Published in final edited form as:

Tob Control. 2020 January ; 29(1): 15–23. doi:10.1136/tobaccocontrol-2018-054502.

Evidence of compensation among waterpipe smokers using harm reduction components

Marielle C Brinkman^{1,2}, Hyoshin Kim³, Stephanie S Buehler⁴, Anna M Adetona⁴, Sydney M Gordon⁴, Pamela I Clark²

¹College of Public Health, The Ohio State University, Columbus, Ohio, USA

²School of Public Health, Tobacco Center of Regulatory Science, University of Maryland, College Park, Maryland, USA

³Battelle Public Health Center for Tobacco Research, Battelle, Seattle, Washington, USA

⁴Battelle Public Health Center for Tobacco Research, Battelle, Columbus, Ohio, USA

Abstract

Objectives—We examined two waterpipe tobacco smoking components advertised to reduce harm to determine if they result in lower levels of biomarkers of acute exposure.

Methods—We conducted a crossover study of 34 experienced waterpipe smokers smoking a research-grade waterpipe in three configurations *ad libitum* in a controlled chamber: control (quick-light charcoal), electric (electric heating) and bubble diffuser (quick-light charcoal and bubble diffuser). We collected data on smoking topography, environmental carbon monoxide (CO), subjective effects, heart rate, plasma nicotine and exhaled CO and benzene.

Results—Smokers' mean plasma nicotine, heart rate, and exhaled benzene and CO boost were all significantly lower for electric compared with control. However, smokers puffed more intensely and took significantly more and larger volume puffs for a larger total puffing volume (2.0 times larger, $p < 0.0001$) when smoking electric; machine yields indicate this was likely due to lower mainstream nicotine. Smokers rated electric smoking experience less satisfying and less pleasant.

Correspondence to: Marielle C Brinkman, College of Public Health, The Ohio State University, Columbus, Ohio 43210, USA; brinkman.224@osu.edu.

Contributors MCB, SMG and PIC were responsible for the conception and design of the study. SSB was responsible for the chemical analysis, and HK and AMA were responsible for the statistical analysis. All contributed to the analysis and interpretation of the data and the preparation of the manuscript.

Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/tobaccocontrol-2018-054502>).

Publisher's Disclaimer: Disclaimer The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or the Food and Drug Administration.

Competing interests None declared.

Patient consent Not required.

Ethics approval The study was approved by the Battelle Internal Review Board (FWA 0004696).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement In accordance with P.L. 110–161, this article is publicly available on PubMed Central. Additional methodology and data are available in the supplementary file.

For charcoal heating, the mean mass of CO emitted into the chamber was ~1 g when participants smoked for a mean of 32 minutes at a typical residential ventilation rate (2.3 hr⁻¹).

Conclusion—Waterpipe smokers engaged in compensation (i.e., increased and more intense puffing) to make up for decreased mainstream nicotine delivery from the same tobacco heated two ways. Waterpipe components can affect human puffing behaviours, exposures and subjective effects. Evidence reported here supports regulation of waterpipe components, smoking bans in multifamily housing and the use of human studies to evaluate modified or reduced risk claims.

INTRODUCTION

The WHO recognises the urgent need for regulation of waterpipe tobacco under the WHO Framework Convention on Tobacco Control (FCTC).¹ Hookah lounges that encourage and thrive on adolescent and young adult early social experimentation with waterpipe and other combustible tobacco products are centrally located near college campuses.²³

The rapid rise in prevalence of use among young adults may be partially attributed to the widespread perception that waterpipe tobacco smoking is less harmful and less addictive than cigarette smoking or other tobacco products.^{14–9} The misconception that the bowl water filters out toxicants from the smoke is commonly held by waterpipe smokers and non-smokers alike.⁷¹⁰¹¹ Indirect measurements made using machine smoking indicate some of the nicotine is retained by the water.¹² Nevertheless, waterpipe tobacco smoke contains addictive levels of nicotine,¹³ and surveys show this is not well understood by US college students.¹⁴¹⁵ In less than a month from initiation, infrequent (6 days/month), low consumption (7.5 waterpipes/month), sole use of waterpipe has been associated with signs of nicotine dependence in youth (12–18 years old).¹⁶ This form of tobacco may facilitate initiation of cigarette smoking.^{17–20} Among dual-users, waterpipe smoking is linked to progression to regular cigarette smoking²¹ and may impede cigarette smoking cessation.²⁰²²

Most waterpipe tobacco contains high levels of a viscous humectant, glycerin,²³ and therefore does not burn without a heat source. A burning lump of charcoal is typically placed on top of the foil-covered head that contains the tobacco. Charcoal heating in waterpipe smoking results in higher mainstream smoke yields of carbon monoxide (CO; >15 times higher) and benzene (>6 times higher), compared with smoking a cigarette.^{24–26} Biomarkers in blood, urine and exhaled breath confirm that increases in levels of these two compounds from water-pipe smoking greatly exceed those from cigarette smoking.^{27–31} Short-term, acute exposure to CO is associated with neurobehavioural and cognitive impairment,³²³³ and numerous cases of acute CO poisoning from waterpipe smoking are reported.^{34–44} Non-smoking bystanders in cafés and residences are also at risk for CO exposure, as levels of sidestream CO emitted from machine smoking a waterpipe in a controlled environmental chamber exceed those for a cigarette by a factor of 30.⁴⁵ Benzene is an International Agency for Research on Cancer Group 1 carcinogen⁴⁶ and a suspected cardiovascular and reproductive toxicant.^{46–49} Nicotine, CO and benzene are all included in the WHO FCTC priority list of toxic contents and emissions in tobacco products⁵⁰⁵¹ and the US Food and Drug Administration's (FDA) list of harmful and potentially harmful constituents.⁴⁸

The US statutory definition of a tobacco product includes components that are reasonably expected to: (1) alter or affect the tobacco product's performance, composition, constituents or characteristics and (2) be used with or for the human consumption of a tobacco product.⁵² Components may not be sold or distributed with health/modified risk claims unless the FDA issues an authorisation order after careful review of the evidence provided in a modified risk tobacco product application.^{52,53} This study examined two commercially available components because of specific health claims in their marketing rhetoric: a puck-like device that sits atop the foil-covered head and uses electrical resistance to heat waterpipe tobacco, and a plastic bubble diffuser that is press-fit onto the end of the waterpipe stem. During puffing, the bubble diffuser forces large bubbles that contain the mainstream smoke through a plastic mesh, creating smaller bubbles and increasing the surface area of water that the smoke contacts prior to being inhaled by the smoker. Manufacturers claim that these components are for 'the healthy hookah smoker', and their use results in increased filtration of the smoke sample (bubble diffuser),⁵⁴ and smokeless, odourless, heating with no CO (electric heater).⁵⁵

WHO's position is that misleading health claims on packaging and labelling of waterpipe components should be regulated to prohibit the use of such statements that infer waterpipe tobacco and charcoal are safe.¹ Modified risk tobacco products in the US are now prohibited to make claims of 'lower risk', 'less harmful' or 'contains a reduced level of a substance' without an FDA order in effect.⁵² Protocols for testing waterpipe emissions are not yet established, and mainstream and sidestream toxicant emissions have been measured using a variety of waterpipes and machine smoking equipment.⁵⁶ However, machine smoking emissions data are not valid measures of human exposure or risk.⁵⁷ To address data gaps and inform regulation of waterpipe components, clinical research is needed to characterise human exposures resulting from use of so-called reduced harm components.

