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Early Symptoms and Correlates of Nicotine Dependence Among Adolescent Waterpipe Smokers

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EARLY SYMPTOMS AND CORRELATES OF NICOTINE DEPENDENCE AMONG ADOLESCENT WATERPIPE SMOKERS

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by

Raed Bahelah

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

This dissertation, written by Raed Bahelah, and entitled Early Symptoms and Correlates of Nicotine Dependence among Adolescent Waterpipe Smokers, 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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Florida International University, 2016

DEDICATION

All praise and thanks are to Allah. I dedicate this work to my mom, my dad, my wife Dawn, and to the students in 8th and 9th grades in Lebanon. You all helped me make my dream comes true.

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ABSTRACT OF THE DISSERTATION

EARLY SYMPTOMS AND CORRELATES OF NICOTINE DEPENDENCE AMONG ADOLESCENT WATERPIPE SMOKERS

by

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Waterpipe (WP; hookah, shisha, narghile) has re-emerged as a global epidemic of tobacco smoking mainly among young people. Although WP smokers show symptoms of nicotine dependence (ND) and face difficulty quitting, no study has examined the early symptoms and factors associated with ND among young WP smokers. Using baseline data from the Waterpipe Dependence in Lebanese Youth (WDLY) study, this research investigated the appearance and timing of early symptoms, factors, and WP-specific smoking patterns associated with ND symptoms among 160 adolescents (mean age ± SD =14.0 ± 1.1 years at baseline) from 8th and 9th grades who reported WP use in the past 30 days. ND symptoms were assessed using Hooked on Nicotine Checklist (HONC) and the full syndrome of ND was evaluated using the International Classification of Diseases-10th revision (ICD-10 ND).

Our analysis shows that 71.3% of WP smokers endorsed at least one HONC symptom, 38.1% developed ICD-10 ND, with craving (25%), feeling addicted (22.5%), and failed quit attempts (14.3%) were the most commonly endorsed early symptoms of ND. The first HONC symptom and full ICD-10 ND were reached 10.9 and 13.9 months, respectively, after the initiation of WP use. Results from multivariable regression models show that depressive symptoms, lower self-esteem, and having at least one sibling who smokes WP were associated with the presence of ND symptoms, while enrollment in public schools, smoking WP ≥30

minutes per session, and believing that cigarette smoking is harmful to health were associated with a higher number of ND symptoms. Smoking a whole WP without sharing and being in 9th grade were associated with the presence and endorsement of a higher number of ND symptoms.

These findings suggest that a large proportion of adolescents experience symptoms of ND within a short time period of initiating WP use. Moreover, we identified specific factors that put adolescents at a higher odds of developing ND symptoms. Therefore, WP prevention and intervention strategies may have greatest impact by educating youth about the harmful and addictive properties of WP, teaching them positive coping skills, targeting those enrolled in public schools, and addressing WP use by family members.

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Introduction

In 2005, the World Health Organization issued its first advisory note on waterpipe tobacco smoking in response to waterpipe's growing threats to public health worldwide (WHO, 2005). Waterpipe (a.k.a. hookah, shisha, narghile, hubble-bubble) is a method of tobacco smoking in which a burned charcoal heats a tobacco separated from the charcoal by a perforated aluminum foil. Tobacco smoke cools down when it passes through a bowl usually filled with water to a hose and finally to a smoker through a mouthpiece (WHO, 2005). For many waterpipe users, the passage of smoke through water "filters" the toxic chemicals found in tobacco smoke and makes waterpipe less harmful and addictive than cigarettes (WHO, 2005; 2015). Contrary to this misperception, research has shown that waterpipe smoking is associated with many adverse health outcomes similar to those caused by cigarette smoking. For example, waterpipe smoking is associated with lung cancer, coronary artery diseases, perinatal and obstetric complications, and nicotine dependence (El-Zaatari et al., 2015).

With respect to nicotine dependence, many waterpipe smokers report failed quit attempts and experience craving/withdrawal symptoms that are suppressed by subsequent waterpipe use similar to cigarettes (Eissenberg & Shihadeh, 2009). However, craving/withdrawal symptoms can be recovered faster among waterpipe smokers than cigarette smokers. For example, a cross-over study among 61 Syrian young adults (mean age=22 years) who completed two 45-min sessions of smoking either waterpipe or cigarettes show that waterpipe comparatively suppressed withdrawal/craving symptoms but craving symptoms were recovered faster during cigarette smoking session (Rastam et al., 2011). Another study with a similar design among 54 US young adults (mean age=21.2 years) found that recovery of craving and urges to smoke symptoms were pronounced during the cigarette session relative to waterpipe at 45 min after smoking (Cobb et al., 2011). Although these studies provide useful insights into waterpipe addictive potentials, their

generalizability is limited by their laboratory-based design. As well, these studies recruited established smokers who may have different smoking profile than beginning smokers. Moreover, to the best of our knowledge no study had examined the early symptoms of nicotine dependence among young waterpipe smokers who are at a higher risk of developing symptoms of nicotine dependence (Lydon et al., 2014). Characterizing the appearance and composition of early nicotine dependence symptoms profile was crucial for reducing youths' cigarette smoking and is equally critical for preventing youths' waterpipe use.

Waterpipe is also characterized by unique smoking patterns, different from cigarette smoking, that are associated with increased risk of harmful and addictive effects (Maziak et al., 2005). For example, waterpipe is usually smoked over long smoking sessions that extend ≥60 min during which smokers inhale large amounts of carbon monoxide, tar, and the addiction-causing drug "nicotine" (Eissenberg & Shihadeh, 2009). Another unique feature of waterpipe is its prominent intermittent smoking patterns. Regardless of being mainly intermittently smoked, a single smoking session of waterpipe exposes smokers to levels of nicotine associated with nicotine dependence particularly among youth (Primack et a., 2016). Moreover, waterpipe smokers show typical features of nicotine dependence such as behavioral adaptations to ensure access to waterpipe, increased use frequency over time, and decreased feelings of control over waterpipe use (Maziak et al., 2005; Aboaziza & Eissenberg, 2015). While waterpipe has a unique social aspect and many users smoke waterpipe in cafés, established smokers tend to smoke waterpipe alone and at home. These observations led some researchers to suggest that in addition to the general symptoms of nicotine dependence, waterpipe users may show additional symptoms of nicotine dependence specific to this unique method of tobacco use (Maziak et al., 2005).

The need for studies that examine nicotine dependence among young waterpipe smokers is evident for three main reasons. First, the majority of adult smokers initiate smoking by their eighteenth birthday (U.S. Department of Health and Human Services, 2014). Therefore,

preventing tobacco initiation should target young people. Second, findings from the most recent Global Youth Tobacco Surveys show that waterpipe use is more prevalent than cigarettes among 13-15 year-olds in many Eastern Mediterranean (EM) countries (Jawad et al., 2015). For example, the prevalence of current (past 30-days) cigarette smoking among 13-15 year-olds in Syria in 2010 was 7.7% compared to 20.1% for current waterpipe smoking. In Lebanon in 2011, 36.9% of 13-15 year-olds currently smoked waterpipe and 13.7% currently smoked cigarettes (Jawad et al., 2015). Waterpipe use is also increasing among young people from other parts of the world. Among US middle and high school students, current cigarette use has significantly decreased during 2011-2015, while current waterpipe use has significantly increased during the same period (Singh et al., 2016). Third, assessment of nicotine dependence among waterpipe smokers requires waterpipe-tailored measures based on waterpipe smokers' experiences and unique smoking context. Adapting measures of nicotine dependence from the cigarette literature is not scientifically sound and cannot capture waterpipe-specific smoking patterns. For example, the item "time to first cigarette after waking up" commonly used to measure the presence and severity of nicotine dependence on cigarette is not suitable for a typically intermittently used, time-consuming smoking method such as the waterpipe (Myers et al., 2016).

In the EM countries where waterpipe was used for centuries, many youth view waterpipe as a symbol of cultural identity and smoke it for the first time with a family member (Maziak et al., 2015). Additionally, waterpipe use among youth and females in many EM countries is socially acceptable and is not tabooed as is the case for cigarettes (Maziak et al., 2005). Social acceptability, marketing strategies, and the lack of effective control policies in the EM countries may facilitate youths' access and use of waterpipe (Jawad et al., 2015). In fact, the highest prevalence of current waterpipe use worldwide was reported among Lebanese youth (36.9%) which makes Lebanon a natural laboratory for studying nicotine dependence among young waterpipe smokers.

The *Waterpipe Dependence in Lebanese Youth (WDLY)* Study is the first prospective study of the development of ND in waterpipe smokers. It aims at determining if waterpipe smokers develop ND with nondaily use and whether the symptoms of ND among waterpipe smokers differ from those among cigarette smokers. It also aims to determine the factors associated with the development of ND among young waterpipe smoker. The findings can guide the development of waterpipe-specific prevention and intervention strategies to limit the unprecedented worldwide use of waterpipe especially among youth.

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EARLY SYMPTOMS OF NICOTINE DEPENDENCE AMONG ADOLESCENT WATERPIPE SMOKERS

Abstract

Background

Although waterpipe smoking is increasingly popular among youth and can lead to nicotine dependence (ND), no studies have documented how ND develops in waterpipe smokers. We examined the emerging symptoms of ND among adolescent waterpipe smokers in Lebanon.

Methods

Individual confidential interviews were used to evaluate ND in 160 waterpipe smokers and 24 cigarette smokers from a sample of 498 students enrolled in 8th and 9th grades in Lebanon.

Results

Among waterpipe smokers, 71.3% endorsed at least one Hooked on Nicotine Checklist (HONC) symptom and 38.1% developed the full syndrome of ND (≥3 criteria using the International Classification of Diseases, 10th revision). The early symptoms of ND among waterpipe smokers were craving (25%), feeling addicted (22.5%), and failed quit attempts (14.3%). Among those who reached the respective milestones, median tobacco use when the first HONC symptom emerged was 7.5 waterpipes/month with smoking frequency of 6 days/month; the median tobacco use for the full syndrome of ND was 15 waterpipes/month with smoking frequency of 15 days/month. Among those who had already reached the milestones, the first HONC symptom appeared 10.9 months after the initiation of waterpipe smoking and the full syndrome of ND was reached at 13.9 months. In addition, cues such as seeing or smelling waterpipe, and the café environment triggered craving in most waterpipe smokers with symptoms of ND.

Conclusions

Symptoms of ND develop among adolescent waterpipe smokers at low levels of consumption and frequency of use. Craving for nicotine triggered by waterpipe-specific cues is reported even at this young age. Waterpipe-specific ND prevention and intervention programs for youth are needed.

Introduction

Tobacco smoking is a major preventable cause of premature death worldwide.[1] Nicotine, a component of tobacco, is addictive and leads to nicotine dependence (ND) that is mostly responsible for failed quit attempts and continued tobacco use (WHO 2002; 2010). Tobacco-related morbidity and mortality are higher than that for all other forms of drug addiction combined (WHO, 2010). Non-cigarette tobacco products deliver significant amounts of nicotine and show addictive potential similar to cigarettes (Fagerström & Eissenberg, 2012; O'Connor, 2012), thus representing a major factor in sustaining ND and contributing to tobacco-related morbidity and mortality (Maziak et al., 2015).

Waterpipe smoking (hookah, narghile, shisha) is an emerging tobacco use method for youth in the Middle East and globally (Maziak et al., 2009). Studies about waterpipe's addictive potential indicate that its use is associated with considerable exposure to nicotine, and some of the known symptoms of ND in tobacco smokers such as abstinence-induced withdrawal and craving that are relieved by subsequent smoking (Maziak et al., 2011; Ward et al., 2005; Aboaziza & Eissenberg, 2014). In a survey of 268 waterpipe smokers (mean age=30 years) in Aleppo-Syria, 59.2% reported unsuccessful quit attempts during the past year (Ward et al., 2005). These studies indicate that waterpipe smoking can lead to ND, yet no study has attempted to characterize the

natural course of ND among adolescent waterpipe smokers or how ND among waterpipe smokers might differ from that in cigarette smokers.

Unlike cigarettes, waterpipe is a predominantly intermittent tobacco use method with long smoking sessions averaging an hour (Eissenberg & Shihadeh, 2009; Maziak et al., 2009). A single waterpipe session exposes smokers to 1.7 times the amount of nicotine, and about 50 times the volume of smoke inhaled compared to a single cigarette (48.6 liters vs. 1 liter) (Eissenberg & Shihadeh, 2009). Accessibility to tobacco is another factor that can influence how ND can develop and its characteristics (Doubeni et al., 2008). Unlike cigarettes, waterpipe is a stationary, multi-component, and social tobacco use method. In addition, the café environment, in which waterpipe smokers usually socialize, provides waterpipe-specific cues that can shape ND amongst them (Maziak et al., 2005). So while limited accessibility and intermittent use might hinder the development of physical dependence, larger amounts of inhaled smoke/nicotine, length of smoking session and its strong social cues may facilitate dependence in a waterpipe-specific fashion (Maziak et al., 2005). It is therefore of interest to examine the timing and characteristics of ND in waterpipe smokers in order to guide the development of waterpipe-specific prevention and intervention strategies.

Lebanon is among the countries most affected by the waterpipe epidemic, with the highest prevalence of current waterpipe smoking among 13-15 year olds globally (36.9%) (Jawad et al., 2015). Therefore, Lebanon provides a natural lab for studying the development of ND among waterpipe smokers.

The *Waterpipe Dependence in Lebanese Youth (WDLY)* Study is the first prospective study of the development of ND in waterpipe smokers. It aims at determining if waterpipe smokers can develop ND with nondaily use and whether the symptoms of ND experienced by waterpipe smokers are the same as those experienced by cigarette smokers. It also aims to determine at what age ND begins among waterpipe smokers. Using baseline data, we describe

symptoms of ND among adolescent waterpipe smokers in relation to the duration, quantity and frequency of waterpipe use.

Methods

The study was conducted in Lebanon, an upper-middle income country with gross national income of US$9,870 per capita and a population of 4.5 million in 2013 (The World Bank, 2013).

Design

The WDLY is a longitudinal study of 498 adolescents enrolled in 8th and 9th grades at baseline (mean age ± standard deviation, 14.0 ± 1.1 years). Since the development of ND can be a protracted process (Kandel et al., 2009), we included in this study waterpipe, cigarette, and susceptible nonsmokers to be able to measure initial and important ND milestones during the 3 year study. We report baseline data for interviews conducted in 2015. The study was approved by the institutional review boards of Florida International University, and the American University of Beirut.

Recruitment

Schools with 8th and 9th grades from 4 regions in Lebanon (Beirut, Mount Lebanon, Nabatiye, South Lebanon) were identified using a list from the Lebanese Ministry of Education. Schools were considered eligible if they agreed to participate and provided space to ensure privacy of interviews. The Ministry of Education list had 178 schools with 8th and 9th grades, of which 38 schools agreed to participate and lent support to the study. Letters requesting parental consent were sent to the parents of all 8th and 9th grade students in the 38 schools. After obtaining written parental consents and students' assents, a brief, in-class, self-administered recruitment survey about students' smoking status was used to determine eligibility.

To allow us to compare cigarette and waterpipe smokers, students were eligible to participate if they currently (past 30 days) smoked either cigarettes or waterpipe, but not both. We

also included those susceptible to initiating smoking in the future, but since the current study focuses on early symptoms of ND, susceptible nonsmokers were excluded from the current analysis.

