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AN INTRODUCTION TO THE ELECTRONIC WATERPIPE

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by

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ABSTRACT

With growing popularity in the U.S., it has been estimated that 10 million adults currently smoke traditional waterpipe (TWP) and 1.4 million use every day or some days. Emerging adults aged 18-24 report the highest rates of TWP smoking. In the U.S., approximately 12.2% of young adults and 10% of college students report past-year TWP use. Despite positive perception of use among current and non-users, TWP has been associated with an increased risk of developing cancer, respiratory disease, cardiovascular disease, and addiction. In addition to TWP, there is a new product has emerged in the marketplace within the past five years that provides users with a non-combustible option; the electronic waterpipe (e-waterpipe; EWP).

The EWP is a large smoking system that is a combination of two commercially available products including 1) the structure of a TWP (a metal stem, water-filled bowl, and hoses to inhale smoke) and 2) an electronic head (e-head) that electronically heats e-liquid which is then vaporized and inhaled. In an e-head, any flavor and any nicotine content e-liquid can be vaporized using a similar heating mechanism as an electronic cigarette (e-cigarette). Based on the literature comparing e-cigarettes and traditional cigarettes, it can be suggested that the EWP has a similar potential to become a popular, and possibly a safer alternative to TWP. However, to date, there are no known studies investigating EWP use or its comparison to TWP use.

Given the gaps in the literature, the purpose of this dissertation was to aid in the development of efforts to identify and evaluate the novel EWP. Specifically, this dissertation included the investigation of the three following aims: 1) define the e-waterpipe and explain how an e-head is used to construct the e-waterpipe, 2) characterize perceptions and intentions of EWP use among first-time users, and 3) compare EWP and TWP total smoke exposure, immediate

physiological responses, and future intentions of use. To address these aims, the three-paper dissertation option was utilized.

The first manuscript (Chapter 2) included a mini review which highlighted a non-combustible, alternative waterpipe product, the EWP, and gave a brief overview of how it functions as a large smoking system (i.e., a combination of an e-head and a TWP structure). It detailed several models on the market which have varying characteristics and how those characteristics may affect smoking behaviors and vapor/nicotine exposure. Additionally, this review rationalized the need for future research to understand EWP prevalence, perceptions of use, and its associated health risks.

In the second manuscript (Chapter 3), pilot data (N=26) from the first known laboratory-based EWP study was analyzed using a descriptive analysis. A factor analysis identified distinct categories among items in a newly-developed EWP questionnaire including 1) perceived health risks, 2) future intentions to use the EWP, and 3) first-time experiences using the EWP. This study's design and results were used to inform the development and implementation of a larger-scale EWP study, which is discussed in Chapter 4. The findings suggest that EWP use has the potential to become popular similar to e-cigarettes based on positive experiences and perceptions and increased intentions of future use.

For the third manuscript (Chapter 4), a laboratory-based study was conducted that allowed smokers (N=36) to attend two experimental sessions, one to smoke the TWP and one to smoke the EWP, where physiological markers were measured pre-and post-smoking. Physiological measurements included change in exhaled carbon monoxide (CO), heart rate (HR), blood pressure (BP), and spirometry parameters (forced expiratory volume (FEV) and estimated lung age). After smoking each device, a questionnaire measured future intentions to use the

respective waterpipe. Mixed effect modeling using repeated measures was used to evaluate the association between the type of waterpipe smoked (TWP or EWP) and total smoke exposure on the associated immediate physiological responses and future intentions of use. This study found that for TWP use compared to EWP use, each one second increase in total smoke exposure was associated with 0.006 greater ΔCO from pre- post-smoking. This study alone cannot suggest that the EWP use is a safer alternative to TWP smoking. However, it can imply that the EWP exposes the smoker to significantly less CO compared to TWP smoking. These results highlight a crucial need for more investigation into the use of EWP, as well as the need for comprehensive EWP regulation.

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ABBREVIATIONS

BP: blood pressure

CO: carbon monoxide

E-HEAD: electronic head

ENDS: electronic nicotine delivery system

EWP: electronic waterpipe, e-waterpipe

FEV: forced expiratory volume

HR: heart rate

LWDS-11: Lebanese Waterpipe Dependence Scale

PEWQ: Perceptions of E-Waterpipe Use Questionnaire

PSECDI: Penn State Electronic Cigarette Dependence Index

TWP: traditional, combustible waterpipe

Δ: average change between pre- and post-smoking

PREFACE

Chapters 2, 3 and 4 are manuscripts on which I, Andrea Stroup, was the first author. For Paper 1 (Chapter 2), I was responsible for the literature and website content review, concept and design of the paper, interpretation of the review findings, and writing. For Papers 2 and 3 (Chapter 3 and 4), I was responsible for the conceptual design, data collection, data analysis, interpretation of the results, and writing.

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CHAPTER 1

Background and Significance

BACKGROUND AND SIGNIFICANCE

The reduction of traditional, combustible waterpipe (TWP) smoking remains a national public health priority because of the known health risks associated with use including cancer, respiratory disease, cardiovascular disease, and addiction. Despite these risks, 10 million adults in the US currently smoke traditional waterpipe (TWP) and 1.4 million use every day or some days [1]. Emerging adults aged 18-24 report the highest rates of TWP smoking [1]. In the U.S., approximately 12.2% of young adults and 10% of college students report past-year TWP use [2]. Several strategies to reduce TWP smoking include increased health education, the development of new interventions, and comprehensive TWP regulation. Additionally, a new product has emerged in the marketplace within the past five years that provides users with a non-combustible option; the electronic waterpipe (e-waterpipe; EWP).

The EWP is a large smoking system that is a combination of two commercially available products including 1) the structure of a TWP (a metal stem, water-filled bowl, and hoses to inhale smoke and 2) an electronic head (e-head) that electronically heats e-liquid which is then vaporized and inhaled. In an e-head, any flavor and any nicotine content e-liquid can be vaporized using a similar heating mechanism as an electronic cigarette (e-cigarette). Based on the literature comparing e-cigarettes and traditional cigarettes, it can be suggested that the EWP has a similar potential to become a popular, and possibly a safer alternative to TWP. However, to date, there are no known studies investigating EWP use or its comparison to TWP use.

Since there is no literature regarding the EWP, it can be assumed that researchers and regulatory agencies have yet to consider the potential benefits, harm, or overall influence of EWP as a potential nicotine delivery system. As previously shown in the literature regarding e-cigarettes, several manuscripts were published, prior to systematic experimental research being conducted, describing the device, its mechanisms, and implications of use. This dissertation produced an introductory paper (Manuscript 1) to address the same concerns regarding the EWP and e-head. The purpose of the paper was to build a platform for researchers and policymakers to identify and analyze the EWP in the future and to help serve the field as a foundation for understanding the potential role of EWP.

Prior to this dissertation, there were no known research studies evaluating perceptions or intentions of EWP use. This dissertation used a previously conducted pilot study (PI: Stroup) as the initial step in exploring the EWP in an experimental setting. It was the first study to use a comprehensive theory-driven approach to identify subjective rating of EWP use. For this dissertation, a descriptive analysis was conducted on the pilot data, allowing for the first known literature explaining perceptions and future intentions of EWP use in first-time EWP users (Manuscript 2). The pilot study was also able to inform the development of the larger scale, proposed dissertation study in terms of design, content, and hypothesis development.

Prior to this dissertation, there were no known studies comparing the short-term health effects between TWP and EWP smoking among college students. The present research was the first to utilize a laboratory-based study to examine difference between TWP and EWP smoking behaviors, immediate physiological responses, and intentions of future use (Manuscript 3). This research is the first step in identifying any potential harm reduction and describing current and TWP smokers' likelihood of transitioning to EWP. These findings may contribute to future research and regulatory action regarding both TWP and EWP use.

Taken together, these three manuscripts provide evidence that EWP use has the potential to become popular similar to e-cigarettes based on positive experiences and perceptions and increased intentions of future use. The results also provide evidence that the EWP use may be a safer alternative to TWP smoking; however, further research is necessary to better understand these findings. These results highlight a crucial need for more investigation into the use of EWP, as well as the need for comprehensive EWP regulation.

CHAPTER 2

An Introduction to the Electronic Waterpipe

Manuscript 1

ABSTRACT

Despite the associated negative health outcomes, waterpipe smoking remains a popular method of tobacco consumption, specifically in young adults. While there have been expanding efforts to decrease waterpipe use, there is a new, non-combustible waterpipe device on the market, the electronic waterpipe (e-waterpipe), that could serve as an alternative to traditional, combustible waterpipe smoking. There is currently no known literature evaluating the e-waterpipe including prevalence of use or its health risks. This mini review defines the e-waterpipe, explains how an e-head is used to construct an e-waterpipe, and describes the various e-head models available for use. The review also discusses implications of e-head use and provides recommendations for future research and regulation.

INTRODUCTION

Waterpipe smoking remains a national research priority as the prevalence of use continues to increase in the US [3]. National estimates suggest that more than one in ten adults have used a traditional, combustible waterpipe [4]. Nearly 10 million adults in the US currently smoke traditional waterpipe (TWP) and 1.4 million use every day or some days [1]. Emerging adults aged 18-24 report the highest rates of TWP smoking [1]. In the U.S., approximately 12.2% of young adults and 10% of college students report past-year TWP use [2]. Despite the high rates of TWP use, there are known health risks that can negatively impact overall health.

TWP smoking has been associated with cancer [5], oral infections [5], and respiratory diseases [6]. Previous literature has shown that during a one-hour TWP smoking session, an individual may inhale as much smoke as consuming 100 cigarettes [7]. In addition, users are exposed to toxic substances that are shown to increase the risk of clogged arteries and heart disease later in life [7–9]. Salivary cotinine levels, reflecting nicotine exposure, are strongly and positively correlated with TWP use, suggesting a risk of tobacco use disorder associated with TWP smoking [10]. Also, scores reported on the Lebanese Waterpipe Dependence Scale (LWDS-11) [11], a validated waterpipe-specific nicotine dependence measure, have been associated with frequency of use, smoking behaviors, and exposure to carbon monoxide (CO) and nicotine [12–14]. Although there are known health risks associated with smoking TWP, the prevalence of use continues to increase in the U.S. [1].

Because of the known addiction and health risks associated with TWP use, there have been increased efforts to prevent TWP use among young smokers, as well as public health messaging aimed at reducing or eliminating use among current users. Additionally, a new product has emerged in the marketplace within the last 5-7 years that provides users with a non-combustible option; the electronic waterpipe (e-waterpipe; EWP) is a battery-powered, electronic vaporizer, with internal mechanisms similar to an e-cigarette that allows smokers to use e-liquid in a waterpipe device.

It is important to differentiate between an EWP and other electronic devices that typically are grouped together including e-cigarettes and e-hookahs. Previously, literature has used the terms e-cigarette and e-hookah to describe handheld, pen-shaped products that electronically heats and vaporizes e-liquid [15]. The term e-waterpipe was constructed by our team because the device is part of a new category of electronic smoking devices and the chosen term reflects the unique aspects of the device that combines an electronic head that heats and vaporizes e-liquid, with a traditional waterpipe base that includes a water bowl and individual hoses that allow multiple smokers to use the device simultaneously. Thus, the EWP is not necessarily a single device, rather is a combination of commercially available products that create a larger smoking system.

Specifically, the EWP consists of two separate elements: the body of the TWP (i.e., a water-filled bowl, stem, and hose) and the "e-head", an electronic component which uses a heating mechanism similar to an e-cigarette. The e-head heats a flavored liquid solution of nicotine and other additives (e-liquid), which is then vaporized into an aerosol and inhaled by the user through the TWP stem and hoses. Because there is no combustion of tobacco using an e-head, it has been suggested that the EWP, like e-cigarettes, may result in lower overall health risks as compared to TWP [16]. However, there is currently no literature on benefits of transitioning from burning tobacco in a TWP to electrically heating e-liquid in an e-head. Likewise, there are no known studies evaluating health consequences associated with e-head use.