For this study, we applied a previously developed boost measurement paradigm for biomarkers of acute exposure⁵⁸ combined with real-time analysis⁵⁹ to estimate nicotine, benzene and CO exposures experienced by established waterpipe users smoking a research-grade waterpipe (RWP) in a standard configuration (control) and equipped with two different components (ie, bubble diffuser and electric heater) purported by the manufacturers to reduce the harm of waterpipe smoking. Human exposure was evaluated via continuous collection of puffing topography and heart rate, and discrete sampling of plasma nicotine and exhaled breath compounds in a crossover study of active waterpipe smokers engaging in laboratory smoking in a controlled chamber ventilated at typical residential levels. Environmental or secondhand exposures were estimated from continuous CO data collected in the participant's breathing zone. Machine smoking according to a human-derived puffing regimen was used to inform compensation estimates.

METHODS

Participants

Using Craigslist, print advertisements, flyers and referrals, we recruited a convenience sample (n=36) of healthy, established waterpipe users aged 18 years and screened for eligibility by telephone. Established user was defined as having smoked water-pipe tobacco

3 times in the previous 6 months and 1 time in the previous month. Exclusion criteria included pregnancy, evident intoxication, respiratory infection, mouth disease and any history of smoking-related disease. Participants refrained from drinking coffee and using any tobacco product 12 and 4 hours prior to their laboratory visits, respectively. Participants were remunerated \$225 for completing all three laboratory smoking sessions.

Study protocol

For this repeated measures design, each participant undertook three laboratory visits to smoke the RWP with: (1) quick-light charcoal (control), (2) electric heating (electric) and (3) quick-light charcoal and stem fitted with bubble diffuser (bubble diffuser). Laboratory visits were scheduled according to Williams design randomisation scheme and separated by 1 week. Participants were instructed to smoke normally until satiated, with no minimum or maximum smoking time required. For the control or bubble diffuser, participants were limited to one quick-light charcoal. The RWP was prepared by laboratory staff, and participants were not allowed to manipulate the heat source during smoking.

During the first visit, smoking history and demographic information were collected, including the Minnesota Nicotine Withdrawal Scale, Brief Questionnaire of Smoking Urges, Direct Effect of Nicotine Scale and Direct Effects of Tobacco Scale. During each visit, participants completed these subjective effects questionnaires before and after smoking the RWP.

Before entering and immediately after exiting the chamber, blood and exhaled breath samples were collected. During smoking, participants were seated in a comfortable chair with a choice of videos for distraction. Participants' puff topography and heart rate were measured and recorded during the smoking session.

Waterpipe configurations and smoking topography data collection

Details regarding the setup, precision and accuracy of the RWP are described elsewhere.⁶⁰ Briefly, the RWP was fitted with a new hose and mouthpiece, the head was loaded with 10.0 ± 0.2 g tobacco (Double Apple, Nakhla) and covered with foil (Reynolds 625, China, 23×23 cm sheet, perforated with 18 holes). For the control and bubble diffuser, a burning quick-light charcoal (40 mm diameter, Three Kings, Holland) was placed on top of the foil after being placed on an electric heater (Type RY0811, 28 mm diameter, Ren Headstream, China) for 2 min. For the electric, the same electric heater was heated for 2 min and then placed on top of the foil. As previously described,⁶⁰ puffing flow rate data were continuously acquired (6 Hz) throughout the smoking session and later analysed to produce puffing topography. For the bubble diffuser, a Large Hookah Diffuser (Heba) was attached to the end of the stem in the bowl water.

Details on the controlled chamber, and methods used to measure exhaled breath CO and benzene, environmental CO levels, heart rate, subjective effects, mainstream smoke nicotine yields, and tobacco and heat source temperatures are described in the online supplementary material. RWP results are also compared with those obtained by other researchers with commercial waterpipes in the supplementary material.

Data analysis

Data were analysed using a linear mixed effects model for the analysis of repeated measures crossover design to assess differences in outcomes between the types of configuration and to account for the correlated data within the same participant. The model includes two within-participant factors: configuration (control, bubble diffuser and electric) and period (1, 2 and 3), and one between-participant factor for order effects. The main effects of configuration and the interaction effects between configuration and period were estimated. None of the interactions were statistically significant, indicating no carryover effects. For paired comparisons, p values were adjusted for multiple testing using Tukey's method. Because the study was predominantly exploratory, p values that are significant at the 0.10 significance level are marked. Data were analysed using *SAS* (V.9.4).

RESULTS

Participants

Data were collected in Columbus, Ohio, 3 November 2010–4 May 2011. Due to a technical error, two participants were excluded from topography analysis. Table 1 describes the study sample characteristics. Most participants first used waterpipe to smoke tobacco an average of 6 years prior to the study in a 'café or restaurant' setting or 'at a friend's home', but past 30-day use showed more smoking at home. Most participants described their waterpipe use as 'at least once a month, but not weekly'. In the past 30 days, participants smoked waterpipe an average of 3 times for 71.5 ± 44.4 min per session. No participants reported daily use, and only one participant responded 'yes' to the question 'Do you consider yourself 'hooked' on waterpipe?' Yet based on the Lebanon Waterpipe Dependence Scale,⁶¹ roughly one-third of the participants were considered dependent (a total score ≥ 10). More than half of the participants (56%) indicated they also smoked combustible cigarettes 'every day' or 'some days'.

Objective study outcomes

Table 2 compares puffing behaviour, exposure measures and charcoal and tobacco consumption by configuration. Generally, there were no significant differences in objective outcomes when participants smoked the RWP using charcoal heating, with the exception being a small increase (14%–18%) in average puff flow rate for the bubble as compared with control.

There were significant differences in almost all the objective outcomes compared with the control when participants smoked the RWP with electric heating. On average, participants took 30% more puffs resulting in almost twice the total puffing volume when smoking electric compared with control. Participants' puffs were 16% longer in duration and 38% larger in volume, with higher average and peak flow rates (18% and 12%, respectively) when smoking electric.

With electric heating, the mass of CO emitted into the chamber was over 1000 times lower compared with control. This was also reflected in the average boost in exhaled breath CO, which was only 3% of what was measured for participants using charcoal heating. Benzene

was detected in the exhaled breath of participants after smoking with charcoal, but not with electric. Plasma nicotine and heart rate boost were both significantly lower for electric compared with control (38% and 32%, respectively). Recovery of nicotine spiked into plasma QC samples averaged $100.5\% \pm 10.3\%$ ($n=14$), and the mean relative SD of participants' duplicate plasma samples ($n=3$) was $5.3\% \pm 4.8\%$ (mean $\pm$ SD), indicating the analytical method performed well.

Figure 1 shows the amount of charcoal and tobacco consumed versus the time each participant spent smoking. Charcoal consumption correlates strongly with smoking time (Spearman $r=0.905$), indicating that the burn rate of the charcoal was hardly affected by the participants' puffing behaviours. The relationship between tobacco consumption and smoking time is weaker ($r=0.607$), indicating puffing behaviour may play a more important role in how much tobacco is burned.

Machine smoking

Temperature may have been the reason why mainstream nicotine yields were significantly lower for the electric configuration. We conducted machine smoking using a human-derived puffing regimen (see online supplementary table S–1) for the control and electric configurations while continuously monitoring the temperature of the tobacco and heating sources (see online supplementary figure S–1 and S–2). Charcoal tobacco temperatures exceed those of electric by as much as 17.5°C at the end of the 33 min smoking session. Curves for the heat sources are significantly different after the first minute, with the charcoal temperature being as much as 76°C higher than the electric device in the first 5 min.

Subjective effects

As shown in table 3, all three configurations provided relief from urges to smoke. Compared with control, the bubble diffuser provided greater relief from 'urges to smoke a waterpipe' and 'craving a waterpipe/nicotine'. Participants rated higher increased drowsiness scores using charcoal heating. 'Desire for sweets' increased slightly after smoking control, while it decreased very little after smoking bubble diffuser or electric.