Data collection

We developed the study questionnaire in line with existing literature on patterns of waterpipe smoking (Maziak et al., 2009; Maziak et al., 2011; Ward et al., 2005; Eissenberg & Shihadeh, 2009; Maziak et al., 2005; Asfar et al., 2005) and domains of ND among adolescents (O'Loughlin et al., 2009; Kandel et al., 2007; DiFranza et al., 2000, 2002, 2007) The questionnaire was pilot-tested in a group of 8th graders who were not part of the study sample. Questionnaires were administered by trained interviewers and are composed of four modules: socio-demographics, smoking-related behaviors, ND, and psychological traits. All modules were translated to Arabic and back translated to English for comparison and fine-tuning following standard techniques (Brislin, 1970). Interviewers met participants individually and all interviews were conducted in private rooms on schools' premises to protect confidentiality and minimize social desirability bias.

Dates of the first symptom of ND and key smoking milestones (smoking initiation, first inhalation, smoking a whole cigarette/waterpipe head) were recorded. Four methods were used to improve recall of appearance of ND symptoms and milestones: bounded recall, decomposition, personal landmarks, and the depiction of these landmarks visually to create a personal calendar for each student (DiFranza et al., 2000, 2002). Following an established methodology (DiFranza et al., 2000, 2002), if exact dates were not recalled, we recorded the 7th of the month for events that occurred at beginning of the month, the 14th for events occurring in the middle of the month, and the 21st for events at end of the month.

Instruments and measures

Stages of Physical Dependence (PD) is a 3-item measurement of the progression of PD on tobacco (DiFranza et al., 2012a). PD develops through stages of wanting, craving and needing (DiFranza et al., 2012a; Huang et al., 2013) which correlate with structural (Huang et al., 2013) and functional (Huang et al., 2014) changes in smoker's brain. This measure has been used with cigarette and smokeless tobacco users (DiFranza et al., 2011, 2012a), but not with waterpipe smokers. Wanting was assessed by the item: "If I go too long without smoking, the first thing I will notice is a mild desire to smoke that I can ignore," craving was assessed by the item: "If I go too long without smoking, the desire for smoking becomes so strong that it is hard to ignore and it interrupts my thinking," and needing was assessed by the item: "If I go too long without smoking, I just cannot function right, and I know I will have to smoke just to feel normal again." Responses were: describes me not at all, describes me a little, describes me pretty well, and describes me very well. Any response above 'describes me not at all' is considered an endorsement (DiFranza et al., 2012a). Participants are assigned to the stage corresponding to the most advanced symptom endorsed (wanting, craving, or needing) (DiFranza et al., 2012a). Participants who do not endorse any of the 3 items do not have PD. As this instrument does not produce a score by tallying items, internal reliability is not applicable.

The World Health Organization's International Classification of Diseases, 10^{th} Revision (ICD-10) has 6 criteria and endorsement of ≥ 3 of these criteria during a 12-month period is required for the diagnosis of the syndrome of tobacco dependence (DiFranza et al., 2007). We also obtained a continuous score of ICD-10 by tallying the number of endorsed criteria (O'Loughlin et al., 2002). Internal reliability (α) of the Arabic version of ICD-10 was 0.76 in this study.

The Hooked on Nicotine Checklist (HONC) is a 10-item measurement of autonomy that assesses symptoms, rather than behaviors, to allow its use with any form of nicotine delivery and

with participants of all ages (Wellman et al., 2006, 2008; DiFranza et al., 2012b). The HONC has been extensively validated among adolescent and adult cigarette and smokeless tobacco users (Wellman et al., 2006, 2008; DiFranza et al., 2012b), but has not been used with waterpipe smokers. Each HONC item represents a symptom of ND and has yes/no options. Endorsement of any item indicates a loss of autonomy over tobacco use. Although a loss of autonomy often leads to a ICD-10 defined syndrome of dependence, a loss of autonomy is not synonymous with ICD-10 tobacco dependence (DiFranza et al., 2002, 2007). We also obtained a continuous score of the HONC by tallying the number of endorsed items (DiFranza et al., 2007). Internal reliability (α) of the Arabic version of HONC was 0.74 in this study.

The Lebanon Waterpipe Dependence Scale (LWDS-10J) is a 10-item measurement that assesses primarily physical dependence and motivation for smoking (Fagerström & Eissenberg, 2012). Scores on this measurement correlate with the number of waterpipe smoking sessions per week and the number of waterpipe heads smoked per session (Primack et al., 2014). We used the modified 10-item measurement as it shows better psychometric properties than the original 11-item LWDS scale (Primack et al., 2014). Internal reliability (α) of the Arabic version of the LWDS-10J was 0.74 in this study.

The Syrian Center for Tobacco Studies-28 (SCTS-28) is a battery of items addressing behaviors, attitudes and symptoms related to waterpipe use and dependence (see Table 5). Items were developed using a theory-driven, iterative process, and review of dependence concepts/domains based on qualitative data from waterpipe smokers (Hammal et al., 2008). It consists of 28-items with response options ‘true’, ‘somewhat true’, and ‘not true’, and scores of 2, 1, and 0, respectively. Any response other than ‘not true’ to an item was considered a positive response to that item. Internal reliability (α) of the Arabic version of the SCTS-28 was 0.80 in this study.

Data analysis

To calculate the mean age (in years) at smoking milestones and appearance of individual symptoms of ND, a participant's date of birth was subtracted from the date when the event of interest took place. Time intervals between each smoking milestone (initiation, inhalation, smoking a whole cigarette/waterpipe head) and ND milestones (the 1st HONC symptom, or the 3rd ICD-10 criterion) were calculated. It should be noted that means were calculated based only on subjects who reached the particular milestones, i.e. they do not represent a survival analysis. When data showed a Poisson distribution, we reported the median amount (waterpipes per month, cigarettes per month) and frequency (days per month) of tobacco use that corresponded to the time when the participant experienced the first HONC symptom, the third ICD-10 criterion, and each stage of PD (Wanting, Craving, Needing).

We employed three symptom-based dependence measures (HONC, ICD-10, PD) to allow for comparisons between waterpipe and cigarette smokers, and two measures specific to waterpipe (SCTS-28, LWDS-10J) to describe the main symptoms of ND among waterpipe smokers. We evaluated the internal reliability of these measures using Cronbach's alpha with a value >0.70 indicating acceptable internal reliability (Santos, 1999). In addition, we evaluated the convergent construct validity of waterpipe-specific ND measurements using two different methods (O'Loughlin et al., 2002). First, because measurements that have good convergent construct validity are highly correlated as they measure the same underlying concept (ND in this case) (O'Loughlin et al., 2002), Spearman's rank-order correlation (r_s) was used to test the association between scores on the HONC, ICD-10, LWDS-10J, and SCTS-28. Second, measurements of ND have good convergent construct validity if they are associated with other indicators of ND (O'Loughlin et al., 2002). Consequently, we tested the relationship between scores on the LWDS-10J, SCTS-28 and the different stages of PD (a component of ND).

Data on socio-demographics, smoking milestones, and symptoms of ND were summarized using percentages and means (with standard deviations (SD)). Pearson's Chi-squared or linear-by-linear association tests, as appropriate, were used to test associations among categorical variables. Normality was checked for quantitative variables and Student's *t* test, or Wilcoxon Mann-Whitney/Kruskal–Wallis tests, as appropriate, were used to compare group differences in quantitative variables. Cramer's V statistic was used to determine the magnitude of association among categorical variables. All tests were two-tailed and a level of significance was set at $p<0.05$. Data were analyzed using SPSS-20 (IBM Corp., Armonk, NY) and SAS-9.3 (SAS Institute Inc., Cary, NC).

Results

Socio-demographics

Out of 498 participants recruited, 298 susceptible nonsmokers and 16 dual users of waterpipe and cigarettes were excluded from the current analysis. Therefore, this study was restricted to 160 current waterpipe and 24 current cigarette smokers (N=184). Overall, 49.5% were females, and 53.8% were recruited from public schools. Females represented 56.9% of waterpipe smokers, and only 8.3% of cigarette smokers (see Table 1 for socio-demographic comparisons). This striking gender difference likely reflects the social acceptability of waterpipe, but not cigarette smoking among females in the Middle Eastern context (Afifi et al., 2013). Because of the small and gender-skewed sample of cigarette smokers, only limited comparisons with waterpipe smokers were undertaken.

Smoking milestones

Table 2 presents the number and percentage of participants who experienced important smoking milestones (initiation, inhalation), and ND (first HONC symptom, ICD-10, PD), and age of attaining each milestone. There were no significant differences in the mean age reported for

experiencing the first HONC symptom (13.9 years for cigarette and 14.1 years for waterpipe; p=0.48), age of attaining ICD-10 (14.7 years for cigarette and 14.6 years for waterpipe, p=0.84), or for reaching the Wanting (p=0.86), Craving (p=0.58), or Needing (p=0.65) stages of PD between waterpipe and cigarette smokers.

Table 3 shows the median time interval between smoking milestones and the appearance of the first HONC symptom or attaining ICD-10 dependence criteria. These data pertain only to those participants who experienced the given outcome.

Early symptoms of ND and patterns of tobacco use

There were no significant differences in the proportion of waterpipe and cigarette smokers who reported HONC symptoms or met ICD-10 dependence criteria. One or more HONC items were endorsed by 75.0% of cigarette smokers and 71.2% of waterpipe smokers (p=0.70). The average number of HONC items endorsed was 2.3 (2.3) for cigarette smokers and 2.0 (2.1) for waterpipe smokers (p=0.67). ICD-10 dependence criteria were met by 25.0% of cigarette smokers and 38.1% of waterpipe smokers (p=0.17). The average number of ICD-10 criteria endorsed was 2.1 (1.3) for cigarette smokers and 2.2 (1.6) for waterpipe smokers (p=0.73).

As measured by the HONC, the earliest emerging symptoms among waterpipe smokers were craving (25.0%), feeling addicted (22.5%), and a failed quit attempt (14.3%) (Table 4). Median tobacco use per month when the first HONC symptom emerged was 7.5 waterpipes and 27.5 cigarettes (p<0.001). Median smoking frequency per month when the first HONC symptom emerged was 6 days for waterpipe and 13.5 days for cigarette smokers (p=0.09).

Based on the appearance of ICD-10 dependence criteria, "A strong desire or sense of compulsion to take tobacco" was the most common first criterion of ND among waterpipe smokers (27.5%), "Difficulties in controlling tobacco-taking behavior in terms of its onset, termination, or levels of use" and "A strong desire or sense of compulsion to take tobacco" were the most common second criteria of ND and were equally endorsed by 23.8% of waterpipe

smokers, while "Difficulties in controlling tobacco-taking behavior in terms of its onset, termination, or levels of use" was the most common third criterion of ND and was endorsed by 24.4% of waterpipe smokers in this study. Median tobacco use per month when ICD-10 criteria were met was 15 waterpipes and 115 cigarettes ($p<0.001$), and a median smoking frequency per month of 15 days for waterpipe and 23 days for cigarette smokers ($p=0.27$).

Waterpipe-specific aspects of ND

Table 5 presents participants' responses to the SCTS-28 among waterpipe users only. A desire to quit smoking *(I want to quit smoking waterpipe)* was endorsed by 78.8% of waterpipe smokers. Sensory cues (*Just the sight or smell of waterpipe is enough to make me want to smoke*, 82.5%), psychological components (*I spend too much money on waterpipe*, 91.9%), withdrawal symptoms (*If I could not smoke waterpipe for a while, I would have difficulty concentrating*, 80.6%), and pleasure (*Smoking waterpipe is a good way to reward myself*, 79.4%) were among the most commonly endorsed items. Only 21.3% of waterpipe smokers usually shared a waterpipe.

Among adolescent waterpipe smokers, at least one HONC item was endorsed by 77.5% of those who endorsed "Just the sight or smell of waterpipe is enough to make me want to smoke," 75.4% of those who endorsed "It would be very difficult to me to be in a restaurant, and not smoke waterpipe," and 83.3% of those who endorsed "I smoke waterpipe usually with friends or in cafés/restaurants" ($p<0.001$, $p=0.03$, $p<0.001$, respectively).

Assessment of waterpipe-specific measures

We compared the LWDS-10J and SCTS-28 with the HONC and ICD-10. All measures were positively correlated with one another. The LWDS-10J and SCTS-28 were highly correlated ($r_s=0.74$), and both the LWDS-10J ($r_s=0.59$) and SCTS-28 ($r_s=0.55$) correlated well with the HONC. Similarly, both the LWDS-10J ($r_s=0.66$) and SCTS-28 ($r_s=0.60$) correlated well with ICD-10 ($p<0.01$ for all).

As well, scores on the SCTS-28 and LWDS-10J increased in proportion to the Stage of PD. Mean (SD) LWDS-10J scores were 5.0 (3.8) for subjects with no PD, 6.9 (4.4) for Wanting, 10.3 (3.5) for Craving, and 16.5 (3.9) for Needing ($p<0.001$). Similar patterns were observed for SCTS-28 scores with 18.9 (6.0) for no PD, 23.5 (8.4) for Wanting, 28.8 (6.1) for Craving, and 37.2 (5.1) for Needing ($p< 0.001$).

Discussion

This is the first study to examine the early symptoms of ND among adolescent waterpipe smokers. We used multiple measures of ND and employed memory-assistance techniques to improve recall of important smoking milestones. The early symptoms of ND among adolescent waterpipe smokers in Lebanon–as measured by ICD-10 and HONC- were craving and feeling addicted. As has been previously reported for cigarette smokers, adolescent waterpipe smokers can meet ICD-10 dependence criteria with nondaily use (DiFranza et al., 2000, 2007). ICD-10 criteria were met by 38.1% of waterpipe smokers, who reported a median tobacco use at the time ICD-10 criteria were met of 15 waterpipes per month and a median smoking frequency of 15 days per month. Our findings extend those of previous research by demonstrating that infrequent use of a non-cigarette tobacco product can induce ICD-10 dependence in adolescents (DiFranza et al., 2012b; Apelberg et al., 2014).

Individual symptoms of ND appear before the full ICD-10 dependence criteria are met. In this study, median tobacco use when the first HONC symptom emerged was 7.5 waterpipes per month with a smoking frequency of 6 days per month. Among those reporting ND symptoms, the first HONC symptom emerged 10.9 months and ICD-10 criteria were met 13.9 months after the initiation of waterpipe smoking. Prior studies have shown large individual differences in the speed with which individual symptoms and the full ND syndrome develop (Hu et al., 2008, 2012; Gervais et al., 2006). At this point in our longitudinal study we would only see dependence in

those individuals prone to develop it rapidly. Over time, the observed median time to onset of ND symptoms will become longer as more youths in this cohort develop symptoms. The important observation is that many youths (average age of 14 years in this analysis) develop ICD-10 dependence within the first year of waterpipe use.

Although the limited sample size of cigarette smokers in this study that did not allow for robust comparison between waterpipe and cigarette smokers on main study outcomes, some general patterns have emerged. These include a similarity between the proportion of those who endorsed at least one HONC symptom or satisfying the ICD-10 dependence criteria, as well as intensity of symptoms (average number of endorsed ND symptoms). However, the appearance of the first HONC symptom and ICD-10 dependence criteria seem to occur earlier (from onset) and at a lower smoking frequency among waterpipe compared to cigarette smokers. On the other hand, the prevalence and early symptoms of ND (craving and feeling addicted) among waterpipe smokers in this study were comparable to those among adolescent cigarette smokers from other studies (Kandel et al., 2007; DiFranza et al., 2002; O'Loughlin et al., 2002; Gervais et al., 2006; Doubeni et al., 2010).

