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DETERMINANTS OF WATERPIPE SMOKING TRAJECTORIES AND THE EFFECTS OF PICTORIAL HEALTH WARNING LABEL AMONG YOUNG WATERPIPE SMOKERS IN THE US

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Prem Gautam

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To: Dean Tomás R. Guilarte
Robert Stempel College of Public Health and Social Work

This dissertation, written by Prem Gautam, and entitled Determinants of Waterpipe Smoking Trajectories and the Effects of Pictorial Health Warning Label Among Young Waterpipe Smokers in the US, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this dissertation and recommend that it be approved.

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The dissertation of Prem Gautam is approved.

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DEDICATION

I dedicate my dissertation to my parents [Father (Maheshor Prasad Gautam), Mother (Sita Devi Gautam)], lovely wife (Srijana), and my cute baby (Nirvan). I also dedicate my dissertation to my dear brother (Lekhnath Gautam), sister-in-law (Sunita Sigdel), nephews (Subarna and Suyash), and parents-in-law (Lal Prasad Acharya and Saraswati Acharya). Words cannot fully express how grateful I am for their sacrifice, hard work, support, and unconditional love. Without their love and support, this work would not have been possible.

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ABSTRACT OF THE DISSERTATION

DETERMINANTS OF WATERPIPE SMOKING TRAJECTORIES AND THE EFFECTS OF PICTORIAL HEALTH WARNING LABEL AMONG YOUNG WATERPIPE SMOKERS IN THE US

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In recent years waterpipe tobacco (WPT) smoking has increased among young people in the United States (US). Adequate characterization of the WPT smoking trajectories (initiation, progression, and cessation), their predictors, and examination of the effects of a pictorial health warning label (PHWL) on WPT smokers is essential to guide interventions and policies to curb WPT smoking among young people in the US. Using the Population Assessment of Tobacco and Health Study (PATH) and clinical lab data, this dissertation assessed: 1) prevalence and predictors of WPT smoking initiation and progression among adolescents and young adults; 2) magnitude and predictors of WPT cessation among young adults, and 3) the effects of PHWL on low- and high-frequency WPT smokers' experiences, toxicant exposures, and puffing behavior.

In the first study, between 2013-2018, 4.8% of the adolescents and 18.5% of young adults initiated WPT smoking. During the same period, 10.6% of adolescent WPT smokers and 14.1% of young adult-WPT smokers progressed in WPT smoking (increase in the frequency of smoking at any subsequent wave). Predictors of WPT initiation among adolescents include lower harm perception (adjusted odds ratio (aHR)=2.89, 95% confidence interval (CI)=2.10-3.98), and other tobacco products use (aHR=3.97,

95% CI=2.73-5.78), while predictors of WPT progression include illicit drug use (aHR=4.60, 95% CI=1.99-10.67). Among young adults, predictors of WPT initiation include lower harm perception (aHR=2.77, 95% CI=2.19-3.50), and other tobacco products use (aHR=3.14, 95% CI=2.25-4.38); while predictors of WPT progression were lower harm perception (aHR=1.80, 95% CI=1.41-2.30), and alcohol use (aHR=1.61, 95% CI=1.13-2.30).

In the second study, 25.13% of the young adult WPT smokers quit smoking between waves 1-5 (2015-2019). The major predictor of WPT smoking cessation was regretting smoking (aHR= 2.33, 95% CI=1.29-4.21) whereas barriers to cessation were the lack of smoking restriction at home (aHR=0.35, 95% CI=0.18-0.70) and alcohol use (aHR=0.62, 95% CI=0.41-0.93) among young adults WPT smokers. A moderate correlation between regret smoking WPT and quit attempts (ρ=0.3, p-value <0.05) was found indicating regretting smoking as a proxy of interest in quitting.

In the third study, both low- and high-frequency smoking groups showed no effect of PHWL on exposure to nicotine and other toxicants. However, there was a reduction in acute subjective experiences of smoking among high-frequency smokers compared to low-frequency smokers after smoking WPT with PHWL compared to the no-PHWL (e.g., puff liking -1.2 vs. -0.5; puff satisfaction -1.0 vs. -0.3) ($p<0.05$ for all).

Overall, we found a high rate of WPT smoking initiation and progression. Several modifiable risk factors including lower harm perception towards WPT and the loopholes in regulating WPT establishments were the drivers of WPT initiation, progression, and continuation. The PHWL on the WPT device showed differential effectiveness among low- and high-frequency smokers. The FDA should mandate PHWL on the WPT device and WPT establishments should not be exempted from smoke-free air legislation and not allowed indirect promotion in social media.

TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS

aHR	Adjusted hazard ratio
ACASI	Audio Computer-administered Self-interview
CI	Confidence interval
DSM	Diagnostic and Statistical Manual Criteria
DSQ	Duke Sensory Questionnaire
eCO	Expired Carbon Monoxide
HAVE	Host, Agent, Vector, Environment
HONC	Hooked on Nicotine Checklist
IPI	Inter-puff Interval
LGBS	Lesbian, Gay, Bisexual, and Other
MAR	Missing at Random
NDSS	Nicotine Dependence Syndrome Scale
NH	non-Hispanic
PATH	Population Assessment of Tobacco and Health
PHWL	Pictorial health warning label
US	United States
WES	Waterpipe Evaluation Scale
WISDM	Wisconsin Inventory of Smoking Dependence Motives
WHO	World Health Organization
WP	Waterpipe
WPT	Waterpipe Tobacco

INTRODUCTION

Every year, tobacco use kills over 8 million people globally (World Health Organization, 2020) including almost half a million in the United States (US) alone (Campaign for Tobacco-Free Kids, 2021). One of the contributors to this burden is waterpipe tobacco (WPT) smoking (aka hookah, shisha, and narghile) which has become popular around the world and in the US, mostly among young people (Jawad et al., 2018; Sidani et al., 2019).

According to the US National Youth Tobacco Surveys from 2011 to 2020, the prevalence rate of current WPT smoking among adolescents in 2020 was 2.1% (estimated ~580,000) and it shows an increasing trend, especially among middle school students (1% in 2011 to 1.3% in 2020) (Gentzke et al., 2019). Additionally, as per the 2016 Population Assessment of Tobacco and Health (PATH) study data, the current WPT smoking rate is high (9.2%) among young adults of age between 18-24 years (Sharma et al., 2020). The popularity of WPT smoking among young people is concerning given the evidence that WPT smoke contains several toxicants and carcinogens known to cause respiratory and cardiovascular diseases as well as lung cancer (Bhatnagar et al., 2019).

Literature review shows that several factors are associated with WPT initiation, progression, and continued use among young people. For example, lower addictive and harm perception compared to cigarettes (Arshad et al., 2019; Heinz et al., 2013; Maziak, 2015; Neergaard et al., 2007; Noonan & Patrick, 2013), socialization (Braun et al., 2012; Smith-Simone et al., 2008), appealing flavors (Villanti et al., 2017) WPT use by peer or family member (Baheiraei et al., 2015) other substances use (e.g., alcohol, marijuana, and other tobacco products) (Abudayyeh et al., 2018; Berg et al., 2011; Braun et al.,

2012; Fielder et al., 2012a, 2013; Jarrett et al., 2012; Palamar et al., 2014; Sterling & Mermelstein, 2011; Sutfin et al., 2011), nicotine dependence and lack of smoking restriction at home (Asfar et al., 2014; Shtaiwi et al., 2021; Soneji et al., 2021). Most of the previous studies, however, are limited due to small sample, cross-sectional study design, short-term follow-up, and lack of an appropriate theoretical framework to guide them (Asfar et al., 2005; Fielder et al., 2012a, 2012b, 2013; Islam & Johnson, 2003; Kassim et al., 2013; Leventhal et al., 2015; McKelvey et al., 2014; Primack et al., 2009, 2010, 2015; Rice et al., 2003, 2006; Shepardson & Hustad, 2016; Sidani et al., 2017; Villanti et al., 2015). Adequate understanding of the magnitude and factors behind WPT smoking initiation, progression, and continued use based on national-level longitudinal data would help to identify salient WPT smoking patterns and their predictors and guide the development of targeted interventions and policies to limit their spread among young people in the US.

One of the major factors attributable to the spread of WPT among young people is the misperception that it is less addictive and harmful compared to cigarettes (Arshad et al., 2019; Heinz et al., 2013; Maziak, 2015). Pictorial health warning label (PHWL), a globally used risk communication strategy for tobacco products, has been found effective in delivering information about the risks associated with WPT smoking as well as reducing its usage (Hammond, 2011; Institute for Global Tobacco Control (2013); Maziak et al., 2019; Nakkash et al., 2018). Examining such effects among WPT smokers who are at different stages of nicotine dependence, low-frequency vs. high frequency potentially representing less dependent vs. high dependent smokers, will help to gauge the potential effect of PHWL policies on a broad range of WPT smokers that exist in society.

To address these gaps in the literature, we aimed to examine the determinants of WPT smoking trajectories (initiation, progression, and cessation) and the potential effectiveness of PHWL policies upon two different types of WPT smokers in the US. We used two sources of data that fit our study objectives: 1) the 5 waves of the PATH Study, a nationally representative longitudinal study designed to characterize and monitor tobacco use in the US over an extended time; 2) the data from the Clinical Research Laboratory for Tobacco Smoking at Florida International University collected among current WPT smokers. The three specific aims of the dissertation are:

Aim 1: Prevalence and predictors of WPT smoking initiation and progression among adolescents and young adults in waves 1-4 (2013-18) of the PATH Study.

Aim 2: Magnitude and predictors of WPT smoking cessation among young adults in five waves (2013-19) of the PATH Study.

Aim 3: The effects of pictorial health warning label on WPT (Low- and High- Frequency) smokers' experiences, toxicant exposures, and puffing behavior.

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MANUSCRIPT 1

Prevalence and Predictors of Waterpipe Smoking Initiation and Progression Among Adolescents and Young Adults in Waves 1-4 (2013-18) of the Population Assessment of Tobacco and Health (PATH) Study

Abstract

Background: Waterpipe tobacco (WPT) smoking has increased among the young population in the United States (US). This study assessed the extent and predictors of WPT smoking initiation and progression among US adolescents (12-17 years) and young adults (18-24 years) longitudinally.

Methods: We analyzed data from 4 waves (2013-2018) of the Population Assessment of Tobacco and Health (PATH) study comprising 10,692 respondents (adolescents=5,428 and young adults=5,264). Kaplan-Meier survival method estimated probabilities of WPT initiation and progression. Cox proportional hazards regression models delineated predictors of the outcomes.

Results: Between 2013 to 2018, 4.8% of adolescents initiated and 10.6% progressed WPT smoking. Among young adults, 18.5% initiated and 14.1% progressed WPT smoking during the same time interval. Predictors among adolescents included, WPT initiation: Hispanic ethnicity (adjusted odds ratio (aHR)=1.75, 95% confidence interval (CI)=1.23-2.49), lower harm perception (aHR=2.89, 95% CI=2.10-3.98), and other tobacco products use (aHR=3.97, 95% CI=2.73-5.78); WPT progression: illicit drug use (aHR=4.60, 95% CI=1.99-10.67). Predictors among young adults included, WPT initiation: non-Hispanic Black (aHR=2.31, 95% CI=1.78-3.00), Hispanic (aHR=1.77, 95% CI=1.34-2.33), lower harm perception (aHR=2.77, 95% CI=2.19-3.50), and other tobacco products use (aHR=3.14, 95% CI=2.25-4.38); WPT progression: non-Hispanic Black

(aHR=1.51 95% CI=1.09-2.10), lower harm perception (aHR=1.80, 95% CI=1.41-2.30), and alcohol use (aHR=1.61, 95% CI=1.13-2.30).

Conclusions: Results indicate a high prevalence of WPT initiation and progression among adolescents and young adults over time, with minority racial/ethnic groups being at greater risk for both. WPT-specific risk communication interventions (e.g., educational campaigns and health warning labels) are warranted to limit WPT smoking among young people.

Background

More than 1 billion people around the world smoke tobacco making it the leading cause of preventable disease and death (World Health Organization, 2020). Every year, tobacco use kills over 8 million people globally (World Health Organization, 2020) including almost half a million in the United States (US) alone (Campaign for Tobacco-Free Kids, 2021). One of the contributors to this burden is waterpipe tobacco (WPT) smoking (aka hookah, shisha, and narghile) which has become popular around the world and in the US, mostly among young people (Jawad et al., 2018; Sidani et al., 2019). The US National Youth Tobacco Survey showed that the past-30-day (current) WPT smoking rate is 2.1% (estimated ~580,000) among adolescents, with increasing trends notably among middle school students (1% to 1.3%) between 2011-2020 (Gentzke et al., 2019, 2020). Additionally, as per the 2016 Population Assessment of Tobacco and Health (PATH) study data, the current WPT smoking rate is highest among young adults aged 18-24 years compared to older adults (9.2% vs. 1.2%) (Sharma et al., 2020). The popularity of WPT smoking among young people is partly attributable to the widespread misperception that WPT smoking is less harmful and addictive than smoking cigarettes, and also the availability of flavors (Arshad et al., 2019; Feirman et al., 2016; Heinz et al., 2013; Maziak, 2015). However, evidence shows that WPT smoke contains tobacco

toxicants and carcinogens known to cause lung cancer, respiratory, and cardiovascular diseases (Bhatnagar et al., 2019). Thus, the spread of WPT smoking among the US young population is likely to put an additional strain on tobacco-related morbidity and mortality.