It is known that tobacco use and experimentation may be influenced by social and environmental factors [17]. Given that EWP use, like TWP use, may typically be done in social settings, and that the EWP may be seen as a “safe” alternative to TWP, EWP may gain popularity and become increasingly socially acceptable similar to e-cigarettes. In order to understand what role EWP may play in the tobacco marketplace, it will be necessary to identify the perceptions of EWP among those most likely to transition from TWP or those at highest risk to experiment with such new products. Given that EWP is a recent development, and that there is little, if any, descriptions or empirical examinations of the EWP, the purpose of this paper was to examine the EWP device, its typically usage, variations in the product, it’s similarities to TWP, and to provide a general introduction for researchers and clinicians to a new nicotine delivery device and potential alternative to TWP.

METHODS

An initial literature search was completed prior to this review in an effort to identify all interchangeable terms associated with TWP, ENDS, and the EWP to ensure a comprehensive comparison to existing products and provide an overview of the EWP. Previous research on existing TWP, ENDS and other tobacco products were analyzed to explain the functionality, uses, and potential harm of the EWP. Literature referenced consisted of English language, peer-reviewed articles accessed via PubMed, Google Scholar and other relevant databases. Next, a search of online tobacco retailers was conducted to identify models of EWP and accessories that are commercially available and to compare models (i.e., battery size, power, cartomizer specifications, and price). The terms e-hookah, e-bowl, and e-head were used by consumer websites and e-head manufacturers to develop product names and were ultimately used in the present search. In order to characterize the e-heads, research staff scanned website content, product packaging and pictures of products. If the manufacturer or retailer websites provided incomplete information about the e-head, then those characteristics were coded as not available in *Table 1* (n/a).

RESULTS

I. E-head and E-Waterpipe Description

A. E-Waterpipe Function

Traditional waterpipes (TWP) use a ceramic or glass head to hold tobacco which is heated by coals. When the head is placed on top of a waterpipe, air is drawn through the coal and tobacco smoke is drawn through the stem, bowl, and hose to the user The EWP is a large smoking system that utilizes an electronic head (e-head), a metal stem, water-filled bowl, and hose, similar to that in a TWP. The component that varies between a TWP and EWP is the type of head used (ceramic/glass vs. electronic). Rather than burning shisha, the e-head electrically heats e-liquid. When a smoker inhales through the hose, it activates a pressure sensor (i.e., similar to the activation of an e-cigarette) that turns on the heating coils, which atomizes the e-liquid. The aerosol is drawn down the stem, into the water found in the bowl, where it travels via bubbles through the water and converts back into vapor in the air pocket above the water. The vapor is then inhaled by the smoker through a hose. To date, there is no information on what temperature the vapor reaches throughout this process or what amount of aerosol, if any, gets filtered when passing through the water. On the bottom of e-heads, there is a triangle-shaped area where a universally-sized grommet, which provides an air-tight seal connecting the e-head to the body, is located. Another option for e-head users is to insert the hose directly into the e-head's grommet to smoke. In this situation, the smoker would no longer be pulling the vapor through water found in the bowl of the TWP body which would be categorized as vaping using an e-head, not an EWP.

B. E-head Internal Mechanisms

The e-heads come equipped with either a clearomizer or cartomizer which is used to store e-liquid and to house a heating coil. The clearomizer/cartomizer can be accessed in most e-heads by unscrewing the device into two pieces. Typically, one piece will contain the battery and the control panel (if applicable) and the other will contain the cartomizer/clearomizer. Cartomizers have differing characteristics such as being pre-filled with e-liquid or being refillable (*Table 1*). The pre-filled cartomizers are disposable and replaceable, whereas the refillable option can be cleaned and reused. Cartomizers contains a polyfill material that carries e-liquid from the chamber to the heating coil [18,19]. Polyfill may decrease the abundance of flavor from the e-liquid and may retain flavor from previous smoking sessions [19]. A clearomizer is a see-through, glass or plastic storage chamber that holds e-liquid. In the middle of the chamber, there is an atomizer which contains the heating coil to electrically heat the e-liquid and wicks to carry the e-liquid from the chamber to the coil [19]. A few benefits of using a clearomizer instead of a cartomizer include the smoker can easily see the level of e-liquid in their device and wicks can often provide a stronger flavor. If there is a preference of a clearomizer or cartomizer, the smoker would need to research the components of each e-head since there is variation among the models.

Cartomizers/clearomizers can hold varying amounts of e-liquid (*Table 1*), with no standardized size across models of e-heads. This review has identified e-heads that have tanks with maximum volumes of 2mL, 8mL, 10mL, 16mL, and 50mL. In some instances, tank size is not labelled or advertised. For example, the Fantasia E-Bowl [20] uses a prefilled, disposable cartomizer that does not disclose the e-liquid capacity. Another e-head gives the option to purchase a refillable cartomizer to replace the disposable cartomizer (i.e., Smoke Free Electronic Hookah Pyramid[21]. When using an e-head, nicotinic or non-nicotinic e-liquid can be used. For e-heads using pre-filled, disposable cartomizers, replacements will vary in nicotine content and flavor, but typically not brand. In contrast, e-heads that come with a clearomizer can be refilled with any e-liquid, including brand, flavor and nicotine variations.

E-liquid is heated by a battery located inside of the e-head and is typically accessible to the smokers. As shown in *Table 1*, there are varying battery sizes in e-heads. Battery power in e-heads are measured in milli-ampere hour (mAh) and range from 900 mAh – 4,440 mAh. In several models, the battery power for the device is not labelled or advertised. All e-heads can be recharged using a wall or USB charger and can be charged while vaping, although the safety of this is undetermined. On most e-heads, there is no on/off switch; it is automatically activated by inhalation and goes to "sleep" after inactivity.

C. E-head Control Panel

A few e-head models have a control panel on the outside of the device that shows the battery life of the e-head. In one technologically-advanced model, the Square E-Head [22], the control panel displays a puff counter and puff duration timer. Although these displayed measurements could be beneficial to research, there is no literature detailing their validity or reliability. This review did not find any other e-heads with these advanced features. Another feature of a control panel is that it provides the ability to adjust the battery-powered heat (i.e., voltage or wattage) within a range. The voltage being used will vary based on the smoker's preference since it may affect flavor intensity and vapor production. In models with this option, the temperature remains the same until it is changed by the smoker. Not all e-heads have a control panel or the option to alter the voltage/wattage being used to heat the e-liquid (*Table 1*). In over half of the identified models, the power is non-variable, meaning the temperature of heat is pre-determined by the manufacturer and cannot be changed by the smoker. Also shown in

Table 1, the pre-set power levels are not always provided by the manufacturer (i.e., Kelvin H1 E-Bowl and Fantasia E-bowl [20,23].

CONCLUSIONS

Based on high rates of TWP and e-cigarette use in young adults, there is reason to believe that the TWP has the ability to become a popular method of nicotine consumption, particularly among youth and young adult users, among whom experimentation with new products may be more common. It is possible that perceptions of the EWP will be similar to the positive perceptions of e-cigarettes including perceptions of reduced addiction potential and reduced health risks [24,25], and those perceptions may influence non-users of TWP to experiment with EWP or current TWP smokers to transition to EWP.

There is a need for studies to determine perceptions of the EWP, experiences of EWP users, levels of exposure to nicotine and other constituents of EWP vapor, the likelihood of TWP smokers, e-cigarette smokers, traditional cigarette smokers and non-smokers using EWP, and if the EWP is viewed as a viable alternative to TWP. Additionally future research should determine if passing the aerosol through water affects nicotine and toxin exposure. Moreover, there is a need to understand smoking behaviors that may be unique to EWP. For example, when using an e-cigarette, shorter and lighter puffs are recommended; however, TWP smokers tend to take longer and deeper puffs. It is not known if TWP users who transition to EWP will alter their puffing behavior or continue to smoke in a manner similar to TWP. Research shows that approximately one hour of TWP smoking consists of approximately 200 puffs (90,000 ml smoke inhaled [26]. If a smoker completes a smoking session (approximately 30-60 minutes) using the EWP, there remains a question regarding the amount of toxicant and nicotine exposure. Finally, it will be important to know if the potential health effects of inhaling e-liquid aerosol in EWP.

Despite these concerns, there may be a reduction of harm associated with EWP use compared to a TWP smoking. First, EWP use should not expose the smoker to carbon monoxide

(CO) based on the heating mechanism in the device which is similar to e-cigarette use [27]. This would be a reduction from TWP CO exposure since one puff of a TWP can have up to ten times the volume of CO than in a conventional cigarette [28], which can be detrimental to health. There are additional risks associated with TWP use including cancer [5], respiratory problems [6] and heart-related issues including clogged arteries, heart disease, and increased heart rate and blood pressure [6,7,29]. Since no studies have investigated the health effects of EWP use, it is too early to determine if it will have similar health risks.

Findings suggest that e-cigarettes produce chemical emissions of carbonyl compounds, metals, NNK (a carcinogen associated with smoking-related cancers), and propylene glycol [30,31]. Exposure to those associated toxins have resulted in increased reports of mouth and throat irritation and dry cough [32]. Additionally, e-cigarette use is associated with elevated diastolic blood pressure [33] and increased respiratory resistance [34]. Many e-liquid flavoring chemicals have also been categorized as unsafe and detrimental to health [33,35]. It was found that of 51 e-cigarette flavors tested, 39 contained diacetyl, 23 contained 2,3-pentanedione, and 46 contained acetoin [35]. Previously, diacetyl has been associated with bronchiolitis obliterans, also known as “popcorn lung” [35]. Given that EWP uses similar mechanisms for heating and vaporing e-liquids, it is possible that the EWP has similar health risks.

Although e-heads are regulated under the FDA’s 2016 deeming rule, there may be a benefit to examining the regulation of the e-head with more scrutiny. For example, the varying levels of power used to regulate the temperature of vapor can be harmful if used incorrectly. Some e-heads come pre-set to one permanent power which may be too strong for a smoker and may burn their throat. If the FDA were to standardize the power, such as limiting the maximum temperature or requiring adjustable levels of powers, this situation could be avoided. However, prior to any comprehensive regulatory action on the EWP could be enacted, a more thorough understanding of its use patterns, potential risk, exposure, and addiction is needed.

TABLE 1

Table 1. Description of Electronic Waterpipe Heads (E-heads)*					
Name/Brand	*Battery*	*Power*	*Cartomizer Specifications*	*Price*	*Similar E-heads*
Aspire Proteus E-Hookah Head	5000 mAh	Non-Variable: 70W	Refillable 10 mL	$49.99-$59.99	n/a
Fantasia E-Bowl	4400 mAh	Non-Variable: n/a	Prefilled, Replaceable, size n/a	$49.99-$79.99	n/a
Flux E-Bowl by Luxury Lites	5000 mAh	Non-Variable: 100W	Refillable 50 mL	$79.99-$99.99	Kangerm Electronic Hookah Bowl, ePuffer E-Hookah
Kelvin H1 E-Bowl	900 mAh	Non-Variable: n/a	Refillable 2 mL	$29.99-$129.99	Rook Electronic Bowl, El-Badia E-Bowl, Ehuqa Electronic Hookah Bowl, Shisha Evolve Electronic Shisha Hookah Device
Smoke Free Electronic Hookah Pyramid	n/a	Non-Variable: n/a	Prefilled, Replaceable; optional refillable cartomizer (16 mL)	$99.99	n/a
Square E-Head	2400 mAh	Range: 3.2- 6.0V	Refillable 8 mL	$99.99-$119.99	n/a
Starbuzz Wireless E-Head	n/a	Range: 10-40W	Refillable 8 mL	$84.99-$159.99	n/a
Volt E-Vapor Hookah Bowl	2400 mAh	Range: 3.2- 6.0V	Refillable 10 mL	$99.99-$149.99	Amanoo E-Head

*There are several styles of e-heads that are identical or similar, but are sold under different brand names (see *Table 1, Similar E-heads*). The e-head models provided in column 1 were randomly selected to represent the category of similar models.

*All columns displaying “not available” (n/a) are those that did not have publically available information (i.e., product label and/or distributor did not provide the information).

CHAPTER 3

Perceptions and Future Intentions of Use of First-Time E-Waterpipe Users: A Pilot Study

Manuscript 2

ABSTRACT

Introduction: The electronic waterpipe (EWP) is a novel nicotine delivery system that combines the equipment used in tradition waterpipe smoking with the electronic vaporization of flavored nicotine-containing liquid, similar to that used in e-cigarettes. Given the increased use of both waterpipes and e-cigarettes in many populations, the appeal of the EWP may be strong for many users. This is the first EWP study to examine responses to first-time use of EWP, including perceptions of use and future intentions to use the novel device.