It is plausible that dependence might develop more rapidly among waterpipe smokers compared to cigarette smokers. Waterpipe smokers must inhale deeply to use the waterpipe, but inhalation is not required for a cigarette. While cigarette smokers spend 5-8 minutes smoking a single cigarette, an average waterpipe smoking session lasts 30-60 minutes (Maziak, 2014; Maziak et al., 2004). During one session, waterpipe smokers are usually exposed to larger doses of nicotine compared to smoking one cigarette (Eissenberg & Shihadeh, 2009). On the other hand, cigarettes are more portable and offer more opportunities to smoke. The number of cigarette smokers in our sample was small, but our data suggest that ICD-10 dependence criteria develops at a lower frequency of use in waterpipe smokers (15 waterpipes vs 115 cigarettes per month ($p<0.001$). These data should be interpreted in light of the differences in the dose of

delivered nicotine between these two smoking methods. However, there is no practical way to measure cumulative nicotine exposure to provide a better metric for comparison.

Even at low levels of use, the majority of waterpipe smokers with ND symptoms reported responding to waterpipe-specific environmental cues, highlighting the importance of such cues for the development of ND in waterpipe smokers. Environmental factors, such as waterpipe sight, smell, and the café environment have been shown previously to affect the "waterpipe experience" (Smith-Simone et al., 2008; Hammal et al., 2008). When systematically measured for the first time in this study using SCTS-28, waterpipe smokers who experienced HONC symptoms of ND were more likely to endorse being responsive to these drug cues. We believe that this is the first study to show that drug cues, such as the sight and smell of waterpipe stimulate a desire to smoke the waterpipe, and thus can be important factors in the development of ND. It is evident that heavy and prolonged use of the waterpipe is not a prerequisite for the development of responsivity to drug cues.

This study has limitations. First, the small number of cigarette smokers provided limited statistical power to detect significant differences between waterpipe and cigarette smokers, but we expect that the sample size for cigarette smokers will increase during follow-up and our study will have more power over time. Second, the sample of cigarette smokers was almost all male. Third, unlike the LWDS-10J, the SCTS-28 was not developed to obtain an overall score of ND. We used scores for SCTS-28 mainly to measure how its items correlate with validated measures of lost autonomy and ND in general (HONC, ICD-10) and those specific to waterpipe (LWDS-10J). While the LWDS-10J assesses ND among waterpipe smokers, the SCTS-28 evaluates waterpipe-specific smoking behaviors and attitudes that are not captured by the LWDS-10J, but are more reflective of the strong social dimension of waterpipe smoking. Fourth, common to all studies of the natural history of ND, both prospective and retrospective, symptoms of ND are self-reported and reported retrospectively. Errors in recalling the dates of events which happened

in the past are possible. However, we minimized such possibilities by the use of methods that improve recall of events (DiFranza et al., 2000, 2002) and enrolled a very young cohort for which all events would be relatively recent. Finally, calculations of the time to onset of an event such as meeting ICD-10 dependence criteria are necessarily based only on those individuals who have already reached the milestone of interest. An analogy would be that the average time to complete a marathon becomes slightly longer each time another runner passes the finish line. In a longitudinal study, the observed median times to reach a milestone become longer with each successive assessment as those who were slower to reach the milestone eventually make it. Therefore, figures reported in Table 3 should be viewed as representing only those individuals with a propensity to develop symptoms rapidly. Our results should be interpreted in light of these limitations.

Conclusions

This study shows that ICD-10 ND can appear within a relatively short time period after the initiation of waterpipe smoking among adolescents, and at a lower frequency of waterpipe use compared to cigarette smokers. Frequency and intensity of ND symptoms did not differ between waterpipe and cigarette smokers, nor did the age at the onset of ND milestones. The types of symptoms experienced, and the order with which symptoms appeared did not differ significantly for the two forms of tobacco. However, our results show how waterpipe smoking involves different use behaviors, social context, and sensory experiences than cigarette smoking and more research is needed to explore how these differences might affect the development of ND or how it manifests behaviorally. Our data indicate that adolescent waterpipe smokers develop symptoms of ND, which indicates that waterpipe-specific prevention and intervention programs targeting youth are needed. These programs need to be tailored to the specifics of waterpipe as a tobacco use method with unique use patterns and a strong social dimension.

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Table 1.1 Selected baseline socio-demographic characteristics of a cohort of adolescent current smokers in Lebanon.

	Waterpipe smokers (n=160)	**Cigarette smokers (n=24)**	**Total (N=184)**	***Cramer's V***	**p-value**
	n (%)	**n (%)**			
Sex				0.33	<0.001
Male	69 (43.1)	22 (91.7)	91 (49.5)		
Female	91 (56.9)	2 (8.3)	93 (50.5)		
School type				0.16	0.03
Public	91 (56.9)	8 (33.3)	99 (53.8)		
Private	69 (43.1)	16 (66.7)	85 (46.2)		
Age				0.06	0.44
12-13 years	41 (25.6)	8 (33.3)	49 (26.6)		
14-15 years	94 (58.8)	13 (54.2)	107 (58.2)		
16-18 years	25 (15.6)	3 (12.5)	28 (15.2)		
Grade				0.06	0.41
8th grade	79 (49.4)	14 (58.3)	93 (50.5)		
9th grade	81 (50.6)	10 (41.7)	91 (49.5)		
Weekly school allowance (LBP)*				0.08	0.37
<10,000	18 (11.3)	1 (4.2)	19 (10.3)		
10,000-20,000	84 (52.5)	13 (54.2)	97 (52.7)		
>20,000	58 (36.2)	10 (41.6)	68 (37.0)		

*1 $US = 1,508 Lebanese Pounds (LBP) as of July 28th, 2015 (http://themoneyconverter.com/USD/LBP.aspx)

Table 1.2 Percentage of participants who attained each milestone and the mean age of attaining each milestone among a cohort of adolescent current smokers in Lebanon.

Milestone (ages are in years)	Waterpipe smokers		Cigarette smokers	
	No. (%)	Mean**(SD)	No. (%)	Mean (SD)
Age of first smoking	160 (100)	12.9 (1.9)	24 (100)	11.3 (4.9)
Age of first inhaling tobacco smoke into lungs*	160 (100)	12.9 (1.9)	16 (66.6)	13.3 (1.4)
Age first HONC item was experienced	114 (71.2)	14.1 (1.4)	18 (75.0)	13.9 (1.1)
Age first experienced Wanting (PD stage 2)	92 (57.5)	13.9 (1.3)	13 (54.2)	13.8 (1.4)
Age of attaining ICD-10 ND	61 (38.1)	14.6 (1.3)	6 (25.0)	14.7 (1.1)
Age first experienced Craving (PD stage 3)	42 (26.2)	14.3 (1.2)	7 (29.2)	14.2 (1.2)
Age first experienced Needing (PD stage 4)	14 (8.8)	15.0 (1.7)	7 (29.2)	14.7 (1.3)

*As inhalation is required for waterpipe smoking, the age of inhaling was assumed to be the same as the age of first smoking a waterpipe.

**None of the differences are statistically significant.

HONC = Hooked on Nicotine Checklist; PD = Stages of Physical Dependence; ICD-10 ND = International Classification of Diseases, Nicotine Dependence (≥3 criteria).

Table 1.3 The median time interval between smoking milestones and the appearance of the first HONC symptom or ICD-10 is shown only for those subjects who had already experienced these outcomes at the baseline survey.

No. (%)	Interval	Months
114 (71.2)	From the first use of waterpipe to appearance of the first HONC symptom	10.9
61 (38.1)	From the first use of waterpipe to ICD-10	13.9
50 (90.9)	From smoking a whole waterpipe head to the appearance of the first HONC symptom	0.6
37 (67.3)	From smoking a whole waterpipe head to ICD-10	5.0

ICD-10= International Classification of Diseases Nicotine Dependence (≥3 criteria).

HONC = Hooked on Nicotine Checklist

Table 1.4 Percentage of waterpipe smokers endorsing each HONC symptom as the first symptom and the total percentage of waterpipe smokers endorsing each symptom (N=160).

HONC Symptom	**No. of participants endorsing this as their first symptom, (%)***	**Total No. of participants endorsing this symptom, (%)**
Have you ever had strong cravings to smoke?	40 (25.0)	59 (36.9)
Have you ever felt like you were addicted to smoking?	36 (22.5)	54 (33.8)
Have you ever felt like you really needed a waterpipe?	18 (11.2)	33 (20.6)
Is it hard to keep from smoking in places where you are not supposed to, like school?	3 (1.8)	11 (6.9)
Have you ever tried to quit smoking but could not do it?	23 (14.3)	40 (25.0)
Do you smoke now because it is really hard to quit?	5 (3.1)	19 (11.9)
Did you find it hard to concentrate because you could not smoke?	13 (8.1)	8 (5.0)
Did you feel more irritable because you could not smoke?	5 (3.1)	20 (12.5)
Did you feel a strong need or urge to smoke?	21 (13.1)	44 (27.5)
Did you feel nervous, restless or anxious because you could not smoke?	11 (6.8)	34 (21.3)

*Percentages do not add up to 100% because some participants experienced more than 1 symptom simultaneously.
HONC = Hooked on Nicotine Checklist

Table 1.5 Early experiences of adolescent waterpipe smokers according to waterpipe-specific dependence measures (SCTS-28 and LWDS-10J).

Syrian Center for Tobacco Studies (SCTS-28) *	**% of waterpipe smokers who endorsed each symptom**
Smoking waterpipe helps me to concentrate	53.1
Smoking waterpipe is a good way to reward myself	79.4
When I smoke waterpipe, I feel less irritable, frustrated, or angry	35.0
When I smoke waterpipe, I feel less sad, blue, or depressed	48.8
When I smoke waterpipe, I have less insomnia or trouble sleeping	43.8
I enjoy blowing waterpipe smoke from my mouth and nose and the feeling of inhaling waterpipe smoke into my mouth and lungs	60.0
I am confident that I can quit smoking waterpipe anytime I want	40.0
I spend too much money on waterpipe	91.9
Smoking waterpipe makes me feel sociable	30.0
Smoking waterpipe makes me feel happy	71.9
Just the sight or smell of waterpipe is enough to make me want to smoke	82.5
Smoking waterpipe makes me feel energetic	34.4
Most of my friends smoke waterpipe	65.6
I smoke waterpipe usually with friends or in cafés/restaurants	54.4
When I smoke waterpipe I usually share it with others	21.3
Even if I was sure that waterpipe is not good for my health, I would still smoke as often	78.8
It would be very difficult to me to be in a restaurant, and not smoke waterpipe	78.1
It would be difficult for me to refuse an invitation to smoke waterpipe	51.9
If I was with someone who objected to my waterpipe smoking, I would smoke it anyway	15.6
My favorite waterpipe is the one I smoke after having gone an extended period without smoking it	17.5
If the cost of waterpipe smoking doubled, I would still smoke as often	69.4
I always make sure I have an adequate supply of waterpipe materials (tobacco, coal, foil, etc.)	35.0
If my waterpipe smoking session was to get interrupted, I would be annoyed	40.6
If I could not smoke waterpipe for a while, I would have difficulty concentrating	80.6
I usually allocate a special time of the day for smoking waterpipe	71.3
If I could not smoke waterpipe for a while, I would feel an urge or craving to smoke	33.1
I want to quit smoking waterpipe	78.8
I have family or friends who would like me to quit smoking waterpipe	91.9
Lebanon Waterpipe Dependence Scale-10J (LWDS-10J)**	**% of waterpipe smokers who endorsed each symptom**
a. Psychosocial	
Do you smoke waterpipe to improve your morale?	65.6
Do you smoke waterpipe to please others?	64.4
b. Relaxation/pleasure	
Do you smoke waterpipe for pleasure?	36.9
Do you smoke waterpipe to relax your nerves?	47.5

c. Physical dependence	
Do you smoke waterpipe when you are seriously ill?	50.6
Do you smoke waterpipe alone?	30.0
Number of times you could stop waterpipe for more than 7 days At least once (vs. none)	50.0
What percentage of income would you spend on waterpipe smoking? ≤50% of monthly income (vs. >50% of monthly income)	98.8
Number of days you could spend without waterpipe >7 days (vs. ≤7 days)	82.5
Number of waterpipes you usually smoke per week <7 waterpipes/week (vs. ≥7 waterpipes/week)	94.4

*These items are specific to waterpipe use patterns and include aspects associated with dependence that are not captured by the LWDS-10J.

** Categories were collapsed due to small cell sizes

Manuscript 2 (published in *Drug and Alcohol Dependence*)

CORRELATES OF NICOTINE DEPENDENCE AMONG ADOLESCENT WATERPIPE SMOKERS

Abstract

Background

Waterpipe smoking is addictive and its use is increasing globally among youth, yet little is known about the factors associated with nicotine dependence (ND) among waterpipe smokers. We investigated the factors associated with ND symptoms among a sample of Lebanese adolescents who smoke waterpipe.

Methods

We collected data on factors potentially associated with ND (individual, socio-demographic, environmental, smoking patterns) among 160 current (past 30 days) waterpipe smokers recruited from 8th and 9th school grades in Lebanon. We assessed the loss of autonomy over tobacco using the Hooked on Nicotine Checklist (HONC), ND using the International Classification of Diseases, 10th revision (ICD-10), and the number of ND symptoms endorsed.

Results

Depressive symptoms, lower self-esteem, and having at least one sibling who smokes waterpipe were associated with the presence of ND symptoms, while enrollment in public schools, smoking waterpipe ≥30 minutes per session, and believing that cigarette smoking is harmful to health were associated with endorsement of a higher number of ND symptoms. Smoking a whole waterpipe head without sharing and being in 9th grade in this study were associated with the presence and endorsement of a higher number of ND symptoms.

Conclusions

We identified specific social and psychological characteristics, waterpipe smoking patterns, and beliefs about harmful effects of smoking associated with the presence of ND among adolescent

waterpipe smokers. Considering these factors when planning policies to prevent ND among waterpipe smokers is warranted.

Introduction

Use of waterpipe (narghile, shisha, hookah) has re-emerged in the global epidemic of tobacco smoking (Maziak et al., 2015). It is associated with adverse health outcomes such as impaired lung function, lung and esophageal cancers (Montazeri et al., 2015), coronary artery disease (Akl et al., 2010; El-Zaatariet et al., 2015), and nicotine dependence (Aboaziza & Eissenberg, 2015; Maziak, 2014; Maziak et al., 2004). In many Eastern Mediterranean countries, where waterpipe use is traditional, it has surpassed cigarettes as the most common tobacco use method among 13-15 year-old schoolchildren (Maziak et al., 2015; WHO, 2015). Alarmingly, tobacco smoking using a waterpipe is increasing among youth in other parts of the world where it is not traditional. For example, current (past 30 days) waterpipe tobacco smoking among US high school students has increased to the extent that its prevalence was similar to that of cigarette smoking (9.4% vs. 9.2%, respectively) by 2014 (Arrazola et al., 2015). Furthermore, many young waterpipe smokers are cigarette-naïve and at higher risk for initiation of cigarette smoking (Jaber et al., 2015a; Soneji et al., 2015). This waterpipe-to-cigarette transition may signal the appearance of nicotine dependence among waterpipe smokers who may find a craving for nicotine easier to satisfy using the easily accessible cigarette as compared to the stationary, less accessible waterpipe (Jaber et al., 2015a). Thus, preventing nicotine dependence among waterpipe smokers is an integral component for the overall success of tobacco control efforts worldwide.

Many youth are attracted to the social aspects of waterpipe and perceive it as a fashionable, safer alternative to cigarettes with a lower potential for addiction (Akl et al., 2013).

