further stratified by device type: Modular-tank (mod, n = 59) or pod-like (pod, n = 64). Red boxes include individuals who had ever exhaled from their nose (e.g., mouth and nose + nose only), and these cumulative nasal exhalation percentages are shown in red. Chi-squared analyses revealed statistically significant differences between all tobacco products and between e-cig devices (*$P \leq .05$).

Regardless of tobacco product, exclusive mouth exhalation was more common than exclusive nose exhalation. However, proportion tests revealed that ATP users (both hookah and e-cigarette) practiced exclusive oral exhalation significantly less often than did cigarette smokers (Table 2, $P < .001$). Surprisingly, people vaping e-cigarettes practiced exclusive nasal exhalation at almost 4 times the rate of cigarette smokers (19.5% vs 4.9%, respectively, Figure 1). Interestingly, hookah smokers were never observed exclusively exhaling from their nose, although 50% did practice dual exhalation.

Within e-cigarette users, device type was significantly associated with nasal exhalation patterns: Pod-like users were more than twice as likely to exclusively exhale from their nose as compared to individuals vaping modular-tank devices (26.6% vs 11.9%, respectively). However, approximately 40% more modular device users (Figure 1) were seen ever exhaling from their nose (cumulative proportion of dual and exclusive nasal exhalation, Table 2, P<.001). Notably, cigarette smokers exhaled out of their nose significantly less often than did either hookah smokers or e-cigarette vapers (22% compared to 50% and 62.6%, respectively, Figure 1).

Discussion

Here, we present the first evidence of ATP-specific aerosol exhalation patterns in which vapers and hookah users retronasally exhale ATP emissions more often than do cigarette smokers. ATP products associated with increased rates of retrohaling could increase the direct exposure of the upper respiratory tract (nose and sinuses) to ATP emissions, which may lead to unique health consequences in these tissues. For example, a recent study found increased levels of inflammatory cytokines in the nose of e-cigarette users and hookah smokers—a phenotype that was not present in the nose of cigarette smokers.[47] Therefore, these findings may have important implications for ATP toxicity and risk evaluations, as these behavioral differences could lead to–and potentially explain–novel product-specific health risks.

Additionally, e-cigarette device type appeared to influence consumer exhalation patterns, with modular-tank users practicing dual exhalation (i.e., both nose and mouth) 40% more frequently than individuals vaping pod-like devices. In fact, persons vaping modular-tank devices had the highest rates of dual exhalation of any group. This dual exhalation may relate to the fact that modular-tank e-cigarettes can generate larger aerosol volumes than pod-like devices,[48] so modular-tank vapers may need both their nose and mouth to facilitate exhalation of larger volumes of inhaled aerosols.[49] Importantly, the reduced coil resistance and higher wattages needed to generate those larger emissions has been found to enhance the toxicity of the resultant aerosol.[50-52] Thus, modular-tank users may be enhancing risks through more frequent nasal exposures to potentially larger volumes of more harmful chemicals.

The abundance of available ATP flavors found in vaping e-liquids and hookah shisha may partly explain the apparent preferential nasal exhalation among their users.[53] Another biological basis for the observed exhalation patterns could be the

complex integration of olfactory and taste sensory networks.[54] Theoretically, nasal exhalation of flavored emissions should enhance how ATP consumers sense a product's "flavor," which in turn may enhance their overall product experience and potentially reinforce this behavior. Intriguingly, chewing tobacco has been shown to attenuate taste perception,[55] whereas individuals who smoke cigarettes consistently demonstrate impairments in olfaction, but not taste.[56,57] Taken together, these data suggest that the reduced olfaction commonly observed among cigarette smokers might explain why we observed so few practicing nasal exhalation.[57,58]

Limitations

While exhalation of tobacco product emissions is not a routine metric, it did permit for the comparison of product-specific breathing patterns that could be observed visually and unbeknownst to research subjects—a vast improvement from classical inhalation research, which has relied heavily on self-reported product behaviors. Unfortunately, the observational nature of this study precluded our knowing the exact constituents of the ATPs used. Despite this experimental limitation, the novel ATP-specific exhalation profiles we observed suggest that the products themselves may be a significant predictor of consumer behavior, rather than intra-product differences (i.e., flavors, brands, or devices), as some have suggested.[59] If so, this would be consistent with the product-specific breathing patterns that have been observed between smokers of different types of combustible tobacco.[17,18]

Final Remarks

Perhaps because of ATP's potential to reduce tobacco harm, most ATP research has evaluated the health risks of ATPs against those of cigarettes.[60-63] However, as has been found with tobacco-smoke inhalation depth, differences in how tobacco products are used can confer different respiratory risks.[16,18] Limiting the scope of studies to established cigarette health endpoints may risk missing ATP-specific behaviors that might foster unique harms. Thus, we recommend that future toxicological of ATP respiratory risk consider the potential for retrohaling to disproportionately—and uniquely—impact upper-respiratory tissues. Designing studies that better reflect potential real-world exposures by honing experimental considerations and biological endpoints will improve our understanding of any health impacts from new and emerging ATPs and better inform clinical recommendations.