Methods: Current e-cigarettes users who have used a traditional, combustible waterpipe in the last year (N=26) were given 20 minutes to smoke the EWP using their own e-liquid (any nicotine content/ flavor). After smoking, participants completed a questionnaire asking about their experiences of using EWP, willingness and likelihood of future use, and perceived health risks.

Results: Approximately 73.1% of participants reported the EWP was both satisfying and enjoyable. Nearly 46.2% of users believed smoking the EWP was safe and 30.8% thought use was healthy. Concurrently, 65.4% of participants perceived EWP use as addictive. There were several individuals who believed that EWP use would not increase the risk of developing long-term illnesses including lung disease (30.8%), gum disease (38.5%), throat and/or lung cancer (30.8%). Nearly all participants (96.1%) were willing to use EWP again in the future.

Conclusions: EWP use may have the potential to become popular based on positive perceptions of the device and the strong willingness to use the device in the future.

INTRODUCTION

Alternative tobacco products, including waterpipes, have grown in popularity over the past decade [36]. Approximately 100 million people worldwide smoke traditional waterpipe (TWP) daily [37]. In the United States, 1.4 million people smoke TWP every day or some days with young adults aged 18-24 reporting the highest rates of use [1]. There are common misconceptions about the safety of TWP smoking which may, in part, influence its popularity and prevalence of use [38]. TWP smoking has been consistently perceived as less addictive and less harmful than cigarette smoking [39,40]. Additional motivating factors for TWP use include socializing, relaxing, peer influence, and social acceptability among peers [39,41,42]. These positive perceptions and attitudes towards TWP smoking have been associated with increased intention to use TWP in the future and increased odds of being a current TWP user [43].

Regardless of the positive perceptions surrounding use, TWP smoking has been associated with elevated blood pressure and heart rate and an increased risk of cardiovascular disease [44]. TWP smoking also exhibits associations with an increased risk of developing several types of cancer, respiratory disease, and periodontal disease [44]. Based on scores reported on the Lebanese Waterpipe Dependence Scale (LWDS-11) and post-smoking salivary cotinine levels, TWP smokers are exposed to levels of nicotine that have a strong potential for developing a tobacco use disorder [10,11]. With increasingly high rates of TWP smoking and the associated health risks, it is essential to identify alternative products that may reduce harm.

A relatively new product on the market is a non-combustible electronic waterpipe (e-waterpipe; EWP). Instead of using charcoals to burn wet flavored tobacco (shisha) in a ceramic head, the EWP uses an electronic head (e-head) to electronically heat e-liquid, which is then vaporized and inhaled. The e-head uses an internal heating mechanism similar to an electronic cigarette (e-cigarette), utilizing a battery, atomizer, and cartomizer/clearomizer that contains the e-liquid. The e-head sits on top of a TWP structure, consisting of a metal stem, water-filled bowl, and hose; the user then draws the vapor from the e-head through the water-filled bowl and hose.

The EWP may have special appeal, based on positive perceptions of use that surround a similar product, the e-cigarette [25]. Compared to cigarettes, e-cigarettes are perceived as healthier, safer, and less addictive [45]. Perceived benefits of e-cigarette use included being cool and fashionable, socially acceptable, safe for bystanders and the environment, and it tastes good [45]. These positive perceptions and experiences have influenced intentions and initiation of e-cigarette use and EWP use may produce similar reactions. However, to date, there is no known research identifying the perceptions of using the EWP, nor any research evaluating predictors or prevalence of use. The current pilot study is the first study to investigate perceptions of EWP use and the willingness and likelihood to use EWP in the future. This study hypothesized that there would be overall positive perceptions and responses to EWP use and that most participants would be willing to use the EWP again and have strong intentions to use EWP in the future.

METHODS

A. Participants

Participants (n=26) were recruited via flyers or a web-based recruitment tool available for all research studies actively recruiting at Penn State University. Inclusion criteria included being 18 years of age or older, having used traditional (combustible) waterpipe at least once in the past year, and having used e-cigarettes, on average, at least once a week over the past 30 days. Participants were excluded if they had used an EWP before participating in the study. Although both males and females were recruited, only males responded to advertisements and participated in the study.

B. Study Procedures

The study was approved by the Pennsylvania State University Institutional Review Board. Informed consent was obtained after verification of study eligibility. Participants were asked to abstain from all nicotine and tobacco products for 12 hours prior to the experimental session. Abstinence was verified by an exhaled breath CO device with a threshold of 10 ppm [46]. Participants completed baseline questionnaires including the Penn State Electronic Cigarette Dependence Index (PSECDI) [47] and basic demographic questions. Research staff then provided basic information about the EWP, such as where the e-liquid is stored in the device and how the device works. Participants were given 20 minutes to smoke the EWP *ad lib* in a laboratory setting using the e-liquid the participants supplied themselves.

The e-head used to convert the TWP structure into an EWP was the Square E-Head [48]. Although this specific model of e-head has variable voltage ranging from 3.2-6.0V, the voltage was set at 4.0V for the entirety of the study and was chosen based on commonly used voltage in e-cigarettes and the assumption that the hookah water would cool the smoke temperature. The smoking session was video recorded to document the total number of puffs taken, the duration of each inhalation, and the time between puffs. Following the smoking session, participants again provided exhaled-breath air samples to measure CO levels and spirometry parameters. Lastly, all participants completed a 64-item post-smoking questionnaire, Perceptions of E-Waterpipe Use Questionnaire (PEWQ), developed specifically for this project. The PEWQ assessed individual experiences with the EWP and perceived health risks, on a 5-point scale: 1) strongly disagree, 2) moderately disagree, 3) neither agree nor disagree, 4) moderately agree, and 5) strongly agree. The PEWQ also assessed participants' willingness and likelihood towards future EWP use on a 4-point scale: 1) not at all willing/likely, 2) slightly willing/likely, 3) moderately willing/likely, and 4) strongly willing/likely. Questionnaire reliability and validity tests were conducted using the pilot study data and results are found in Appendix A.

RESULTS

A. Sample Characteristics

The average e-liquid nicotine content used was 6.08mg (SD= 5.49, min= 0, max= 20). The e-liquids consumed varied across three flavor categories including fruity (50.0%), sweets/desserts (30.8%), and savory (19.2%). Approximately 96.2% (n=25) of participants ever smoked cigarettes and 50.0% (n=13) of those smoked in the past 30 days. The average age of first-time cigarette use was 16.8 years old (SD=2.15, min=10, max=21). All participants reported previous use of combustible waterpipe (TWP) and e-cigarettes. For TWP, 3.8% (n=1) reported weekly use, 34.6% (n=9) monthly use, and 38.5% (n=10) yearly use. The average age of first-time TWP use was 18.1 years old (SD=3.60, min=15, max=33). Participants reported smoking TWP in various settings including a friend's house (19.2%, n=5), their own house (23.1%, n=6), a fraternity/sorority (7.7%, n=1), and a hookah lounge/café (61.5%, n=16).

In regard to e-cigarette use, 61.5% (n=16) reported daily use, 19.2% (n=5) weekly use, and 11.5% (n=3) monthly use. The average age of first-time e-cigarette use was 19.5 years old (SD=4.25, min=16, max=33). Nearly 96.2% (n=25) of participants described their electronic smoking device as a "rechargeable device with a refillable tank" and 3.8% (n=1) described their device as "not rechargeable and disposable." The PSECDI[47] demonstrated that 38.5% (n=10) of individuals were not dependent on e-cigarettes, 30.8% had low dependence, 19.2% (n=5) moderate dependence, and 11.5% (n=3) high dependence. Participants' demographic characteristics are shown in *Table 2*.

B. Experiences with First-Time EWP Use

Approximately 73.1% (n=19) reported that smoking the EWP was both satisfying and enjoyable. Participants expressed that smoking the EWP was calming (42.3%, n=11), helped them concentrate (19.2%, n=5), and made them feel more awake (19.2%, n=5) and less irritable (30.8%, n=8). The majority reported that EWP smoke tasted good (65.4%, n=17) and provided enjoyable sensations in the throat and chest (57.7%, n=15). Additional short-term health effects included reports of reduced hunger cravings (26.9%, n=7), feeling dizzy (26.9%, n=7), and feeling nauseous (30.8%, n=8). Among those individuals who reported feeling dizzy and feeling nauseous, the average e-liquid nicotine content used was higher than the sample average, respectively, 8.44mg (SD=6.86) and 8.20mg (SD=6.85).

C. Perceived Health Outcomes

Nearly 42.3% (n=11) of participants believed smoking the EWP was safe and 30.8% (n=8) thought EWP use was healthy. In contrast, a majority of participants (65.4%, n=17) perceived EWP use as addictive. As expected, most smokers were unsure of the possible long-term risks associated with EWP use. However, there were several participants who moderately or strongly believed that EWP use would not increase the risk of developing long-term illnesses including heart disease (23.1%, n=6), lung disease (30.8%, n=8), gum disease (38.5%, n=10), throat and/or lung cancer (30.8%, n=8), and heart attack (23.1%, n=6).

D. Likelihood and Willingness to Use TWP

Participants reported their willingness and likelihood of participating in a number of behaviors related to the EWP. For this study, "Willingness" was defined as "*something you haven't really thought about doing but would be open to doing if the opportunity presented itself*;" and "Likelihood" was defined as "*something you have thought about and plan to do in the near future.*" As shown in *Table 3*, there are differences in participant's willingness to perform a behavior and the likelihood or actuality of partaking in that behavior.

CONCLUSIONS

This pilot study is the first known research to measure responses to first-time use of EWP, including perceptions of use and future intentions to use the novel device. A majority of first-time users had positive experiences while using the EWP such that it was satisfying, enjoyable, and tasted good. Additional short-term effects reported include that it was calming, improved concentration, and made them feel more awake. It was also suggested that it reduced hunger cravings and provided enjoyable sensations the throat and chest. Similar experiences and short-term effects were previously reported by individuals who used e-cigarettes [25,45] and TWP [39–42]. It can be assumed that since there are comparable short-term effects and perceptions of these products, individuals may be willing to transition from a combustible TWP to a non-combustible EWP.

There were a few reports of negative short-term EWP experiences including feeling dizzy and/or nauseous, which were similar to subjective responses (dizziness, coughing, and nausea) reported by first-time e-cigarette and TWP smokers [49]. One reason for these side effects may be because of confusion surrounding how to smoke the device. For example, smoking behaviors could vary between long, inhaled puffs similar to TWP smoking and shorter, more frequent puffs similar to e-cigarette use. Another possible reason for these side effects could be the amount of nicotine in the e-liquid used. For example, a smoker may be exposed to unsafe levels of nicotine if a highly nicotinic e-liquid is consumed using intense smoking behaviors (e.g., high puff count, long puff duration, and less time between puffs). It is recommended that future studies control for e-liquid nicotine content and nicotine dependence as precautionary measures.

This study showed that a majority of EWP users have positive perceptions of EWP use. Many participants believed that EWP use is safe, healthy, and would not increase their risk of developing long-term illnesses including heart, lung, and gum disease, heart attack, and cancer. In addition, some smokers perceived EWP use as non-addictive. This demonstrates that young adults should be informed about the health risks of using electronic nicotine delivery systems (ENDS) and consuming nicotinic e-liquid. It can be suggested that the non-combustible EWP will have less harmful effects on health based on literature showing that e-cigarettes may be a less harmful alternative to smoking conventional cigarettes[16]. However, to date, there is no literature identifying the benefits of transitioning from burning shisha in TWP to electrically heating e-liquid in EWP.

First-time EWP users also reported their willingness and likelihood of behaviors associated with EWP use. A majority of participants were equally willing and likely to investigate the new smoking device, share their EWP smoking experience with others, and speak positively about their EWP experience. Approximately two-thirds of smokers were willing and likely to purchase an EWP. It is important to highlight that although nearly half of participants were highly willing to use an EWP in the future, the actual likelihood of use was lower. A primary reason for this could be that smokers are unaware of where the device can be accessed or purchased because it is relatively new. To date, there are no known reports of prevalence of EWP use or ownership, therefore, it will be important for future research to provide initial surveillance of use patterns.