The 'intention to smoke WP' and 'relief from withdrawal' decreased across all three configurations. Participants reported increased subjective nicotine effects after smoking all three configurations (see table 3). More specifically, participants showed significantly higher effects in dizzy and lightheaded when smoking control compared with electric. Participants rated satisfying, pleasant and sleepy higher after smoking the two charcoal configurations compared with electric. Between control and bubble diffuser, calm, awake, reduce hunger, and sick were significantly higher for bubble diffuser than for control.

Comparison of toxicants in residential-like chamber and café smoking

Table 4 compares increases in toxicant levels in participants' exhaled breath and the chamber air to those reported for waterpipe café smokers and workers in the USA, Iran, Turkey, Russia, Egypt and Canada. Average boost in our participants' exhaled benzene exceeded indoor café smokers' exhaled⁶² and café environmental air benzene levels⁶³ by a factor of 5. Our participants' average boost in exhaled CO exceeded that measured in

waterpipe café employees after a ~10-hour shift⁶⁴ and that measured in field staff after being in a waterpipe café for 2 hours.⁶⁵

DISCUSSION

The study results have several policy and regulatory implications regarding infrequent waterpipe smokers, tobacco product standards and waterpipe tobacco smoking consumer education, marketing regulations and passive exposure protections.

Smoker compensation and signs of addiction

The heating source had a significant effect on smokers' puffing behaviours, toxicant exposures and subjective experiences. Participants rated the electric configuration less satisfying and pleasant, yet they took significantly more and larger puffs for almost twice the total puffing volume compared with charcoal heating. Although exposures associated with the burning charcoal, e.g., CO and benzene, were significantly lower, inhaling twice as much smoke when using the electric heat source would result in higher exposures to toxicants associated with the burning tobacco, such as furans and carbonyls. Outcomes related to nicotine delivery and the burning charcoal, e.g., plasma nicotine, heart rate, and exhaled benzene and CO boost, were significantly lower when using electric heating compared with charcoal. Initial symptoms of acute and chronic CO exposure, such as dizziness and lightheadedness,³³ were also significantly reduced when participants used electric heating. Ironically, the reduction of these symptoms may enable smokers to better tolerate more aggressive puffing to obtain the nicotine they desire and/or frustrate smokers who consider these sensations a pleasurable part of waterpipe smoking. Testing tobaccos and components using machine smoking would not have revealed increased toxicant exposure due to human compensation, and therefore, human studies are critical to informing tobacco product standards.

Machine smoking according to a standardised puffing regimen is a useful tool for regulation because yields can be used to compare tobaccos and components, but they cannot predict actual human exposures.⁶⁶ Nicotine yields indicated that the more aggressive puffing behaviour when using the electric component was likely in response to lower mainstream nicotine delivery associated with electric heating. Average boost in heart rate with electric heating was half that seen with charcoal heating, which may also be in response to lower mainstream nicotine delivery. We hypothesise that participants were engaging in compensation, or changing their puffing behaviour to compensate for lower nicotine levels in mainstream smoke.^{67,68} Mainstream nicotine yield was significantly lower for the electric configuration as compared with control (0.32 vs 1.44 mg/session). Although nicotine yield was almost a factor of 5 lower when using the electric heat source, participant plasma nicotine levels were only a factor of 2 lower. Average compensation level was 68% when participants smoked the RWP in the electric configuration compared with the control.^{67,68} Like addicted cigarette smokers,⁶⁷ the study participants appeared to upregulate their nicotine intake when inhaling waterpipe tobacco smoke with lower levels of nicotine. Cobb *et al*⁶⁹ first reported evidence of increased puffing when high-use frequency waterpipe smokers (20 waterpipes/month) smoked a nicotine-free herbal versus a nicotine-containing

product in the laboratory. Ours is the first study to quantify compensation in low-use frequency waterpipe smokers (3.1 ± 3.0 waterpipes/month) when smoking the same tobacco heated using two different components (quick-light charcoal and electric). This finding supports previous reports that even infrequent water-pipe use is associated with signs of nicotine dependence.¹⁶ It also indicates that waterpipe components can affect the ‘elasticity’ of the waterpipe by causing the smoker to actively obtain more than the yield value of nicotine.⁷⁰ The lower nicotine yield can be explained by the fact that the maximum temperature achieved by the electric heat source was lower than charcoal (see online supplementary figure S–1). Similar to what was reported for heated cigarettes,⁷¹ a direct relationship between temperature of the heated tobacco and mainstream nicotine yields is likely for waterpipe tobacco, but more data are needed. Should this relationship prove robust, product standards regarding the acceptable range of power for electric waterpipe heating devices would be warranted.

Ventilation: residential versus indoor café smoking

This study’s average environmental CO concentration, when adjusted from a 1-hour time-weighted average (TWA) to a 10-hour or 8-hour workday (9.39 mg/m^3 and 11.7 mg/m^3 , respectively), does not exceed the US National Institute for Occupational Safety and Health (NIOSH) and the US Occupational Safety and Health Administration TWAs (40 mg/m^3 and 55 mg/m^3 , respectively).^{72,73} However, chamber air levels were very close to the NIOSH ceiling level (229 mg/m^3), and therefore this ventilation level is not recommended for future work. The environmental CO levels measured here are cause for concern because the ventilation rate of the chamber (2.3 hour^{-1}) was almost four times higher than median residential air exchange rates reported for three major US metropolitan areas,⁷⁴ and the Passive House Standard⁷⁵ for energy efficient construction (0.71 and 0.60 hr^{-1} , respectively). Therefore, smoking a single waterpipe with charcoal heating at home with the windows closed may generate CO and benzene levels that significantly exceed permissible occupational exposure thresholds worldwide^{72,73,76–81} and, ironically, may also exceed those encountered in indoor hookah cafés where numerous people are smoking waterpipes.

Benzene is generated primarily by the burning charcoal,²⁵ and thus was not detected in participants’ breath when they smoked the electric configuration. This was corroborated by the lower average increase in heart rate and that they reported feeling less sleepy, drowsy and dizzy when smoking the electric configuration, all symptoms of acute exposure to high levels of benzene ($700\text{--}3000 \text{ ppm}$).⁸⁵ In our study, in a room that was ventilated at a rate comparable to most residences, smokers’ exhaled breath benzene levels for charcoal smoking were significantly higher than those reported by Samarghandi *et al* for waterpipe café smokers.⁶²

Charcoal heating also resulted in a considerable mass of CO in the chamber, ranging from 0.34 g to 1.7 g , during the smoking session, whereas electric generated very little CO. Waterpipe smoking with charcoal generates levels of CO that are 25–30 times greater than those from a cigarette.^{26,45} Roughly 17% of the average mass of charcoal consumed during the smoking session (see table 2) was measured as environmental CO. Yet charcoal

manufacturers are not required to provide warnings about smoking indoors or near residences, nor educational material regarding the importance of a smoke-free home as part of their consumer packaging.

CO emissions from waterpipe smoking are also concerning because CO is slightly lighter than air and can diffuse evenly throughout rooms in a house or units in multifamily housing, including into bedrooms where vulnerable occupants, such as children and older adults, are sleeping. A majority of our participants first smoked waterpipe in a café or restaurant setting, but their recent smoking shows a shift towards smoking more in the home. Smoking bans in public spaces are now prevalent throughout the world, yet passive exposure in multifamily homes is not similarly protected. One recent exception to this worldwide gap in legislation is that the US Department of Housing and Urban Development now prohibits smoking, including waterpipes, inside and within 25 feet of any public housing.⁸⁶ Whether the US ban can be successfully implemented remains to be seen. In the case of waterpipe, to squarely address the mistaken perception that this form of tobacco use is less harmful, concurrent public education through the use of media campaigns and mandated warning labels and educational package inserts may be critical to the success of smoke-free housing.