Contrary to this misperception, a growing body of research shows that waterpipe smokers are exposed to significant amounts of nicotine and experience symptoms of nicotine dependence similar to those among cigarette smokers such as drug seeking behavior, loss of control over waterpipe use, and difficulty quitting (Aboaziza & Eissenberg, 2015; Ward et al., 2005; Eissenberg & Shihadeh, 2009; Maziak et al., 2011). Moreover, evidence from the few studies that examined nicotine dependence among adult waterpipe smokers found that a higher frequency of waterpipe use (proxy of nicotine dependence) was associated with self-perception of being hooked on waterpipe and behavioral adaptations to support access to waterpipe including carrying/owning a waterpipe, and smoking mainly alone and at home (Maziak et al., 2004; Ward et al., 2007). Other studies that applied modified versions of the Lebanon Waterpipe Dependence Scale found that factors such as daily use, Arab ethnicity, age of initiation, length of smoking session, number of waterpipes owned, average sessions per week, and average waterpipe heads used per session were risk factors for nicotine dependence among waterpipe smokers (Primack et al., 2014; Kassim et al., 2014). However, some of these studies relied on participants' self-perception of being addicted to waterpipe (Maziak et al. 2004; Ward et al. 2007), while others applied nicotine dependence measures that may not be sensitive to nicotine dependence symptoms at low levels of tobacco use (Primack et al., 2014; Kassim et al., 2014), and no study so far has examined the factors associated with nicotine dependence among adolescent waterpipe smokers.

In the first report from the *Waterpipe Dependence among Lebanese Youth (WDLY)* study, we described the early symptoms of nicotine dependence among adolescent waterpipe smokers and showed that nicotine dependence symptoms can be experienced earlier among waterpipe smokers than cigarette smokers (Bahelah et al., 2016). Building on that work, the current study aims to identify factors associated with nicotine dependence among adolescent waterpipe smokers using baseline data from the WDLY. Such knowledge is important to identify youth at a

higher risk of becoming addicted to waterpipe and who can potentially benefit from early prevention and intervention strategies.

Methods

Participants and procedures

The WDLY is a cohort study of 498 adolescent smokers and non-smokers (mean± SD age at baseline for the whole sample =14.1±1.1 years) enrolled in 8th and 9th school grades from 4 regions in Lebanon (Beirut, Mount Lebanon, Nabatiye, South Lebanon) (Figure 1). Details about the study design and procedures can be found elsewhere (Bahelah et al., 2016). Briefly, among 178 schools with 8th and 9th grades from these 4 regions, 38 schools agreed to participate and provided private rooms on schools' premises to insure confidentiality of interviews. A brief, in-classroom, self-administered survey was distributed to all students who provided parental consents and their assent in order to determine eligibility. For smokers, those who smoked waterpipe or cigarettes, but not both, at least once during the past 30 days were eligible to participate. Because this report focuses on the factors associated with ND, only those who reported smoking waterpipe at baseline (N=160) were included in the analysis.

Data on waterpipe use patterns (Maziak et al., 2004, 2005; Primack et al., 2014), attitudes towards waterpipe (Hammal et al., 2008; Maziak et al., 2004; Ward et al., 2005), and the factors associated with nicotine dependence among adolescent smokers (Kleinjan et al., 2012; DiFranza et al., 2007a; Racicot et al., 2013; O'Loughlin et al., 2002) were obtained using a pilot-tested, interviewer-administered questionnaire. The questionnaire was translated into Arabic, and back translated to English for comparison and fine-tuning using standard methods (Brislin, 1970). Four techniques were used to improve recall of past events: decomposition, bounded recall, personal landmarks, and the depiction of these landmarks visually to create a personal calendar for each

student (DiFranza et al., 2007b; DiFranza et al., 2009). Students provided personal landmarks (e.g., birthday, entry into school) which were depicted on a calendar for each student to aid in recalling past events such as dates of smoking milestones (initiation of waterpipe smoking, smoking a whole waterpipe head without sharing) and appearance of nicotine dependence symptoms. The study protocol was approved by the institutional review boards of Florida International University and the American University of Beirut.

Measures

Explanatory variables

The selection of the factors potentially associated with nicotine dependence among adolescent waterpipe smokers was guided by the literature on nicotine dependence among adolescent smokers and waterpipe-specific use patterns. A description of these variables follows.

1) Smoking-related factors. Smoking milestones, average time spent during a waterpipe smoking session (<30 min, 30-60 min, >60 min), past month smoking frequency (did not smoke waterpipe in the past 30 days, smoked less than once a week, smoked at least once a week but not every day, smoked every day/almost every day), and quantity (number of waterpipes smoked in the past 30 days) were obtained. Students were also asked whether they had experienced any of several reactions the first time they inhaled from a waterpipe (felt relaxed, felt high/buzz sensation, experienced burning throat/bad taste). Beliefs and attitudes towards waterpipe were evaluated by asking students if they believe waterpipe smokers look more attractive than nonsmokers, have more friends, if waterpipe smoking makes a person lose weight, and if waterpipe smoking is harmful to health (Jaber et al., 2015b)

2) Socio-demographics and environmental factors. Socio-demographics include age, gender, school type (public, private), regular physical activity (at least once per week), school grade (8^{th}, 9^{th}), and years of education for each parent. Environmental factors include smoking by parents, siblings, close friends, and exposure to pro-tobacco advertisements (Kleinjan et al., 2012).

3) Psychological characteristics associated with nicotine dependence among youth were also measured (DiFranza et al., 2007a; Racicot et al., 2013; O'Loughlin et al., 2009).

1. *Stress* during the past 6 months was measured by a list of 15 life events that represent common stressors for adolescents (e.g., body weight, parental divorce) (Racicot et al., 2013; O'Loughlin et al., 2009). Students rated their stress level to each item on a four-point Likert scale (Not at all to A whole lot) with a total score of 0-45; higher scores indicate higher stress. Cronbach's alpha for the stress scale in this study was 0.79.
2. *Depressive symptoms* during the past 6 months were measured using a six-item Depressive Symptom Scale (DSS) on a four-point Likert scale (Never to Often) (Brunet et al., 2014), with a total score of 0-18. Higher score indicates more depressive symptoms. Cronbach's alpha for the DSS in this study was 0.75.
3. *Novelty seeking* was measured using nine items from Cloninger's Personality Questionnaire (DiFranza et al., 2007a) on a five-point Likert scale (Not at all true to Very true) with 0-36 total score. Higher score indicates higher novelty. Cronbach's alpha for the novelty seeking scale in this study was 0.76.
4. *Impulsivity* was measured using seven items on a five-point Likert scale (Not at all true to Very true) with 0-28 total score (DiFranza et al., 2007a), and higher score indicates higher impulsivity. Cronbach's alpha for the impulsivity scale in this study was 0.81.
5. *Distractibility* was measured using six items on a five-point Likert scale (Never to Always) with 0-24 total score (DiFranza et al., 2007a). Higher score indicates higher distractibility. Cronbach's alpha for the distractibility scale in this study was 0.63.
6. *Self-esteem* was measured using a ten-item Rosenberg's Self-Esteem Scale assessed on a four-point Likert scale (Strongly Disagree to Strongly Agree), with total score of 0-30 (Waters et al., 2006). Higher score indicates higher self-esteem. Cronbach's alpha for the self-esteem scale in this study was 0.79.

Outcome variables

Table 1 shows the 19 survey items used to measure the three outcomes in this study: the loss of autonomy, nicotine dependence, and the number of nicotine dependence items endorsed. Each item represents a symptom of nicotine dependence and was validated among adolescent smokers in previous studies (DiFranza et al., 2007a; O'Loughlin et al., 2002). Each item has Yes/No response option and a "Yes" response indicates endorsement of that item.

Smokers lose autonomy over tobacco when quitting requires an effort or involves discomfort. The loss of autonomy is an early indicator of developing nicotine dependence (DiFranza et al., 2007a; DiFranza et al., 2002), and can be measured using a 10-item Hooked on Nicotine Checklist (HONC). Endorsement of at least 1 HONC item indicates a loss of autonomy. HONC is a validated, sensitive indicator of symptoms of nicotine dependence presenting with infrequent tobacco use (DiFranza et al., 2002; Wheeler et al., 2004). HONC scores are computed by summing the number of symptoms endorsed (range 0–10) and its scores correlate with addiction-related changes in neural structures of smoker's brain (Huang et al., 2013).

Nicotine dependence was measured using the WHO's International Classification of Diseases – Tenth Revision (ICD-10). ICD-10 consists of 6 criteria of nicotine dependence and endorsement of at least 3 of these criteria over a 12-month period is required for the diagnosis of ICD-10 nicotine dependence (DiFranza et al., 2007a; O'Loughlin et al., 2002). Finally, we used the number of nicotine dependence items endorsed (from a total of 19 items shown in Table 1) as a proxy measure of the level of nicotine dependence among adolescent waterpipe smokers, in which a higher number of endorsed items indicates an advanced level of nicotine dependence (Apelberg et al., 2014; Caraballo et al., 2009).

Both the HONC and ICD-10 have shown acceptable internal consistency among waterpipe smokers in this cohort (Bahelah et al., 2016). We further tested the correlation among the HONC, ICD-10, and the number of nicotine dependence items endorsed in this study. The

third measure (number of nicotine dependence items endorsed) has an average inter-item correlation of 0.14 and an acceptable internal consistency as shown by Cronbach' alpha of 0.76 in this study.

Data analysis

Summary statistics were presented for categorical variables using frequencies/percentages, and mean ± standard deviation (SD) for continuous variables. At the bivariate level, associations among categorical variables were tested using chi-squared or Fisher Exact tests, while t-test (when normality was met) or Mann-Whitney *U*/Kruskal-Wallis tests (when normality was violated) were used to test group differences in continuous variables. We assessed the magnitude of association between the number of nicotine dependence items endorsed with ICD-10 and HONC separately using point-biserial Pearson correlation coefficient, while the magnitude of association between ICD-10 and HONC was assessed using Phi correlation coefficient.

All explanatory variables (smoking-related, socio-demographics, environmental, psychological characteristics) significant at $p<0.15$ in the bivariate models were entered into separate multivariable logistic regression models to identify the factors associated with the loss of autonomy (0=No, 1=Yes), and ICD-10 nicotine dependence (0=No, 1=Yes) (Bursac et al. 2008). Odds ratios (OR) with 95% confidence intervals (CI) were reported from these models. As the third outcome (number of nicotine dependence items endorsed) in this study is a count variable, multivariable Poisson regression model was used to identify the factors associated with this outcome, and regression parameters (*b*) with 95% CI were reported from this model (Coxe et al. 2009). We accounted for over-dispersion in the Poisson regression model and adjusted the standard errors of regression parameters by using "scale=Pearson" option in SAS 9.3 (SAS Institute Inc., NC; USA) (Lee et al. 2012). Age at baseline and gender were included in all models. We checked for multicollinearity among explanatory variables using the variance

inflation factor (VIF). All VIF values were less than 5 indicating multicollinearity did not affect our models (Nazar et al. 2015). All tests were two-tailed and the statistical significance was set at $p<0.05$.

Results

Sample characteristics

The sample for this study consisted of 160 current (past 30 days) waterpipe smokers, of whom 56.8% were girls. Overall, 71.2% endorsed ≥1 HONC item (i.e., lost autonomy), and 38.1% met ICD-10 criteria for nicotine dependence (endorsed ≥3 criteria). Table 1 presents the percentage of participants who endorsed each item of nicotine dependence used in this study.

Correlation among measures of nicotine dependence

All measures of nicotine dependence were positively correlated with one another. The number of nicotine dependence items endorsed correlated significantly with ICD-10 nicotine dependence (Point-biserial coefficient=0.74, $p<0.001$) and HONC (Point-biserial coefficient=0.61, $p<0.001$), while both ICD-10 nicotine dependence and HONC correlated well with one another (Phi coefficient=0.42, $p<0.001$).

Results from bivariate analyses

Table 2 presents bivariate associations between the explanatory variables and the 3 studied outcomes: loss of autonomy, nicotine dependence, and number of nicotine dependence items endorsed. There were no significant gender differences in the loss of autonomy ($p=0.44$), nicotine dependence ($p=0.91$), or number of nicotine dependence items endorsed ($p=0.92$). Although a higher proportion of participants who lost autonomy came from public schools ($p=0.01$), school type was not associated with either nicotine dependence ($p=0.15$) or number of nicotine dependence items endorsed ($p=0.08$). School grade was associated with nicotine dependence ($p=0.02$), number of nicotine dependence items endorsed ($p=0.01$), but not with loss of autonomy

(p=0.08). Those who lost autonomy had higher mean levels for stress, depression, distractibility, novelty seeking, impulsivity, and a lower mean score on self-esteem than those who did not lose autonomy (all p-values <0.05). Number of nicotine dependence items endorsed was positively associated with depression, distractibility, and novelty-seeking (all p-values <0.05). Waterpipe smoking by at least one parent or at least one sibling was associated with nicotine dependence (p=0.01), while having a favorite waterpipe advertisement was associated with the loss of autonomy (p=0.01) and number of nicotine dependence items endorsed (p=0.002). Believing that waterpipe smokers look more attractive and have more friends were positively associated with nicotine dependence and number of nicotine dependence items endorsed, while believing that waterpipe smoking is harmful to health was negatively associated with number of nicotine dependence items endorsed (all p-values <0.05). Smoking a whole waterpipe head without sharing, past month smoking frequency and number of waterpipes smoked, and average time during waterpipe smoking session were all associated with loss of autonomy, nicotine dependence, and number of nicotine dependence items endorsed (all p-values <0.05) (Table 2).

Results from multivariable analyses

Table 3 shows the results of separate multivariable logistic regression models for the factors associated with loss of autonomy and nicotine dependence, and table 4 shows the results of a multivariable Poisson regression model for the factors associated with the number of nicotine dependence items endorsed. Covariates included in all models were: age at baseline, gender, past month smoking quantity and frequency, age of smoking initiation, and the average time spent during a smoking session.

Factors associated with the loss of autonomy were enrollment in public schools (OR=2.8, 95% CI=1.1 - 7.5, p=0.03), regular physical activity (OR=8.6, 95% CI=2.6 - 28.3, p<0.001), depression (OR=1.2, 95% CI=1.1 - 1.3, p=0.02), smoking a whole waterpipe head without sharing (OR=5.8, 95% CI=1.6 - 21.1, p<0.007), smoking waterpipe for 30-60 minutes (OR=3.6,

95% CI=1.1 - 11.8, p=0.03) or >60 minutes (OR=7.1, 95% CI=1.4 - 34.7, p=0.01), and self-esteem (OR=0.8, 95% CI=0.7 - 0.9, p=0.03).

Ninth graders were more likely than eight graders to be nicotine dependence (OR=2.6, 95% CI=1.2 - 5.9, p=0.02). Other correlates of nicotine dependence included having at least one sibling who smokes waterpipe (OR=2.5, 95% CI=1.1 - 6.1, p=0.04), and smoking a whole waterpipe head without sharing (OR=4.6, 95% CI=2.0 - 10.7, p<0.001).

Endorsement of a higher number of nicotine dependence symptoms was associated with enrollment in public schools (*b*=0.22, 95% CI=0.01 - 0.44, p=0.04), being in 9th grade (*b*=0.31, 95% CI=0.09 - 0.53, p=0.005), smoking a whole waterpipe head without sharing (*b*=0.49, 95% CI=0.26 - 0.72, p<0.0001), smoking waterpipe for 30-60 minutes (*b*=0.30, 95% CI=0.02 - 0.57, p=0.03) or >60 minutes (*b*=0.36, 95% CI=0.05 - 0.68, p=0.02), and believing that cigarette smoking is harmful to health (*b*=0.28, 95% CI=0.02 - 0.54, p=0.03).