In the US, according to the PATH study (2013-16), the past 12-month WPT initiation rate was 8.9% among adolescents (12-17 years) and 14.1% among young adults (18-24 years) (Stanton et al., 2020). Among those initiating WPT, the rate of progression to regular use between wave 1 and wave 2 was 9.9 % among adolescents and 6.4% among adults (Soneji et al.). Evidence indicates that WPT initiation among young people is associated with individual factors such as low addictive and harm perception compared to cigarettes (Arshad et al., 2019; Heinz et al., 2013; Maziak, 2015; Neergaard et al., 2013), socialization (Braun et al., 2012; Smith-Simone et al., 2008), appealing flavors (Villanti et al., 2017), and sensation seeking (Hampson et al., 2015; Ramji et al., 2015) as well as social factors (e.g., peer or family influence) (Baheiraei et al., 2015) and other substance use (e.g., alcohol, marijuana, and other tobacco products) (Abudayyeh et al., 2018; Berg et al., 2011; Braun et al., 2012; Fielder et al., 2012a, 2013; Jarrett et al., 2012; Palamar et al., 2014; Sterling & Mermelstein, 2011; Sutfin et al., 2011). Whereas, progression in WPT among this population is associated with additional factors (Haider et al., 2015; Jaber et al., 2015) such as nicotine dependence (Salameh et al., 2008) and owning a WPT smoking device (Robinson et al., 2017). Most of the available evidence, however, is based on small samples, cross-sectional data, limited span longitudinal data, or lacks an appropriate theoretical framework (Asfar et al., 2005; Fielder et al., 2012a, 2012b, 2013; Islam & Johnson, 2003; Kassim et al., 2013; Leventhal et al., 2015; McKelvey et al., 2014; Primack et al.,

2009, 2010, 2015; Rice et al., 2003, 2006; Shepardson & Hustad, 2016; Sidani et al., 2017; Villanti et al., 2015).

The PATH study offers a unique opportunity to monitor the progression of and factors influencing WPT smoking in a national US sample over an extended period. The selection of study variables in our study was guided by the Host, Agent, Vector, Environment (HAVE) conceptual model of the PATH study (Hyland et al., 2017) and a review of the literature (Abudayyeh et al., 2018; Arshad et al., 2019; Baheiraei et al., 2015; Berg et al., 2011; Braun et al., 2012; Fielder et al., 2012a, 2013; Haider et al., 2015; Hampson et al., 2015; Heinz et al., 2013; Jaber et al., 2015; Jarrett et al., 2012; Maziak, 2015; Neergaard et al., 2007; Noonan & Patrick, 2013; Palamar et al., 2014; Ramji et al., 2015; Robinson et al., 2017; Salameh et al., 2008; Smith-Simone et al., 2008; Sterling & Mermelstein, 2011; Sutfin et al., 2011; Villanti et al., 2017). According to the HAVE model, behavioral and health outcomes are influenced by the interactions between these four critical domains. *Host* factors are related to individuals who are tobacco users or at risk of becoming tobacco users and include perceptions and demographic characteristics. *Agent* factors are specific to the tobacco use method features and formulation (e.g., the unique morphology of WPT apparatus). A *vector* is a promoter or facilitator of interaction between *host*, *agent*, and *environments*. *Environmental* factors include current policies as well as social, cultural, and geographical influences. In this study, we aimed to characterize the magnitude and predictors of WPT smoking initiation and progression among US adolescents (ages 12-17) and young adults (ages 18-24) across four waves (2013-18) of the PATH study. Such characterization may aid in the development of targeted interventions and/or WPT-specific health policy changes to curb WPT smoking among young people in the US and beyond.

Methods

Data source and study design

The PATH Study is a nationally representative longitudinal study of 45,791 non-institutionalized US adolescents and adults which characterizes tobacco use and its effects on health. The study collects data through audio computer-administered self-interview (ACASI) methods in both English and Spanish. Study recruitment at Wave 1 employed a stratified address-based, area-probability sampling design that oversampled adult tobacco users, young adults (aged 18-24), and African American adults. An in-person screener was used to randomly select adolescents (aged 12-17) and adults (aged 18+) from households for participation in the study. Details on interview procedures, questionnaires, sampling, weighting, response rates, and accessing the data are described in the PATH Study Restricted-Use Files User Guide at https://doi.org/10.3886/Series606. The study was approved by the Westat Institutional Review Board. Adult respondents provided informed consent. Participants aged 12-17 years provided assent and their legal parent/guardian provided consent. A detailed description of the PATH study design and methods can be found elsewhere (United States Department of Health and Human Services, 2021).

Measures: Outcomes

i) *WPT initiation* was operationalized as never-use of WPT at wave 1 and ever-use of WPT in either wave 2, 3, or 4. At waves 2, 3, and 4, participants were asked if they had ever smoked WTP in the past year. Those who responded, “No, they had never smoked WPT, even one or two puffs” were designated as never smokers, else as ever smokers.

ii) At each wave, participants were also asked “Which of the following choices best describes your WPT smoking?” and the response options were “Every day”, “Weekly”, “Monthly”, “Every couple of months” and “About once a year”. *WPT progression* was operationalized as an increase in the frequency of WPT smoking (for the first time) at any subsequent wave (for example, change in smoking frequency from “About once a year” in wave 1 to either “Every day” or “Weekly” or “Monthly” or “Every couple of months” in wave 2).

Measures: Covariates

Covariates of interest were categorized as host factors and environmental factors. A detailed description of these covariates is as follows (variable levels used as a reference group in the regression model are underlined).

Host factors:

a) *Demographics*: included gender (male/female), sexual orientation (straight/lesbian, gay, bisexual and other), race/ethnicity (non-Hispanic White/non-Hispanic Black/Hispanic/non-Hispanic other), education (adolescents: ≤8th grade/≥9th grade, young adults: <high school/≥ some college), income (< 50,000/≥50,000), and US census region (Northeast/Midwest/South/West).

b) *Harm perception* was dichotomized (less harmful vs. same/more harmful) based on the question, “Is WPT smoking tobacco less harmful, about the same, or more harmful than smoking cigarettes?”.

c) *Sensation seeking* was assessed based on three modified items from the Brief Sensation Seeking Scale: 1) “I like to do frightening things”, 2) “I like new and exciting experiences even if I have to break the rules”, and 3) “I prefer friends who are exciting

and unpredictable". Response options for each item (4=strongly agree, 3=agree, 2=neither agree nor disagree, 1=disagree, and 0=strongly disagree) were summed to create overall (range: 0–12) and mean scores. The scale was found to be internally consistent among adolescents in the PATH Study (Cronbach's α=0.76) (Silveira et al., 2018). Sensation seeking was not measured among young adults.

d) *Overall health* was dichotomized (good vs. poor/fair) based on the response from the parents "In general, would you say [Child's first name]'s overall health is excellent, very good, good, fair, or poor?". Overall health was not measured among young adults.

e) *Mental health* was dichotomized (good vs. poor/fair) based on the question "In general, how would you rate your mental health, which includes stress, depression, and problems with emotions?". Mental health was not measured among adolescents.

f) *Grade performance* was dichotomized (D/Fs vs. ABCs) based on the question asked to parents "How would you describe how [Child's first name] has performed at school in the past 12 months? Would you say [Child's first name]'s grades are…?". Grade performance was not measured among young adults.

g) *Nicotine dependence* was quantified based on 16 tobacco dependence symptoms derived from the Wisconsin Inventory of Smoking Dependence Motives (WISDM: 11 items), Nicotine Dependence Syndrome Scale (NDSS: 4 items), Hooked on Nicotine Checklist (HONC: 3 items), and Diagnostic and Statistical Manual criteria (DSM: 1 item) assessed in the PATH Study (Strong et al., 2018). It is a validated scale for this population and the score ranged from 0 (low/no dependence) to 100 (high dependence) (Strong et al., 2018). Nicotine dependence was not measured among adolescents.

Substance use: Ever use of other substances below were dichotomized (yes vs. no) based on a “yes” response to the respective questions:

h) *Alcohol use*: “Have you ever used alcohol at all including sips of someone's drink or your own drink?”.

i) *Marijuana use*: “Have you ever used marijuana, hash, THC, grass, pot, or weed?”.

j) *Illicit drug use*: “Have you ever used any of the following substances…?”: 1) Cocaine or crack, 2) Stimulants like methamphetamine or speed, or 3) Any other drugs like heroin, inhalants, solvents, or hallucinogens.

k) *Prescription drug abuse*: “Have you ever used any of the following prescription drugs that were not prescribed for you or that you took only for the experience or feeling they caused: Painkillers, sedatives, or tranquilizers?”.

l) *Other tobacco product use*: “Have you ever used/smoked tobacco products…”: cigarettes, e-cigarettes, traditional cigars, cigarillos, filtered cigars, pipe, smokeless tobacco (loose snus, moist, snuff, dip, spit, or chewing tobacco), snus pouches, kreteks, bidis, or dissolvable tobacco. Information about kreteks, bidis, and dissolvable tobacco use was not available in the datasets after wave 2.

Environmental factors:

m) *Social norms about tobacco* were dichotomized based on the questions; young adults (positive vs. neutral/negative): “Thinking about the people who are important to you, how would you describe their opinion on using tobacco?”; adolescents (be very upset vs. no reaction/upset): “If your parents or guardians found you using tobacco, how do you think they would react? Would they…”.

n) *Passive exposure to tobacco products* was dichotomized (yes vs. no) based on questions asking “Does anyone who lives with you now smoke/use any of the following...”: cigarettes, smokeless tobacco (such as chewing tobacco, snuff, dip, or snus), cigars, cigarillos, or filtered cigars or any other form of tobacco.

Data analysis

Data analyses were conducted in five steps. First, we created four datasets [adolescents: initiation (n=5,192) and progression (n=236); young adults: initiation (n=2,635) and progression (n=2,629)] based on never (initiation) and current frequency of WTP smoking (progression) as shown in Supplementary Figure 1. Second, a programming statement method was used to incorporate time-dependent variables (all the variables presented in Table 1 and 2 except gender, sexual orientation, race, and US census region) measured from waves 1-4 in the regression analyses (Powell & Bagnell, 2012). The programming statement method generated only one record for each individual which corresponded to the time point when initiation/progression occurred (Allison, 2010). Third, descriptive statistics for the baseline characteristics of the study sample were reported as frequency and percentages. The percentages were weighted using all-waves weight and replicate weights for the wave 1 cohort to represent the US adolescent and young adult population. Fourth, Kaplan-Meier (product-limit) survival estimates were used to estimate the hazard probabilities of WPT smoking initiation and progression. Fifth, the Cox proportional hazards regression models were used to evaluate the hazard ratios of WPT smoking initiation and progression (Powell & Bagnell, 2012). The procedure PROC SURVEYPHREG was used for analyses in SAS (Statistical Analysis System Institute, Cary, NC, USA, version 9.4). All-waves weight and replicate weights for the wave 1 cohort were applied to compensate for variable probabilities of

selection, differential non-response rates, and possible deficiencies in the sampling frame (e.g., under coverage of certain population groups). Unadjusted and adjusted hazard ratios (aHRs) with 95% confidence intervals (CI) were reported. Results with a p-value <0.05 were considered statistically significant.

Multiple imputations by chained equations (30 imputations) were applied for missing data in the independent variables. Sensitivity analyses were performed by refitting the Cox regression models using the full dataset to test if the missing-at-random (MAR) assumption had been violated across multiple imputations.

Results

Baseline characteristics

Among adolescents, more than half (51.4%) of the never WPT smoking participants and less than half (48.1%) of the ever WPT smoking participants were males and the rest were females. Whereas the gender distribution of never and ever WPT smoking participants among young adults was in opposite direction to adolescents. More than half (52.6%) of the never WPT smoking participants and less than half (46.0%) of the ever WPT smoking participants were females and the rest were males. The higher proportion of both adolescent (Table 1) and young adult (Table 2) WPT initiators and progressors were other than non-Hispanic Whites ethnic groups.