Manufacturers' marketing claims

Because participants engaged in compensation when smoking with the electric heat source, the anticipated higher active and passive particulate matter and tobacco smoke-related toxicants (besides nicotine) associated with that compensation, although not measured in this study, may offset any reduced risk that may be associated with the lower CO and benzene exposures. Puffing behaviour and exposures when using the bubble diffuser were not substantially different from the control, and thus the manufacturer's health claim of greater filtration is unsubstantiated. However, the bubble diffuser did provide roughly twice as much relief from urges to smoke and craving a waterpipe, and reduced desiring sweets compared with the control, suggesting this component may make waterpipe tobacco smoking more appealing. More work is needed to understand the public health effects of using these components.

Limitations

There are limitations to the data reported for this study. Because of the convenience sample, our results are not generalisable to the larger waterpipe tobacco smoking community. Although we believe the study provides convincing evidence of compensatory smoking in waterpipe tobacco smokers, this conclusion is not robust because mainstream charcoal emissions were not present when participants smoked the electric configuration. It is possible that charcoal emissions by themselves are reinforcing and established waterpipe smokers might puff more intensely because they are missing this stimulus when using electric heating. However, we would expect this behaviour to decay quickly because, unlike increases in nicotine delivery, there would be no reward for this more intense puffing. To further study compensation, one could test participants smoking the RWP with the same tobacco being electrically heated at two different temperatures, or in the control configuration using two different plastic hoses, one with and one without air ventilation holes.

Although the RWP is a predictable and precise tool that is well accepted by established waterpipe tobacco smokers,⁶⁰⁸⁷ the data presented cannot be generalised for the variety of commercial waterpipes sold worldwide. However, where available, our study outcomes agree with those reported by other researchers using commercial waterpipes. A laboratory study may not yield puffing behaviour representative of behaviour in more relaxed, social settings. Nevertheless, the reliability of this tool, combined with the crossover study design, allows us to make valid comparisons of exposures when smokers use different waterpipe components.

CONCLUSION

Considering misconceptions about waterpipe being non-addictive, and increasing prevalence of use, youth and young adults are a vulnerable population that is susceptible to the promise of reduced harm. Results from this study suggest that waterpipe smokers exhibit compensatory behaviour associated with nicotine addiction by inhaling much larger volumes of smoke per smoking session when using a component that results in lower levels of mainstream nicotine. In addition, smoking waterpipe at home may result in smokers and non-smokers being exposed to harmful levels of benzene and CO that significantly exceed worldwide occupational exposure limits. Future work should include a wider panel of biomarkers representing toxicants generated by the tobacco to more thoroughly understand exposures associated with electric heating. Data reported here support regulating waterpipe components as stringently as tobacco products to enhance public health.

To combat the mistaken perception that waterpipe smoking is a less harmful form of tobacco use and increase consumer education, we recommend mandating indelible (non-removable) health warning labels on components that warn users of the product's potential to initiate nicotine addiction (for the waterpipe itself), cause smokers to inhale more smoke (for heating sources) and produce poisonous levels of CO and benzene indoors (for charcoal). These data also strongly support banning manufacturers' claims that any component results in a lower risk from water-pipe smoking until regulatory agencies can evaluate carefully designed human studies to determine the real toxicant exposures associated with components purported to reduce harm.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors would like to thank Dawn M Deojay, Robyn R Kroeger and Iza L Reyes for their assistance with processing participants and data collection.

Funding Research was supported by grant number R01CA133149; the preparation of the manuscript was supported by P50CA180523 from the Office of the Director, National Institutes of Health (OD), National Cancer Institute and the FDA Center for Tobacco Products.

REFERENCES

1. World Health Organization (WHO). Advisory Note: Waterpipe tobacco smoking: health effects, research needs and recommended actions for regulations. 2nd Edition: WHO Study Group on Tobacco Product Regulation (TobReg), 2015 ISBN: 9789241508469.
2. Martinasek MP, Gibson-Young LM, Davis JN, et al. Waterpipe tobacco smoking impact on public health: implications for policy. *Risk Manag Healthc Policy* 2015;8:121. [PubMed: 26346473]
3. Kates FR, Salloum RG, Thrasher JF, et al. Geographic proximity of waterpipe smoking establishments to colleges in the U.S. *Am J Prev Med* 2016;50:e9–e14. [PubMed: 26346294]
4. Villanti AC, Cobb CO, Cohn AM, et al. Correlates of hookah use and predictors of hookah trial in U.S. young adults. *Am J Prev Med* 2015;48:742–6. [PubMed: 25890683]
5. Ambrose BK, Day HR, Rostron B, et al. Flavored tobacco product use among US youth aged 12–17 Years, 2013–2014. *JAMA* 2015;314:1871–3. [PubMed: 26502219]
6. Gathuru IM, Tarter RE, Klein-Fedyshin M. Review of hookah tobacco smoking among college students: policy implications and research recommendations. *Am J Drug Alcohol Abuse* 2015;41:272–80. [PubMed: 26057153]
7. Akl EA, Jawad M, Lam WY, et al. Motives, beliefs and attitudes towards waterpipe tobacco smoking: a systematic review. *Harm Reduct J* 2013;10:12. [PubMed: 23816366]
8. Minaker LM, Shuh A, Burkhalter RJ, et al. Hookah use prevalence, predictors, and perceptions among Canadian youth: findings from the 2012/2013 Youth Smoking Survey. *Cancer Causes Control* 2015;26:831–8. [PubMed: 25783457]
9. Berg CJ, Stratton E, Schauer GL, et al. Perceived harm, addictiveness, and social acceptability of tobacco products and marijuana among young adults: marijuana, hookah, and electronic cigarettes win. *Subst Use Misuse* 2015;50:79–89. [PubMed: 25268294]
10. Aljarrah K, Ababneh ZQ, Al-Delaimy WK. Perceptions of hookah smoking harmfulness: predictors and characteristics among current hookah users. *Tob Induc Dis* 2009;5:16. [PubMed: 20021672]
11. Daniels KE, Roman NV. A descriptive study of the perceptions and behaviors of waterpipe use by university students in the Western Cape, South Africa. *Tob Induc Dis* 2013;11:4. [PubMed: 23394683]
12. Shihadeh A Investigation of mainstream smoke aerosol of the argileh water pipe. *Food Chem Toxicol* 2003;41:143–52. [PubMed: 12453738]
13. Aboaziza E, Eissenberg T. Waterpipe tobacco smoking: what is the evidence that it supports nicotine/tobacco dependence? *Tob Control* 2015;24 Suppl 1(Suppl 1):i44–i53. [PubMed: 25492935]
14. Creamer MR, Loukas A, Li X, et al. College students' perceptions and knowledge of hookah use. *Drug Alcohol Depen* 2016;168:191–5.
15. Nuzzo E, Shensa A, Kim KH, et al. Associations between hookah tobacco smoking knowledge and hookah smoking behavior among US college students. *Health Educ Res* 2013;28:92–100. [PubMed: 22987864]
16. Bahelah R, DiFranza JR, Fouad FM, et al. Early symptoms of nicotine dependence among adolescent waterpipe smokers. *Tob Control* 2016;25:e127–e134. [PubMed: 27113610]
17. Jaber R, Madhivanan P, Veledar E, et al. Waterpipe a gateway to cigarette smoking initiation among adolescents in Irbid, Jordan: a longitudinal study. *Int J Tuberc Lung Dis* 2015;19:481–7. [PubMed: 25860006]
18. Salloum RG, Haider MR, Barnett TE, et al. Waterpipe tobacco smoking and susceptibility to cigarette smoking among young adults in the United States, 2012–2013. *Prev Chronic Dis* 2016;13:E24. [PubMed: 26890407]
19. Jensen PD, Cortes R, Engholm G, et al. Waterpipe use predicts progression to regular cigarette smoking among Danish youth. *Subst Use Misuse* 2010;45:1245–61. [PubMed: 20441461]
20. Asfar T, Weg MV, Maziak W, et al. Outcomes and adherence in Syria's first smoking cessation trial. *Am J Health Behav* 2008;32:146–56. [PubMed: 18052855]