Generally, parameter estimates obtained from a Poisson regression reflect the change in the log-count of the outcome variable for a 1 unit change in the predictor, holding all other explanatory variables in the model constant (Hilbe, 2014). For example, attending public schools increases the log-count of endorsed nicotine dependence symptoms by 0.22 compared to private schools, holding all other variables constant. All other parameter estimates from Poisson regression in this study can be interpreted in the same way.

Discussion

This is the first study to examine the factors associated with nicotine dependence among adolescent waterpipe smokers using validated measures. Our results show that specific psychological characteristics (depressive symptoms, lower self-esteem), waterpipe-related use patterns (e.g., smoking a whole waterpipe head without sharing), believing that cigarette smoking is harmful to health, enrollment in public schools, and having at least one sibling who smokes

waterpipe were associated with nicotine dependence among waterpipe smokers. Furthermore, this study highlights two modifiable factors uniquely associated with nicotine dependence among adolescent waterpipe smokers: believing that cigarette smoking is harmful to health and longer smoking sessions of waterpipe. Collectively, these findings provide novel insights into the characteristics of young waterpipe smokers more likely to become addicted to waterpipe and identify specific areas that can be targeted for preventing nicotine dependence among waterpipe smokers. Incorporating educational materials on tobacco-related harm and addiction in school curricula, targeting those enrolled in public schools, and addressing waterpipe use by family members are strategies that can be implemented to prevent nicotine dependence among young waterpipe smokers.

The co-existence of certain psychological characteristics and symptoms of nicotine dependence among adolescent cigarette smokers has been well characterized (Kleinjan et al., 2012; DiFranza et al., 2007a; Racicot et al., 2013). In this study, we identified two such factors – depression and self-esteem – that were associated with the loss of autonomy among adolescent waterpipe smokers. Generally, self-esteem is an important psychological characteristic that can distinguish adolescent smokers from non-smokers (Guillon et al., 2007). Given the high prevalence of waterpipe use among youth in Lebanon and other Middle Eastern countries coupled with its prominent social aspect, adolescents with lower self-esteem may smoke waterpipe as a means to cope with their personal discontent and can get easily hooked on waterpipe. In fact, low self-esteem was a predictor of current (past 30 days) waterpipe smoking among a sample of male adolescents from Iran (mean age=16.7 years) (Karimy et al., 2013). Moreover; adolescents with low self-esteem usually have low refusal self-efficacy skills, which, in turn, predicts higher frequency of waterpipe use among adolescents (Jaber et al., 2015b) and the appearance of nicotine dependence.

Previous studies among adolescent cigarette smokers show that smokers report more depressive symptoms than nonsmokers (Goodman & Capitman, 2000), and depressive symptoms predict progression to regular smoking (Karp et al., 2006), and nicotine dependence (DiFranza et al., 2007a). In this study, adolescents with depressive symptoms have a higher risk of experiencing nicotine dependence symptoms. It is likely that adolescents with depression symptoms smoke waterpipe to alleviate the negative affective experiences associated with these symptoms. In fact, dealing with depressive symptoms was reported as one of the main motives for smoking waterpipe among Middle Eastern youth (Akl et al., 2013). The relationship between depression and nicotine dependence symptoms may arise as a result of a repeated exposure to waterpipe (i.e., self-medication) to cope with depressive symptoms which results in physiological adaptations that lead to the appearance of nicotine dependence (Pomerleau, 1995). On the other hand, genetic and environmental factors common to both depression and nicotine dependence symptoms were also proposed as the link between these two conditions (DiFranza et al., 2007a)

In Lebanon and other Middle Eastern countries, many young people view waterpipe as a symbol of cultural identity and smoke it for the first time with a family member (Afifi et al. 2013; Asfar et al. 2005). Specifically, previous studies among Middle Eastern youth showed that having a sibling who smokes waterpipe was a predictor of initiation (McKelvey et al., 2014) and higher use (Jaber et al. 2015b) of waterpipe. In line with these findings, waterpipe smokers in this study who have at least one sibling who smokes waterpipe were twice as likely to become addicted to waterpipe. As explained by the social learning model of nicotine dependence among adolescent cigarette smokers, imitation and social reinforcement (e.g., positive attitudes toward smoking) delineate the influence of siblings' smoking on nicotine dependence among adolescents (Hu et al., 2011). Moreover, findings from studies among adolescent cigarette smokers have shown that cigarette smoking among siblings can facilitate access to and continued use of cigarettes (Kandel et al., 2007; Doubeni et al., 2010), which determine the appearance of nicotine dependence

among adolescents (Kandel et al., 2007; Doubeni et al., 2010). These same theories can be applied to explain a higher risk of nicotine dependence among adolescent waterpipe smokers who have at least one sibling who smokes waterpipe. Another interesting finding in this study is that enrollment in public schools, as compared to private schools, was associated with loss of autonomy and endorsement of a higher number of nicotine dependence symptoms. This can be due to less tolerance to smoking in private schools that may enforce stricter rules against smoking by students and school personnel, which has been shown to prevent waterpipe smoking progression among a cohort of schoolchildren in Jordan (median age≈13 years at baseline) (Jaber et al., 2015b).

The global resurgence of waterpipe among youth can be attributed to a mistaken belief that waterpipe is less health-damaging and addictive than cigarettes (Maziak, 2014; Maziak et al., 2015; WHO, 2015). The predominantly intermittent smoking patterns of waterpipe and a presumed "filtering" effect of its smoke when it passes through a water bowl are the main drivers for this wrong belief (Maziak et al., 2015; Maziak, 2014; WHO, 2015). Of note, believing that waterpipe is less harmful and addictive than cigarettes was a predictor of current waterpipe use among youth (Sutfin et al., 2011; Eissenberg et al., 2008; Alzyoud et al., 2013). This study shows that adolescent waterpipe smokers who believed that cigarette smoking is harmful to health were more likely to endorse a higher number of nicotine dependence symptoms. Although not statistically significant, adolescents in this study who do not believe that waterpipe is harmful to health were more likely to endorse more nicotine dependence symptoms ($p=0.32$, data not shown). This finding is consistent with results from a cohort study of Canadian young waterpipe smokers (N=777, mean age=20 years at baseline) which found that those who smoke cigarettes infrequently were more likely to sustain waterpipe use 4 years later (Dugas et al., 2014). The lower harm perception of waterpipe tobacco smoking compared to cigarettes can lead to sustained use of waterpipe (Dugas et al., 2014) and endorsement of higher number of nicotine dependence

symptoms among young waterpipe smokers. This wrong perception is augmented, at a population level, by the societal acceptability of waterpipe use among youth, marketing strategies, and the lack of effective regulatory policies to prevent its use among youth.

Physical activity has been shown to protect against cigarette smoking in youth (Ali et al., 2015). Contrary to this observation, youth who were physically active were more likely to report smoking waterpipe than those who were not physically active (Primack et al., 2010). Moreover, higher physical activity was a predictor of initiation (McKelvey et al., 2014) and progression (Jaber et al., 2015b) on waterpipe smoking among a cohort of schoolchildren in Jordan (median age≈13 years at baseline). In line with these findings, our study shows that youth who are physically active are more likely to loss autonomy over waterpipe smoking. It is possible that youth who perform regular physical activity underestimate the harmful effects of waterpipe and are attracted to the social nature common to both waterpipe and physical activity (McKelvey et al., 2014).

This study highlights the importance of intensity and smoking patterns of waterpipe in the appearance of nicotine dependence symptoms among adolescents. Smoking a whole waterpipe head without sharing was the only factor associated with all 3 outcomes of this study (loss of autonomy, nicotine dependence, number of nicotine dependence items endorsed). Interestingly, the association between the duration of a smoking session and the number of nicotine dependence items endorsed was stronger for sessions that last over 60 min than those lasting 30-60 min, possibly reflecting a dose-response relationship. Longer smoking sessions expose smokers to higher doses of nicotine and this greater nicotine exposure can be associated with endorsement of a higher number of nicotine dependence symptoms. Findings from previous studies documented a positive correlation between the duration of waterpipe smoking session and the boost in plasma nicotine (the difference between pre-smoking and post-smoking nicotine plasma concentration) (Maziak et al., 2011; Eissenberg & Shihadeh, 2009). In addition, the

number of puffs on a waterpipe, which is greater during longer smoking sessions, correlate positively with the maximal plasma nicotine concentration in waterpipe smokers (Jacob et al., 2011). However, it is also possible that more addicted smokers require more nicotine resulting in longer smoking sessions which will be further investigated in our longitudinal study. One last observation is that the number of waterpipes smoked in the past 30 days was not associated with the presence of nicotine dependence among waterpipe smokers in this study. As tolerance to nicotine develops over time, adolescent waterpipe smokers may need to smoke greater number of waterpipes in order to achieve pleasurable effects and avoid withdrawal symptoms.

Limitations of this study include the possibility of recall errors of past events. To minimize this limitation, we employed four recall assistance methods to improve the recall of past events (DiFranza et al., 2007b; DiFranza et al., 2009). Another limitation is that some explanatory variables did not reach statistical significance perhaps as a result of a relatively small sample size. However, inclusion of the explanatory variables in our models was informed by a review of the important factors associated with nicotine dependence among adolescent smokers (Kleinjan et al., 2012; DiFranza et al., 2007a; Racicot et al., 2013). In addition, our ongoing study will have more power to detect significant differences as the sample size of youth who use waterpipe increases. Making causal inferences is limited by the cross-sectional nature of the study. Finally, our results may not be generalizable to adolescent waterpipe smokers from other countries and there is a need for additional research elsewhere (e.g., the U.S.) to continue to build this important body of knowledge. Despite these limitations, this exploratory study represents the first attempt to examine the factors associated with the presence of nicotine dependence among adolescent waterpipe smokers.

Conclusions

This study demonstrates that certain sociodemographic characteristics (public vs. private school attendance, being in 9th grade), psychological characteristics (depression and self-esteem), exposure to siblings' waterpipe use, and greater use of waterpipe (e.g., smoking a whole waterpipe head without sharing, longer duration of smoking sessions) are associated with nicotine dependence symptomatology among adolescent waterpipe smokers. Therefore, waterpipe prevention and intervention strategies may have greatest impact by educating youth about the harmful and addictive properties of waterpipe, teaching them positive coping skills, targeting those enrolled in public schools, and addressing waterpipe use by family members.

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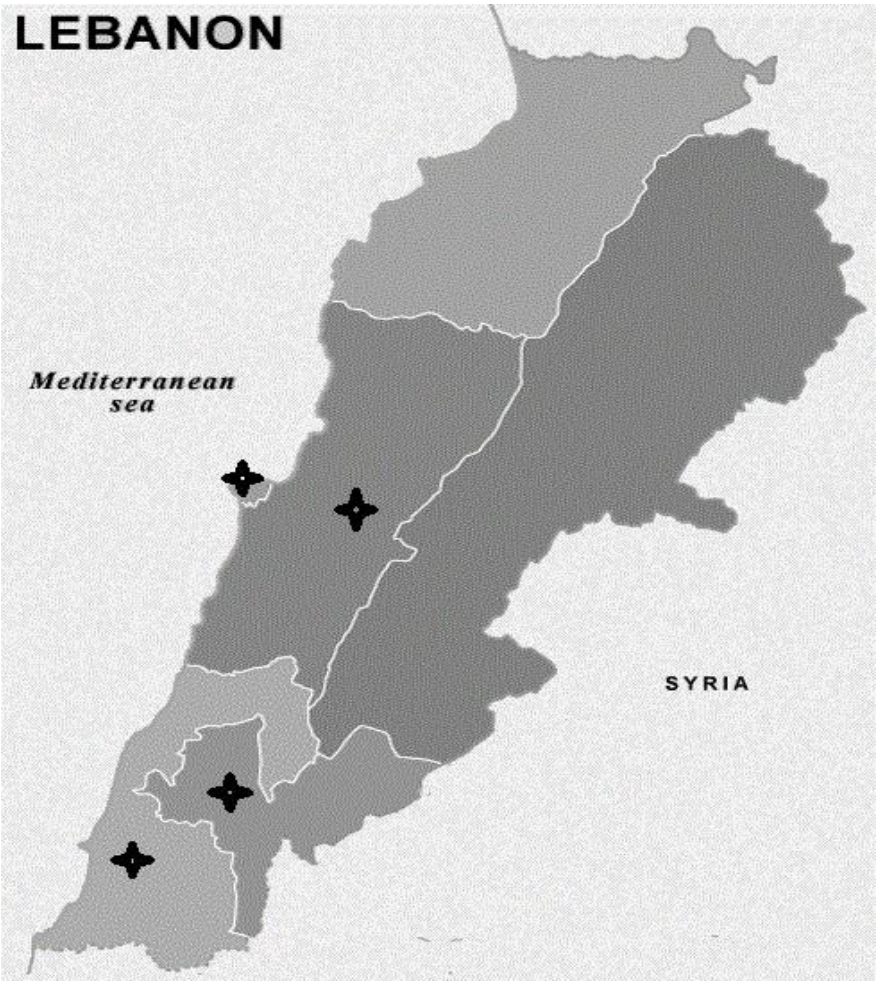

Figure 2.1. A map of Lebanon showing the four regions where study participants were recruited from.

Table 2.1 Survey items used to measure loss of autonomy and nicotine dependence among adolescent waterpipe smokers in Lebanon[ǂ]

Item		Number (%) of participants endorsing this item
1.	A strong desire or sense of compulsion to use tobacco* (4 items)	
	a. Have you ever had strong cravings to smoke waterpipe?[¶]	59 (36.9)
	b. Have you ever felt like you were addicted to waterpipe?[¶]	54 (33.8)
	c. Have you ever felt like you really needed a waterpipe?[¶]	33 (20.6)
	d. Is it hard to keep from smoking waterpipe in places where you are not supposed to, like school?[¶]	11 (6.9)
2.	Difficulties in controlling tobacco-taking behaviour in terms of its onset, termination, or levels of use* (3 items)	
	a. Have you ever tried to quit waterpipe smoking but could not do it?[¶]	40 (25.0)
	b. Do you smoke waterpipe now because it is really hard to quit?[¶]	19 (11.9)
	c. Are you smoking waterpipe more now than you planned to when you started?	72 (45.0)
3.	A physiological withdrawal state* (5 items)	
	When you have tried to stop smoking or when you have not been able to smoke…	
	a. Did you find it hard to concentrate because you could not smoke waterpipe?[¶]	8 (5.0)
	b. Did you feel more irritable because you could not smoke waterpipe?[¶]	20 (12.5)
	c. Did you feel a strong need or urge to smoke waterpipe?[¶]	44 (27.5)
	d. Did you feel nervous, restless, or anxious because you could not smoke waterpipe?[¶]	34 (21.3)
	e. Do you smoke waterpipe to avoid withdrawal symptoms?	18 (11.3)
4.	Evidence of tolerance* (2 items)	
	a. Do you find that you need to smoke waterpipe more often than you used to?	27 (16.9)
	b. Do you have to smoke waterpipe more often now to feel relaxed than you used to?	25 (15.6)
5.	Neglect of alternative pleasures* (4 items)	
	a. Do you find that you are spending more of your free time trying to get waterpipe?	53 (33.1)
	b. Have you cut down on your physical activities or sports because you smoke waterpipe?	30 (18.8)
	c. Do you ever give up going places or doing things because waterpipe smoking is not allowed?	17 (10.6)
	d. Have you stopped hanging out with certain friends because you smoke waterpipe?	4 (2.5)
6.	Use despite harm* (1 item)	
	a. Has a doctor or nurse told you that you should quit smoking waterpipe because it was damaging your health?	38 (23.8)

[ǂ]These survey items represent the 6 criteria of nicotine dependence based on the International Classification of Diseases-10th revision and include the 10 items of Hooked on Nicotine Checklist.
*The 6 criteria of nicotine dependence based on the International Classification of Diseases, 10-revision (ICD-10). Endorsement of any 1 item in a criterion (any 2 items in criterion 3) represents endorsement of that criterion, and the presence of ≥3 criteria over a 12-month period is needed for the diagnosis of nicotine dependence.
[¶]The 10 items of Hooked on Nicotine Checklist (HONC). Endorsement of any HONC item indicates that a smoker has lost autonomy over tobacco use.