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REFERENCES

1. Loukas A, Marti CN, Pasch KE, Harrell MB, Wilkinson AV, Perry CL. Rising vape pod popularity disrupted declining use of electronic nicotine delivery systems among young adults in Texas, USA from 2014 to 2019. *Addiction*. 2021.
2. Huang J, Duan Z, Kwok J, et al. Vaping versus JUULing: How the extraordinary growth and marketing of JUUL transformed the US retail e-cigarette market. *Tobac Control*. 2019;28(2):146-151.
3. Mirbolouk M, Charkhchi P, Kianoush S, et al. Prevalence and distribution of E-Cigarette use among U.S. Adults: Behavioral risk factor surveillance system, 2016. *Ann Intern Med*. 2018;169(7):429-438.
4. Soule EK, Lipato T, Eissenberg T. Waterpipe tobacco-smoking: A new smoking epidemic among the young? *Current Pulmonology Reports*. 2015;4(4):163-172.
5. Soulakova JN, Pham T, Owens VL, Crockett LJ. Prevalence and factors associated with use of hookah tobacco among young adults in the U.S. *Addict Behav*. 2018;85:21-25.
6. Stepanov I, Woodward A. Heated tobacco products: things we do and do not know. *Tobac Control*. 2018;27(suppl 1):s7.
7. Elsayed Y, Dalibalta S, El Kouche M. Chemical characterization and safety assessment of dokha: An emerging alternative tobacco product. *Sci Total Environ*. 2018;615:9-14.
8. Gordon T, Karey E, Rebuli ME, Escobar Y, Jaspers I, Chen LC. E-cigarette Toxicology. *Annu Rev Pharmacol Toxicol*. 2021:62. (In Press).
9. Elsayed Y, Dalibalta S, Abu-Farha N. Chemical analysis and potential health risks of hookah charcoal. *Sci Total Environ*. 2016;569-570:262-268.
10. Cox S, Kośmider L, McRobbie H, et al. E-cigarette puffing patterns associated with high and low nicotine e-liquid strength: effects on toxicant and carcinogen exposure. *BMC Publ Health*. 2016;16(1):999.
11. Erythropel HC, Garcia Torres DS, Woodrow JG, et al. Quantification of flavorants and nicotine in waterpipe tobacco and mainstream smoke and comparison to E-cigarette aerosol. *Nicotine Tob Res*. 2021;23(3):600-604.
12. Soule EK, Ramôa C, Eissenberg T, Cobb CO. Differences in puff topography, toxicant exposure, and subjective response between waterpipe tobacco smoking men and women. *Exp Clin Psychopharmacol*. 2018;26(5):440-447.
13. McMillen R, Maduka J, Winickoff J. Use of emerging tobacco products in the United States. *Journal of Environmental and Public Health*. 2012;2012:989474.
14. Meišutovič-Akhtarieva M, Prasauskas T, Čiužas D, Kaunelienė V, Martuzevičius D. The dynamics of exhaled aerosol following the usage of heated tobacco product, electronic cigarette, and conventional cigarette. *Aerosol Air Qual Res*. 2021;21(8):200653.
15. Lee YO, Nonnemaker JM, Bradfield B, Hensel EC, Robinson RJ. Examining daily electronic cigarette puff topography among established and nonestablished cigarette smokers in their natural environment. *Nicotine Tob Res*. 2018;20(10):1283-1288.
16. Benhamou S, Benhamou E, Flamant R. Lung cancer risk associated with cigar and pipe smoking. *Int J Cancer*. 1986;37(6):825-829.
17. Wynder EL, Stellman SD. Comparative epidemiology of tobacco-related cancers. *Cancer Res*. 1977;37(12):4608-4622.
18. Rodenstein DO, Stănescu DC. Pattern of inhalation of tobacco smoke in pipe, cigarette, and never smokers. *Am Rev Respir Dis*. 1985;132(3):628-632.
19. Webb GB. The effect of the inhalation of cigarette smoke on the lungs. *Am Rev Tubercul*. 1918;2(1):25-27.
20. Rimington J. Cigarette smokers' chronic bronchitis: Inhalers and non-inhalers compared. *Br J Dis Chest*. 1974;68:161-165.
21. Fukumoto K, Ito H, Matsuo K, et al. Cigarette smoke inhalation and risk of lung cancer: a case-control study in a large Japanese population. *Eur J Cancer Prev : The Official Journal of the European Cancer Prevention Organisation (ECP)*. 2015;24(3):195-200.
22. Ramroth H, Dietz A, Becher H. Intensity and inhalation of smoking in the aetiology of laryngeal cancer. *Int J Environ Res Publ Health*. 2011;8(4):976-984.
23. Lubin JH, Richter BS, Blot WJ. Lung cancer risk with cigar and pipe use. *JNCI (J Natl Cancer Inst): J Natl Cancer Inst*. 1984;73(2):377-381.
24. Lubin JH, Blot WJ, Berrino F, et al. Patterns of lung cancer risk according to type of cigarette smoked. *Int J Cancer*. 1984;33(5):569-576.
25. Lubin JH, Jun-Yao L, Xiang-Ghen X, et al. Risk of lung cancer among cigarette and pipe smokers in Southern China. *Int J Cancer*. 1992;51(3):390-395.
26. Levin ML, Goldstein H, Gerhardt PR. Cancer and Tobacco Smoking. *J Am Med Assoc*. 1950;143(4):336-338.
27. Chow W-H, Schuman LM, McLaughlin JK, et al. A cohort study of tobacco use, diet, occupation, and lung cancer mortality. *Cancer Causes Control*. 1992;3(3):247-254.
28. Schwartz D, Flamant R, Lellouch J, Denoix PF. Results of a French Survey on the Role of Tobacco, Particularly Inhalation, in Different Cancer Sites. *J Natl Cancer Inst*. 1961;26(5):1085-1108.
29. McM. TurnerTurner JA, Sillett RW, McNicol MW. The inhaling habits of pipe smokers. *Br J Dis Chest*. 1981;75(1):71-76.
30. McGrath C, Warren N, Biggs P, McAughey J. Real-time measurement of inhaled and exhaled cigarette smoke: Implications for dose. *J Phys Conf*. 2009;151:012018.
31. Baker RR, Dixon M. The retention of tobacco smoke constituents in the human respiratory tract. *Inhal Toxicol*. 2006;18(4):255-294.
32. 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(2):150-157.