21. Doran N, Godfrey KM, Myers MG. Hookah use predicts cigarette smoking progression among college smokers. *Nicotine Tob Res* 2015;17:1347–53. [PubMed: 25586774]
22. Hammal F, Mock J, Ward KD, et al. A pleasure among friends: how narghile (waterpipe) smoking differs from cigarette smoking in Syria. *Tob Control* 2008;17:e3. [PubMed: 18375726]
23. Schubert J, Bewersdorff J, Luch A, et al. Waterpipe smoke: a considerable source of human exposure against furanic compounds. *Anal Chim Acta* 2012;709:105–12. [PubMed: 22122938]
24. Monzer B, Sepetdjian E, Saliba N, et al. Charcoal emissions as a source of CO and carcinogenic PAH in mainstream narghile waterpipe smoke. *Food Chem Toxicol* 2008;46:2991–5. [PubMed: 18573302]
25. Schubert J, Müller FD, Schmidt R, et al. Waterpipe smoke: source of toxic and carcinogenic VOCs, phenols and heavy metals? *Arch Toxicol* 2015;89:2129–39. [PubMed: 25248501]
26. Shihadeh A, Schubert J, Klaiany J, et al. Toxicant content, physical properties and biological activity of waterpipe tobacco smoke and its tobacco-free alternatives. *Tob Control* 2015;24 Suppl 1:i22–i30. [PubMed: 25666550]
27. Kassem NO, Kassem NO, Jackson SR, et al. Benzene uptake in Hookah smokers and non-smokers attending Hookah social events: regulatory implications. *Cancer Epidemiol Biomarkers Prev* 2014;23:2793–809. [PubMed: 25416714]
28. St Helen G, Benowitz NL, Dains KM, et al. Nicotine and carcinogen exposure after water pipe smoking in hookah bars. *Cancer Epidemiol Biomarkers Prev* 2014;23.
29. Bentur L, Hellou E, Goldbart A, et al. Laboratory and clinical acute effects of active and passive indoor group water-pipe (narghile) smoking. *Chest* 2014;145:803–9. [PubMed: 24158379]
30. Eissenberg T, Shihadeh A. Waterpipe tobacco and cigarette smoking: direct comparison of toxicant exposure. *Am J Prev Med* 2009;37:518–23. [PubMed: 19944918]
31. Jacob P, Abu Raddaha AH, Dempsey D, et al. Nicotine, carbon monoxide, and carcinogen exposure after a single use of a water pipe. *Cancer Epidemiol Biomarkers Prev* 2011;20:2345–53. [PubMed: 21908725]
32. Raub JA, Mathieu-Nolf M, Hampson NB, et al. Carbon monoxide poisoning-a public health perspective. *Toxicology* 2000;145:1–14. [PubMed: 10771127]
33. Kao LW, Nañagas KA. Toxicity associated with carbon monoxide. *Clin Lab Med* 2006;26:99–125. [PubMed: 16567227]
34. Lim BL, Lim GH, Seow E. Case of carbon monoxide poisoning after smoking shisha. *Int J Emerg Med* 2009;2:121–2. [PubMed: 20157455]
35. Cavus UY, Rehber ZH, Ozeke O, et al. Carbon monoxide poisoning associated with narghile use. *Emerg Med J* 2010;27:406. [PubMed: 20442182]
36. La Fauci G, Weiser G, Steiner IP, et al. Carbon monoxide poisoning in narghile (water pipe) tobacco smokers. *CJEM* 2012;14:57–9. [PubMed: 22417961]
37. Ashurst JV, Urquhart M, Cook MD. Carbon monoxide poisoning secondary to hookah smoking. *J Am Osteopath Assoc* 2012;112:686–8. [PubMed: 23055468]
38. Clarke SF, Stephens C, Farhan M, et al. Multiple patients with carbon monoxide toxicity from water-pipe smoking. *Prehosp Disaster Med* 2012;27:612–4. [PubMed: 23174041]
39. Karaca Y, Eryigit U, Aksut N, et al. Syncope associated with water pipe smoking. *BMJ Case Rep* 2013;2013:bcr2013009526.
40. Ozkan S, Ozturk T, Ozmen Y, et al. Syncope associated with carbon monoxide poisoning due to narghile smoking. *Case Rep Emerg Med* 2013;2013.
41. von Rappard J, Schönenberger M, Bärlocher L. Carbon monoxide poisoning following use of a water pipe/hookah. *Dtsch Arztebl Int* 2014;111:674. [PubMed: 25346357]
42. Wang LW, He EY, Ghosh D, et al. Severe carbon monoxide poisoning from waterpipe smoking: a public health concern. *Med J Aust* 2015;202:446–7. [PubMed: 25929510]
43. Medford MA, Gasier HG, Hexdall E, et al. Research report: Charcoal type used for hookah smoking influences CO production. *Undersea Hyperb Med* 2015;42:375–80. [PubMed: 26403022]
44. Retzky SS, Spiller HA, Callahan-Lyon P. Calls to Poison Centers for hookah smoking exposures. *Clin Toxicol* 2018;56:442–5.