Estimates of WPT smoking initiation and progression

Among adolescents, 4.8% of the never-smokers (4.6% of males vs. 5.3% of females) initiated WPT use between waves 1-4, and 10.6% of the ever-smokers (12.1% of males vs. 9.5% of females) progressed in WPT use during the same period. Among young adults, 18.5% of the never-smokers (17.2% of males vs. 14.8% of females)

initiated WPT use and 14.1% of the ever-smokers (14.0% of males vs. 13.3% of females) progressed in WPT use between waves 1-4.

Predictors of WPT initiation and progression

Adolescents: Adjusted models indicated that factors that increased the likelihood of WPT initiation among adolescents (Table 3), included Hispanic ethnicity (adjusted odds ratio (aHR)= 1.75, 95% confidence interval (CI)=1.23-2.49), Northeast region (aHR=1.59, 95% CI=1.05-2.41), lower harm perception (aHR=2.89, 95% CI=2.10-3.98), sensation seeking (aHR=1.12, 95% CI=1.07-1.17), alcohol use (aHR=1.46, 95% CI=1.07-1.98), illicit drug use (aHR=1.88, 95% CI=1.11-3.17), prescription drug abuse (aHR=2.11, 95% CI=1.53-2.90), other tobacco product use (aHR=3.97, 95% CI=2.73-5.78), and passive exposure to tobacco products (aHR=1.45, 95% CI=1.07-1.96). Progression in WPT smoking among adolescents was increased only by illicit drug use (aHR=4.60, 95% CI=1.99-10.67).

Young adults: Adjusted models indicated that predictors of WPT initiation among young adults (Table 4), included non-Hispanic Black ethnicity (aHR=2.31, 95% CI=1.78-3.00) and Hispanic ethnicity (aHR=1.77, 95% CI=1.34-2.33), lower harm perception (aHR=2.77, 95% CI=2.19-3.50), alcohol use (aHR=1.57, 95% CI=1.21-2.03), marijuana use (aHR=1.64, 95% CI=1.16-2.30), other tobacco product use (aHR=3.14, 95% CI=2.25-4.38), and passive exposure to tobacco products (aHR=1.40, 95% CI=1.09-1.79). Progression in WPT smoking among young adults was higher for non-Hispanic Black ethnicity (aHR=1.51, 95% CI=1.09-2.10), lower harm perception (aHR=1.80, 95% CI=1.41-2.30), alcohol use (aHR=1.61, 95% CI=1.13-2.30), and passive exposure to tobacco products (aHR=1.42, 95% CI=1.05-1.93).

Discussion

This is the first national longitudinal study to examine the magnitude and predictors of WPT initiation and progression among adolescents and young adults using four-time points. The key findings indicate that among adolescents, 4.8% initiated and 10.6% progressed in WPT smoking between 2013 and 2018. Among young adults, 18.5% initiated and 14.1% progressed in WPT smoking during the same time interval. Hispanic ethnicity, lower harm perception compared to cigarettes, use of other tobacco products, and alcohol were strong predictors of WPT initiation among both adolescents and young adults. Progression in WPT use among adolescents was predicted only by illicit drug use whereas, among young adults, predictors of progression included being non-Hispanic Black, lower harm perception compared to cigarettes, alcohol use, and passive exposure to tobacco products. These outcomes highlight a substantial rate of WPT initiation and progression among adolescents and young adults in the US. Addressing at-risk groups (e.g., Hispanics and non-Hispanic Blacks) and the identified modifiable determinants (e.g., lower harm perception, use of other tobacco products, alcohol, and passive exposure to tobacco products) may facilitate reduction of WPT initiation and progression and, in turn, tobacco-related morbidity and mortality.

The past 12-month rate of WPT initiation among young adults was higher than the rate of cigarette initiation [18.5% (wave 1-4) vs. 10.3% (wave 1-3)]. More concerning is that the past 12-month progression of WPT smoking among young adults appears to be accelerating, based on a comparison of rates in the same population for waves 1-4 (14.1%) compared to waves 1-2 (6.4%) (Soneji et al.). Such high rates of WPT initiation and progression among young adults are likely to be detrimental to tobacco control and public health as WPT smoke contains a number of tobacco toxicants and carcinogens

known to cause lung cancer, respiratory and cardiovascular diseases (Bhatnagar et al., 2019). Additionally, WPT smoking can lead to nicotine dependence (Aboaziza & Eissenberg, 2015), potentially serve as a gateway to cigarettes and electronic cigarettes (Al et al., 2019; Case et al., 2018), and may hinder smoking cessation among cigarette smokers (Rastam et al., 2011).

Among both adolescents and young adults, ethnic minorities such as Hispanics and non-Hispanic Blacks in our study were about two times more likely to initiate and progress WPT use compared to non-Hispanic Whites. Several explanations could account for these disparities, including the targeting of minorities by WPT companies and the use of appealing flavors (e.g., menthol, candy, fruit, or other sweets). Historically, tobacco companies have targeted marketing campaigns at ethnic minority populations (Iglesias-Rios & Parascandola, 2013; Yerger et al., 2007). Ethnic minorities are more likely to engage in tobacco product-related information (e.g., reading articles, watching videos, signing up to receive e-mails, and following social media) compared to non-Hispanic White peers (Soneji et al., 2019). In addition to promotion and marketing, flavors seem to be more appealing to ethnic minority populations. For example, the National Adult Tobacco Survey (2013-2014) showed that a greater proportion of non-Hispanic Blacks and Hispanics smoke flavored WPT tobacco compared to non-Hispanic Whites (90% vs. 80%) (Bonhomme et al., 2016). Reasons why tobacco flavors may be more appealing among ethnic minorities remain to be explored by future studies.

We found that youths indicating lower harm perception of WPT relative to cigarette smoking were more likely to initiate (3 times) and progress (2 times) WPT use. Some reasons behind this may include, 1) misperception that water in the WPT bowl “filters” out toxic chemicals present in the smoke (Akl et al., 2013), and 2) belief that

intermittent or occasional use of WPT is safe (Griffiths et al., 2011). Despite such misperceptions, WPT smoke is known to contain a number of toxicants and carcinogens (Bhatnagar et al., 2019; Jawad et al., 2019). Interventions promoting awareness of the harmful effects associated with WPT smoking (e.g., public education campaigns, health warning labels) should be of high priority. Evidence shows that counseling and educational support sessions by medical professionals as well as mass media campaigns through television, radio, and newspaper have been successful in educating people about the harms of smoking, changing smoking-related attitudes and beliefs, increasing intentions to quit, and decreasing smoking (Kader et al., 2019; Sadeghi R, 2020). Also, the use of social media (Facebook, Twitter, and YouTube) campaigns seems promising in delivering information about the dangers of WPT smoking as they can reach out to a large number of audiences in a short period of time (Jawad et al., 2015). Additionally, health warnings labels, especially pictorial warning labels, have been found effective in delivering information about the harmful effects of WPT smoking and motivating smokers to quit (Maziak et al., 2019; Nakkash et al., 2018). Specifically, health warning labels on the WPT device provide extended exposure to the warning due to prolonged use session (averaging an hour) and thus offers a promising avenue to address health beliefs in WPT smokers (Maziak et al., 2019; Salloum et al., 20160.

The use of substances (i.e., marijuana, other tobacco products, alcohol, and illicit drugs) increased the likelihood of initiating WPT smoking by ~4 times and progression by ~5 times among youth. This association may be related to the unique characteristics of WPT smoking. For example, cigarette smokers might become attracted to WPT smoking because of the flavored tobacco, less irritating smoke, or the social acceptance of smoking indoors unlike cigarette smoking which is typically prohibited indoors (Maziak, 2011). Additionally, some individuals may have an underlying propensity (e.g.,

sensation seeking) to generally engage in tobacco use (Vanyukov et al., 2012). Our findings indicate that future interventions to control WPT smoking should incorporate poly tobacco, alcohol, and marijuana use that appears to be relatively common among young WPT smokers (Heinz et al., 2013).

In our study, passive exposure to tobacco products such as tobacco use by someone living with predicted WPT initiation among adolescents and both initiation and progression among young adults. One reason for such influence might be related to the socializing aspect of WPT smoking. A single smoking session may last up to an hour, providing enough time to learn about WPT smoking from peers or a family member through direct observation (Maziak, 2011; Sharma et al., 2013; Smith-Simone et al., 2008). Additionally, family members might own a WPT device which may increase access and the likelihood of experimentation (Griffiths et al., 2011; Jamil et al., 2011; Smith-Simone et al., 2008). Adding to this concern, WPT home delivery is burgeoning in the US and beyond which puts youths at risk of initiation and progression due to the lack of WTP-specific regulations (Kalan et al., 2021). These observations suggest that future interventions such as educational campaigns should provide information on how to handle peer pressure and social influences. Especially, the interventions should focus on increasing self-efficacy to resist pro-drug social influences (Ellickson & Hays, 1990).

Additionally, expanding restrictions in shipping WPT and accessories at home like in cigarettes, and other tobacco products might make WPT less accessible to young people (Prevent All Cigarette Trafficking Act, 2010).

Our study has some limitations. First, the information on WPT smoking characteristics was self-reported, so it is likely to be self-reported bias. However, previous studies have demonstrated robust relationships between self-reported tobacco

smoking behavior and biomarkers of tobacco exposure among young people (Brener et al., 2003). Second, the assessment of passive exposure to tobacco products in the study did not differentiate the use of tobacco products by peers or family members. Third, some of the important variables related to WPT smoking such as flavor and preferred location of WPT smoking (e.g., hookah café) were not included in the study due to high missingness (>60%) across waves. Nonetheless, the study has sufficient relevant variables guided by the HAVE model and the literature review. Lastly, the use of weighted longitudinal analyses over the four waves excluded participants with missing information at any of the waves. However, this does not affect our analytical findings as the weights adequately compensate for differential nonresponse rates as well as variable probabilities of selection and deficiencies in the sampling frame.

Despite these limitations, our study has major strengths. The PATH study data is nationally representative so, the results are generalizable to the youth population of the US. Additionally, this is the first study, to our knowledge, examining the scope and predictors of WPT initiation and progression among young people in the US using a national-level longitudinal study.

Conclusions

The results show high rates of WPT initiation and progression among adolescents and young adults in the US. Hispanic and non-Hispanic Black ethnic groups are the at-risk groups for WPT initiation and progression. Lower harm perception relative to cigarettes, passive exposure to tobacco products, and other substance use strongly predicted WPT initiation and progression.

Implication for interventions and policies

The HAVE model assumes that behavioral outcomes such as WPT initiation and progression are influenced by the interactions between *host, agent, vector*, and *environmental* factors (Hyland et al., 2017). The model provides a framework to understand how different factors relate to each other to impact WPT initiation and progression and does not indicate a causal chain of events (Asfar et al., 2020). In the study, we have identified *host* and *environmental* factors predicting WPT smoking outcomes that can inform future interventions and policies to limit WPT spread. The *host* factor, lower harm perception of WPT relative to cigarettes, implies that awareness interventions about the harmful effects of WPT smoking (e.g., counseling, educational support, and mass media campaigns) and policy changes such as health warning labels could affect smoking behavior. The *environmental* factor, passive exposure to tobacco products, implies that future interventions should focus on promoting self-efficacy to resist prodrug social influence among young people. Additionally, intervening on an *agent* factor i.e., implementing restrictions in shipping WPT and accessories at home might play a significant role in limiting access to WPT.

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Table 1. Baseline characteristics of adolescents according to their smoking status.				
Variables	WPT Initiation		WPT Progression	
	Total, N (weighted %)	Initiators, n (weighted %)	Total, N (weighted %)	Progressors, n (weighted %)
Gender				
Male	2672 (51.4)	117 (4.6)	109 (48.1)	13 (12.1)
Female	2520 (48.6)	130 (5.3)	127 (51.9)	12 (9.5)
Race/ethnicity				
NH-White	2458 (54.2)	106 (4.5)		
NH-Black	732 (14.0)	26 (4.1)		
Hispanic	1527 (22.5)	95 (7.1)		
NH-other	475 (9.2)	20 (3.3)		
White alone			153 (65.4)	16 (10.1)
Other			83 (34.6)	9 (12.0)
Geographical region				
Northeast	684 (16.2)	56 (8.3)	NA	
Midwest	1163 (21.9)	56 (4.6)		
South	1961 (38.2)	63 (3.4)		
West	1384 (23.8)	72 (5.5)		
Education[#]				
≤8th grade	123 (2.2)	37 (30.6)	10 (3.7)	1 (0.3)
≥9th grade	5058 (97.8)	210 (4.4)	225 (96.3)	24 (10.5)
Alcohol use[#]				
Yes	1690 (34.0)	141 (8.5)	106 (45.0)	14 (11.5)
No	3485 (66.0)	102 (3.0)	127 (55.0)	10 (9.7)
Marijuana use[#]				
Yes	390 (8.7)	40 (10.2)	22 (15.0)	1 (3.8)
No	4254 (91.3)	105 (2.5)	116 (85.0)	8 (6.8)
Illicit drug use[#]				
Yes	104 (2.1)	27 (27.1)	27 (11.5)	9 (32.3)
No	5059 (97.9)	219 (4.5)	209 (88.5)	16 (8.0)
Prescription drug use[#]				
Yes	514 (9.9)	61 (1.3)	53 (22.4)	7 (11.7)
No	4661 (90.1)	185 (3.6)	182 (77.6)	18 (10.5)
Other tobacco product use[#]				
Yes	1503 (31.8)	183 (12.5)	NA	
No	3344 (68.2)	57 (1.7)		

Abbreviations: WPT-Waterpipe tobacco; NH-non-Hispanic; NA-Not available.