33. Eddingsaas NC, Hensel EC, O'Dea S, Kunselman P, DiFrancesco AG, Robinson RJ. Effect of user puffing topography on total particulate matter, nicotine and volatile carbonyl emissions from narghile waterpipes. *Tobac Control*. 2020;29(suppl 2):s117.
34. Owens VL, Ha T, Soulakova JN. Widespread use of flavored e-cigarettes and hookah tobacco in the United States. *Preventive Medicine Reports*. 2019;14:100854.
35. Shepherd GM. New perspectives on olfactory processing and human smell. In: Menini A, ed. *The Neurobiology of Olfaction*. Boca Raton, FL: CRC Press/Taylor & Francis; 2010.
36. Djordjevic J, Zatorre RJ, Jones-Gotman M. Effects of perceived and imagined odors on taste detection. *Chem Senses*. 2004;29(3):199-208.
37. Rivas F. *Puffing Away, Stogie Style: Black Smoke Miami Celebrates Black Cigar Smokers*. Miami, FL: The Miami Times; 2019. Lifestyles.
38. Nagesh A. Do you vape? Don't blow it through your nose. Metro. *April*. 2016;13.
39. Verhagen JV. A role for lung retention in the sense of retronasal smell. *Chemosensory Perception*. 2015;8(2):78-84.
40. Gilreath TD, Leventhal A, Barrington-Trimis JL, et al. Patterns of alternative tobacco product use: Emergence of hookah and e-cigarettes as preferred products amongst youth. *J Adolesc Health*. 2016;58(2):181-185.
41. Treur JL, Rozema AD, Mathijssen JJP, van Oers H, Vink JM. E-cigarette and waterpipe use in two adolescent cohorts: cross-sectional and longitudinal associations with conventional cigarette smoking. *Eur J Epidemiol*. 2018;33(3):323-334.
42. Williams M, Talbot P. Design features in multiple generations of electronic cigarette atomizers. *Int J Environ Res Publ Health*. 2019;16(16).
43. Clapp PW, Jaspers I. Electronic cigarettes: Their constituents and potential links to asthma. *Curr Allergy Asthma Rep*. 2017;17(11):79.
44. Sussman S, Hahn G, Dent CW, Stacy AW, Burton D, Flay BR. Naturalistic observation of adolescent tobacco use. *Int J Addict*. 1993;28(9):803-811.
45. Sussman S, Allem J-P, Garcia J, Unger JB, Cruz TB, Garcia R, et al. Who walks into vape shops in Southern California?: A naturalistic observation of customers. *Tob Induc Dis*. 2016;14(1):18.
46. McHugh ML. The chi-square test of independence. *Biochem Med*. 2013;23(2):143-149.
47. Karey E, Hess J, Farrell K, et al. The nose knows: sniffing out the unique immunological risk of alternative tobacco products. *Am J Respir Cell Mol Biol*. 2021. (Accepted Ahead of Print.).
48. Gillman IG, Kistler KA, Stewart EW, Paolantonio AR. Effect of variable power levels on the yield of total aerosol mass and formation of aldehydes in e-cigarette aerosols. *Regul Toxicol Pharmacol*. 2016;75:58-65.