TABLE 2

Table 2. Sample Demographic Characteristics

	Frequency	**Mean (*SD*)**
Age		21.3 (*SD*=4.1)
Gender		
Male	26 (100.0%)	
Race		
Caucasian	18 (69.2%)	
Black or African American	2 (0.1%)	
Native Hawaiian/ Other Pacific Islander	4 (15.4%)	
Asian	0 (0.0%)	
Hispanic	0 (0.0%)	
American Indian/Alaska Native	3 (11.5%)	
Unknown/ Other	1 (0.03%)	
Household Income		
< $25,000	7 (27.0%)	
$25,000 - $50,000	2 (0.1%)	
$50,000 - $75,000	1 (0.03%)	
$75,000 - $100,000	6 (23.1%)	
> $100,000	10 (38.5%)	
Highest Education Level		
High School Graduate	7 (27.0%)	
Currently in College/ University (or at least one year of specialized technical training)	13 (50.0%)	
College/University Graduate	3 (11.5%)	
Graduate School or Professional Training	3 (11.5%)	

TABLE 3

Table 3. Future Intentions to Use Electronic Waterpipe

	Future Intentions to Use		
	Not at all	Slightly/Moderately	Highly
Willingness (next 30 days)			
To use EWP	1 (3.8%)	14 (53.8%)	11 (42.3%)
To purchase an EWP	9 (34.6%)	14 (53.8%)	3 (11.5%)
To research and collect EWP information	0 (0.0%)	15 (57.7%)	11 (42.3%)
To share your EWP smoking experience	1 (3.8%)	11 (42.3%)	14 (53.8%)
To speak positively about your EWP smoking experience	3 (11.5%)	13 (50.0%)	10 (38.5%)
Likelihood (next 30 days)			
To use EWP	4 (15.4%)	20 (76.9%)	2 (7.7%)
To purchase an EWP	10 (38.5%)	14 (53.8%)	2 (7.7%)
To research and collect EWP information	1 (3.8%)	14 (53.8%)	11 (42.3%)
To share your EWP smoking experience	1 (3.8%)	10 (38.5%)	15 (57.7%)
To speak positively about your EWP smoking experience	3 (11.5%)	12 (46.2%)	11 (42.3%)

CHAPTER 4

Comparing Immediate Physiological Responses and Future Intentions of Use between Combustible and Electronic Waterpipe Users

Manuscript 3

ABSTRACT

Introduction: The reduction of waterpipe smoking remains a national public health priority based on the health risks associated with use including cancer, respiratory disease, cardiovascular disease, and tobacco use disorder. Despite continuous efforts to decrease waterpipe use, use prevalence has increased over the past decade, particularly in young adults and college students. In addition to combustible waterpipe, there is relatively new, non-combustible waterpipe that may be seen as a "safer" alternative; the electronic waterpipe (e-waterpipe; EWP). This is the first known study comparing the immediate physiological responses between combustible and electronic waterpipe use among young adults. The present study also identifies future intentions of use of the new EWP compared to traditional, combustible waterpipe (TWP).

Methods: Data were collected from 36 individuals on two separate days, one day to smoke the TWP and one day to smoke the EWP. Physiological measurements including change in exhaled carbon monoxide (CO), heart rate (HR), blood pressure (BP systolic and BP diastolic), and spirometry parameters (forced expiratory volume [FEV] and estimated lung age) were measured pre-and post-smoking. After smoking each device, a questionnaire measured future intentions to use the respective waterpipe. Mixed effect modeling using repeated measures was used to evaluate the association between the type of waterpipe smoked (TWP or EWP) and total smoke exposure on the associated immediate physiological responses and future intentions of use.

Results: Smoking EWP compared to TWP was associated with a significantly smaller average change (Δ) in CO (b= -9.965, SE=0.821, $p<0.001$), Δ HR (b= -7.607, SE=1.694, $p<0.001$), and Δ FEV (b= -0.259, SE=0.111, $p=0.026$). Total smoke exposure from TWP compared to EWP was associated with a greater ΔCO from pre- to post-smoking (b=0.092, SE=0.019, $p<0.001$), a greater ΔHR from pre- to post-smoking (b=0.065, SE=0.021, $p=0.004$), and predicted more

future intentions to use the EWP (*b*= 0.039, *SE*=0.019, p=0.047). The results showed that for TWP use compared to EWP use, each one second increase in total smoke exposure was associated with 0.006 greater ΔCO from pre- post-smoking. Therefore, EWP smoke exposure compared to TWP smoke exposure resulted less ΔCO.

Discussion: The present findings represent a small sample size, which may not be representative of the population, meaning this study alone cannot suggest that the EWP use is a safer alternative to TWP smoking. However, it can be suggested that the EWP exposes the smoker to significantly less CO compared to TWP smoking. Further research is necessary to better understand these findings. One option is to conduct a large-scale, longitudinal study to compare long-term health outcomes between combustible and non-combustible waterpipe smokers. Overall, the results highlight a crucial need for more investigation into the use of EWP, as well as the need for comprehensive EWP regulation.

INTRODUCTION

Although there have been expanding efforts to decrease use, prevalence of traditional, combustible waterpipe (TWP) smoking has increased over the past decade, specifically in young adults and college students [50]. Young adults aged 18-24 report the highest rates of TWP smoking [1]. In the U.S., nearly 12.2% of young adults and 10% of college students reported TWP use in the past year [2]. A national assessment found that among college students who report past 30-day TWP smoking, 62.4% smoked TWP one to two days, whereas 6% used TWP daily or almost daily [51]. Increasing prevalence of TWP smoking has been associated with perceived social acceptability, peer influence, and misconceptions about its health risks [9,39,52].

Despite the positive perceptions surrounding use, TWP smoking has shown to be detrimental to smokers' health. One study demonstrated that more toxic substances including carbon monoxide (CO) and tar are absorbed while smoking TWP compared to cigarettes because of TWP intense smoking behaviors [26]. About one hour of TWP smoking consists of approximately 200 puffs (90,000 ml smoke inhaled), whereas smoking a cigarette involves approximately 20 puffs (500-600 ml smoke inhaled) [53]. TWP smokers can inhale roughly ten times as much CO from burning coals compared to the CO exposure from cigarettes, which can lead to CO poisoning [54].

One factor that may increase TWP smoke exposure includes the social environment in which it is smoked (i.e., smoking in group settings). A study comparing TWP smoking behaviors between smoking alone and smoking in a two-person group showed that those in groups took more frequent puffs and more overall puffs [53]. Compared to smoking TWP alone, smoking in a group setting was associated with lower CO and higher concentration of toxicants in the smoke [53]. Therefore, in the current study it will be important to allow the participants to smoke in groups, with their friends, to create a real-world environment and to avoid significantly altered results due to unfamiliarity with other participants. By allowing smokers to have typical waterpipe smoking distractions (i.e., phones, music, conversation, etc.), topography measurements will be more similar to those groups smoking in a hookah lounge. It should be noted that there are no studies identifying common smoking behaviors among EWP users or comparing EWP and similar tobacco product smoking behaviors. In the present study, it will be important to determine if the total exposure to smoke, in both an EWP and TWP, affect the immediate physiological responses.

In addition to harmful smoke, CO, and toxicant exposure, TWP smokers are exposed to varying amounts of nicotine in shisha (wet flavored tobacco). Data has shown that post-smoking salivary cotinine levels, which indicate levels of nicotine exposure, were positively and strongly correlated with TWP smoking [55]. It has been suggested that TWP smoking can provide the same or a greater dose of nicotine compared to smoking a cigarette [56], which can result in a tobacco use disorder. Tobacco use disorder is a DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition) diagnosis assigned to individuals who are dependent on the nicotine due to continued use of tobacco products [57,58].

In a previous study using automated smoking machines, it was demonstrated that e-cigarettes delivered less nicotine per puff than conventional cigarettes [59]. Another study showed that 5 minutes after taking a similar number of puffs, plasma nicotine levels after smoking an e-cigarette were significantly lower compared to after smoking a traditional cigarette [60]. It should be noted, however, that when comparing experienced e-cigarette users and conventional cigarette smokers, both achieved similar nicotine concentrations [59]. Despite this information, it is unknown if or how the EWP exposes the smokers to similar levels of nicotine as when smoking TWP.

TWP smoking exhibits significant associations with several types of cancer, oral infections, and respiratory problems [5,6]. Specifically, TWP smoke exposure was associated with heart-related issues including clogged arteries, heart disease, and increased heart rate and blood pressure [5,6,26,53,61]. Combustible waterpipe smoking can cause respiratory complications such as airway obstruction, which can mimic premature lung aging [62]. Previous literature also showed that short-term tobacco smoke exposure significantly, negatively affected lung function (reduced forced expiratory volume [FEV]), while e-cigarette vapor exposure did not significantly impact lung function (FEV) [63,64]. When using a spirometer, a smokers' FEV is used, in part, to estimate lung age. Lung age refers to the average age of a nonsmoker with an FEV equal to that of the individual being tested [65]. The purpose of identifying a lung age, historically, was to influence smokers to quit smoking by providing them with a more relatable figure than spirometry values like FEV [65]. Although lung age is not the standard measure used when testing lung function in experimental smoking studies, the current investigators felt that all spirometry parameters recorded should be reported as part of this study to inform the literature of the EWP's overall impact on short-term health.

Based on the known health risks and increasing rates of use, it is important to identify any means of harm reduction for current and future TWP smokers. Recently, a non-combustible waterpipe has emerged on the market called the electronic waterpipe or e-waterpipe (EWP) that may be seen as a "safer" alternative device. The EWP is a smoking device that combines the body of a TWP (i.e., a water-filled bowl, metal stem, and sharable hoses) and a new non-combustible element deemed an "e-head." In one review, approximately 15 different brands of e-heads were identified with varying characteristics including battery size, power range, and cartomizer size and type (disposable vs. refillable) [66]. An e-head electronically heats e-liquid using mechanisms similar to an e-cigarette (i.e., using an atomizer, cartomizer, and battery) which is then vaporized and inhaled by the user [66].

E-liquid is a fluid used in e-cigarettes that is primarily made up of propylene glycol, vegetable glycerin, flavoring, chemical additives, and optional nicotine [67]. Several health outcomes associated with exposure to e-liquid include elevated diastolic blood pressure [33], increased respiratory resistance [34], and an increased risk of developing a respiratory infection [68]. Within 30 minutes of e-cigarette smoking, it has been demonstrated that using nicotine-containing e-cigarettes could result in increased arterial stiffness, heart rate, and the blood pressure [69]. There are several toxic chemical emissions generated from heating e-liquid including carbonyl compounds, NNK (a tobacco-related carcinogen), and metals [30,31,70]. E-liquid flavoring chemicals have been deemed potentially unsafe and detrimental to health [16,35]. For example, one e-liquid flavoring ingredient, diacetyl, has been associated with bronchiolitis obliterans, which is also known as “popcorn lung” [35]. Based on the heating methods and use of e-liquid, it can be presumed that EWP use health risks may be similar to those associated with e-cigarette use. However, to date, no study has identified the risks or benefits of using EWP compared to using TWP. It can be suggested that there are different chemicals in shisha tobacco and e-liquid, or in their respective smoke that affect acute health impacts.

The present study is the first-known study investigating the EWP, specifically comparing TWP and EWP immediate physiological responses, total smoke exposure, and future intentions of use. Approximately equal nicotine levels were consumed from the EWP and TWP; therefore, it was hypothesized that using the EWP compared to the TWP will not significantly affect

ΔBP_{sys} (Hypothesis 1.1), ΔBP_{dia} (Hypothesis 2.1), or ΔHR (Hypothesis 3.1). In contrast, it was expected that a higher total smoke exposure would independently and significantly increase ΔBP_{sys} (Hypothesis 1.2), ΔBP_{dia} (Hypothesis 2.2), and ΔHR (Hypothesis 3.2).