45. Daher N, Saleh R, Jaroudi E, et al. Comparison of carcinogen, carbon monoxide, and ultrafine particle emissions from narghile waterpipe and cigarette smoking: Sidestream smoke measurements and assessment of second-hand smoke emission factors. *Atmos Environ* 2010;44:8–14.
46. International Agency for Research on Cancer (IARC), 2012 IARC Monographs on the evaluation of carcinogenic risks to humans. Volume 100F: a review of human carcinogens: chemical agents and related occupations. Available here <http://monographs.iarc.fr/ENG/Monographs/vol100F/ono100F-24.pdf>
47. US Environmental Protection Agency. Benzene: 71-43-2. Summary created in April 1992, updated in January 2000 and January 2012. <https://www.epa.gov/sites/production/files/2016-09/documents/benzene.pdf>.
48. US Food Drug Administration. Harmful and potentially harmful constituents in tobacco products and tobacco smoke; established list. *Fed Regist* 2012;77:20034–7.
49. Bahadar H, Mostafalou S, Abdollahi M. Current understandings and perspectives on non-cancer health effects of benzene: a global concern. *Toxicol Appl Pharmacol* 2014;276:83–94. [PubMed: 24589379]
50. World Health Organization. The Scientific Basis of Tobacco product Regulation. Second report of a WHO study group. 951, 45–125: World Health Organization WHO Technical Report Series, 2008 http://www.who.int/tobacco/global_interaction/tobreg/publications/9789241209519.pdf.
51. World Health Organization, WHO framework convention on tobacco control. 2003 http://www.who.int/tobacco/framework/WHO_FCTC_english.pdf.
52. Food and Drug Administration, HHS. Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products. Final rule. *Fed Regist* 2016;81:28973. [PubMed: 27192730]
53. Food and Drug Administration (FDA). U.S. Department of Health and Human Services (HHS), 2012. Guidance for Industry Modified Risk Tobacco Product Applications Draft Guidance. <https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM297751.pdf>.
54. <https://www.hookah-shisha.com/hookahlove/85-the-heba-diffuser-why-a-little-piece-plastic-makes-of-a-huge-difference.Html>
55. <http://www.hookahshisha.org/hookah-charcoal-electronic-hookah-shisha-charcoal-large-40mm-plugin-p-1102.Html>
56. World Health Organization. WHO study group on tobacco product regulation: report on the scientific basis of tobacco product regulation: sixth report of a WHO study group, 2017 <http://apps.who.int/iris/bitstream/10665/260245/1/9789241210010-eng.pdf?ua=1>.
57. World Health Organization. WHO Tobacco Free Initiative. Standard operating procedure for intense smoking of cigarettes. 2012 http://apps.who.int/iris/bitstream/handle/10665/75261/9789241503891_eng.pdf;jsessionid=5E3D61464957BF3E7D53B26E8136B1D1?sequence=1
58. Brinkman MC, Chuang JC, Gordon SM, et al. Exposure to and deposition of fine and ultrafine particles in smokers of menthol and nonmenthol cigarettes. *Inhal Toxicol* 2012;24:255–69. [PubMed: 22486344]
59. Gordon SM, Brinkman MC, Meng RQ, et al. Effect of cigarette menthol content on mainstream smoke emissions. *Chem Res Toxicol* 2011;24:1744–53. [PubMed: 21888394]
60. Brinkman MC, Kim H, Gordon SM, et al. Design and validation of a research-grade waterpipe equipped with puff topography analyzer. *Nicotine Tob Res* 2016;18:785–93. [PubMed: 26377514]
61. Salameh P, Waked M, Aoun Z. Waterpipe smoking: construction and validation of the Lebanon Waterpipe Dependence Scale (LWDS-11). *Nicotine Tob Res* 2008;10:149–58. [PubMed: 18188755]
62. Samarghandi M, Mehrilipour J, Shabanlo A, et al. The evaluation of personal exposure to BTEX compounds in the traditional restaurants in Hamadan in 2013. *Sci J Hamadan Univ Med Sci* 2014;21:231–9.
63. Hazrati S, Rostami R, Fazlzadeh M. BTEX in indoor air of waterpipe cafés: Levels and factors influencing their concentrations. *Sci Total Environ* 2015;524–525:347–53.

64. Zhou S, Behrooz L, Weitzman M, et al. Secondhand hookah smoke: an occupational hazard for hookah bar employees. *Tob Control* 2017;26:40–5. [PubMed: 26811352]
65. Zhang B, Haji F, Kaufman P, et al. ‘Enter at your own risk’: a multimethod study of air quality and biological measures in Canadian waterpipe cafes. *Tob Control* 2015;24:175–81. [PubMed: 24161999]
66. Burns DM, Dybing E, Gray N, et al. Mandated lowering of toxicants in cigarette smoke: a description of the World Health Organization TobReg proposal. *Tob Control* 2008;17:132–41. [PubMed: 18375736]
67. Benowitz NL. Compensatory smoking of low-yield cigarettes, National Cancer Institute Risks associated with smoking cigarettes with low machine yields of tar and nicotine Smoking and Tobacco Control Monograph No. 2001;13:39–63.
68. Stephen A, Frost C, Thompson S, et al. Estimating the extent of compensatory smoking. Nicotine, smoking and the low tar programme 1989:100–15.
69. Cobb CO, Sahmarani K, Eissenberg T, et al. Acute toxicant exposure and cardiac autonomic dysfunction from smoking a single narghile waterpipe with tobacco and with a “healthy” tobacco-free alternative. *Toxicol Lett* 2012;215:70–5. [PubMed: 23059956]
70. Manipulation: Imperial Tobacco & Its Cigarettes: The Engineering of Canadian Cigarettes, British American Tobacco Records, 1999 Bates No. 321932254–321932258. <https://www.industrydocumentslibrary.ucsf.edu/tobacco/docs/kmgn0204>.
71. Forster M, Liu C, Duke MG, et al. An experimental method to study emissions from heated tobacco between 100–200°C. *Chem Cent J* 2015;9:20. [PubMed: 25941536]
72. NIOSH. NIOSH Pocket Guide to Chemical Hazards, Books Express Publishing, 1600 Clifton Rd. Atlanta, GA 30329, USA, 2012.
73. OSHA. Occupational Exposure Limits. Occupational Safety & Health Administration, 200 Constitution Ave. NW, Washington, DC 20210, USA, 2014.
74. Yamamoto N, Shendell DG, Winer AM, et al. Residential air exchange rates in three major US metropolitan areas: results from the Relationship Among Indoor, Outdoor, and Personal Air Study 1999–2001. *Indoor Air* 2010;20:85–90. [PubMed: 19874401]
75. Passive House Certification Criteria, International Passive House Association. https://www.passivehouse-international.org/index.php?page_id=150
76. MHMEI. Occupational Exposure Limits: Center EOH, Tehran, 2012.
77. HSE. Eh40/2005 Workplace Exposure Limits. London: Health and Safety Executive, 2011.
78. USEPA. United States Environmental Protection Agency, Reference concentration for chronic inhalation exposure. 2007 <http://www.epa.gov/iris>.
79. Attias L, Boccardi P, Boeije G, et al. European union system for the evaluation of substances: the second version. *Chemosphere* 2005;59:473–85. [PubMed: 15788170]
80. American Conference of Governmental Industrial Hygienists. Carbon Monoxide: TLV(R) Chemical Substances 7th Edition Documentation, Signature Publications, 2001 <https://www.acgih.org/forms/store/ProductFormPublic/carbon-monoxide-tlv-r-chemical-substances-7th-edition-documentation>
81. ACGIH. American Conference of Governmental Industrial Hygienists. Benzene: TLV(R) Chemical Substances 7th Edition Documentation, Signature Publications, 2001 <https://www.acgih.org/forms/store/ProductFormPublic/benzene-tlv-r-chemical-substances-7th-edition-documentation>.
82. Torrey CM, Moon KA, Williams DA, et al. Waterpipe cafes in Baltimore, Maryland: Carbon monoxide, particulate matter, and nicotine exposure. *J Expo Sci Environ Epidemiol* 2015;25:405–10. [PubMed: 24736103]
83. Zhou S, Weitzman M, Vilcassim R, et al. Air quality in New York City hookah bars. *Tob Control* 2015;24:e193–e198. [PubMed: 25232045]
84. Kumar SR, Davies S, Weitzman M, et al. A review of air quality, biological indicators and health effects of second-hand waterpipe smoke exposure. *Tob Control* 2015;24 Suppl 1:i54–i59. [PubMed: 25480544]
85. U.S. Department of Health and Human Services. Agency for Toxic Substance and Disease Registry (ATSDR): In. Toxicological profile for Benzene, 2007 <https://www.atsdr.cdc.gov/toxprofiles/tp3.pdf>

86. Department of Housing and Urban Development. Instituting Smoke-Free Public Housing. 24 CFR Parts 965 and 966, Docket No. 2016. FR 5597-F-03, RIN 2577-AC97 <https://archives.hud.gov/news/2016/pr16-184-smokefreephfinalrule.pdf>.
87. Kim H, Brinkman MC, Sharma E, et al. Variability in puff topography and exhaled CO in waterpipe tobacco smoking. *Tob Regul Sci* 2016;2:301–8. [PubMed: 28670606]