Note: Due to a small sample size of adolescents (WPT progression), ethnicity was divided into “White alone” and “Other”. Geographical region and other tobacco product use were not available. Baseline characteristics for time-changing variables (#sign) represent their measurement at event-time (WPT initiation/progression).

Table 2. Baseline characteristics of young adults according to their smoking status.				
Variables	WPT Initiation		WPT Progression	
	Total, N (weighted %)	Initiators, n (weighted %)	Total, N (weighted %)	Progressors, n (weighted %)
Gender				
Male	1182 (47.4)	231 (17.2)	1329 (54.0)	194 (14.0)
Female	1453 (52.6)	257 (14.8)	1300 (46.0)	176 (13.3)
Sexual orientation				
LGBO	247 (7.4)	67 (22.5)	356 (11.9)	52 (13.4)
Straight	2354 (92.6)	419 (15.6)	2254 (88.1)	315 (13.7)
Race/ethnicity				
NH-White	1240 (52.3)	166 (12.2)	1214 (51.7)	152 (12.4)
NH-Black	534 (15.6)	142 (24.2)	460 (14.1)	80 (16.8)
Hispanic	617 (20.1)	126 (19.4)	687 (22.5)	100 (14.7)
NH-other	244 (12.0)	54 (15.8)	268 (11.6)	38 (13.7)
Geographical region				
Northeast	362 (16.9)	76 (18.1)	391 (18.4)	57 (14.2)
Midwest	594 (20.4)	97 (12.5)	578 (18.9)	89 (14.7)
South	1142 (40.9)	213 (16.3)	935 (35.4)	124 (13.2)
West	537 (21.9)	102 (16.9)	725 (27.2)	100 (13.2)
Education[#]				
< high school	1135 (34.5)	229 (17.9)	906 (29.6)	123 (13.8)
≥ some college	1497 (65.5)	258 (14.9)	1715 (70.4)	247 (13.7)
Income[#]				
< 50,000	1799 (66.9)	357 (16.9)	1789 (66.7)	273 (14.8)
≥50,000	683 (33.1)	105 (14.2)	713 (33.3)	83 (11.8)
Alcohol use[#]				
Yes	1684 (66.1)	357 (18.8)	208 (80.1)	307 (14.6)
No	943 (33.9)	129 (10.3)	560 (19.9)	60 (9.3)
Marijuana use[#]				
Yes	219 (8.7)	60 (26.9)	344 (22.0)	43 (10.9)
No	2004 (91.3)	242 (10.7)	1236 (78.0)	131 (10.6)
Illicit drug use[#]				
Yes	63 (1.9)	24 (37.1)	301 (12.1)	42 (13.4)
No	2569 (98.1)	464 (15.6)	2327 (87.9)	328 (13.7)
Prescription drug use[#]				
Yes	199 (7.3)	53 (23.3)	375 (14.1)	63 (15.5)
No	2432 (92.7)	434 (15.4)	2253 (85.9)	307 (13.4)
Other tobacco product use[#]				
Yes	1682 (53.7)	419 (24.2)	2474 (93.5)	348 (13.8)
No	931 (46.3)	67 (6.7)	142 (6.5)	20 (12.3)

Abbreviations: WPT-Waterpipe tobacco; LGBO- Lesbian, Gay, Bisexual, and other; NH-non-Hispanic.

Baseline characteristics for time-changing variables ([#]sign) represent their measurement at event-time (WPT initiation/progression).

Table 3. Unadjusted and adjusted hazard ratios (HR) of WPT initiation and progression among adolescents.				
Variables	WPT Initiation		WPT Progression	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Host factors				
Gender (Ref=Male)				
Female	1.14 (0.88-1.46)	1.02 (0.79-1.33)	0.68 (0.30-1.54)	0.55 (0.25-1.20)
Race/ethnicity				
NH-White	Ref	Ref		
NH-Black	0.90 (0.59-1.39)	1.18 (0.73-1.90)		
Hispanic	**1.60 (1.16-2.20)**	**1.75 (1.23-2.49)**		
NH-other	0.73 (0.43-1.25)	0.79 (0.45-1.39)		
White alone			Ref	Ref
Other			1.17 (0.47-2.90)	1.37 (0.47-3.97)
Geographical region (Ref=West)				
Northeast	**1.53 (1.02-2.30)**	**1.59 (1.05-2.41)**	NA	
Midwest	0.84 (0.59-1.20)	0.91 (0.64-1.29)		
South	**0.61 (0.41-0.93)**	0.65 (0.42-1.01)		
Education (Ref=≥9th grade)				
≤8th grade	**9.10 (5.91-14.01)**	**12.13 (7.63-19.28)**	0.34 (0.02-5.20)	0.59 (0.04-8.55)
Harm perception (Ref= Same/more harmful)				
Less harmful	**3.60 (2.71-4.78)**	**2.89 (2.10-3.98)**	1.02 (0.31-3.35)	1.07 (0.31-3.72)
Sensation seeking	**1.22 (1.17-1.27)**	**1.12 (1.07-1.17)**	NA	
Grade performance (Ref= ABC's)				
D/F's	**2.26 (1.43-3.57)**	1.17 (0.66-2.10)	0.33 (0.02-5.55)	0.35 (0.02-5.96)
Overall health (Ref= Poor/fair)				
Good	0.86 (0.38-1.94)	0.98 (0.45-2.16)	1.20 (0.08-18.78)	0.55 (0.03-11.03)
Substance use (Ref=No)				
Alcohol use	**2.87 (2.22-3.72)**	**1.46 (1.07-1.98)**	1.09 (0.41-2.85)	1.31 (0.32-5.30)
Marijuana use	**3.67 (2.56-5.26)**	1.12 (0.74-1.69)	1.06 (0.28-4.08)	0.79 (0.16-3.82)
Illicit drug use	**7.03 (4.36-11.33)**	**1.88 (1.11-3.17)**	**3.87 (1.71-8.77)**	**4.60 (1.99-10.67)**
Prescription drug abuse	**3.59 (2.62-4.94)**	**2.11 (1.53-2.90)**	1.04 (0.39-2.84)	0.52 (0.20-1.35)
Other tobacco product use	**7.26 (5.25-10.07)**	**3.97 (2.73-5.78)**	NA	
Environmental factors				
Social norms about tobacco (Ref= No reaction/upset)				
Be very upset	**0.35 (0.25-0.48)**	**0.64 (0.46-0.89)**	**0.35 (0.15-0.83)**	0.40 (0.15-1.08)
Passive exposure to tobacco products (Ref=No)				
Yes	**2.37 (1.79-3.14)**	**1.45 (1.07-1.96)**	0.92 (0.35-2.41)	0.92 (0.28-2.98)

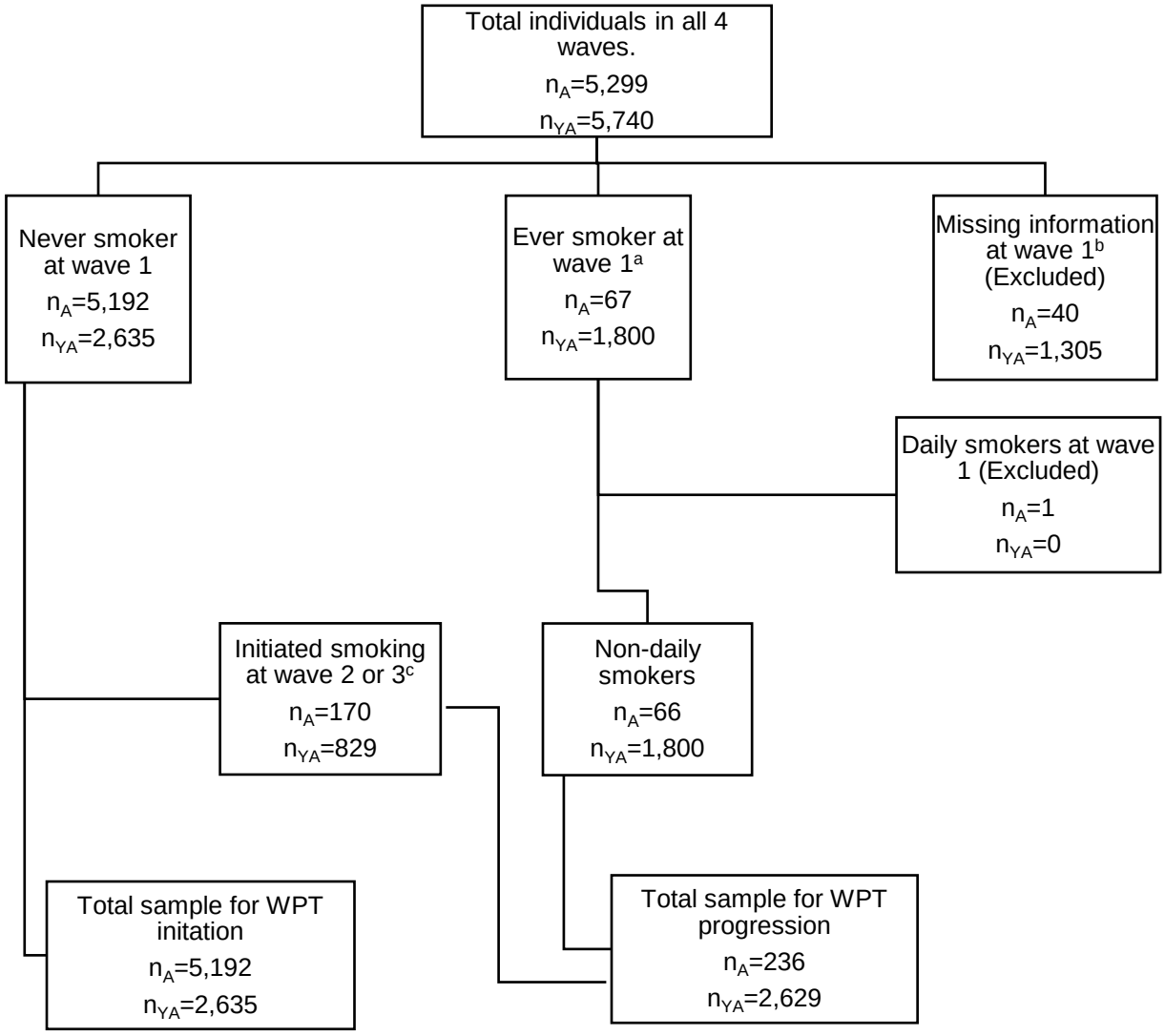
Abbreviations: WPT-Waterpipe tobacco; NH-non-Hispanic; Ref= reference; NA-Not applicable.

Bold values indicate statistical significance at p-value <0.05. Note: Due to a small sample size of adolescents (WPT progression), ethnicity was divided into "White alone" and "Other", and the geographical region was not available.