It was hypothesized that, independently, using the EWP compared to the TWP, a higher total smoke exposure, and the interaction term (type of waterpipe smoked X total smoke exposure) would have a significant decrease in ΔCO (Hypothesis 4) and in Δ estimated lung age (Hypothesis 5). It was also hypothesized that, independently, using the EWP compared to the TWP, a higher total smoke exposure would significantly increase Δ FEV (Hypothesis 6) and would result in someone being more likely to have future intentions to use (Hypothesis 7).

METHODS

A. Participants

Participants (N=36) were 12 groups of 3 college-aged individuals from central Pennsylvania. To qualify for study inclusion, participants were at least age 18 and no older than age 24 in order to represent the young adult population who reports the highest rates of TWP use. Participants were required to have used TWP at least once in the past year, used an electronic nicotine delivery system (ENDS) at least once prior to participation in the study, and used any tobacco product in the past 30 days. The listed requirements are necessary to avoid exposing non-users to a product that they may not normally smoke regularly. To control for the novelty of the EWP, participants must not have ever used an EWP prior to study participation. Potential participants were excluded if they had an illness that was adversely affected by smoking, tested positive for pregnancy, were breastfeeding, or had health problems that could interfere with attending or completing the two experimental sessions.

B. Recruitment & Data Collection

Participants were recruited via flyers, a university-provided recruitment website, radio advertisements, and word-of-mouth. This study utilized the snowball effect to recruit friends of the initial person interested in the study to participate as a triad (groups of 3 smokers). The initial eligible participant contacted their peers to participate; the recruitment of friends simulated a group-based smoking experience that would not be significantly altered due to unfamiliarity with other participants. Prior to participating, friends independently contacted the researchers (rather than being solicited by the research team) and also completed a brief screening survey by phone to verify eligibility and willingness to participate. Together, the three eligible participants will schedule two, one-hour appointment times, one day for TW smoking and one day for EW smoking. Smoking sessions were completed only when all group members were able to attend together. It was important to allow the participants to smoke in groups, with their friends, to better create a real-world environment. By allowing smokers to have typical waterpipe smoking distractions (i.e., phones, music, and conversation), topography measurements were more similar to groups smoking in a hookah lounge/café.

C. Study Procedures

Participants attended 2 experimental sessions over a 2-day period, with the same group of friends. On day one of the two-day study, following screening, but prior to any other data collection, participants provided consent and completed an electronic baseline questionnaire that assessed demographic characteristics and tobacco use history. Nicotine and specific tobacco product (e-cigarette, cigarette, and TWP) dependence were measured using a battery of validated and reliable questionnaires.

For both experimental session days, participants were asked to abstain from all tobacco and nicotine products for 12 hours prior to their laboratory sessions, allowing for three half-lives for CO elimination [71]. Abstinence was verified by an exhaled breath CO device with a threshold of 10 ppm which is commonly used to verify abstinence in the literature [72]. After smoking each waterpipe, exhaled breath CO levels were again recorded. At both laboratory sessions, participants provided additional pre-and post-smoking biological samples including blood pressure (BP) and heart rate (HR) using an automatic BP and HR monitor. Both BP (systolic and diastolic) and HR were collected two times, with a five minute interval between measurements, to ensure a valid and reliable reading. Pre- and post-smoking each waterpipe, participants also exhaled into a standardized spirometer to determine lung function, with measurements including estimated lung age (ELA) and forced expiratory volume (FEV).

For both laboratory sessions, triads smoked in a ventilated smoking laboratory room that was set up to replicate a hookah lounge (i.e., a couch, television, and coffee table). During the first experimental session, blueberry-flavored shisha (nicotine: 0.3% total volume) was smoked out of the TWP and during the second session, a blueberry-flavored e-liquid (nicotine: 3 mg/mL) was vaporized using the EWP. A previously conducted pilot EWP study demonstrated that blueberry-flavored e-liquid was the most common flavor smoked from the EWP. Since the EWP is relatively new and there is no public knowledge of its safety or how participants will smoke the device (i.e., heavy vs. light smoking behaviors), research staff and the ethical review board determined that the safety of the participants is of the utmost importance. Therefore, the nicotine concentrations were selected based on the lowest nicotine content available, besides zero, in each product.

Participants were given brief instructions on how to use the waterpipe being smoked each day and were allowed to use their phones, play music, and read magazines during the 20-minute smoking sessions. On both days, smoking sessions were video recorded to observe topography measures, including an individual's total puff count, average puff duration, and total exposure to smoke (seconds). Finally, individuals completed a post-smoking questionnaire identified as a modified version of the Perceptions of E-Waterpipe Questionnaire (mPEWQ) [66], which measured future intentions of use of each device. Individuals were compensated $10.00 after the first smoking session and $20.00 after the second smoking session ($30.00 total for study participation). This study was approved by the Institutional Review Board at Pennsylvania State University.

D. Measures

a. Demographics

Demographic information was collected including sex, age, and race. In each model, age was grand-mean centered (continuous variable) to more easily interpret the regression coefficients and race was controlled for using dummy-coded variables (African American/Black, Asian, Hispanic, and Other, with White as the reference group). Previous research has shown racial differences in tobacco product use [73], and therefore, was accounted for in the present statistical models.

b. Nicotine Dependence

For the present analyses, the Hooked on Nicotine Checklist (HONC) questionnaire was used as an indicator of loss of autonomy over nicotine use [74]. The HONC has superior psychometric properties including high internal consistency and evidence of content and construct validity [75]. It consists of 10 dichotomous (yes/no) items and all endorsed responses were summed to create a score ranging from 0-10. The endorsement of any one item indicated the loss of some autonomy and the total number of items endorsed indicated the level to which autonomy had been lost [74].

c. EWP and TWP Topography

During both 20-minute smoking sessions, topography measures were video recorded and further analyzed to obtain individual smoking behaviors including total number of puffs taken, average puff duration (e.g., each smoker's puffs [in seconds] were summed and divided by the total number of puffs taken), and total smoke exposure (e.g., each smoker's puffs [in seconds] summed). As shown in *Table 6*, there are differences in EWP and TWP smoking behaviors.

The principal investigator coded the videos following study completion using the video's built-in timer/clock. For each puff, the start time was defined as the time on the clock, in which the hose touched their lips and there was evidence of a puff such as the bowl lighting up or a bubbling sound. For each puff, the end time was defined as the time on the clock, in which the hose left the smoker's lips. If necessary, the smoking videos were paused or put on rewind to assure accurate coding. Two research staff were trained together on two occasions by the principal investigator using video examples from a previous pilot EWP study. A random-subset of videos were selected and were coded by the trained staff. Chronbach's alpha was used to test for inter-rater reliability. An alpha (α) $\geq$ 0.9 was determined to be an excellent level of correlation between the different coders' observed values and $0.9 > \alpha \geq 0.8$ was determined to be a good level of correlation. All coded values in the present study met the inter-rater reliability criteria of $\alpha \geq 0.8$.

For the current analyses, total smoke exposure (in seconds) was selected as the predictor variable because the purpose of the study was to compare the relationship between total exposure, the type of waterpipe smoked, and the associated physiological responses. For the current analyses, the continuous variable, total smoke exposure, was centered to avoid multicollinearity issues, which could affect model convergence.

d. Future Intentions of EWP and TWP Use

Since there are no studies comparing the TWP and EWP, there is not a widely-accepted questionnaire to compare subjective ratings of use between the two waterpipes. However, previous literature addressing perceptions of TWP use was systematically reviewed, and consequently, questions previously used in literature and questions used in an EWP pilot study influenced the development of the post-smoking questionnaire. The modified Perceptions of E-Waterpipe Use Questionnaire (mPEWQ) assessed participants' willingness and likelihood towards future EWP/TWP use on a 4-point scale: 1) not at all willing/likely, 2) slightly willing/likely, 3) moderately willing/likely, and 4) strongly willing/likely. These two items, willingness and likelihood of engaging in specific behaviors, were summed to reflect a single "future intentions of engaging in a specific behavior" variable. These items were summed because they were significantly correlated, with *r* ranging from .56 to .89. The "future intentions" variable is defined as the difference between the summed values regarding smoking the EWP and smoking the TWP. Questionnaire reliability and validity tests were conducted using the pilot study data and the current study data; results are found in Appendix A.

e. Average Change in Exhaled Carbon Monoxide

A standard, non-invasive device measured recent carbon monoxide (CO) exposure levels from exhaled breath samples. The device used to measure exhaled CO levels was Bedfont's LungLife by CoVita [76]. CO levels were reported in parts per million (ppm) and were collected approximately five minutes before and after each waterpipe smoking session. To create the average change (Δ) CO variable, the difference between pre-and post-smoking CO values for both smoking sessions (TWP and EWP) was computed.

f. Average Change in Spirometry Parameters

The non-invasive device used to assess lung function was the Vitalograph Lung Age Model 4000 [77] which reported an estimation of lung age and forced expiratory volume (FEV). FEV measures the amount of air that can be exhaled during a forced breath in one second. Estimated lung age was calculated by the spirometer by using a standard formula that includes a smokers' FEV. When the spirometer measures FEV and lung age, it accounts for age, height, and sex. Each participant provided an exhaled breath sample approximately five minutes before and after smoking each waterpipe. To create the average change (Δ) FEV and lung age variables, the difference between pre-and post-smoking spirometry values for both smoking sessions (TWP and EWP) was computed.

g. *Average Change in Blood Pressure and Heart Rate*

To measure HR and BP, the non-invasive Omron HEM-705CP Automatic Digital Blood Pressure Monitor was used [78]. Each participant was asked to sit calmly, with their feet flat on the floor, for five minutes prior to providing each measurement. HR and BP (systolic and diastolic) were collected approximately five minutes before and after smoking each waterpipe. To create the average change (Δ) HR and BP variables, the difference between pre-and post-smoking values for both smoking sessions (TWP and EWP) was computed.

E. Data Analysis

A power analysis using G*Power software was utilized to ensure that the sample size provided sufficient power to detect significant effects [79]. Results of the power analysis suggested that a sample size of 36 was sufficient to achieve a minimum power of .80, $\alpha = .05$, detecting a moderate/large effect size ($f^2=0.30$). This sample size is required to detect an interaction between two predictor variables (one binary and one continuous) with repeated measures of a continuous outcome variable. A simulation study examines the statistical power associated with the resulting sample sizes in a mixed-effects linear regression model with a random intercept. Linear mixed effect modeling for repeated measures was conducted using SAS v9.4 software[80] to test all hypotheses. Commonly used data assumptions were checked for including linearity, homogeneity of variance, and normal distribution. There were no missing data for any variable in any model and there was no attrition on any day. Additionally, preliminary analyses were conducted to identify any mean differences between pre- and post-smoking values, as well as between EWP and TWP smoking values (paired sample t-tests).

To estimate the coefficients, restricted maximum likelihood (REML) was used. REML allows for changing variances and for spatial and/or temporal correlations, making it appropriate for repeated measures analysis [81]. Since the data include repeated measures and the time points of data collection were evenly spaced, different covariance matrix types were considered including compound symmetry and the unstructured covariance structure. For the present study, one outcome variable (Δ CO) was selected as a representative model and it was determined based on model fit criteria that the unstructured covariance structure was the best to capture correlations among the residual variances. This type of structure has no constraints on estimating variance, resulting in each variance and covariance value being very close to what the data actually reflect. For each outcome variable, separate multilevel models were conducted. Although not the primary focus of this study, an intercept-only model (with no predictors) was conducted for each outcome variable to determine if there was significant variation at Level 2. Once it was determined that there was unexplained variation in the model, full models (with all predictors) were conducted to explain the variability. A primary purpose of this study was to identify significant interactions in the models; therefore, all models with non-significant interaction terms were re-analyzed using the same procedures, except the interaction term was not included in the model so the main effects could be interpreted more easily.

The intraclass correlation coefficient (ICC) was calculated for all models, representing the proportion of the variance in the outcome variable not explained by the covariates but a result of variation between the two types of waterpipes smoked (intercept-only model). Then, the ICC was reported for all models to represent to proportion of the variance in the outcome variables explained by all covariates (full/maximal model). A small ICC suggested that the extent of shared variance among the tested variables in the model was low. If an ICC approached 1, then there was no unexplained variance at the individual level (i.e., all participants are the same) [82]. For all models, pseudo R-squared was calculated to express the percent of variance explained by all covariates in the model [83]. Although pseudo R-squared are not interpreted the same as an ordinary least squares (OLS) R-squared, higher values reflect a better model fit [83]. It should be noted that negative pseudo R-squared are possible and in that situation, the negative value should be interpreted as zero percent variance being explained by the model.