What this paper adds

It is widely accepted in the tobacco regulatory science community that waterpipe tobacco smoking delivers sufficient levels of nicotine to initiate and sustain addiction, and active and passive exposures to CO and benzene exceed those from smoking a cigarette. Our results have regulatory implications in that they: It is widely accepted in the tobacco regulatory science community that waterpipe tobacco smoking delivers sufficient levels of nicotine to initiate and sustain addiction, and active and passive exposures to CO and benzene exceed those from smoking a cigarette. Our results have regulatory implications in that they:

- Suggest that waterpipe smokers are addicted to nicotine and therefore will engage in more frequent and aggressive puffing to compensate for lower mainstream nicotine delivery. Thus, reduced harm or modified risk claims cannot be evaluated based on machine smoking yield data alone and require testing with human cohorts to better understand waterpipe tobacco smokers' actual exposures when using these components.
- Demonstrate the importance of waterpipe components to the active and passive toxicant exposures experienced by waterpipe smokers and passively exposed non-smokers. These data support the regulation and controlled testing of waterpipe components.
- Suggest that waterpipe smoking at home exposes smokers and non-smokers to harmful levels of benzene, CO and other toxicants. These data support the inclusion of 'waterpipe tobacco smoking' as banned behaviour in and near multifamily public housing.

Figure 1.
Relationship of tobacco and charcoal consumption to smoking session duration for participant laboratory smoking of the research-grade waterpipe in three different configurations.

Table 1

Study sample characteristics

Characteristic	Mean±SD	Range
Age (years)	24.4±5.5	20–40
Sex (%)		
Male	70.6 [*]	
Female	29.4	
Race (%)		
Asian	8.8	
Black, or African-American	14.7	
White	76.5	
Education (years, GED=12 years)	14.5±1.7	12–17
Where were you when you used a waterpipe to smoke tobacco? (%)	First use	Past 30 days
In a café or restaurant	58.8	50.0
In my own house	0	25.0
At a friend's home	26.5	25.0
At a family member's house	5.9	0
At a fraternity house	0	0
Dorm room	0	0
Other	8.8	0
Age at first waterpipe use (years)	18.6±4.1	15–34
Which of the following choices best describes how often you smoke tobacco using a waterpipe? (%)		
At least once a year, but not monthly	5.9	
At least once a month, but not weekly	58.8	
At least once a week, but not daily	35.3	
At least once a day, or most days each month	0	
Do you own your own waterpipe? (%)		
Yes	50.0	
Approximately how many times did you use a waterpipe to smoke tobacco in the past 30 days? (times)	3.1±3.0	1–17.5
Approximately how many bowls (or heads) of tobacco did you smoke using a waterpipe in the past 30 days? (heads)	4.3±4.0	1–20
When you used a waterpipe to smoke tobacco in the past 30 days, how long did a typical 'waterpipe session' last? (min)	71.5±44.4	12.5–180
Lebanon Waterpipe Independence Scale (LWDS-11)	8.5±3.2	3–17
Do you consider yourself 'hooked' on a waterpipe? (%)	3	
Do you now smoke cigarettes every day some days, or not at all? (%)		
Every day	32.4	
Some days	23.5	
Not at all	44.1	
How many cigarettes do you smoke in a normal day? (cigarettes)	7.5±7.1	0–20

^{*} All percent values are expressed as a fraction of the total participants (n=34).

Table 2

Descriptive statistics and paired statistical comparisons for human topography and biomarker outcome measures from participants (n=34 unless specified) smoking the RWP in three configurations: control, bubble diffuser and electric

	Mean±SD		P values for statistical comparison*		
	Control	Bubble diffuser	Electric	Bubble diffuser versus control	Electric versus control
Topography measures					
Number of puffs	70.9±37.8	73.4±37.2	92.5±39.8	ns	P<0.01
Puff volume (L)	0.65±0.27	0.73±0.37	0.90±0.43	ns	P<0.0001
Puff duration (s)	4.4±2.1	4.3±2.3	5.1±2.2	ns	P<0.10
Puff interval (s)	26.2±14.4	28.2±17.3	22.6±16.1	ns	ns
Puff peak flow (L/min)	15.8±4.8	17.1±5.4	17.7±5.2	ns	P<0.01
Puff average flow (L/min)	10.1±3.8	11.5±4.6	11.9±4.4	P<0.05	P<0.001
Total puff volume (L)	41.7±25.8	48.7±35.8	82.6±63.8	ns	P<0.0001
Duration of smoking (min)	31.6±14.5	32.5±12.1	38.5±26	ns	ns
Exposure measures					
Environmental CO (mg/session)	980.5±368.5	1012±274.8	1.7±3.1 (n=25)[†]	ns	P<0.0001
Exhaled CO boost (ppmv)	51.7±19.9 (n=33) [‡]	56.5±36.1 (n=33) [‡]	0.1±1.3	ns	P<0.0001
Exhaled benzene boost (ppmv)	8.5±5.4 (n=31) [§]	8.4±4.9 (n=32) [§]	-0.1±0.3	ns	P<0.0001
Plasma nicotine (ng/mL)	12.2±12.7	13.7±13.6	7.5±6.7	ns	P<0.05
Heart rate boost (bpm)	13.9±10.6 (n=29) [¶]	15.8±11.5 (n=33) [¶]	9.4±9.7 (n=33)[¶]	ns	P<0.10
Maximum heart rate (bpm)	112±15.2 (n=29) [¶]	113±13.1 (n=33) [¶]	112±10.9 (n=33)[¶]	ns	P<0.05
Tobacco and charcoal consumption					
Tobacco consumed (g)	2.1±0.7 (n=33) ^{**}	2.2±0.8 (n=34)	2.0±0.8 (n=33) ^{**}	ns	ns
Tobacco consumed (%)	21.0±7.1 (n=33) ^{**}	22.2±8.0 (n=34)	20.4±8.2 (n=33) ^{**}	ns	ns
Charcoal consumed (g)	5.8±1.1 (n=34)	6.0±0.9 (n=33) ^{***}	-	ns	ns
Charcoal consumed (%)	55.5±11.0 (n=34)	57.0±10.5 (n=33) ^{***}	-	ns	ns

Both control and bubble diffuser use charcoal heating of the tobacco, whereas electric uses electric heating.

* Statistical comparisons were made between control and each configuration. Bolded entry indicates significant difference from control at a p value of 0.10 or smaller. The p values were adjusted for multiple testing.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

⁷ The CO monitor was inoperable during nine electric smoking sessions.

⁷ Exhaled CO not collected for one control and one bubble diffuser session.

⁸ Exhaled benzene not collected for three control and two bubble diffuser sessions.

⁹ Heart rate data collection file was incomplete for five controls, one bubble diffuser and one electric session.

^{**} Final tobacco weight not recorded for one control and one electric session.

^{***} Final charcoal weight not recorded for one bubble diffuser session.

bpm, beats per minute; CO, carbon monoxide; n, sample size; ns, not significant; ppmv, parts per million by volume.