Table 4. Unadjusted and adjusted hazard ratios of WPT initiation and progression among young adults.				
Variables	WPT initiation		WPT Progression	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Host factors				
Gender (Ref=Male)				
Female	0.85 (0.68-1.06)	0.92 (0.73-1.16)	0.91 (0.71-1.17)	0.89 (0.70-1.14)
Sexual orientation (Ref=Straight)				
LGBO	**1.50 (1.03-2.18)**	1.04 (0.87-2.29)	0.93 (0.69-1.26)	0.89 (0.65-1.22)
Race/ethnicity (Ref=NH-White)				
NH-Black	**2.14 (1.65-2.77)**	**2.31 (1.78-3.00)**	**1.51 (1.12-2.03)**	**1.51 (1.09-2.10)**
Hispanic	**1.67 (1.25-2.23)**	**1.77 (1.34-2.33)**	1.28 (0.95-1.72)	**1.37 (1.00-1.87)**
NH-other	1.34 (0.80-2.23)	1.41 (0.87-2.29)	1.11 (0.68-1.82)	1.23 (0.76-1.98)
Geographical region (Ref=West)				
Northeast	1.08 (0.66-1.76)	1.03 (0.66-1.61)	1.00 (0.68-1.49)	1.15 (0.77-1.71)
Midwest	0.72 (0.46-1.12)	0.69 (0.47-1.03)	1.14 (0.83-1.57)	1.23 (0.88-1.71)
South	0.94 (0.62-1.43)	0.84 (0.60-1.17)	1.02 (0.73-1.43)	1.05 (0.74-1.49)
Education (Ref= ≥ some college)				
< high school	1.25 (0.99-1.58)	1.12 (0.88-1.42)	1.12 (0.86-1.46)	1.13 (0.87-1.46)
Income (Ref= ≥ 50,000)				
< 50,000	1.21 (0.94-1.55)	1.14 (0.88-1.48)	1.32 (0.97-1.79)	1.32 (0.95-1.84)
Harm perception (Ref=Same/more harmful)				
Less harmful	**2.69 (2.11-3.43)**	**2.77 (2.19-3.50)**	**1.74 (1.37-2.21)**	**1.80 (1.41-2.30)**
Mental health (Ref=Poor/fair)				
Good	**0.70 (0.55-0.90)**	0.94 (0.73-1.21)	1.26 (0.90-1.76)	1.33 (0.94-1.87)
Nicotine dependence	NA		1.00 (0.99-1.00)	1.00 (0.99-1.00)
Substance use (Ref=No)				
Alcohol use	**1.89 (1.45-2.47)**	**1.57 (1.21-2.03)**	1.43 (1.00-2.06)	**1.61 (1.13-2.30)**
Marijuana use	**2.48 (1.85-3.32)**	**1.64 (1.16-2.30)**	0.98 (0.71-1.37)	1.02 (0.71-1.45)
Illicit drug use	**2.62 (1.62-4.24)**	1.20 (0.67-2.17)	0.90 (0.60-1.34)	0.92 (0.57-1.47)
Prescription drug abuse	**1.57 (1.13-2.19)**	1.14 (0.85-1.54)	1.15 (0.82-1.62)	1.17 (0.80-1.70)
Other tobacco product use	**3.98 (2.83-5.60)**	**3.14 (2.25-4.38)**	0.86 (0.46-1.62)	0.84 (0.44-1.57)
Environmental factors				
Social norms about tobacco (Ref=Neutral/negative)				
Positive	1.24 (0.87-1.77)	1.00 (0.72-1.38)	1.22 (0.78-1.90)	1.15 (0.74-1.78)
Passive exposure to tobacco products (Ref=No)				
Yes	**1.80 (1.40-2.30)**	**1.40 (1.09-1.79)**	**1.38 (1.04-1.83)**	**1.42 (1.05-1.93)**

Abbreviations: WPT-Waterpipe tobacco; LGBO-Lesbian, Gay, Bisexual and Other; NH=Non-Hispanic; Ref= reference; NA-Not applicable.

Bold values indicate statistical significance at p-value <0.05. Note: Nicotine dependence among adolescents was not measured due to the lack of a validated scale suitable for this population.



Supplementary Figure 1: Flowchart showing participant selection from the PATH study to examine the predictors of WPT smoking initiation and progression.

Abbreviations: n_A-number of adolescents; n_{YA}-number of young adults.

Note: a-includes ever smokers who reported current frequency of smoking (“Every day” or “Weekly”, “Monthly” or “Every couple of months” or “About once a year”).

b-includes ever smokers who did not report their current frequency of smoking.

c-includes those who initiated and reported their current frequency of smoking as well.

MANUSCRIPT 2

Magnitude and Predictors of Waterpipe Smoking Cessation Among Young Adults in the Population Assessment of Tobacco and Health (PATH) Study

Abstract

Background: The prevalence of waterpipe tobacco (WPT) smoking is high among young adults in the US. Adequate understanding of the factors predicting WPT smoking cessation among the young population is essential to tobacco control efforts. This study assessed the magnitude and predictors of WPT smoking cessation among young adults.

Methods: The population assessment of tobacco and health (PATH) study data (waves 1-5) was used for the study. A total sample of 561 young adults exclusively using WPT (past 30-days) was used for the analysis. The probability of WPT smoking cessation (no use in the past 12 months) was estimated using the Kaplan-Meier survival method, and the predictors were assessed using the Cox proportional hazards regression model.

Results: During the five waves, 25.13% of the young adult WPT smokers quit smoking. Among them, 58.2% were females and the remaining were males. The Hispanics (40.2%) had the highest rate of cessation among the ethnic groups. Regret smoking increased the likelihood (adjusted odds ratio (aHR)= 2.33, 95% confidence interval (CI)=1.29-4.21) whereas the lack of smoking restriction at home (aHR=0.35, 95% CI=0.18-0.70) and alcohol use (aHR=0.62, 95% CI=0.41-0.93) decreased the likelihood of cessation among the young adult WPT smokers.

Conclusions: Communicating the health and economic consequences associated with WPT smoking (e.g., pictorial health warning labels), involving smoker's household members in WPT awareness campaigns, and closing regulatory loopholes related to

WPT venues will increase the WPT smoking cessation rate among the young population in the US.

Introduction

More than 8 million people die of tobacco use every year globally (World Health Organization, 2020), including about half a million in the United States (US) alone (Campaign for Tobacco-Free Kids, 2021). Waterpipe tobacco (WPT) smoking (aka hookah, shisha, and narghile) is one of the tobacco products contributing to this burden World Health Organization, 2020). Over the past decade, WPT smoking was spreading around the world including the US, mostly among young people (Jawad et al., 2018; Sidani et al., 2019). According to the Population Assessment of Tobacco and Health (PATH) study (2016), the prevalence of current use (past 30-days) of WPT among young adults (18-24 years) reached 9.2% (Sharma et al., 2020). The high prevalence of WPT among young people is likely to increase tobacco-related morbidity and mortality in the US as the evidence shows that WPT smoke contains carcinogens and toxicants causing lung cancer, cardiovascular and respiratory diseases (Bhatnagar et al., 2019). Additionally, WPT smoking increases the likelihood of cigarette smoking initiation (Al et al, 2019).

Even though the prevalence of WPT smoking is high among young people, successful quitting has been low. A systematic review shows that most WPT smokers (79-98%) feel confident that they could quit smoking at any time (Akl et al., 2013). Unfortunately, studies among adolescents and adults from the Middle East show that nearly 64% of WPT smokers make unsuccessful quit attempts every year (Jaber et al., 2016; Ward et al., 2005). Several factors have been found associated with WPT cessation such as lower level of nicotine dependence, the less appealing flavor of

tobacco, past quit attempts, successful quit history for a shorter period, smoking restriction in the house, and not sharing WPT with others (Asfar et al., 2014; Shtaiwi et al., 2021; Soneji et al., 2021). A recent systematic review (2016) of interventions for WPT smoking cessation shows that most of the interventions (e.g., pharmacotherapies like bupropion and, legislative like smoke-free air laws) lack evidence of effectiveness (Jawad et al., 2016). Whereas behavioral cessation interventions are promising but limited due to the pilot nature of the studies, short-term follow-up, and mostly focused on determinants of cigarette smoking (Jawad et al., 2016; Maziak et al., 2015). Population-based knowledge about factors influencing cessation success would be valuable in informing policies to limit WPT among the young population. In this study, we aimed to determine the magnitude and predictors of WPT smoking cessation among young adults (18-24 years) using waves 1 to 5 (2013-2019) of the PATH study.

Methods

Data source and study design

The PATH Study is an ongoing nationally representative, longitudinal cohort study of 45,791 non-institutionalized US adolescents and adults in the US. The study collects self-reported information on tobacco use and its effects on health. Audio computer-administered self-interview (ACASI) methods in both English and Spanish are used to collect the information. A detailed description of the PATH study design and methods can be found elsewhere (Hyland et al., 2017). The PATH study was guided by the *Host*, *Agent*, *Vector, Environment* (HAVE) conceptual framework for data collection (Hyland et al., 2017). According to the HAVE model, an interaction between the above four domains lead to behavioral and health outcomes. *Host* factors are the variables related to individuals at risk of tobacco use. *Agent* factors are the variables related to tobacco use method features (e.g., WPT device). *Vector* is a facilitator of the interaction

between host, agent, and environments. *Environments* are the policies and social, cultural, and geographical factors. The study was approved by the Westat Institutional Review Board, whereby participants older than 18 years provided informed consent (Hyland et al., 2017).

Outcome

WPT smoking cessation was operationalized as exclusive current use (past 30-days) at wave 1 or 2 or 3 or 4 and no use (past 12-months) in the subsequent wave/s. The cessation means no current use (past 30-days) of any other tobacco products as well.

Covariates

Variables of interest in our study were selected based on literature review (Akl et al., 2013; Asfar et al., 2014; Gautam P, 2022; Jaber et al., 2016; Jawad et al., 2018; Shtaiwi et al., 2021; Sidani et al., 2019; Soneji et al., 2021; Ward et al., 2005) and the conceptual framework of the PATH study (Hyland et al., 2017). Variables were categorized into host factors, agent factors, vector factors, and environmental factors. A detailed description is presented below (underlined variable level represents the reference group in the regression model).

Host factors

a) Demographics: include gender (male/female), sexual orientation (straight/lesbian, gay, bisexual, and other), race/ethnicity (non-Hispanic White/non-Hispanic Black/Hispanic/non-Hispanic other), education (<high school/≥ some college), income (< 50,000/≥50,000), and Geographical region (Northeast/Midwest/South/West).

b) Harm perception (less harmful vs. same/more harmful) was assessed based on the question, “Is WPT tobacco smoking less harmful, about the same, or more harmful than smoking cigarettes?”

c) Socialize (yes vs. no) was assessed based on the response to the question, “Smoke / smoked WPT because: Like / liked socializing while smoking it”.

d) Regret smoking WPT (yes vs. no) was assessed based on the responses to the question, “If you had to do it over again, you would have started using WPT?”. Those who responded definitely would not or probably would not were categorized as “yes”, and probably would or definitely would were categorized as “no”.

e) Mental health (good vs. poor) was assessed based on the question, “In general, how would you rate your mental health, which includes stress, depression, and problems with emotions?”. Those who responded “excellent” or “very good” or “good” were categorized as “good”, and those who responded “fair” or “poor” were categorized as “poor”.

Substance use: Respective questions below were used to dichotomize substances use (yes vs. no):

f) Alcohol use: “Have you ever used alcohol at all including sips of someone's drink or your own drink?”.

g) Marijuana use: “Have you ever used marijuana, hash, THC, grass, pot, or weed?”.

h) Illicit drug use: “Have you ever used any of the following substances…?”: 1) Cocaine or crack, 2) Stimulants like methamphetamine or speed, or 3) Any other drugs like heroin, inhalants, solvents, or hallucinogens.

i) Prescription drug abuse: “Have you ever used any of the following prescription drugs that were not prescribed for you or that you took only for the experience or feeling they caused: Painkillers, sedatives, or tranquilizers?”.

Agent factors

j) Preferred flavor (yes vs. no) was assessed based on the question, “Smoke/smoked WPT because: It comes/came in flavors I like/liked”. It was assessed in the preceding wave of cessation outcome.

k) Nicotine dependence was measured using 16 tobacco dependence indicators derived from the Wisconsin Inventory of Smoking Dependence Motives (WISDM: 11 items), Nicotine Dependence Syndrome Scale (NDSS: 4 items), Hooked on Nicotine Checklist (HONC: 3 items), and Diagnostic and Statistical Manual criteria (DSM: 1 item) in the PATH Study (David R. Strong et al., 2017). It is a validated scale for this population and the score ranged from 0 (low/no dependence) to 100 (high dependence) (David R. Strong et al., 2017).

Vector factor

l) Smoking in café (yes vs. no) was assessed based on the response to the question, “Where do/did you usually smoke WPT: In a hookah bar or café?.”

Environmental factors

m) Social norm about tobacco (non-positive vs. positive) was assessed based on the question, “Thinking about the people who are important to you, how would you describe their opinion on using tobacco?”.

n) Passive exposure to tobacco products (yes vs. no) was assessed based on questions, “Does anyone who lives with you now smoke/use any of the following..?”: cigarettes, smokeless tobacco (such as chewing tobacco, snuff, dip, or snus), cigars, cigarillos, or filtered cigars or any other form of tobacco.

o) Advice to quit (yes vs. no) was assessed based on the question, “In the past 12 months, did any medical doctor, dentist, or other health professional advise you to stop using tobacco?”

p) Home smoking restriction (yes vs. no) at home was assessed based on the question, “For tobacco products that are burned, such as cigarettes, cigars, pipes, or hookah, which statement best describes the rules about smoking a tobacco product inside your home?”. Those who were allowed sometime or somewhere were categorized as “yes”, and those who were not allowed anywhere and at any time were categorized as “no”.