For the models specified, fixed effects (Level 1) for the type of waterpipe smoked, total smoke exposure (in seconds), and their interaction were estimated and a random intercept was specified to accommodate the repeated measures design [84]. The total variance of the outcome variables (physiological responses /future intentions) is partitioned into between-person and within-person variability. Mixed modeling was used to identify associations of total smoke exposure and type of waterpipe used with several different immediate physiological responses, including average change (Δ) in CO, Δ HR, Δ BP*systolic*, Δ BP*diastolic*, Δ FEV, and Δ estimated lung age, and future intentions of use. Each model included covariates known to be associated with smoking behaviors, including age, gender, race, and nicotine dependence and were tested at Level 2 (person-specific variables). In the present study, α of 0.05 was used to determined statistical significance.

RESULTS

A. Sample Characteristics

Participants' demographic characteristics are shown in *Table 4*. Participants' nicotine and tobacco-product specific dependence levels and tobacco use history are shown in *Table 5*. HONC[74] scores were positively correlated with the LWDS-11[11] scores (r=0.284, p=0.015), but were not correlated with the PSECDI [47] scores (r=0.173, p=0.146). After further consideration, the investigators felt it was important to account for nicotine dependence, rather than tobacco-product specific dependence and HONC scores were selected to represent participants' levels of nicotine dependence. Despite its inclusion in the models, HONC scores did not significantly predict any immediate physiological responses, nor future intentions of use ($p > 0.05$).

B. Preliminary Results

1. Differences in Pre- and Post-Smoking Measurements by Device

a. TWP Smoking

TWP smoking pre- and post-smoking biological samples were positively correlated; CO (r=0.453, p=0.006), FEV (r=0.799, p=0.000), lung age (r=0.952, p= 0.000), systolic BP (r=0.782, p=0.000), diastolic BP (r=0.673, p=0.000), and HR (r=0.760, p=0.000). Paired-samples t-tests were conducted to identify any significant differences between pre- and post-smoking biological measures including CO, spirometry parameters, BP, and HR. On average, TWP post-smoking CO values were 9.14 part per million (ppm) higher than TWP pre-smoking CO values (t_{35}=8.87, 95% CI [7.03, 11.25], p=0.000). There was a significant average difference between pre- and post-TWP smoking HR levels (t_{35}=2.94, 95% CI [1.43, 7.80], p=0.006). No significant differences were identified in TWP pre-and post-smoking measures including: FEV (t_{35}=1.87, p=0.069), lung age (t_{35}=-0.097, p= 0.923), systolic BP (t_{35}=-0.226, p=0.822), and diastolic BP (t_{35}=0.315, p=0.754).

b. EWP Smoking

EWP smoking pre- and post-smoking biological samples were strongly and positively correlated; CO (r=0.887, p=0.000), FEV (r=0.833, p=0.000), lung age (r=0.930, p= 0.000), systolic BP (r=0.851, p=0.000), diastolic BP (r=0.819, p=0.000), and HR (r=0.726, p=0.000). Paired-sample t-tests showed there was a significant difference in systolic BP levels for pre- and post-smoking levels (t_{35}=2.34, 95% CI [0.547, 7.79], p= 0.025). There were no significant differences in EWP pre-and post-smoking measures including: CO (t_{35}=1.36, p=0.182), FEV (t_{35}=1.07, p=0.293), lung age (t_{35}=-0.829, p= 0.413), diastolic BP (t_{35}=1.26, p=0.215), and HR (t_{35}=1.59, p=0.122).

2. Differences between Smoking TWP and EWP

a. Immediate Physiological Responses

Analyses found no significant correlations among the following EWP and TWP smoking biological sample values; CO (r=0.134, p=0.437), FEV (r=0.170, p=0.321), lung age (r=-0.057, p= 0.740), systolic BP (r=-0.028, p=0.871), diastolic BP (r=0.203, p=0.234). There was a weak but significant correlation between EWP and TWP smoking HR levels (r=0.360, p=0.031). Paired-samples t-tests identified significant differences between EWP and TWP smoking CO levels (t_{35}=9.06, 95% CI [7.24, 11.43], p=0.000), FEV levels (t_{35}=2.30, 95% CI [0.030, 0.472], p=0.027), and HR levels (t_{35}=4.06, 95% CI [3.39, 10.17], p=0.000). There were no significant differences between EWP and TWP smoking biological samples including lung age (t_{35}=-0.649, p= 0.520), systolic BP (t_{35}=1.27, p=0.211), and diastolic BP (t_{35}=1.14, p=0.261).

b. Future Intentions of Use

Results showed there was a significant, positive correlation between EWP and TWP future intentions of use (r=0.631, p=0.000). A paired sample t-test suggested that there was no significant difference between EWP and TWP future intentions of use (t_{35}=-0.027, p=0.978).

c. Topography Measures

In addition to the outcome variables, various topography measures were analyzed to identify differences between EWP and TWP smoking behaviors. The total number of puffs taken when smoking an EWP and when smoking a TWP were highly correlated (r=0.704, p =0.000). Similarly, results showed a significant correlation between EWP and TWP average puff duration (r=0.665, p=0.000) and between EWP and TWP total smoke exposure (r=0.542, p=0.001). Paired t-tests found no significant differences between EWP and TWP total number of puffs (t_{35}=-1.635, p=0.111). However, there were significant mean differences between EWP and TWP average puff duration (t_{35}=4.617, 95% CI [0.388, 0.997], p=0.000) and between EWP and TWP total smoke exposure (t_{35}=1.804, 95% CI [-1.605, 27.216], p=0.000).

C. Hypotheses and Findings

Model fit statistics (AIC, AICC, BIC, and -2 Log Likelihood) for all models can be found in *Table 8*. As previously mentioned, the ICC was calculated for all models including intercept-only models, main effects models (excluding covariates), and the full model (including all main effects and covariates). An ICC is the proportion of total variance in the outcome variable accounted for by clustering within-person. A small ICC suggested that the extent of shared variance among the tested variables in the model was low. Intraclass correlations and pseudo R-squared effect sizes for all models are provided in *Table 9*.

1. Δ *Systolic Blood Pressure (BPsys)*

Hypotheses: Approximately equal nicotine levels were consumed from the EWP and TWP; therefore, it was hypothesized that using the EWP compared to the TWP will not significantly affect ΔBP*sys* from pre- to post-smoking (Hypothesis 1.1).

For this model, the ICC was almost zero (0.001), which explains why the model was unable to explain any variation in ΔBP*sys* (pseudo R^2= 0.0%).When holding all predictors equal to zero, the mean ΔBP*sys* for TWP use was -10.862 (*SE*=2.598, p<0.001). Findings suggest that for mean smoke exposure, EWP use compared to TWP use was associated with 4.372 lower ΔBP*sys* from pre- to post-smoking (*b*= -4.372, *SE*=3.040, p=0.160). In this model, for every one second increase in total smoke exposure, there was a 0.055 greater ΔBP*sys* from pre- to post-smoking (*b*= 0.055, *SE*=0.028, p=0.060). In this model, those who endorsed being White (*b*=7.725, *SE* =3.079, p=0.017), Hispanic (*b*=12.723, *SE*=0.926, p<0.001), and Asian (*b*=12.328, *SE*=5.366, p=0.028) demonstrated a significantly greater ΔBP*sys* from pre- to post-smoking. However, sex (*b*=0.590, *SE* =2.510, p=0.816), age (*b*=-1.051, *SE*=0.904, p=0.253), HONC scores (*b*=0.322, *SE* =0.445, p=0.475), and specific ethnicities including being Black (*b*=1.990, *SE*=2.120, p=0.354) and of an Other/Unknown race (*b*=5.901, *SE*=4.770, p=0.225) had no significant association with ΔBP*sys* pre- post-smoking. All model estimates are shown in *Table 7*.

2. Δ *Diastolic Blood Pressure (BPdia)*

Hypotheses: Approximately equal nicotine levels were consumed from the EWP and TWP; therefore, it was hypothesized that using the EWP compared to the TWP will not significantly affect ΔBP*dia* from pre- to post-smoking (Hypothesis 2.1) In contrast, it was expected that a higher total smoke exposure would demonstrate a significantly greater ΔBP*dia* (Hypothesis 2.2).

For this model, although there was a small amount of variability in *BPdia* (ICC= 0.193) the model was able to explain 13.9% of that variation. When holding all predictors equal to zero, the mean ΔBP*dia* for TWP use was -7.332 (*SE*=11.785, p=0.539). For mean smoke exposure, EWP use compared to TWP use was associated with 2.158 lower ΔBP*dia* from pre- to post-smoking (*b*= -2.158, *SE*=1.786, p=0.235). Additionally, for every one second increase in total smoke exposure, there was a 0.017 greater ΔBP*dia* from pre- to post-smoking (*b*= 0.017, *SE*= 0.021, p=0.424). In this model, specific ethnicities including being White (*b*=12.547, *SE*=2.622, p<0.001), Black (*b*=4.271, *SE*=1.417, p=0.005), Asian (*b*=14.670, *SE*=3.743, p<0.001), Hispanic (*b*=17.642, *SE*=0.815, p<0.001), and Other/Unknown (*b*=14.623, *SE*=3.646, p<0.001) were associated with a significantly greater ΔBP*dia* from pre- to post-smoking. In contrast, sex (*b*=2.699, *SE*=2.201, p=0.229), age (*b*=-0.415, *SE*=0.567, p=0.470), and HONC scores (*b*=0.266, *SE*=0.382, p=0.491) were not significantly associated with ΔBP*dia* from pre- to post-smoking.

3. Δ *Heart Rate (HR)*

Hypotheses Approximately equal nicotine levels were consumed from the EWP and TWP; therefore, it was hypothesized that using the EWP compared to the TWP will not significantly affect ΔHR from pre- to post-smoking (Hypothesis 3.1). In contrast, it was expected that a higher total smoke exposure would provide a significantly greater ΔHR (Hypothesis 3.2).

For this model, there was a small amount of variability in HR (ICC =0.191) and the model was unable to explain any variation in ΔHR (pseudo R^2= 0.0%).When holding all predictors equal to zero, the mean ΔHR for TWP use was 13.730 (*SE*=2.580, p<0.001). For mean smoke exposure, EWP use compared to TWP use was associated with 7.607 lower ΔHR from pre- to post-smoking (*b*= -7.607, *SE*=1.694, p<0.001). In contrast, for every one second increase in total smoke exposure, there was a 0.065 greater ΔHR from pre- to post-smoking (*b*= 0.065, *SE*=0.021, p=0.004). In this model, being White (*b* =-11.039, *SE*=2.598, p<0.001), Black (*b*=-13.127, *SE*=2.043, p<0.001), Hispanic (*b*=-7.303, *SE*=0.830, p<0.001), and Other/Unknown (*b*=-16.343, *SE*=3.054, p<0.001) were associated with a significantly smaller ΔHR from pre- to post-smoking. However, sex (*b*=1.774, *SE*=2.145, p=0.414), age (*b*=-0.049, *SE*=1.015, p=0.962), total HONC scores (*b*=0.005, *SE*=0.476, p=0.991), and being Asian (*b*=-6.443, *SE*=3.270, p=0.057) had no significant associations with ΔHR from pre- to post-smoking.

4. Δ *Carbon Monoxide (CO)*

Hypotheses: Independently, using the EWP compared to the TWP, a higher total smoke exposure, and the interaction term (type of waterpipe smoked X total smoke exposure) would provide a significantly smaller ΔCO (Hypothesis 4).