Table 2.2 Bivariate associations between explanatory variables and the three studied outcomes: loss of autonomy, ICD-10 nicotine dependence, and number of nicotine dependence items endorsed

Explanatory variables	Loss of Autonomy*			ICD-10 Nicotine Dependence**			Number of nicotine dependence items endorsed ǂ	
	No (n=46), % or mean (SD)	Yes (n=114), % or mean (SD)	p-value	No (n=99), % or mean (SD)	Yes (n=61), % or mean (SD)	p-value	Correlation coefficient§	p-value
Socio-demographics								
Gender (% female)	52.2	58.8	0.44	56.6	57.4	0.91	0.01	0.92
Type of school (% public)¶	**41.3**	**63.2**	**0.01**	52.5	63.9	0.15	-0.14	0.08
School grade (% 9th)¶	39.1	55.3	0.08	**43.4**	**62.3**	**0.02**	**0.20**	**0.01**
School performance (below average)	10.8	10.5	0.86	11.1	9.8	0.46	0.03	0.72
Weekly allowance (% >20,000 LBP)	30.4	38.6	0.39	34.3	39.3	0.34	-0.02	0.78
Performing regular physical activity*	63.0	76.9	0.07	72.4	73.7	0.85	0.03	0.74
Father's years of education (% ≥12 years)	34.8	23.7	0.19	**32.3**	**18.0**	**0.04**	**-0.16**	**0.03**
Mother's years of education (% ≥12 years)	32.6	36.0	0.59	40.4	26.2	0.08	-0.11	0.15
Age at baseline	14.1 (1.2)	14.4 (1.3)	0.09	14.2 (1.2)	14.5 (1.3)	0.16	0.15	0.05
Psychological factors								
Stress¶	**6.9 (6.2)**	**9.5 (6.9)**	**0.03**	8.2 (6.0)	9.7 (8.0)	0.45	0.15	0.05
Depression¶	**5.6 (4.4)**	**8.9 (4.3)**	**<0.001**	7.6 (4.8)	8.5 (4.2)	0.25	**0.22**	**0.004**
Distractibility¶	**6.3 (3.5)**	**9.5 (5.0)**	**<0.001**	8.0 (4.3)	9.5 (5.4)	0.16	**0.21**	**0.01**
Novelty seeking¶	**12.6 (6.0)**	**16.1 (7.6)**	**0.007**	14.3 (6.7)	16.4 (8.1)	0.08	**0.21**	**0.005**
Impulsivity¶	**9.2 (5.5)**	**12.6 (7.0)**	**0.009**	11.5 (6.8)	11.9 (6.9)	0.72	0.13	0.10
Self-esteem¶	**22.9 (4.3)**	**20.8 (4.4)**	**0.01**	21.4 (4.7)	21.5 (4.1)	0.80	-0.08	0.29
Beliefs about smoking								
Waterpipe smokers look more attractive (% agree)¶	15.2	32.5	0.08	**19.2**	**40.9**	**0.01**	**0.21**	**0.01**
Waterpipe smokers have more friends (% agree) ¶	32.6	35.1	0.85	**24.2**	**50.8**	**0.006**	**0.24**	**0.002**
Waterpipe smoking makes a person lose weight (% agree)	6.5	12.3	0.52	11.1	9.8	0.96	0.02	0.83
Waterpipe smoking is harmful to health (% agree)	100.0	96.4	0.57	98.9	95.1	0.15	**-0.22**	**0.004**
Cigarette smokers look more attractive (% agree)	4.3	11.4	0.35	9.1	9.8	0.96	0.03	0.69
Cigarette smokers have more friends (% agree)	21.7	16.7	0.67	15.1	22.9	0.33	0.01	0.88
Cigarette smoking makes a person lose weight (% agree)	6.5	7.9	0.39	10.1	3.3	0.28	-0.05	0.50

Cigarette smoking is harmful to health (% agree)	95.6	100.0	0.08	97.9	100.0	0.52	0.11	0.15
Environmental factors								
Father and/or mother smokes waterpipe¶	60.8	47.4	0.16	**43.4**	**63.9**	**0.01**	0.06	0.40
One or more sibling smokes waterpipe¶	71.7	62.3	0.25	**57.6**	**77.0**	**0.01**	0.13	0.11
One or more close friend smokes waterpipe	89.1	93.9	0.30	91.9	93.4	0.72	0.13	0.10
Having a favorite waterpipe advertisement¶	**4.3**	**19.3**	**0.01**	11.1	21.3	0.08	**0.28**	**0.002**
Father and/or mother smokes cigarettes	67.4	77.2	0.19	72.7	77.0	0.54	0.04	0.58
One or more sibling smokes cigarettes	36.9	27.2	0.22	31.3	27.8	0.64	-0.02	0.74
One or more close friend smokes cigarettes	43.4	53.5	0.25	49.5	52.4	0.71	**0.18**	**0.02**
Having a favorite cigarette advertisement	4.3	8.8	0.51	7.1	8.2	0.76	0.14	0.08
Patterns of waterpipe use and reactions to first inhalation								
Average usual time during a waterpipe smoking session (% 30-60 minutes)	**15.5**	**47.4**	**<0.001**	**27.5**	**55.7**	**<0.001**	**0.51**	**<0.001**
Waterpipe smoking frequency in past 30 days (% smoked at least once a week but not everyday)	**26.1**	**42.1**	**0.003**	**32.3**	**45.9**	**<0.001**	**0.50**	**<0.001**
Number of waterpipes smoked in past 30 days¶	**4.6 (9.3)**	**12.8 (23.9)**	**0.002**	**6.1 (18.6)**	**17.5 (23.2)**	**0.008**	**0.52**	**<0.001**
Age first smoked waterpipe	12.9 (1.8)	12.8 (1.9)	0.89	12.8 (1.9)	13.0 (1.8)	0.47	-0.11	0.15
Ever smoked a whole waterpipe head without sharing¶	**10.8**	**43.8**	**<0.001**	**18.2**	**60.6**	**<0.001**	**0.52**	**<0.001**
Felt relaxed the first time inhaled tobacco smoke	31.5	39.6	0.59	31.8	46.4	0.21	0.13	0.28
Felt high or buzz the first time inhaled tobacco smoke	36.8	26.4	0.39	27.2	32.1	0.65	-0.02	0.87
Experienced coughing, burning throat, or bad taste the first time inhaled tobacco smoke	73.6	75.4	0.87	79.5	67.8	0.26	-0.08	0.46

*Loss of autonomy was measured by Hooked on Nicotine Checklist (HONC); endorsement of ≥1 HONC item indicates a loss of autonomy.

**Nicotine dependence (ICD-10 nicotine dependence) was measured by the 6 criteria of nicotine dependence of the International Classification of Diseases, 10th revision (ICD-10). Endorsement of ≥3 of these criteria over a 12-month period is needed for a diagnosis of ICD-10 nicotine dependence.

¶ p<0.05 indicated in bold. P-value was obtained from chi-squared or Fisher Exact tests (percentages); t-test, Mann-Whitney U, or Kruskal-Wallis tests (means).

§Spearman or Point biserial correlation coefficient

ǂThis measure has an average (SD) composite symptom count of 3.8 (3.1) and a range of 0-15.

Table 2.3 Odds Ratios (OR) and 95% confidence intervals (CI) of the significant factors associated with the loss of autonomy and ICD-10 nicotine dependence

	Loss of autonomy			ICD-10 Nicotine dependence		
Explanatory variables	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Type of school						
Private	Ref			--	--	--
Public	2.8	1.1 - 7.5	0.04			
School grade						
8th	--	--	--	Ref		
9th				2.6	1.2 - 5.9	0.01
Performing regular physical activity*				--	--	--
No	Ref					
Yes	8.6	2.6 - 28.3	0.004			
Depression	1.2	1.1 - 1.3	0.01	--	--	--
Self-esteem	0.8	0.7 - 0.9	0.04	--	--	--
Waterpipe smoking among siblings						
None/do not know	--	--	--	Ref	1.1 - 6.1	0.03
At least one				2.5		
Smoked a whole waterpipe head						
No	Ref			Ref		
Yes	5.8	1.6 - 21.1	0.02	4.6	2.0 - 10.7	0.001
Average usual time during a waterpipe smoking session						
<30 min	Ref					
30-60 min	3.6	1.1 - 11.8	0.02	--	--	--
>60 min	7.1	1.4 - 34.7	0.01			

*at least once/week
(--) Non-significant at $p<0.05$

Table 2.4 Regression parameters (*b*) and 95% confidence intervals (CI) of the significant factors associated with the number of nicotine dependence items endorsed

Explanatory variable	***b***	**95% CI**	**p-value**
Type of school			
Private	Ref		
Public	0.22	0.01 - 0.44	0.04
School grade			
8th	Ref		
9th	0.31	0.09 - 0.53	0.005
Smoked a whole waterpipe head			
No	Ref		
Yes	0.49	0.26 - 0.72	<0.001
Average usual time during a waterpipe smoking session			
<30 min	Ref		
30-60 min	0.30	0.02 - 0.57	0.03
>60 min	0.36	0.05 - 0.68	0.02
Cigarette smoking is harmful to health			
Disagree	Ref		
Agree	0.28	0.02 - 0.54	0.03

Manuscript 3 (Submitted and under review in *Nicotine & Tobacco Research*)

WATERPIPE SMOKING PATTERNS AND SYMPTOMS OF NICOTINE DEPENDENCE: THE WDLY STUDY

Abstract

Background

Waterpipe is typically intermittently smoked over long smoking sessions. Waterpipe is addictive and its users show symptoms of nicotine dependence (ND). This study examined the risk of developing ND symptoms across waterpipe use patterns among Lebanese youth.

Methods

Waterpipe use patterns (length of smoking session, smoking a whole waterpipe without sharing, past-30 day use frequency, and number of waterpipes smoked) were assessed. Symptoms of ND were assessed using the 10-item Hooked on Nicotine Checklist (HONC; endorsement of ≥1 symptom) and the 6 criteria of the International Classification of Diseases-10th revision (ICD-10 ND; presence of ≥3 criteria during 12 months).

Results

Both the proportion of participants endorsing ND symptoms and the average number of endorsed ND symptoms increased with increasing waterpipe use frequency, number of waterpipes smoked, and length of smoking session. The risk of endorsing ≥1 HONC symptom increased with increasing number of waterpipes smoked in the past 30-days (≥10 vs. <4 waterpipes; Hazard ratio (HR) =2.05, 95% CI: 1.52-2.58, p=0.007), and session length (>60 min vs. <30 min; HR=2.87, 95% CI: 2.83-2.91, p=0.001). The risk of attaining ICD-10 ND increased with increasing number of waterpipes used in the past 30-days (≥10 vs. <4 waterpipes; HR=2.56, 95% CI: 1.89-3.22, p=0.006), and smoking every day/almost every day vs. less than once weekly (HR=2.86, 95% CI: 2.12-3.60, p=0.007).

Conclusions

Increasing use frequency, number of waterpipes smoked, and longer smoking sessions were associated with higher risk of ND. The length of smoking session emerged as a novel indicator of ND among waterpipe smokers.

Introduction

Waterpipe use has emerged as a new strain of the global tobacco epidemic, mainly affecting youth (WHO, 2015). In many Eastern Mediterranean countries, waterpipe has exceeded cigarettes as the most common tobacco used among youth (WHO, 2015). Waterpipe users are exposed to the same toxic chemicals found in cigarettes, such as polycyclic aromatic hydrocarbons, carbon monoxide, and nicotine (Eissenberg & Shihadeh, 2009). Many waterpipe users suffer from smoking-related health problems such as lung cancer, cardio-respiratory illnesses (El-Zaatari et al., 2015), and nicotine dependence (ND) (Aboaziza & Eissenberg, 2015). In contrast to cigarettes, waterpipe consists of different components (head, body, water bowl, hose), being less accessible (Maziak et al., 2015), and is usually smoked intermittently over smoking sessions that can last ≥60 minutes (Sidani et al., 2016). During these long smoking sessions, waterpipe smokers inhale approximately 50-80 L of tobacco smoke compared with 0.5-0.8 L from smoking a single cigarette (Eissenberg, 2013). Moreover, the time spent during a single smoking session and total volume of inhaled nicotine-containing tobacco smoke correlate positively with plasma nicotine levels (Maziak et al., 2011). Thus, the buildup of high levels of plasma nicotine over long smoking sessions may explain why waterpipe smokers take more time, compared with cigarette smokers, to experience abstinence-induced withdrawal/craving symptoms (Cobb et al., 2011; Rastam et al., 2011).

Waterpipe smoking patterns may influence ND symptoms differently than cigarettes (Aboaziza & Eissenberg, 2015). Few studies have examined the association between use patterns and ND symptoms among waterpipe smokers and these studies suffer from considerable drawbacks. For example, some studies failed to control for important factors related to ND (e.g., use of cigarettes/other tobacco) (Primack et al., 2014; Kassim et al., 2014), while others applied cigarette-based measures of ND that may not be applicable to waterpipe-specific use patterns (Kassim et al., 2014; Sidani et al., 2016).

The available evidence from the cigarette literature shows that smoking frequency (number of smoking days per month) and amount (number of cigarettes used on the days smoked) play a role in the development of ND symptoms among adolescent smokers (Caraballo et al., 2009; O'Loughlin et al., 2003; Lessov-Schlaggar et al., 2008). Moreover, there is a widespread assumption among young people that by being less frequently smoked the waterpipe is less addictive than cigarettes (Jawad et al., 2013). Interestingly, waterpipe smokers do not seem to be a homogeneous group (Ward et al., 2007). Waterpipe is characterized by intermittent use patterns; nonetheless, daily use is more common among older smokers. Older smokers are also less willing to quit waterpipe and have lower prevalence of current (past 30-day) cigarette smoking compared to younger waterpipe smokers (Asfar et al., 2005). Indeed, this difference in smoking patterns between younger and older waterpipe smokers underscores the need for targeted interventions and that "one-size-fits-all" strategies may not be effective.

Using baseline data from the *Waterpipe Dependence in Lebanese Youth* (WDLY) study, we showed that smoking a whole waterpipe without sharing and the length of a smoking session were among the factors strongly associated with ND (Bahelah et al., 2016). The current study aims to examine whether the proportion of smokers reporting ND symptoms and average number of endorsed ND symptoms increase with increasing waterpipe use frequency, intensity, and length of smoking session. It also aims to examine if the risk of reporting the first ND symptom

and the full syndrome of ND differs by waterpipe use frequency, intensity, and length of smoking session. Findings from this study will facilitate the understanding of the contribution of waterpipe use patterns to the development of ND, and help identify waterpipe smokers who are more likely to develop ND for targeted interventions.