Data analysis

Data analyses were completed in the following five steps: 1) a dataset of exclusive WPT smokers (past 30-days) was created, 2) time-changing variables measured from waves 1-5 (all the variables presented in table 2 except gender, sexual orientation, race/ethnicity, geographical region, preferred flavor, and nicotine dependence) were created using a programming statement method to incorporate them in the regression analyses (Gautam et al., 2022). The programming statement method generated one record for an individual corresponding to the time point when WPT cessation occurred. 3) descriptive statistics and chi-square analysis p-values of the sample baseline characteristics were calculated, 4) hazard probability of WPT cessation was estimated by the Kaplan-Meier (product-limit) survival estimates, and 5) hazard ratios of WPT cessation were estimated by the Cox proportional hazards regression

model (Survival Analysis Using SAS, 2011). The PROC SURVEYPHREG procedure was used for the analyses in SAS (Statistical Analysis System Institute, Cary, NC, USA, version 9.4). Unadjusted and adjusted hazard ratios (aHRs) of WPT cessation with 95% confidence intervals (CI) were reported. The significance level for the results was set up at a p-value <0.05.

Missingness in the independent variables was addressed by applying multiple imputations by chained equations (30 imputations). To test if the missing-at-random (MAR) assumption had been violated across multiple imputations, sensitivity analyses were performed by refitting the Cox regression model using the full dataset.

Results

Baseline characteristics

About 58% of the young adult WPT quitters were females and the rest were males. Among ethnic groups, the highest proportion of WPT quitters were Hispanics (40.2%). Nearly 69% of the WPT quitters had some college degree or higher education. More than 60% of the WPT quitters had income less than $50,000. More details about baseline characteristics of WPT quitters are available in Table 1.

Estimates and predictors of WPT smoking cessation

Between waves 1 and 5, 25.13% of exclusive WPT smokers quit smoking. Regret smoking WPT increased the likelihood of cessation (adjusted odds ratio (aHR)= 2.33, 95% confidence interval (CI)=1.29-4.21) whereas the absence of home smoking restriction (aHR=0.35, 95% CI=0.18-0.70), and alcohol use (aHR=0.62, 95% CI=0.41-0.93) decreased the likelihood of cessation. Details about the effects of other variables on WPT cessation are available in Table 2.

Discussion

Our study is the first national longitudinal study to examine the magnitude and predictors of WPT smoking cessation among young adults in the US. We found that between 2013-2019, 25.13% of young adults quit WPT smoking. The strongest factor affecting waterpipe cessation was regretting smoking WPT, while lack of rules restricting smoking at home, and alcohol use were associated with decreased cessation among young adult WPT smokers. Implementing risk communication interventions (e.g., pictorial health warning labels), adopting measures to control the sale of alcohol in WPT smoking venues, and discouraging household smoking (e.g., smoke-free air policies) might increase the WPT cessation rate among the young population.

In the current study, smokers who regret smoking WPT were more than two times more likely to quit smoking compared to those who do not. In cigarette smokers, regretting smoking is mostly related to concerns about the serious health and economic consequences of smoking (Nayak et al., 2017; O'Connor et al., 2016). Similarly, WPT smokers are found to be worried about serious health consequences of their WPT smoking including cancer, the likelihood of addiction, and higher expenses (Kothari & Berg, 2018; Isaac et al., 2018). This highlights the importance of health communication strategies about WPT's detrimental effects on smokers and their families (Dogar et al., 2014; Lipkus et al., 2011). Pictorial health warning labels have been found to adequately deliver evidence-based risk information to tobacco users and it is a principal strategy for reducing tobacco use globally (Hammond, 2011; Institute for Global Tobacco Control, 2013). In this regard, pictorial health warnings can be a promising path to proceed with as there is evidence of their effectiveness in communicating health risks to WPT smokers and motivating cessation among them. For example, a clinical laboratory study

among WPT smokers by Maziak et al. showed that smoking WPT with pictorial health warning labels on it significantly increased harm perception and decreased positive smoking experiences (Maziak et al., 2019).

We found that the use of alcohol among WPT smokers decreased the likelihood of cessation by nearly a half. Studies show that co-use of alcohol is common among WPT smokers (Cohn et al., 2017; Heinz et al., 2013; Sutfin et al., 2011). For example, Leavens and colleagues found that alcohol use among WPT smokers was associated with enhanced smoking experience, increased urge to smoke, and exposure to a higher level of nicotine (Leavens et al., 2020). The context and setting of WPT can explain this association. It is well documented that young people, such as college students smoke the WPT in special venues (e.g. hookah lounges, hookah cafés) that also serve food and drinks and facilitate socializing around WPT (Kassem et al., 2015; Sutfin et al., 2011; Ward et al., 2007). These venues exploit current regulatory loopholes by advertising their products heavily to college-aged students through social media, as well as get exempted from clean indoor air legislation when they are designated as tobacco retail establishments rather than cafes or bars (Allem et al., 2017; Noonan, 2010).

Consistent with the findings from previous studies, WPT smokers in our study who had strict rules of not smoking at home were more likely to quit (Collins et al., 2019; Farkas et al., 1999; Haardörfer et al., 2018; Shtaiwi et al., 2021). This indicates the importance of home environment and family attitude towards smoking in young people's smoking behavior. More so, as a stationary and prolonged form of tobacco use, WPT smoking requires a dedicated space as well as an extended time to smoke inside the house compared to cigarette smoking which is a quick and easily concealed behavior. This explains the perhaps more salient role for the home environment for WPT smoking

and the importance of involving family and household members in efforts to communicate the negative consequences of this tobacco use method (Centers for Disease Control and Prevention, 2021).

Nicotine dependence did not have any effect on the WPT cessation in our study, in contrast to the findings from previous studies (Haider et al., 2015; Shtaiwi et al., 2021). The lack of effect might be due to the inability of the scale used in the PATH to capture an accurate level of nicotine dependence and predictive outcomes among WPT smokers. This assumption is supported by the findings of a recent study by Strong et. al. that examined the predictive association between biomarkers of nicotine exposure and the 16 self-reported items of tobacco dependence and smoking outcomes in the PATH study (wave 1-2) (David R Strong et al., 2021). They found, using the 16-items scale, a lower score of tobacco dependence among WPT smokers (mean=8.4) compared to cigarette smokers (mean=54.8) at wave 1 and the score did not show any predictive relationship with change in frequency as well as quitting WPT in wave 2 (David R Strong et al., 2021). Perhaps using WPT-specific nicotine dependence assessment instruments like the Syrian Center for Tobacco Studies-13 (SCTS-13) (Alam et al., 2020) in the future can clarify the role of this important factor in cessation success.

Our study has some limitations. First, due to the low response rate (~10%), we could not precisely measure the WPT smokers' intention to quit. However, based on subset analysis of the sample (n=128), where information about interest in quitting existed, a moderate correlation between regret smoking WPT and quit attempts (ρ=0.3, p-value <0.05) indicates that regretting smoking can be a proxy of interest in quitting. Second, the high missingness of the participants in one of the 5 waves limited the application of population weights in the regression analysis resulting in the lack of

generalizability of findings to the US population. However, the use of 5 waves provided an opportunity to include participants who entered later in the study resulting in increased sample size and precision of the results.

Conclusion

Our findings show that the adequate delivery of information about the impact of WPT smoking on health and finances and approaches to close loopholes in policies and regulations might help to increase WPT cessation. Specifically, developing WPT specific risk communication approach (e.g., pictorial health warning labels on the waterpipe device), closing loopholes regarding WPT venues, and involving family and household members in WPT awareness campaigns seem to be promising strategies to encourage WPT cessation. Future studies applying more WPT-specific measures of interest in quitting and nicotine dependence in WPT smokers can help elucidate further the role of these factors in waterpipe cessation success.

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Table 1. Baseline characteristics of young adult WPT smokers.			
Variables	Quitters (n=141)	Non-quitters (n=420)	
	unweighted no. (%)	unweighted no. (%)	*p*-value
Gender			
Male	59 (41.8)	150 (40.1)	0.763
Female	82 (58.2)	224 (59.9)	
Sexual orientation			
LGBO	17 (12.1)	39 (10.5)	0.635
Straight	124 (87.9)	334 (89.5)	
Race/Ethnicity			
NH-White	45 (32.9)	127 (34.5)	0.068
NH-Black	21 (15.3)	88 (23.9)	
Hispanic	55 (40.2)	108 (29.4)	
NH-Other	16 (11.7)	45 (12.2)	
Geographical region			
Northeast	14 (15.4)	70 (23.2)	**0.045**
Midwest	25 (27.5)	48 (15.6)	
South	31 (34.1)	96 (31.8)	
West	21(23.1)	88 (29.1)	
Education[*]			
< high school	44 (31.2)	70 (26.7)	0.355
≥ some college	97 (68.8)	192 (73.2)	
Income[*]			
< 50,000	82 (60.7)	167 (66.5)	0.257
≥50,000	53 (39.3)	84 (33.5)	
Alcohol use[*]			
Yes	93 (66.0)	209 (80.1)	**0.002**
No	48 (34.0)	52 (19.9)	
Regret smoking WPT[*]			
Yes	103 (88.8)	146 (60.3)	**<0.001**
No	13 (11.2)	96 (39.7)	
Home smoking restriction[*]			
Yes	129 (91.5)	82 (31.2)	**<0.001**
No	12 (8.5)	181 (68.8)	
Nicotine dependence[a]	3.24 (7.0)	5.48 (9.9)	**0.024**

Abbreviations: WPT-Waterpipe tobacco; LGBO- Lesbian, Gay, Bisexual, and other; NH-non-Hispanic.

Bold values indicate statistical significance at $p<0.05$.

Note: Baseline characteristics for time-changing variables (*Sign) represent their measurement at event-time (WPT cessation).

Table 2. Unadjusted and adjusted hazard ratios (aHRs) of WPT smoking cessation among young adults.		
Variables	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Host factors		
Gender (Female vs. Male)	1.05 (0.75-1.47)	0.89 (0.61-1.30)
Sexual orientation (LGBO vs. straight)	1.11 (0.67-1.90)	1.32 (0.73-2.38)
Race/Ethnicity (Ref=NH-White)		
NH-Black	0.70 (0.42-1.18)	0.62 (0.35-1.08)
Hispanic	1.33 (0.90-1.97)	1.28 (0.83-1.98)
NH-other	0.98 (0.56-1.75)	1.00 (0.53-1.87)
Geographical region (Ref=West)		
Northeast	0.85 (0.43-1.67)	0.83 (0.44-1.56)
Midwest	**2.01 (1.13-3.57)**	**2.11 (1.16-3.84)**
South	1.35 (0.78-2.34)	1.18 (0.70-2.01)
Education (< high school vs. ≥ Some college)	1.19 (0.83-1.69)	1.16 (0.78-1.74)
Income (< 50,000 vs. ≥ 50,000)	0.82 (0.58-1.20)	0.79 (0.53-1.18)
Harm perception (Less harmful vs. Same/more harmful)	**0.57 (0.38-0.85)**	0.74 (0.47-1.19)
Mental health (Good vs. Poor)	1.53 (0.93-2.52)	1.28 (0.71-2.29)
Socialize (Yes vs. No)	0.56 (0.28-1.13)	0.98 (0.64-1.51)
Regret smoking WPT (Yes vs. No)	**4.20 (2.31-7.40)**	**2.33 (1.24-4.36)**
Substance use (Yes vs. No)		
Alcohol use	**0.56 (0.40-0.80)**	**0.62 (0.41-0.93)**
Marijuana use	0.59 (0.33-1.04)	0.82 (0.44-1.52)
Illicit drug use	1.04 (0.46-2.34)	1.50 (0.57-3.98)
Prescription drug abuse	0.95 (0.51-1.75)	1.03 (0.51-2.07)
Agent factors		
Preferred flavor (Yes vs. No)	**0.65 (0.47-0.91)**	1.20 (0.81-1.76)
Nicotine Dependence	0.97 (0.93-1.01)	0.99 (0.96-1.03)
Vector factor		
Smoking in café (Yes vs. No)	0.53 (0.27-1.04)	0.87 (0.54-1.41)
Environmental factors		
Social norms about tobacco (Positive vs. Negative)	**0.57 (0.37-0.87)**	0.80 (0.49-1.29)
Passive exposure to tobacco products (Yes vs. No)	**0.67 (0.45-0.99)**	0.96 (0.59-1.55)
Advice to quit (Yes vs. No)	0.19 (0.03-1.38)	0.42 (0.10-1.70)
Home smoking restriction (No vs. Yes)	0.26 (0.14-0.46)	**0.35 (0.17-0.71)**

Abbreviations: WPT-Waterpipe tobacco; LGBO-Lesbian, Gay, Bisexual and Other; NH=Non-Hispanic; Ref= reference.

Bold value indicates a p-value <0.05. Unadjusted models include complete case analysis.