For this model, although there was a small amount of variability in ΔCO (ICC= 0.119) the model was able to explain 87.4% of that variation. When holding all predictors equal to zero, the mean ΔCO for TWP use was 11.846 (*SE*=1.138, p<0.001). For mean smoke exposure, EWP use compared to TWP use was associated with 9.965 lower ΔCO from pre- to post-smoking (*b*= -9.965, *SE*=0.821, p<0.001). In this model, for every one second increase in total smoke exposure, there was a 0.092 greater ΔCO from pre- to post-smoking (*b*= 0.092, *SE*=0.019, p<0.001). The interaction between the type of waterpipe smoked, total smoke exposure, and ΔCO was significant (b= -0.086, *SE*=0.019, p<0.001), indicating that for TWP use, each one second increase in total smoke exposure was associated with 0.006 greater ΔCO from pre- post-smoking. The plot displaying the significant interaction can be found in *Figure 1*.

In this model, being female (*b*=-2.225, *SE*=0.727, p=0.004), Hispanic (*b*=-1.274, *SE*=0.305, p=0.002), and of Other/Unknown race (*b*=4.806, *SE*=1.624, p=0.006) were associated with a significantly smaller ΔCO from pre- to post-smoking. In contrast, being older (*b*=0.092, *SE*=0.286, p=0.751), HONC scores (*b*=-0.114, *SE*=0.147, p=0.442), and being of specific ethnicities including White (*b*=-1.182, *SE*=1.064, p=0.275), Black (*b*=-1.710, *SE*=0.961, p=0.084), and Asian (*b*=0.331, *SE*=1.277, p=0.767) had no significant association with ΔCO pre- to post-smoking.

5. Δ *Estimated Lung Age*

<u>Hypotheses</u>: Independently, using the EWP compared to the TWP and a higher total smoke exposure would provide a significantly smaller Δ estimated lung age (Hypothesis 5).

For this model, the ICC was almost zero (0.002), which explains why the model was unable to explain any variation in Δ estimated lung age (pseudo R^2= 0.0%).When holding all predictors equal to zero, the mean Δ estimated lung age for TWP use was -1.931 (*SE*=2.060, p=0.357). Data showed that for mean smoke exposure, EWP use compared to TWP use was associated with 1.079 greater Δ estimated lung age from pre- to post-smoking (*b*= 1.079, *SE*=2.066, p=0.605). Also, for every one second increase in total smoke exposure, there was a 0.024 greater Δ estimated lung age from pre- to post-smoking (*b*= 0.024, *SE*=0.017, p=0.165). In this model, self-identifying as Black (*b*=9.108, *SE*=1.759, p<0.001) was associated with a significantly greater Δ estimated lung age from pre- to post-smoking. In contrast, sex (*b*=-0.441, *SE*=1.895, p=0.817), age (*b*=0.484, *SE*=0.627, p=0.446), HONC scores (*b*=-0.103, *SE*=0.320, p=0.749), and specific ethnicities including being White (*b*=3.127, *SE*=2.745, p=0.263), Asian (*b*=-0.437, *SE*=2.414, p=0.857), Hispanic (*b*=1.243, *SE*=0.680, p=0.076), and Other/Unknown race (*b*=2.285, *SE*=2.239, p=0.315) had no significant association with Δ estimated lung age from pre- to post-smoking.

6. Δ *Forced Expiratory Volume (FEV)*

Hypotheses: Independently, using the EWP compared to the TWP and a higher total smoke exposure would demonstrate a significantly greater ΔFEV (Hypothesis 6).

For this model, the ICC was low (0.115) and the model was unable to explain any variation in ΔFEV (pseudo R^2= 0.0%).When holding all predictors equal to zero, the mean ΔFEV for TWP use was 0.328 (*SE*=0.121, p=0.011). Findings suggest that for mean smoke exposure, EWP use compared to TWP use was associated with 0.259 lower ΔFEV from pre- to post-smoking (*b* = -0.259, *SE*=0.111, p=0.026). In contrast, for every one second increase in total smoke exposure, there was a 0.001 greater ΔFEV from pre- to post-smoking (*b*= 0.001, *SE*=0.001, p=0.681). In this model, being older (*b*=-0.096, *SE*=0.042, p=0.028) and self-identifying as Black (*b*=-0.505, *SE*=0.100, p<0.001) and Other/Unknown race (*b*=-0.756, *SE*=0.235, p=0.003) were associated with a significantly smaller ΔFEV from pre- to post-smoking. However, sex (*b*=-0.001, *SE*=0.125, p=0.992), HONC scores (*b*=0.008, *SE*=0.025, p=0.767), and being of specific ethnicities including White (*b*=-0.182, *SE*=0.196, p=0.362), Asian (*b*=-0.189, *SE*=0.235, p=0.427), and Hispanic (*b*=0.024, *SE*=0.061, p=0.699) were not associated with ΔFEV from pre- to post-smoking.

7. Future Intentions of Use

Hypotheses: Independently, using the EWP compared to the TWP and a higher total smoke exposure would significantly increase the likelihood of having future intentions to use the EWP compared to the TWP (Hypothesis 7).

For this model, although there was a large amount of variability in future intentions to use EWP (ICC= 0.593), the model was unable to explain any of that variation (pseudo R^2 = 0.0%), meaning that unaccounted for factors may be influencing the variation in future intentions to use EWP. When holding all predictors equal to zero, the average future intentions to use for TWP use was 36.056 (*SE*=1.769, p<0.001). The model showed that for mean smoke exposure, EWP use compared to TWP use was associated with a 0.523 decrease in intentions of future EWP use (*b*= -0.523, *SE*=0.927, p=0.576). In contrast, for every one second increase in total smoke exposure, there was a 0.039 increase in intentions to use EWP in the future (*b*= 0.039, *SE*=0.019, p=0.047). In this model, identifying as female compared to male (*b*=-4.369, *SE*=2.049, p=0.040) and being of specific ethnicities including White (*b* =-7.150, *SE*=2.323, p=0.004), Asian (*b*=-7.418, *SE*=2.623, p=0.008), Hispanic (*b*=-8.980, *SE*=0.683, p<0.001), and Other/Unknown (*b*=-12.865, *SE*=3.528, p=0.001) were associated with having less future intentions to use EWP compared to future intentions to use TWP. In contrast, age (*b*=-0.247, *SE*=0.769, p=0.750), HONC scores (*b*=0.107, *SE*=0.414, p=0.798), and identifying as Black (*b*=-1.954, *SE*=1.992, p=0.334) showed no significant associations with future intentions to use the EWP compared to TWP.

CONCLUSIONS

The present study compared TWP and EWP immediate physiological responses, total smoke exposure, and future intentions of use. It was hypothesized that, independently, using the EWP compared to the TWP, a higher total smoke exposure, and the interaction term (type of waterpipe smoked X total smoke exposure) would provide a significantly smaller average change in carbon monoxide levels. Similar to previous comparisons between e-cigarettes and cigarettes [16,27], this study demonstrated that those who smoked the EWP demonstrated a significantly smaller average change in carbon monoxide compared to smoking the TWP. This outcome was expected since one TWP puff can have up to ten times the volume of carbon monoxide than in a cigarette [28] which is a result of using lit coals to directly burn shisha. In contrast, the EWP use should not expose the smoker to any carbon monoxide based on the non-combustible, electronic heating mechanism in the device which is comparable to e-cigarettes [27,66]. There are several secondary effects associated with these findings, such that, smokers who switch from combustible to non-combustible waterpipe would have a drastic reduction in the number of toxic CO exposure occurrences and they would be less likely to burn themselves (i.e., no longer the risk of touching or dropping a burning coal).

Interestingly, in this model, being female, being Hispanic, and being of an Other/Unknown race was associated with a significantly lower average change in carbon monoxide from pre- to post-smoking. This may have occurred because these specific groups smoked the TWP with less intensity, resulting in them having a smaller difference in carbon monoxide exposure between TWP pre- and post-smoking, and therefore, a smaller difference in carbon monoxide between TWP and EWP smoking sessions. Similarly, having higher levels of nicotine dependence may be associated with a lower average change in carbon monoxide from pre- to post-smoking. One nationally representative sample showed that young adult males and being of specific race/ethnicities including being White and Hispanic report the highest rates of TWP use [85]. The present findings may have occurred because individuals with greater dependence may have higher tolerance of nicotine and tobacco products. Despite these findings, future research should use larger sample sizes with a more representative sample of all race/ethnicities, which was a limitation of this study, to further explain what may be influencing racial/ethnic differences in exposure to carbon monoxide. In sum, this is the first-known study to examine the differences between TWP and EWP exposure on carbon monoxide levels and to produce evidence that suggests that EWP smokers may not be exposed to any carbon monoxide while smoking. By knowing the device's heating process [66], it may be safe to imply that the EWP is a safer alternative in regard to exposure to CO.

This study hypothesized that, independently, using the EWP compared to the TWP and a higher total smoke exposure would demonstrate a significantly greater average change in FEV from pre- to post-smoking. Results showed that using an EWP compared to a TWP was associated with a significantly smaller average change in FEV; however, total smoke exposure was not associated with significant changes in FEV. These findings do not support similar research that showed tobacco cigarette smoke significantly reducing FEV, while e-cigarette vapor exposure was not significantly associated with a change in FEV[63]. The present study demonstrates that some other factor, besides smoking behaviors, may have influenced the relationship between using a EWP and TWP and the outcome variable. As an alternative explanation, one study showed that physical activity before spirometry measures could affect the variability in FEV over a 20-minute period [86]. For example, since participants were college students, they may have been exercising at the gym, participating in athletics, or may have walked a fair amount prior to attending one of the smoking sessions. It is possible that prior physical activity could have influenced these results on one smoking day and not the other.

In this model, being older, Black, and of Other/Unknown race was significantly associated with a smaller change in FEV from pre- to post-smoking. Although the spirometer used accounted for height, weight, and sex of a smoker, race/ethnicity was not an option to specify prior to measurement. Previous literature suggests that evaluating lung function based on racial/ethnic differences should be interpreted with caution as non-whites are at risk for erroneous assessment because there is a lack of use of race specific reference values[87]. However, it has been suggested that ethnic difference affect lung function in adults and may be due to differences in inspiratory muscle strength or lung compliance [87]. Additionally, it has been established that lower lung function is associated with social conditions, such as poverty, and the environment [88]. In terms of physiology, it still remains unknown as to how social class and race are associated with lung function, specifically FEV [88].

This study hypothesized that, independently, using the EWP compared to the TWP and total smoke exposure would provide a significantly smaller average change in estimated lung age. However, the data showed no significant relationships between the predictors and outcome variables. Combustible smoking can cause respiratory complications such as airway obstruction, which can mimic premature lung aging [62]. When using a spirometer, a smokers' FEV is used, in part, to estimate lung age. Based on this information, it can be assumed that as FEV changes in a 20-minute smoking session, the estimated lung age will also vary. In the present model, the average change in FEV between EWP and TWP pre- and post-smoking was not significantly different, therefore, the estimated lung age was not affected. However, self-identifying as Black was associated with a significantly greater change in estimated lung age from pre- to post-smoking. As mentioned previously, the spirometer does not adjust for race/ethnicity which could have influenced the measurement validity. Race-related demographics such as type of employment, income, and environmental characteristics (rural vs. urban) should be accounted for based on the information known about its effects on lung function (as previously discussed) [88]. Literature advises that lung function tests are prone to over- and under-estimate lung age and should be interpreted with caution [89].

Since no other studies have investigated EWP use, it is too early to determine the associated long-term cardiovascular health risks. However, it was possible to measure immediate physiological responses including average change in blood pressure (systolic and diastolic) and heart rate. In the study, approximately equal nicotine levels were used while smoking the EWP and TWP; therefore, it was hypothesized that using the EWP compared to the TWP would not significantly affect any cardiovascular-related health responses (average change in systolic and diastolic blood pressure and heart rate) from pre- to post-smoking. Previous studies showed that nicotinic TWP use is associated with an increased risk of developing clogged arteries, heart disease, and elevated heart rate and blood pressure [6,7,29,44]. Similarly, it has been demonstrated that using e-cigarette containing nicotinic e-liquid for 30 minutes resulted in increased arterial stiffness, heart rate, and blood pressure [70]. The present findings demonstrated that smoking an EWP compared to TWP was associated with a significantly smaller average change in heart rate from pre- to post-smoking, but no significant change in systolic or diastolic blood pressure. It is possible that higher levels of nicotine exposure occur while using the TWP compared to the EWP. In a previous study using automated smoking machines, it was demonstrated that e-cigarettes delivered less nicotine per puff than conventional cigarettes [59]. Another study showed that 5 minutes after taking a similar number of puffs, plasma nicotine levels after smoking an e-cigarette were significantly lower compared to after smoking a traditional cigarette [60]. It should be noted, however, that when comparing experienced e-cigarette users and conventional cigarette smokers, both achieved similar nicotine concentrations[59]. Despite this information, it is unknown if or how the EWP exposes the smokers to similar levels of nicotine as when smoking TWP. It will be important in future studies to identify any differences in nicotine uptake in EWP compared to TWP.