Methods

Participants

The sample for this study consists of 160 current waterpipe smokers recruited at baseline from the WDLY study. WDLY is a cohort study of 498 adolescent smokers and never smokers (mean± SD age at baseline for the whole sample =14.1±1.1 years) enrolled in 8th and 9th school grades from 4 regions in Lebanon (Beirut, Mount Lebanon, Nabatiye, South Lebanon). Inclusion criteria were evaluated using in-class, self-administered questionnaires. Never smokers who had the intention to initiate smoking and those who smoked either waterpipe or cigarettes, but not both, in the past 30 days were eligible to participate. Refusal to provide consent by parents or assent by participants, dual use of waterpipe and cigarettes, and not intending to initiate smoking were exclusion criteria. More details about the WDLY study can be found elsewhere (Bahelah et al., 2016).

Procedures

Using interviewer-administered questionnaires, participants provided information about their tobacco use patterns and responded to measures of ND validated among adolescent smokers (Bahelah et al., 2016; DiFranza et al., 2007). Interviewers met participants individually in private rooms on school premises and school personnel were not allowed during interviews to minimize social-desirability bias. During interviews, participants provided exact dates for first developing important milestones that include smoking a whole waterpipe without sharing, endorsement of ND symptoms from the Hooked on Nicotine Checklist (HONC), and the criteria of ND using the

International Classification of Diseases-10th revision (ICD-10 ND). Recall of the dates of these milestones was facilitated by the use of 4 techniques proved to improve recall of past events: decomposition, bounded recall, personal landmarks, and the depiction of these landmarks visually to create a personal calendar for each student (Bahelah et al., 2016; DiFranza et al., 2007). However, if the exact date could not be recalled, we recorded the 7th for events in the beginning of the month, the 14th for middle of the month, and the 21st for events toward the end of the month (Bahelah et al., 2016). The study protocol was approved by the institutional review boards of Florida International University and the American University of Beirut.

Measures

Selection of smoking patterns and important covariates in this study was guided by a review of the factors associated with ND among adolescent smokers (Kleinjan et al., 2012; Racicot et al., 2013) and symptoms of ND among waterpipe smokers (Bahelah et al., 2016; Maziak et al., 2005). Smoking patterns assessed in this study were: (a) *Past 30-day use frequency* (smoked waterpipe less than once a week, smoked at least once a week but not every day, smoked every day/almost every day), (b) *Past 30-day number of waterpipes smoked* (divided into 3 categories: <4, 4-9, and ≥10), (c) *Usual length of a waterpipe smoking session* (<30 min, 30-60 min, >60 min), and (d) *Ever smoking a whole waterpipe without sharing* (yes, no).

Outcomes assessed were the loss of autonomy and ND. Loss of autonomy is a useful concept to describe the onset of ND, especially among adolescent smokers (DiFranza et al., 2007). Endorsement of at least one among the 10 HONC items is an acceptable approach to detect smokers who have "lost autonomy" over tobacco. Loss of autonomy implies that physical or psychological sequelae of tobacco use present a barrier to quitting (DiFranza et al., 2007). The HONC is sensitive to ND symptoms at low levels of use (DiFranza et al., 2007). Presence of ≥3 among the 6 ICD-10 criteria were used to make a diagnosis of ND (O'Loughlin et al., 2002). We chose the HONC and ICD-10 to assess ND in this study because these two measures do not

include any item on tobacco use frequency, making them suitable for assessing ND regardless of the tobacco product. Both the HONC and the ICD-10 were pilot-tested and translated into Arabic, the official language in Lebanon, with back translation into English for comparison and fine-tuning following standard methods (Brislin, 1970).

Statistical analysis

We compared the proportion of participants who lost autonomy (≥1 HONC) or developed ICD-10 ND (≥3 ICD-10 criteria) in relation to smoking patterns using Mantel-Haenszel test for linear trend. We also compared the average number of endorsed HONC items and ICD-10 ND criteria in relation to smoking patterns using Mann-Whitney *U* or Kruskal-Wallis tests as appropriate. Time interval (in months) between smoking initiation and experiencing the 1st HONC symptom or attaining the 3rd criterion of ICD-10 ND was obtained by subtracting the date of smoking initiation from the date when the 1st HONC symptom or 3rd criterion of ICD-10 ND were endorsed.

Time-to-event intervals were plotted using Kaplan-Meier survival curves stratified by smoking patterns (past 30-day smoking frequency, past 30-day number of waterpipes smoked, smoking a whole waterpipe without sharing, usual length of smoking session). Because the proportional hazards assumption was violated in this sample, a Weighted Cox regression model (Kohl et al., 2015) was applied to test the hazards of experiencing the 1st HONC symptom or attaining ICD-10 ND diagnosis across levels of each waterpipe use pattern. Covariates included in all models were gender, age at baseline, age at smoking initiation, school type, depression, self-esteem, and waterpipe smoking among siblings. Analyses accounted for clustering of students within schools using SAS 9.3 (SAS Institute Inc., Cary, NC, USA). All statistical tests were two-tailed and statistical significance was set at $p<0.05$.

Results

Among 160 current waterpipe smokers, 46.9% smoked less than once per week, 37.5% smoked weekly but not every day, and 15.6% smoked every day/almost every day. In terms of the number of waterpipes smoked in the past 30 days, 45.9% smoked <4, 27.7% smoked 4-9, and 26.4% smoked ≥10. Almost half (47.8%) of participants usually smoke waterpipe for <30 min, 38.4% for 30-60 min, and 13.8% for >60 min. Finally, 34.4% participants ever smoked a whole waterpipe without sharing.

Bivariate associations between waterpipe use patterns and loss of autonomy/ICD-10 ND

Table 1 presents the proportion of participants who lost autonomy and met ICD-10 ND across levels of each waterpipe use pattern. Overall, the proportion of participants who lost autonomy and who had an ICD-10 ND diagnosis increased with increasing levels of waterpipe use. For example, a loss of autonomy was present in 57.3% of those who smoked waterpipe less than once a week, in 80% with weekly use, and in 88% with daily use. For these same use levels, ICD-10 ND was present in 18.7%, 46.7% and 76%, respectively. Also shown in table 1 are the average number of endorsed HONC symptoms and ICD-10 ND criteria by waterpipe use patterns. Similarly, a consistent pattern was observed with the average number of endorsed HONC symptoms and ICD-10 ND criteria increasing as a function of smoking frequency/number of waterpipes smoked, longer smoking sessions, and ever smoking a whole waterpipe without sharing (Table 1).

Kaplan-Meier survival curves for the loss of autonomy and ICD-10 ND

Several Kaplan-Meier curves were plotted to show the time (in months) from initiating waterpipe use till reaching the first HONC symptom (loss of autonomy, figure 1) or attaining ICD-10 ND (figure 2) stratified by the 4 studied use patterns. There were no statistical differences in time to reaching the first HONC symptom between those who smoked a whole waterpipe without sharing and those who did not (Logrank p=0.26, figure 1-A,). Time to reaching the first

HONC symptom was significantly different by length of smoking session (Logrank p=0.04, figure 1-B), past 30-day smoking frequency (Logrank p=0.04, figure 1-C), and past 30-day waterpipes smoked (Logrank p=0.03, figure 1-D).

Time to meeting ICD-10 ND was significantly different in relation to smoking a whole waterpipe without sharing (Logrank p=0.002, figure 2-A), length of smoking session (Logrank p=0.01, figure 2-B), past 30-day smoking frequency (Logrank p=0.001, figure 2-C), and past 30-day number of waterpipes smoked (Logrank p<0.001, figure 2-D).

Weighted Cox regression hazards models

Table 2 shows unadjusted and adjusted hazard ratios (HR) from Cox regression models with time to the loss of autonomy and time to ICD-10 ND since initiating waterpipe use as outcomes (both in months). In the unadjusted models, smoking ≥10 waterpipes, smoking waterpipe for 30-60 min, and smoking every day/almost every day were associated with higher hazards for both the loss of autonomy and meeting ICD-10 ND criteria. Ever smoking a whole waterpipe without sharing was associated with higher hazards of meeting ICD-10 ND (Table 2).

Results from adjusted model for the loss of autonomy show that smoking ≥10 waterpipes in the past 30-days was associated with higher hazards for the loss of autonomy compared with smoking <4 waterpipes (HR=2.05, p=0.007). Smoking waterpipe for >60 minutes was associated with higher hazards for the loss of autonomy compared with smoking waterpipe <30 minutes (HR=2.87, p=0.001). Results from adjusted Cox regression model for ICD-10 ND show that smoking waterpipe every day/almost every day was associated with higher hazards of meeting ICD-10 ND relative to smoking waterpipe less than once a week (HR=2.87, p=0.007). Finally, smoking ≥10 waterpipes in the past 30-days was associated with higher hazards of meeting ICD-10 ND compared with smoking <4 waterpipes (HR=2.56, p=0.006).

Discussion

This study is the first to systematically examine the association between waterpipe-specific use patterns and ND symptoms using validated measures of ND among adolescent smokers. This study shows that higher use frequency of waterpipe, increasing number of waterpipes smoked, and longer smoking sessions were associated with a higher risk of attaining ND symptoms, and can be targeted for prevention interventions. Additionally, the length of smoking session emerged as a novel indicator, easy-to-use, single item measure of ND symptoms among adolescent waterpipe smokers.

Although research on symptomatology and factors associated with ND has typically focused on cigarettes (Fagerström & Eissenberg, 2012), tobacco smoking using a waterpipe is addictive and its use is increasing globally among youth (Aboaziza & Eissenberg, 2015; Maziak et al., 2015). Similar to cigarettes, waterpipe users experience abstinence-induced withdrawal symptoms that are relieved by subsequent waterpipe use (Aboaziza & Eissenberg, 2015). However, waterpipe has unique features and use patterns that can influence the development of ND in a way different than cigarettes. For example, waterpipe consists of multiple components (head, body, bowl, hose) which make it less mobile and accessible than cigarettes, and thus mainly intermittently smoked (Maziak et al., 2005). As waterpipe is characterized by intermittent smoking patterns and is misperceived as less addictive than cigarettes, many waterpipe smokers show little interest in quitting (Ward et al., 2005, 2015). Another typical use pattern of waterpipe is its long smoking sessions during which smokers inhale about 1.7 times the amount of nicotine obtained from smoking a single cigarette (Eissenberg & Shihadeh, 2009). So while less accessibility and intermittent smoking might reduce the exposure to nicotine, the length of a smoking session can play an important role in exposure to higher doses of nicotine and emergence of ND symptoms among waterpipe smokers.

In line with these unique use patterns of waterpipe, several observations have emerged in this study and deserve further discussion. First, although waterpipe is typically intermittently smoked, those with higher levels of ND may need to smoke more frequently to satisfy craving for nicotine and thus progress to daily smoking. Higher use frequency also may imply more accessibility to waterpipe among youth who can smoke it either at home or have the financial means to smoke it at a waterpipe café. Our ongoing longitudinal study provides a unique opportunity to examine the association among accessibility, progression on waterpipe tobacco smoking, and appearance of ND symptoms. Second, the risk of attaining ICD-10 ND increased with increasing number of waterpipes smoked. This observation is consistent with findings from a study among young adult men (mean age=29.5 years, 58% Arabs) in the UK in which ND scores, measured by the Lebanon Waterpipe Dependence Scale, increased in dose-response fashion with increasing number of waterpipes smoked per week (Kassim et al., 2014). Third, this study shows that the risk of developing early symptoms of ND increased in relation to the length of a smoking session. As waterpipe is less accessible and thus smoked less frequently, the length of a smoking session becomes an essential parameter of exposure to nicotine and developing ND symptoms among warterpipe smokers. During these long sessions, waterpipe smokers inhale doses of nicotine sufficient for developing symptoms of ND especially among adolescent smokers (Primack et al., 2016).

The development and trajectories of ND have been explained using different theories. One of such theories that can provide a relevant model for explaining the onset and trajectories of ND among waterpipe smokers is the *Sensitization-Homeostasis Theory*. This theory holds that withdrawal symptoms can appear during infrequent tobacco use and defines the latency to withdrawal as the time interval between finishing smoking and the onset of withdrawal symptoms (DiFranza & Ursprung, 2008). Moreover, as tolerance develops, smokers find that their latency to withdrawal shortens and they must smoke more frequently to keep withdrawal symptoms at bay

(DiFranza, 2015). This physiological phenomenon explains why ND measures correlate moderately with measures of the frequency of tobacco use. The observation that two measures of ND were related to multiple patterns of waterpipe use in this study extends prior observations for cigarette smoking to the waterpipe. A study of adolescent cigarette smokers demonstrated that ND symptoms and smoking frequency increased in a mutually reinforcing upward spiral (Doubeni et al., 2010). The observed increase in the number of HONC and ICD-10 symptoms in relation to multiple patterns of waterpipe use in this study is consistent with the picture of a mutually reinforcing spiral. As the latency to withdrawal shortens, addicted smokers must smoke more frequently, and more frequent exposures to nicotine contribute to the development of more advanced symptoms of ND. This can be true for waterpipe smokers as it is for cigarette smokers, despite the less frequent use patterns associated with waterpipe smoking. As observed in this study, an ICD-10 diagnosis of ND could be made in nearly half (47%) of youths who smoked at least once per week, but not daily, and eighty percent of weekly users had experienced a loss of autonomy (table 1). The temporality among ND symptoms and waterpipe use patterns can be further investigated in our longitudinal study.

This study has limitations. Recall errors of past events is possible. We minimized this limitation by the use of four recall assistance methods to maximize recall accuracy of past events (DiFranza et al., 2007). Another limitation is that some variables in the weighted Cox regression model did not reach statistical significance perhaps as a result of a relatively small sample size. This study will have more power as the sample size of smokers will likely increase during follow up. Finally, smoking status and ND symptoms were self-reported and no biochemical tests (e.g., cotinine) were used. Generally, self-reports of smoking status and ND symptoms among adolescents are valid (O'Loughlin et al., 2003). In spite of these limitations, this study is the first to examine smoking patterns and their association with the development of ND symptoms among adolescent waterpipe smokers. The observed associations with multiple measures of tobacco use

provide evidence for the concurrent validity of the HONC and ICD-10 criteria for use among adolescent waterpipe smokers. The use of two validated measures of ND is one of the strengths of this study.

Conclusions

In summary, these findings highlight the association between waterpipe-specific use patterns and the development of ND symptoms among waterpipe smokers. These findings also suggest that it might be helpful to adapt current guidelines derived from the cigarette literature to address some unique use patterns of the waterpipe. Specifically, the length of a smoking session emerged as a novel marker of ND that can be considered in future psychometric work to refine instruments of ND among adolescent waterpipe users, and as an easy-to-assess, single item measure of ND in clinical practice (e.g., by pediatricians and substance use counselors).