MANUSCRIPT 3

The Effects of Pictorial Health Warning Label on Waterpipe (Low- and High-Frequency) Smokers' Experiences, Toxicant Exposures and Puffing Behavior

Abstract

Background: Pictorial health warning label (PHWL) is an effective risk communication measure among cigarette smokers. However, there is a lack of knowledge regarding the effect of PHWL on low and high-frequency waterpipe (WP) smokers. This study examined the effects of PHWL on puffing behavior, subjective experiences, and toxicant exposures among low and high-frequency WP smokers in the United States (US).

Methods: Sixty current (past-month) WP smokers (low- frequency; n=30 and high-frequency; n=30) completed two 45-minute ad libitum WP smoking sessions in a cross-over design study (WP with no-PHWL vs WP with PHWL). We compared the mean differences of puff topography, expired carbon monoxide (eCO), plasma nicotine concentration, and subjective experiences between the two smoking groups.

Results: Mean age of low- frequency smokers was 21.5 years and high-frequency smokers was 21.3 years. Compared to high-frequency, low-frequency smokers had significant reduction in average total smoking time [mean difference (SD) =-7.6 (10.2) min vs -2.6 (6.7) min, p=0.03)] and number of puffs [mean difference (SD) =-33.37 (70.7) vs -0.70 (29.2), p=0.02] following exposure to PHWL compared to no-PHWL condition. Post-session subjective experiences were lower among high-frequency smokers compared to low-frequency smokers following smoking WP with PHWL compared to no-PHWL session (puff liking -1.2 vs. -0.5; puff satisfaction -1.0 vs. -0.3; craving reduction -0.5 vs. 1.2) ($p<0.05$ for all).

Conclusion: Our findings indicate that placing PHWL on the WP device may be a promising strategy with differential effectiveness among WP smokers; low-frequency (reduce puffing behaviors) and high-frequency (reduce smoking experience).

Introduction

Tobacco smoking remains a leading cause of morbidity and mortality worldwide (World Health Organization, 2020). A contributor to this burden is a centuries-old form of tobacco use known as waterpipe (WP; narghile, hookah) smoking (World Health Organization, 2015). According to the 2019 National Health Interview Survey, the rate of current (every day/someday) WP smoking is highest in the age group 18-24 years old (1.7% or 408,000) among US adults (Cornelius et al., 2020). One of the drivers of WP smoking popularity among young people is the misperception that WP smoking is less harmful and addictive relative to cigarette smoking (Arshad et al., 2019; Heinz et al., 2013; Maziak, 2015). This misperception, however, is at odds with accumulating evidence showing that WP smoking is associated with exposure to many toxicants and carcinogens known to cause lung cancer, respiratory and cardiovascular diseases (Bhatnagar et al., 2019).

Several systematic reviews and consensus reports have addressed the adverse health effects of WP smoking such as increased blood pressure, chronic bronchitis, emphysema, and coronary artery disease (Bhatnagar et al., 2019; Ziad et al., 2015). A systematic review and meta-analysis of 13 case-control studies show that WP smoking increases the odds of lung cancer about 5 times and esophageal cancer about 4 times (Montazeri et al., 2017). Some other health effects associated with WP smoking include metabolic syndrome, and deterioration of mental health (Waziry et al., 2016). Appropriate measures are needed to control WP smoking and tobacco-related morbidity and mortality among young people. Because of the extended WP smoking session

averaging an hour, and intensive exposure to combustion smoke during each session, adverse health events have been reported even after a single session of smoking (e.g., heart rate increased from 80.4 ±10 beats/minute to 95.6 ±17 beats/minute) (El-Zaatari et al., 2015; Hakim et al., 2011; Yalcin et al., 2017).

As with other addictive behaviors, WP smokers tend to increase use frequency and develop nicotine dependence (Bahelah et al., 2017). According to a study among Lebanese adolescents, half of the WP smokers lost autonomy over their smoking behavior within 9.7 months and developed full symptoms of nicotine dependence within 15 months of smoking onset (Ebrahimi et al., 2020). Several studies conducted among young WP smokers in the Middle East show that more frequent patterns of WP smoking reflect smokers' level of dependence on nicotine (Asfar et al., 2005; Jaber et al., 2015).

Pictorial health warning label (hereafter PHWL) communicates evidence-based risk information to tobacco users and has been a principal strategy for reducing tobacco use globally (Hammond, 2011; Institute for Global Tobacco Control, 2013). Unlike cigarettes packs where PHWL is usually placed, WP is unique in that the smoker, especially in a "hookah café" setting, is not usually exposed to the tobacco packaging (Islam et al., 2016). Due to the extended time of WP smoking session averaging an hour, the WP device provides ample contact time that can maximize the effect of PHWL (Islam et al., 2016). So far, limited studies have examined the use of PHWL among WP smokers. For example, an explorative study among adult WP smokers and non-smokers suggested that the WP device is an optimal location for placing PHWL that could potentially deter initiation and promote cessation, mostly among non-established smokers (Mostafa et al., 2019). Our team as well as others have shown that placing PHWL on the WP device might be an effective policy to educate smokers about the harmful effects of WP smoking and reducing smoking-related risk (Maziak et al., 2019;

Nakkash et al., 2018). Building on our previous work, in this study, we aim to investigate further the effects of PHWL among WP smokers at different levels of nicotine dependence. This can be achieved by looking at low vs. high-frequency WP smokers. This study is important to gauge the potential effect of PHWL policies on a broad range of WP smokers likely to exist in society.

Methods and materials

Study sample and procedures

Sixty current (past-month) WP smokers aged 18-30 years old, were recruited from the metropolitan area of Miami, Florida via flyers, word of mouth, and snowball sampling in late 2018 and early 2019. Exclusion criteria included a self-reported history of chronic health problems, psychiatric conditions, regular use of prescription medications (other than vitamins or birth control pills), and current use of >5 cigarettes or other tobacco/nicotine products in the past month preceding the study. Women were excluded if they were breastfeeding or tested positive for pregnancy (verified by urinalysis) at the time of screening. This study was approved by the Institutional Review Board of Florida International University and was conducted at the clinical research lab for tobacco smoking in the University. Participants provided informed consent for the study.

As shown in Figure 1, two different PHWLs developed by our team using an international Delphi approach were placed on WP devices (Asfar et al., 2020). The location and size of the PHWL were constant on the WP device and was placed at eye level of the participants' seat. Participants completed the first session using WP without PHWL and the second session with one of the two randomly assigned PHWLs. The study sessions were an addition to a study looking for the effect of flavor on WPT smokers (Maziak et al., 2019). Accordingly, the non-PHWL condition came always first.

The sessions were separated by a 48-hour washout period, preceded by >12 hours tobacco/nicotine abstinence and confirmed by eCO<5 ppm. Participants were instructed to smoke the same brand and their preferred flavor ad libitum for up to 45 minutes in both sessions. During each session, participants were seated in a private room with a comfortable reclining chair and were given a choice to watch movies while smoking WP. Puff topography was measured throughout the WP smoking sessions. Blood samples and eCO measurements were collected in pre and post WP smoking sessions. Subjective responses were assessed in the post-WP smoking session. Further details of the study procedures are published elsewhere (Ben Taleb et al., 2018).

Smoking groups

Among past-month WP smokers, those who reported smoking WP less than once a week in the past 6-months were categorized as low-frequency WP smokers, and those who reported smoking WP at least once a week were categorized as high-frequency WP smokers (Maziak et al., 2019).

Outcome measures

WP puff topography

Puff topography parameters included total smoking time, total puff time, puff duration, inter-puff interval (IPI), number of puffs, total volume inhaled, and average puff volume (Shihadeh et al., 2004, 2005).

Plasma nicotine and expired carbon monoxide (eCO)

Blood was drawn within 10 minutes of the beginning and end of each session. eCO was measured by Breath CO monitor (Vitalograph, Lenexa, Kansas, USA) prior to the start of the 45-minute smoking session and within 5 minutes after it ended (Jacob et al., 2000). Nicotine and eCO boosts were assessed by subtracting the respective pre-WP smoking session measurements from the post-WP smoking session measurements.

Subjective measures

The 11-item WP Evaluation Scale (WES) was used to evaluate the participants' perception of the smoked WP (e.g., satisfying, tastes good, and makes you dizzy) (Malson et al., 2002; Rose et al., 2000). Participants' sensory experience of the inhaled tobacco product (e.g., How satisfying were the puffs?) was assessed by the 9-item Duke Sensory Questionnaire (DSQ) (Pickworth et al., 2002). Harm perception was measured based on an item scale 'In your opinion, how harmful is the WP to general health?' from previous literature (Popova & Ling, 2013). The subjective measures were administered post-WP smoking session and the responses were on a 7-point Likert scale, ranging from 1 ("not at all") to 7 ("extremely").

Data analysis

Baseline descriptive statistics of the participants were summarized as means (M) and standard deviations (SDs) or proportions. The generalized linear mixed model was used to examine the effects of placing PHWL on the puffing parameters among the smoking groups. Interaction between the smoking group and the condition of smoking (PHWL vs. the no-PHWL) for each puffing parameter was examined. Planned comparisons using Student's t-test to examine mean differences in puffing parameters, eCO, plasma nicotine, and subjective measures such as WES, DSQ, and harm perception between smoking conditions (PHWL vs. no-PHWL) among the smoking groups (Keppel G. Design and Analysis, 1991). The level of significance was set at $p < 0.05$. All the analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

Results

A total of 60 participants were equally distributed as low-frequency (n=30) and high-frequency (n=30) smokers. Sixty percent of the low-frequency smokers (n=18) and 70% of high-frequency smokers (n=21) were male and the remaining were female. The

mean age were 21.5 (SD=2.8) years for low-frequency smokers and 21.3 (SD=2.2) years for high-frequency smokers. The majority (≥50%) of the low- and high-frequency smokers were Whites. Detailed information on descriptive characteristics of the sample by the smoking group is available in Supplementary Table 1.

WP puff topography

A significant smoking group by condition interaction was observed for total smoking time [F (1,58) =5.09, p=0.03] and the number of puffs [F (1,58) =5.47, p=0.02] meaning that changes in total smoking time and the number of puffs across smoking groups were dependent upon the PHWL. Compared to high-frequency smokers, low-frequency smokers had significant reduction in average total smoking time [mean difference (SD) =-7.6 (10.2) min vs -2.6 (6.7) min, p=0.03)] and number of puffs [mean difference (SD) =-33.37 (70.7) vs -0.70 (29.2), p=0.02] following exposure to PHWL compared to no-PHWL condition (Table 1).

Plasma nicotine and eCO

Plasma nicotine and eCO boost did not differ significantly between low- and high-frequency WP smokers following exposure to PHWL vs. the no-PHWL condition (Table 1).

Subjective measures

Figure 2 shows a difference in WES (A) and DSQ (B) scores between the two study conditions by smoking groups. WES scores: compared to low-frequency WP smokers, a greater decrease in satisfaction (-1.2 vs. -0.5) and craving reduction (-0.5 vs. 1.2) was reported by high-frequency WP smokers after smoking WP with PHWL compared to no-PHWL (p values <0.05). DSQ scores: compared with low-frequency WP smokers, high-frequency WP smokers reported a greater reduction in scores for puff liking (-1.2 vs. -0.5), puff satisfaction (-1.0 vs. -0.3), and strengths of puffs on the tongue

(-0.4 vs. 0.4) following smoking the WP with PHWL compared to no-PHWL (p values <0.05). Perceived harm towards WP smoking did not change significantly between both smoking groups after smoking WP with and without PHWL (p values >0.05).

Discussion

In this study, we compared the effects of PHWL on WP smokers' puffing behavior, subjective experiences, and toxicant exposures at different levels of nicotine dependence of WP smoking. This knowledge is important to predict the effect of PHWLs policies on a wide range of WP smokers in real life. The results show that following smoking the WP with PHWL (vs. no-PHWL) there was a significantly higher reduction in product satisfaction and liking among high-frequency WP smokers compared to low-frequency WP smokers. In contrast, low-frequency WP smokers had a shorter smoking time and number of puffs during the PHWL compared to high-frequency WP smokers. These findings indicate that PHWL on the WP device is a differentially effective means of risk communication with greater potential to negatively affect smoking experience among high-frequency and puffing behaviors among low-frequency smokers.

It was interesting to notice the differential responses to PHWL among low-frequency and high-frequency WP smokers. On one hand, while high-frequency WP smokers showed a more pronounced negative response to PHWL in terms of satisfaction and smoking experience, it was the low-frequency WP smokers who responded with shortening smoking time and reducing puff numbers. Apparently, for the high-frequency smokers, WP smoking represents a planned, positively cued, and important activity within their routine rather than an occasional occurrence (Maziak et al., 2004; Salameh et al., 2008). Disruption to such daily ritual, when exposed to PHWL, resulted in a significant negative sensory effect among high-frequency smokers. On the other hand, these are the smokers that are likely to be nicotine dependent with greater

loss of autonomy over their smoking behavior. The latter perhaps explains why it was the low-frequency who could respond to the PHWL by shortening smoking time and taking fewer puffs.