Table 3

Descriptive statistics and paired statistical comparisons for subjective effect measures from participants (n=34 unless specified) smoking the RWP in three configurations: control, bubble diffuser and electric

	Mean±SD		P value for statistical comparison*		
	Control	Bubble diffuser	Electric	Bubble diffuser versus control	Electric versus control
Minnesota Nicotine Withdrawal Scale (MNWS) Difference Score (postsampling minus presampling) ^{†‡}					
Urges to smoke a waterpipe	-16.9±28.1	-30.7±32.9	-25.5±29.9	P<0.01	ns
Irritability/frustration/anger	-3.3±12.5	-0.7±17.6	0.6±5.6	ns	ns
Anxious	-0.2±15.5	-0.1±16.0	1.0±19.1	ns	ns
Difficulty concentrating	4.7±19.9	6.7±21.9	1.6±15.5	ns	ns
Restlessness	4.6±20.6	0.2±13.6	-0.2±13.3	ns	ns
Hunger	6.2±23.3	4.5±17.5	5.0±19.1	ns	ns
Impatient	0.4±15.9	1.4±20.8	-3.5±13.2	ns	ns
Craving a waterpipe/nicotine	-15.6±22.9	-27.0±29.5	-24.9±28.9	P<0.05	P<0.10
Drowsiness	11.6±29.3	2.6±26.7	-4.0±22.1	ns	P<0.05
Depression/feeling blue	1.8±14.7	-2.6±10.1	0.3±12.7	ns	ns
Desire for sweets	5.5±15.6	-1.7±8.5	-0.4±10.6	P<0.05	P<0.05
Waterpipe-modified Brief Questionnaire on Smoking Urges (QSU-brief); difference score (postsampling minus presampling)					
Intention to smoke (factor 1)	-2.0±1.5 [§]	-2.5±1.6	-2.2±1.6	P<0.10	ns
Relief from withdrawal (factor 2)	-0.9±1.0	-1.1±1.0	-0.8±1.2	ns	ns
Direct Effects of Nicotine Scale (DENS); difference score (postsampling minus presampling) [‡]					
Nauseous	7.8±19.8	13.8±19.4	3.3±11.5	ns	ns
Dizzy	18.9±25.0	22.9±27.8	8.7±15.2	ns	P<0.10
Lightheaded	26.6±25.6	30.3±28.1	10.2±19.2	ns	P<0.05
Nervous	1.1±14.0	3.5±20.0	-0.3±12.3	ns	ns
Sweaty	10.8±24.6	12.9±22.6	7.1±15.9	ns	ns
Headache	4.2±16.0	7.5±14.8	1.5±8.3	ns	ns
Excess salivation	3.6±11.8	6.2±14.0	7.8±16.4	ns	ns
Heart pounding	8.5±19.6	13.2±19.9	7.0±13.9	ns	ns
Confused	5.2±16.6	6.5±18.1	1.8±6.8	ns	ns
Weak	6.5±20.3	12.4±19.7	2.3±10.5	ns	ns

	Mean±SD		P value for statistical comparison [*]			
	Control	Bubble diffuser	Electric	Bubble diffuser versus control	Electric versus control	
Direct Effects of Tobacco Scale (DETS); postsmoking score [‡]						
Satisfying	59.2±22.3	62.5±23.4	47.0±25.8	ns	P<0.10	
Pleasant	61.8±18.1	61.0±25.3	47.4±24.1	ns	P<0.01	
Taste good	61.2±24.4	63.9±24.5	52.7±25.6	ns	ns	
Taste bad	16.9±17.1	15.2±17.7	22.3±22.1	ns	ns	
Dizzy	35.5±30.6	36.6±27.9	24.3±21.1	ns	ns	
Calm	40.9±25.1	47.2±26.6	33.8±25.6	P<0.10	ns	
Confused	15.2±21.7	13.6±16.9	9.7±10.9	ns	ns	
Concentrate	21.1±17.3	24.0±20.7	22.5±23.7	ns	ns	
Awake	25.4±21.9	32.0±25.3	23.0±22.4	P<0.10	ns	
Reduce hunger	18.8±17.8	27.2±25.1	23.3±21.2	P<0.05	ns	
Sick	14.1±17.7	20.4±17.9	11.5±15.1	P<0.10	ns	
Sleepy	28.9±25.6	29.3±27.3	16.6±20.1	ns	P<0.01	
Like to smoke another WP right now	14.9±18.7	14.6±19.1	16.8±22.1	ns	ns	

^{*} Statistical comparisons were made between control and each configuration. Bolded entry indicates significant difference from control at a p value of 0.10 or smaller. The p values were adjusted for multiple testing.

[‡] Responses from one participant were not collected.

[‡] MNWS, DENS and DETS are VAS ranging from 0 to 100 (not at all to extremely); QSU-brief is Likert scale ranging from 1 to 7 (strongly disagree to strongly agree).

[§] One participant had a missing value in QSU (post item #3) for control, so when creating a mean value for factor 1 the mean was substituted for the missing value.

DETS items were rated postsampling only. Both control and bubble diffuser use charcoal heating of the tobacco, whereas electric uses electric heating. Except for the DETS, scores used for analysis were difference scores (postsampling minus presampling).

ns, not significant; VAS, visual analogue scales.

Table 4

Toxicant increases in exhaled breath and environmental concentrations in waterpipe café studies compared with a single active smoker in a controlled chamber ventilated at 2.3 hr⁻¹ (this study)

Study	Geographic location (sample size)	Boost in exhaled breath (mg/m ³)		Environmental concentration (mg/m ³)	
Benzene		Mean±SD	Range	Mean±SD	Range
This study [*]	Columbus, Ohio, USA (n=31 waterpipe smokers)	27.1±17.2	0.30–66.2	-	-
Hazrati <i>et al</i> ^{63 †}	Ardabil, Iran (n=81 cafés)	-	-	4.96±2.63	0.37–11.64
Samarghandi <i>et al</i> ^{62 ‡}	Hamadan, Iran (n=25 waterpipe smokers)	4.78±0.73	1.76–7.99	-	-
CO		Mean±SD	Range	Mean±SD	Range
This study [*]	Columbus, Ohio, USA (n=33 waterpipe smokers and smoking sessions)	59.2±22.8	16.0–117	93.9±50.4	6.34–234
Zhou 2017 [§]	New York City, New York, USA (n=4 cafés; n=10 non-smoking café workers)	47.11 [¶]	NS	14.8±5.67	10.9–25.8
Torrey <i>et al</i> ^{82 ¶}	Baltimore, Maryland, USA (n=7 cafés)	-	-	21±26	2.3–61
Moon ^{82 **}	Istanbul, Turkey (n=9 cafés)	-	-	4.2 ^{††}	1.6–23 ^{‡‡}
	Moscow, Russia (n=17 cafés)	-	-	2.9 ^{††}	1.5–4.1 ^{‡‡}
	Cairo, Egypt (n=20 cafés)	-	-	27 ^{††}	9.3–110 ^{‡‡}
Zhang 2015 ^{§§}	Toronto, Canada (n=12 indoor cafés; n=23 non-smoking field staff)	17.3±24.1	1.72–80.2	20.3±23.9	0–137

^{*} Control configuration; environmental concentration expressed as 1-hour time-weighted average.

[†] Hazrati S, Rostami R, Fazlzadeh M, *et al*⁶³

[‡] Samarghandi M, Mehrilipour J, Shabanlo A, *et al*⁶² and personal communication with the author.

[§] Boost estimated from difference between post- and pre-shift average exhaled CO from waterpipe cafe workers working average shift of 10.3 ± 1.4 hours ; Zhou S, Behrooz L, Weitzman M, *et al*⁶⁴

[¶] Torrey CM, Moon KA, D'Ann LW, *et al*⁸².

^{**} Moon KA, Magid H, Torrey C, Rule AM, Ferguson J, Susan J. & Radwan GN. Secondhand smoke in waterpipe tobacco venues in Istanbul, Moscow, and Cairo. *Environ Res* 2015;142:568–574.

^{††} Median.

^{‡‡} IQR.

^{§§} Boost taken as value for breath sample collected after conducting 2-hour sampling session; Zhang B, Haji F, Kaufman P, *et al*⁶⁵.

CO, carbon monoxide; NS, not specified.