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Table 3.1 Proportion of participants who lost autonomy and met criteria of nicotine dependence and the average number of endorsed Hooked on Nicotine Checklist (HONC) symptoms and criteria of nicotine dependence by waterpipe use patterns

Waterpipe use pattern	Lost autonomy n (%)	Mean number of HONC symptoms Mean (SD)	Nicotine dependent n (%)	Mean number of nicotine dependence criteria Mean (SD)
Smoking frequency in past 30 days				
Smoked less than once a week	43 (57.3)[a]	1.2 (1.4)[d]	14 (18.7)[a]	1.4 (1.4)[d]
Smoked at least once a week but not every day	48 (80.0)[a]	2.3 (2.1)[d]	28 (46.7)[a]	2.7 (1.5)[d]
Smoked every day or almost every day	22 (88.0)[a]	3.7 (2.4)[d]	19 (76.0)[a]	3.4 (1.2)[d]
Number of waterpipes smoked in past 30 days				
<4	43 (58.9)[a]	1.2 (1.3)[d]	14 (19.2)[a]	1.5 (1.4)[d]
4-9	32 (72.7)[a]	2.0 (1.9)[d]	16 (36.4)[a]	2.3 (1.5)[d]
≥10	38 (90.5)[a]	3.5 (2.4)[d]	31 (73.8)[a]	3.5 (1.3)[d]
Usual length of a waterpipe smoking session				
<30 min	41 (53.9)[a]	1.0 (1.3)[d]	16 (21.1)[a]	1.5 (1.4)[d]
30-60 min	53 (86.9)[a]	2.9 (2.1)[d]	34 (55.7)[a]	2.9 (1.6)[d]
>60 min	19 (86.4)[a]	3.0 (2.6)[d]	11 (50.0)[a]	2.8 (1.1)[d]
Smoked a whole waterpipe head without sharing				
No	64 (61.0)[e]	1.3 (1.6)[h]	24 (22.9)[e]	1.6 (1.4)[h]
Yes	49 (89.1)[e]	3.3 (2.3)[h]	37 (67.3)[e]	3.3 (1.5)[h]

[a] $p<0.01$ using the Mantel-Haenszel linear-by-linear association test (for linear trend)
[d] $p<0.001$ using Kruskal-Wallis test
[e] $p<0.01$ using Person Chi-Square test
[h] $p<0.001$ using Mann-Whitney U test
Loss of autonomy was defined as endorsement of ≥1 Hooked on Nicotine Checklist (HONC) symptom, and nicotine dependence was defined as the presence of ≥3 criteria of the International Classification of Diseases-10th revision (ICD-10 ND) over a 12-month period.

Table 3.2 Results of Weighted Cox regression models for the loss of autonomy and nicotine dependence by waterpipe use patterns

	Loss of autonomy				**Nicotine dependence**			
	Unadjusted HR (95% CI)	**p-value**	**Adjusted HR* (95% CI)**	**p-value**	**Unadjusted HR (95% CI)**	**p-value**	**Adjusted HR* (95% CI)**	**p-value**
Smoking frequency in past 30 days								
Smoked less than once a week	Ref		Ref		Ref		Ref	
Smoked at least once a week but not every day	1.21 (0.79-1.83)	0.36	0.79 (0.45-1.14)	0.19	**2.13 (1.12-4.04)**	**0.02**	1.00 (0.49-1.51)	0.98
Smoked every day or almost every day	**1.95 (1.15-3.29)**	**0.01**	1.73 (1.10-2.35)	0.08	**3.75 (1.87-7.51)**	**0.0002**	**2.86 (2.12-3.60)**	**0.007**
Number of waterpipes smoked in past 30 days								
<4	Ref		Ref		Ref		Ref	
4-9	1.05 (0.60-1.51)	0.83	1.03 (0.65-1.40)	0.87	1.60 (0.78-3.29)	0.19	1.25 (0.43-2.07)	0.58
≥10	**1.72 (1.45-2.47)**	**0.02**	**2.05 (1.52-2.58)**	**0.007**	**3.45 (1.83-6.50)**	**0.0001**	**2.56 (1.89-3.22)**	**0.006**
Usual length of a waterpipe smoking session								
<30 min	Ref		Ref		Ref		Ref	
30-60 min	**1.62 (1.07-2.44)**	**0.02**	1.13 (0.74-1.52)	0.53	**2.35 (1.29-4.28)**	**0.005**	1.36 (0.53-2.18)	0.44
>60 min	1.03 (0.55-1.69)	0.90	**2.87 (2.83-2.91)**	**0.001**	1.18 (0.38-1.85)	0.66	1.34 (0.47-2.20)	0.51
Smoked a whole waterpipe head without sharing								
No	Ref		Ref		Ref		Ref	
Yes	1.24 (0.55-1.17)	0.26	1.36 (0.55-2.16)	0.44	**2.15 (1.32-2.18)**	**0.004**	1.79 (0.98-2.59)	0.07

*Adjusted for school type, depression, self-esteem, gender, age at baseline, age at smoking initiation, waterpipe smoking among siblings
Bold indicates $p<0.05$
Loss of autonomy was defined as endorsement of ≥1 Hooked on Nicotine Checklist (HONC) symptom, while nicotine dependence was defined as the presence of ≥3 criteria of the International Classification of Diseases-10th revision (ICD-10 ND) over a 12-month period.

Figure 3.1 Kaplan-Meier survival curves for time to the loss of autonomy (in months, X-axis) and survival probability (Y-axis) by: (A) smoking a whole waterpipe without sharing, (B) length of smoking session, (C) past 30-day smoking frequency, and (D) past 30-day number of waterpipes smoked.

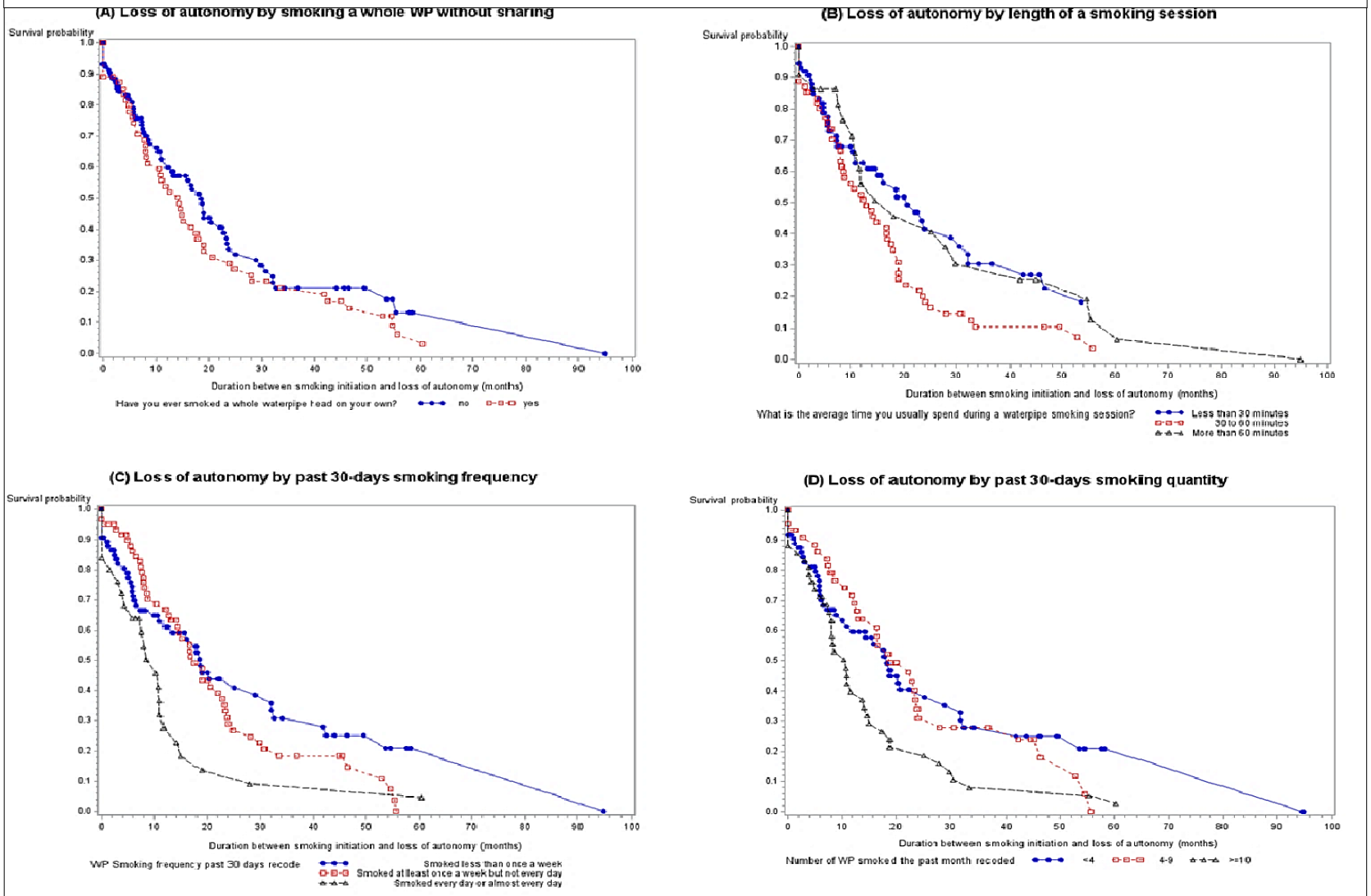
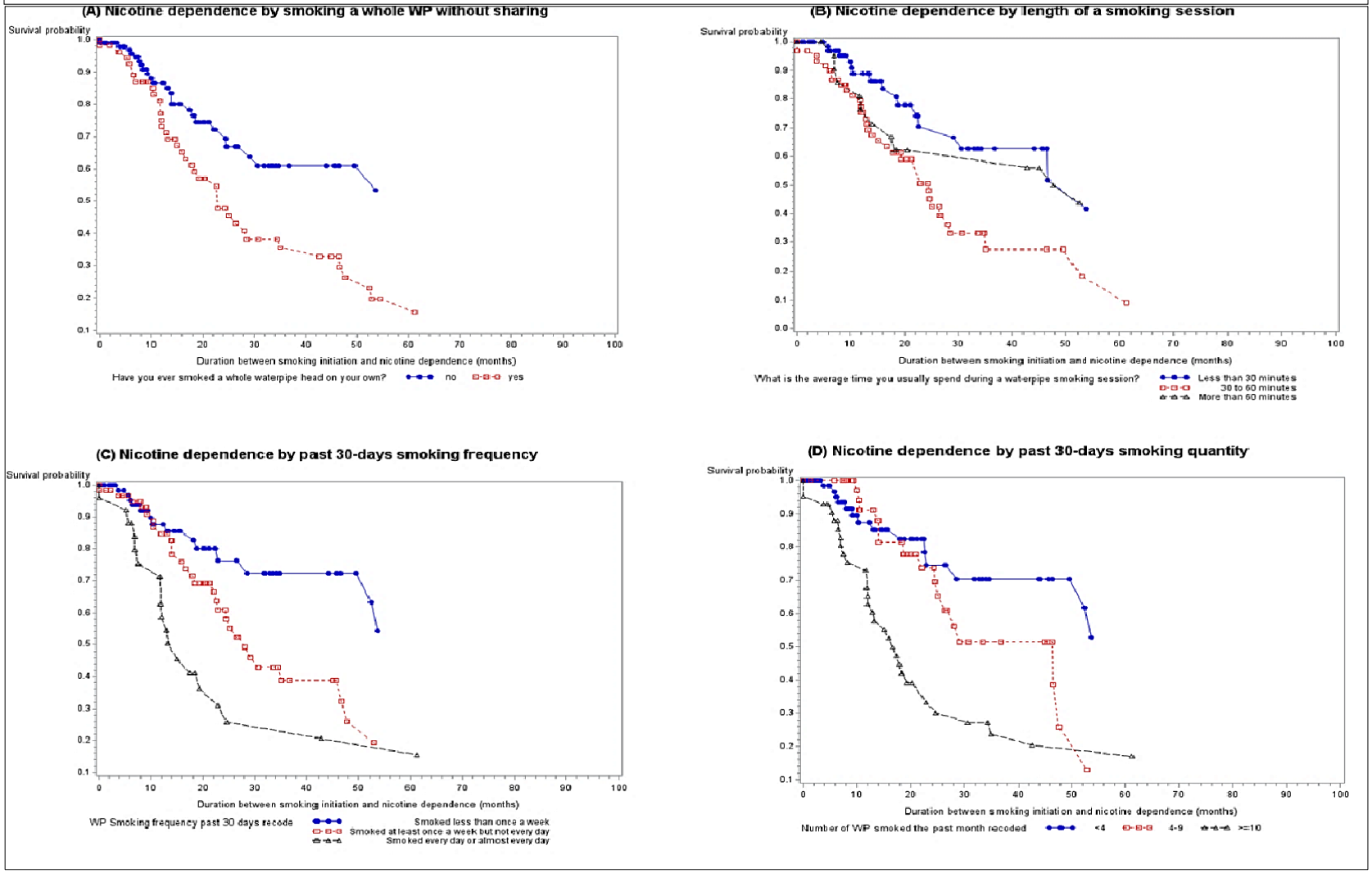


Figure 3.2 Kaplan-Meier survival curves for time to nicotine dependence (in months, X-axis) and survival probability (Y-axis) by: (A) smoking a whole waterpipe without sharing, (B) length of smoking session, (C) past 30-day smoking frequency, and (D) past 30-day number of waterpipes smoked.



Conclusions

Waterpipe smoking represents a main public health problem and is increasingly used by many youth around the world. This increased use was faced by a lack of effective control policies to limit its spread. The lack of knowledge regarding waterpipe's addictive potentials is among the factors that contributed to a lack of effective policies to control waterpipe among youth. This research provides the first systematic attempt to examine the early symptoms of waterpipe and the factors associated with increased risk of developing symptoms of nicotine dependence among young waterpipe smokers.

The first manuscript shows that ICD-10 nicotine dependence can appear within a relatively short time period after the initiation of waterpipe smoking among adolescents, and at a lower frequency of waterpipe use compared to cigarette smokers. Frequency and intensity of nicotine dependence symptoms did not differ between waterpipe and cigarette smokers, nor did the age at the onset of nicotine dependence milestones. The types of symptoms experienced, and the order with which symptoms appeared did not differ significantly for the two forms of tobacco. However, our results show how waterpipe smoking involves different use behaviors, social context, and sensory experiences than cigarette smoking and more research is needed to explore how these differences might affect the development of nicotine dependence or how it manifests behaviorally.

The second manuscript examines the factors that put adolescents at a higher risk of developing symptoms of nicotine dependence. Factors such as depressive symptoms, lower self-esteem, and having at least one sibling who smokes waterpipe were associated with the presence of nicotine dependence symptoms, while enrollment in public schools, smoking waterpipe ≥30 minutes per session, and believing that cigarette smoking is harmful to health were associated with endorsement of a higher number of nicotine dependence symptoms. Smoking a whole

waterpipe without sharing and being in 9th grade in this study were associated with the presence and endorsement of a higher number of nicotine dependence symptoms.

The third manuscript specifically addressed the association between waterpipe-specific smoking patterns and nicotine dependence symptoms. It shows that the prevalence and average number of endorsed symptoms of nicotine dependence increased markedly with higher levels of past 30-days smoking frequency, past-30 days number of waterpipes smoked, length of smoking session, and smoking a whole waterpipe without sharing. Smoking ≥10 waterpipes in the past 30-days and smoking sessions that last over 60 minutes were associated with higher hazards for the loss of autonomy, while smoking waterpipe every day/almost every day and smoking ≥10 waterpipes in the past 30-days were associated with higher hazards of meeting ICD-10 ND.

Overall, our findings suggest that adolescent waterpipe smokers develop symptoms of nicotine dependence at lower levels and with intermittent use of waterpipe. As symptoms of nicotine dependence can be experienced at very low levels of waterpipe use, early prevention and intervention strategies are warranted. Additionally, these findings suggest that waterpipe prevention and intervention strategies should to be tailored to waterpipe-unique use patterns and that these strategies will have greatest impact by educating youth about the harmful and addictive properties of waterpipe, teaching them positive coping skills, targeting those enrolled in public schools, and addressing waterpipe use by family members. Finally, the length of a smoking session emerged as a novel marker of nicotine dependence that can be considered in future psychometric work to refine instruments of nicotine dependence among adolescent waterpipe users, and as an easy-to-assess, single item measure of nicotine dependence in clinical practice (e.g., by pediatricians and substance use counselors).

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