49. Smets J, Baeyens F, Chaumont M, Adriaens K, Van Gucht D. When Less is More: Vaping Low-Nicotine vs. High-Nicotine E-Liquid is Compensated by Increased Wattage and Higher Liquid Consumption. *Int J Environ Res Publ Health*. 2019;16(5).
50. Noël A, Hossain E, Perveen Z, Zaman H, Penn AL. Sub-ohm vaping increases the levels of carbonyls, is cytotoxic, and alters gene expression in human bronchial epithelial cells exposed at the air-liquid interface. *Respir Res*. 2020;21(1):305.
51. El-Hellani A, Al-Moussawi S, El-Hage R, et al. Carbon monoxide and small hydrocarbon emissions from sub-ohm electronic cigarettes. *Chem Res Toxicol*. 2019;32(2):312-317.
52. Talih S, Salman R, Karaoghlanian N, et al. "Juice Monsters": Sub-Ohm vaping and toxic volatile aldehyde emissions. *Chem Res Toxicol*. 2017;30(10):1791-1793.
53. Bonhomme MG, Holder-Hayes E, Ambrose BK, et al. Flavoured non-cigarette tobacco product use among US adults: 2013-2014. *Tobac Control*. 2016;25(suppl 2):ii4.
54. Small DM, Prescott J. Odor/taste integration and the perception of flavor. *Exp Brain Res*. 2005;166(3):345-357.
55. Kale YS, Vibhute N, Belgaumi U, Kadashetti V, Bommanavar S, Kamate W. Effect of using tobacco on taste perception. *J Fam Med Prim Care*. 2019;8(8):2699-2702.
56. Frye RE, Schwartz BS, Doty RL. Dose-Related effects of cigarette smoking on olfactory function. *JAMA: JAMA, J Am Med Assoc*. 1990;263(9):1233-1236.
57. Vennemann MM, Hummel T, Berger K. The association between smoking and smell and taste impairment in the general population. *J Neurol*. 2008;255(8):1121-1126.
58. Glennon S-G, Huedo-Medina T, Rawal S, Hoffman HJ, Litt MD, Duffy VB. Chronic cigarette smoking associates directly and indirectly with self-reported olfactory alterations: Analysis of the 2011-2014 national health and nutrition examination survey. *Nicotine Tob Res*. 2019;21(6):818-827.
59. Zhao J, Nelson J, Dada O, Pyrgiotakis G, Kavouras IG, Demokritou P. Assessing electronic cigarette emissions: linking physico-chemical properties to product brand, e-liquid flavoring additives, operational voltage and user puffing patterns. *Inhal Toxicol*. 2018;30(2):78-88.
60. Polosa R, Farsalinos K, Prisco D. Health impact of electronic cigarettes and heated tobacco systems. *Internal and Emergency Medicine*. 2019;14(6):817-820.
61. Brinkman MC, Kim H, Buehler SS, Adetona AM, Gordon SM, Clark PI. Evidence of compensation among waterpipe smokers using harm reduction components. *Tobac Control*. 2020;29(1):15-23.
62. McCarthy M. US plan gives greater role to electronic cigarettes in tobacco harm reduction. *BMJ*. 2017;358:j3689.
63. Ford EW, Chan KS, Parikh M, Lowe KB, Huerta TR. E-cigarette and hookah adoption patterns: Is the harm reduction theory just so much smoke? *Addictive Behaviors Reports*. 2020;11:100246.