Both low- and high-frequency smoking groups showed no effect of PHWL on exposure to nicotine and other toxicants. As with studies of different tobacco products, it seems that nicotine dependence is the dominant factor affecting puffing behavior and subsequent exposures (Maziak et al., 2019; Vargas-Rivera et al., 2021). In our previous clinical study among WP smokers, pre-session withdrawal rather than study condition (change in flavor), was found to be highly correlated with nicotine boost and puffing patterns (Ben Taleb et al., 2020). As such, although PHWLs seem to have an impact on WP smokers' attitudes to smoking, their puffing behavior and exposure to inhaled toxicants seem more under the control of nicotine dependence. Especially among high-frequency WP smokers, even though the changes in puffing parameters were not significantly different after exposure to PHWL (vs. no-PHWL), their overall puffing parameters were higher than low-frequency smokers regardless of the PHWL condition.

Though we found no difference in exposure to toxicants among the smoking groups following the PHWL session, adverse health effects of WP smoking (e.g., increased blood pressure and heart rate, carbon monoxide intoxication, tissue oxygenation) have been established (Ziad et al., 2015). Therefore, preventive measures should target all WP smokers regardless of their smoking frequency or duration of exposure.

While our study addresses the important knowledge gap about the effect of PHWL among low and high-frequency WP smokers, it has several limitations. First, our study utilizes an acute lab model that is not suitable to assess the effect of health warnings on long-term outcomes such as smoking and quitting behavior. Second, we

use smoking frequency as a proxy of level of nicotine dependence and experience with smoking based on a substantial body of evidence showing that waterpipe smokers progress in their smoking habit with time in terms of frequency and regularity (Bahelah et al., 2017; Ebrahimi Kalan et al., 2020; Maziak et al., 2005; Soneji et al., 2021). We believe that such framing of our study population helps the reader understand the potential impact of health warning label policy on different smokers in the society rather than clinically defined groups. Third, though efforts were made to match WP smoking atmosphere such as a comfortable chair, opportunity to watch movies of choice, and access to cell phones, the lab setup is different from the popular WP café setting for example. Since the lab conditions were similar for all sessions and only the exposure of interest (PHWL) was manipulated, the documented differences likely represent real responses to the health warning (Maziak et al., 2019).

Our findings imply that placing PHWL on the WP device reduces positive smoking experiences more in high-frequency WP smokers compared to low-frequency smokers. As frequent WP smokers are at higher risk of smoking-related health effects, PHWL on the WP device has the potential to limit or reduce WP smoking experience among these smokers. Also, while our acute response lab model gives an idea of the expected impact of implementing PHWLs in society, such application raised several considerations. For example, as a multi-component tobacco use method, it is expected that the maximum effect can be achieved by applying health warnings on its different parts (device, tobacco, charcoal), and in its popular setting of a hookah café (e.g., on the menu). Moreover, long-term application of health warning labels will perhaps require a battery of tested HWLs so they can be renewed and rotated to avoid wearing off of their effect (Woelbert & d'Hombres, 2019). Future studies, therefore, can focus on looking at the long-term effects of HWLs on harm perception, quit intent, and quitting behavior in

smokers as well as an initiation in nonsmokers. In particular, the long-term effects of PHWLs on low-frequency WP smokers can be informative, given that this group is expected to have an easier time quitting WP smoking compared to more high-frequency smokers (Hyland et al., 2006).

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Figure 1: Illustration of the WP devices with no-PHWL (first condition) and PHWL (second condition).

Table 1: Change in waterpipe smoking topography measures, eCO and plasma nicotine among low and high-frequency smokers following exposure to PHWL vs. no-PHWL.

Measures	Low-frequency (N=30)		High-frequency (N=30)		
	Mean difference	SD	Mean difference	SD	p-value
Smoking time (min)	-7.61	10.24	-2.56	6.73	**0.028**
Puffing time (min)	-1.97	4.12	-1.23	3.20	0.438
Puff duration (s)	-0.28	1.31	-0.62	1.37	0.331
Inter-puff interval (s)	5.02	23.37	-1.12	12.89	0.227
Number of puffs	-33.37	70.72	-0.70	29.21	**0.023**
Total volume (L)	-16.61	43.13	-24.78	46.21	0.482
Puff volume (L)	-0.09	0.37	-0.26	0.43	0.098
eCO boost (ppm)	-3.33	9.37	-6.77	17.99	0.358
Nicotine boost (ng/ml)	0.66	4.49	-0.45	6.65	0.476

Bold numbers indicate significant difference between low and high-frequency smokers ($p<0.05$).

eCO, expired carbon monoxide.

PHWL, pictorial health warning label.

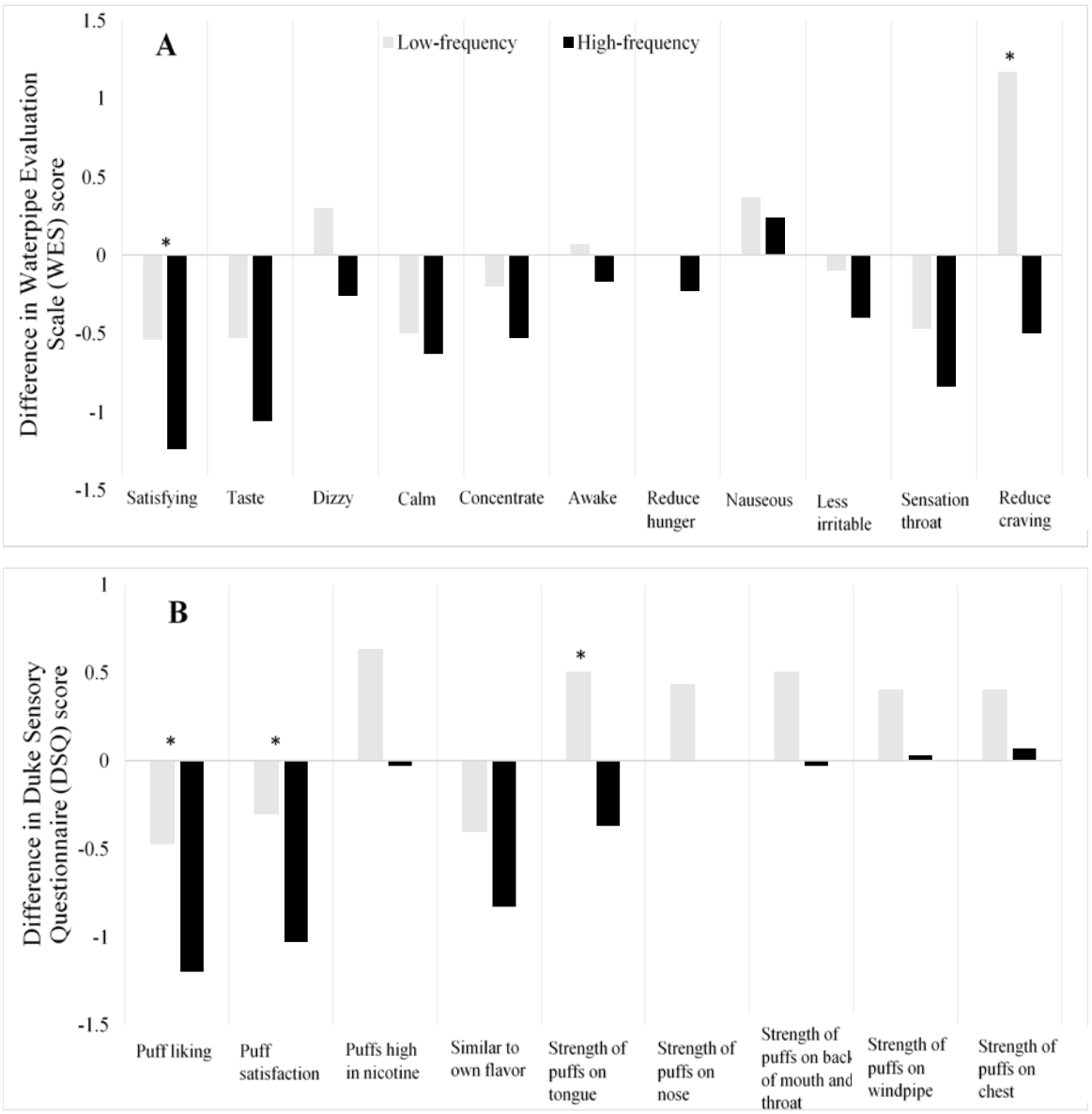

Figure 2, A: Differences in participants' post-WP smoking session Waterpipe Evaluation Scale (WES) score between PHWL and no-PHWL condition among low and high-frequency smokers (N=60).
B: Differences in participants' post-WP smoking session Duke Sensory Questionnaire (DSQ) score between PHWL and no-PHWL condition among low and high frequency smokers (N=60).
*Indicates a significant difference between low and high-frequency smokers after exposure to PHWL compared to no-PHWL ($p < 0.05$).

Supplementary table 1: Descriptive characteristics of the sample by smoking group (N=60)			
Baseline characteristics	Low-frequency (N=30)	High-frequency (N=30)	*p*-value
	N (%)	N (%)	
Gender (Male)	18 (60.0)	21 (70.0)	0.589
Hispanic (Yes)	16 (53.3)	21 (70.0)	0.288
Race			
White	20 (66.67)	15 (50.00)	0.449
Black (African/American)	6 (20.00)	10 (33.33)	
Other	4 (13.33)	5 (16.67)	
Have you smoked cigarettes in the past year? (Yes)	11 (36.37)	12 (40.00)	1.00
When did you start smoking WP in a monthly manner?			
Within past 6 months	4 (13.33)	1 (3.33)	0.389
More than 6 months but less than a year	6 (20.00)	5 (16.67)	
More than 1 year ago	20 (66.67)	24 (80.00)	
What is the average time you usually spend smoking WP? (minutes)			
<30	5 (16.67)	3 (10.00)	0.449
30-60	20 (66.67)	18 (60.00)	
>60	5 (16.67)	9 (30.00)	
	Mean (SD)	Mean (SD)	
Age in years	21.50 (2.81)	21.33 (2.15)	0.879
During the past 6 months, on average how many WPs (head/bowls) you smoke per month?	2.34 (1.53)	6.43 (4.64)	**<0.001**
At what age did you smoke WP for the first time in your life?	17.87 (1.55)	17.60 (1.98)	0.274

Note: Bold number indicate significant difference between low and high-frequency smokers ($p<0.05$).

CONCLUSIONS

The objective of this dissertation was to examine the magnitude and predictors of waterpipe smoking trajectories (initiation, progression, and cessation) and the potential effectiveness of PHWL policies upon WPT smokers at different stages of smoking that exist in society.

In the first study, we assessed the prevalence and predictors of WPT smoking initiation and progression among adolescents and young adults in the US. The results show past 12-month rates of WPT initiation up to 19% and progression up to 14% among these young people. The strong predictors of WPT smoking initiation and progression included lower harm perception towards WPT compared to cigarettes and co-use of alcohol and other tobacco products.

In the second study, we assessed the magnitude and predictors of cessation among young adults WPT smokers in the US. We found a rate of cessation of about 25%. Regret smoking strongly predicted cessation whereas the lack of smoking restriction rules at home and co-use of alcohol hindered the cessation.

In the third study, we examined the effectiveness of potential PHWL policy upon low and high-frequency WPT smokers in a clinical setting. The participants smoked WPT without PHWL in the first session and with PHWL in the second session. The PHWL did not have any effects on overall nicotine and other toxicants exposure in both groups following smoking WPT with PHWL vs. no-PHWL. However, the acute subjective experiences of WPT smoking (e.g., puff liking and puff satisfaction) were more reduced among high-frequency smokers and puffing behaviors (e.g., total smoking time and the number of puffs) were more reduced among low-frequency smokers indicating differential effectiveness of this potential strategy to decrease smoking.

In summary, we found a substantial rate of WPT smoking initiation and progression. Lower harm perception towards WPT and the lack of adequate regulations of WPT establishments (exemption from smoke-free air legislation and indirect social media promotion) facilitated the uptake and continuation of WPT smoking behavior among young people. This implies that future approaches to control WPT should focus on eradicating the highly prevalent misperception towards WPT and regulating WPT smoking venues. The differential effectiveness of PHWL upon low- and high-frequency WPT smokers adds evidence to findings from previous studies to consider PHWL policy for FDA as it shows potential to reduce WPT smoking and prevent tobacco smoking-related morbidities and mortalities.

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