Nicotine is the primary ingredient in tobacco products known to elevate heart rate and blood pressure [44,70]. In the present study, both e-liquid and shisha contained similar or equivalent levels of nicotine. Therefore, this study hypothesized that a higher total smoke exposure to either device would provide a significantly greater average change in systolic and diastolic blood pressure and heart rate. The findings demonstrated that a higher total smoke exposure was associated with a significantly greater average change in heart rate, but was not associated with a change in systolic nor diastolic blood pressure. These results may be explained by simple anatomy, in that, when heart rate increases, blood vessels dilate to allow more blood to flow through the body, allowing for a very small increase in blood pressure, if any [90]. When heart rate increases, it does not automatically mean that blood pressure increases. It can be suggested that as smoke exposure increased, the level of nicotine exposure also increased, thus resulting in a faster heartbeat. In contrast, smoke exposure did not influence a significant change in systolic or diastolic blood pressure from pre- to post-smoking, implying that low, moderate, and heavy smokers of either device may be at an equal risk for a change in blood pressure between pre- and post-smoking. A reason for this occurrence could be that any level of smoke exposure, from either device, results in similar changes in cardiovascular function. These findings are similar to previous studies showing that both, nicotinic e-cigarette and conventional cigarette smoking, were associated with increased heart rate and blood pressure [6,53,61,69,70]. Future studies would benefit from replicating this study, but collecting cardiovascular measurements for a longer period of time after smoking each device. This could inform the literature about the lasting effects each device has on the body, rather than just the acute physiological responses. Also, it would be interesting to know if various levels of nicotine in shisha and e-liquid would affect the models tested in the present study.

As predicted, results showed that being of any listed race was associated with a significantly greater change in diastolic blood pressure from pre- to post-smoking. However, only those who endorsed being White or Hispanic demonstrated a significantly greater average change in systolic blood pressure from pre- to post-smoking compared to their counterparts. The results suggest that these two racial groups may have been exposed to more nicotine via smoking behaviors, which ended in a greater change in systolic blood pressure from pre- to post-smoking. Another explanation for these findings would be that this sample of Whites and Hispanics may have had a lower average baseline systolic blood pressure compared to other races which led to a greater difference in pre- to post-smoking blood pressure levels. Another explanation may be that Hispanics may have a higher threshold of the maximum pressure exerted on the blood vessel walls (systolic blood pressure) compared to other races[91]. Literature suggests that there are racial differences in the rate of nicotine metabolism, specifically, African Americans have a slower average rate of nicotine metabolism compared to Whites [91]. The body may have been able to better regulate the effects of nicotine on systolic blood pressure in other races. Further research, such as a clinical study, is necessary to explain the racial differences in blood pressure changes when using an EWP compared to a TWP.

As a final hypothesis, it was expected that, independently, using the EWP compared to the TWP and a higher total smoke exposure would significantly predict more future intentions to use the EWP compared to the TWP. Initially, it was believed that the novelty of the EWP would result in a higher smoke intake compared to the TWP, as well as reflect a greater intention to use the device. However, the results displayed no significant associations between any predictors and future intentions to use. There may be alternative explanations as to why smokers were not more inclined to have intentions to use one waterpipe over the other. For example, smokers may not have been informed enough about the EWP to make a decision about future use or transitioning from TWP to EWP. Smokers may not have liked the blueberry-flavoring and that alone could result in participants' lack of future intentions to use either device. Although participants were able to smoke each device for 20 minutes, they may not have been able to make a decision in that timeframe whether they liked the new waterpipe or not. It will be important in future research to identify regular EWP users and measure their perceptions of use and health beliefs associated with use, as these could influence whether someone has intentions to initiate and continue use of a product. This model also showed that all races, excluding being Black, were associated with an increased likelihood of having future intentions of EWP compared to TWP. This implies that those who self-identify as black are not willing to make a change from combustible to non-combustible waterpipe use. It is possible that they disliked the e-liquid flavor or nicotine content, they had a bad experience using the device, or it simply did not meet or exceed their expectation. It will be important in future research identify racial differences in EWP and TWP use, particularly who would be more likely to transition from TWP to EWP or use the EWP as their first waterpipe experience.

Prior to this study, there were no known systematic studies comparing the effect of total smoke exposure from EWP and TWP on immediate physiological responses including lung and cardiovascular function and carbon monoxide levels. Overall, the present study was not able to conclude that the EWP use is a safer alternative to TWP smoking; however, the results did suggest that the EWP may expose a smoker to significantly less carbon monoxide compared to smoking TWP. Although the long-term health effects of ENDS use are not clear, the current literature suggests that non-combustible smoking may be a safer alternative to combustible smoking. Further research is necessary to understand the health risks of EWP smoking and to provide critical data on potential harm reduction and potential benefits of advocating switching products. For example, a large-scale, prospective cohort study can compare the development of long-term health outcomes between non-smokers, and combustible and non-combustible waterpipe smokers. Another option would be to conduct a cross-sectional study to identify associations between current tobacco product use and related health complications at a specific point in time.

A. Limitations

Since there is no existing EWP-related literature describing expected health outcomes of EWP use, these findings should be interpreted with caution. It will be important to identify prevalence of EWP use overall and in comparison to TWP use to determine if people are even using the device and to determine if there are enough users to participate in an EWP health-related longitudinal study. If it is determined that a large subgroup of the population are currently using or plan to use EWP and additional research provides evidence about its safety, then national efforts can be made to identify TWP and EWP use as a national health priority.

Statistical and data limitations were apparent in this research study. Specifically, the study used a small sample size which limited the statistical approaches to analyzing the data. One simulation study demonstrated that a small sample size of 50 or less led to biased estimates of the standard errors, whereas in all other samples sizes (that were greater than 50), regression coefficients, variance components, and standard errors were unbiased and accurate [92]. Prior to conducting future EWP studies that use multilevel modeling or other advanced statistics, it may be beneficial to conduct a similar simulation study to plot curves of how power increases with sample size. Using a larger sample size will allow for different methods of estimating parameters.

Additionally, this study should be replicated using a larger sample size to more reliably reflect the population. Although the current findings suggest that specific races may explain part of the variance in the outcome variables, it should be addressed that not all race/ethnicities were equally represented in the sample and in some cases, were represented by only a few individuals. Despite this, investigators felt that all collected data should be included in the analyses for purposes of maintaining power and to serving as a starting point for the literature. Since there are no known studies examining the EWP, it is more beneficial for future studies to utilize what little information there is about racial/ethnic differences surrounding use than to conduct a study without knowing any details. For this study, individuals aged 18-24 were considered eligible. In future research, it would be beneficial to include all adults over the age of 18 who smoke TWP and e-cigarettes to establish a more representative sample.

A limitation of the study was the use of a newly-developed EWP and TWP questionnaire. The original questionnaire that was developed for a previous pilot study, only included questions regarding EWP use. For this dissertation study, identical questions were asked about EWP and

TWP. Although tests of reliability and validity were conducted on both the previous pilot study questionnaire and the present EWP/TWP questionnaire, further research and analyses should continue to assess the reliability and validity of measurement using larger sample sizes. Additionally, because self-report was used in the EWP/TWP questionnaire and several nicotine and tobacco product-specific dependence questionnaires, the measures may be subject to under- or over-reporting that could influence the results [93]. These are common occurrences in tobacco research, particularly in emerging adults, who may be trying to hide tobacco use from their parents, friends, or a significant other or accentuate their frequency of using tobacco products to make themselves look "cool" among their peers [94].

Another limitation was that participants' were not asked about specific existing medical conditions prior to participating in the study. Participants were asked if a doctor ever recommended them to quit smoking due to a health complication or medicine interaction; however, questions about specific medical conditions that could influence the physiological markers, such as cardiovascular health, were not asked. For example, initially asking about BMI could help determine if a participant would be more inclined to have cardiovascular or respiratory complications compared to their healthier counterparts. Despite the aforementioned limitations, the results from this study represent plausible explanations and should provide a foundation for future research to compare the effects of smoking EWP and TWP on immediate physiological responses.

TABLE 4

Table 4. Sample Demographic Characteristics (N=36)

	Frequency	**Mean (*SD*)**
Age		20.08 (*SD*=1.32)
Gender		
Male	18 (50.0%)	
Race		
White/Caucasian	16 (44.4%)	
Hispanic	12 (33.3%)	
Asian	6 (16.7%)	
Black/African American	2 (5.6%)	
American Indian/Alaska Native	0 (0.0%)	
Native Hawaiian/Other Pacific Islander	0 (0.0%)	
Unknown/ Other	1 (2.8%)	
Ethnicity (if Hispanic)		
White/Caucasian	7 (19.4%)	
Hispanic/Latino Only	9 (25.0%)	
Black/African American	1 (2.8%)	

TABLE 5

Table 5. Sample Nicotine and Product-Specific Dependence

	Frequency	**Mean (*SD*)**
PSECDI		3.72 (*SD*=2.49)
Not EC dependent	14 (38.9%)	
Low EC dependence	21 (58.3%)	
Medium EC dependence	1 (2.8%)	
High EC dependence	0 (0.0%)	
LWDS-11		5.86 (*SD*=2.43)
Not TWP dependent	33 (91.7%)	
Moderate TWP dependence	3 (8.3%)	
High TWP dependence	0 (0.0%)	
FTND (current cigarette smokers only)		1.00 (*SD*=1.49)
Very low dependence	7 (19.4 %)	
Low dependence	2 (5.6%)	
Medium, high, or very high dependence	0 (0.0%)	
HONC		1.34 (*SD*=2.24)
Full autonomy	20 (55.6%)	
Little loss of autonomy (endorsement of 1-3 items), had, and had	10 (27.8%)	
Moderate loss of autonomy (endorsement of 4-7 items)	4 (11.1%)	
Complete loss of autonomy (endorsement of all 10 items)	2 (5.6%)	
Ever cigarette use	9 (25.0%)	
Past 30 day cigarette use		
0 days	18 (50.0%)	

1-5 days	8 (22.2%)
6-10 days	5 (13.9%)
11-20 days	2 (5.6%)
21-29 days	0 (0.0%)
All 30 days	0 (0.0%)
Ever waterpipe use	36 (100.0%)
Past 30 days waterpipe use	
0 days	9 (25.0)
1-5 days	20 (55.6%)
6-10 days	3 (8.3%)
11-20 days	1 (2.8%)
21-29 days	3 (8.3%)
All 30 days	0 (0.0%)
Ever e-cigarette use	36 (100.0%)
Past 30 day e-cigarette use	
0 days	9 (25.0)
1-5 days	14 (38.9%)
6-10 days	9 (25.0%)
11-20 days	1 (2.8%)
21-29 days	0 (0.0%)
All 30 days	3 (8.3%)
Personal e-liquid nicotine content	
0 mg/mL	4 (11.1%)
1-3 mg/ mL	10 (27.8%)
4-6 mg/ mL	3 (8.3%)
7-12 mg/ mL	1 (2.8%)
> 20 mg/ mL	2 (5.6%)
I don’t know.	16 (44.4%)
Ever marijuana use	25 (69.4%)
Past 30 day marijuana use	
0 days	2 (5.6%)

1-5 days	6 (16.8%)	
6-10 days	6 (16.8%)	
11-20 days	3 (8.3%)	
21-29 days	3 (8.3%)	
All 30 days	3 (8.3%)	
Most amount of alcoholic drinks in one day– past 30 days		7.91 (*SD*=5.53)

*Below is a brief description of how each response was scored for individual questionnaires.

TABLE 6

Table 6. Topography Measures		
Device	**EWP**	**TWP**
Variable	**Mean (*SD*)**	**Mean (*SD*)**
Total Smoke Exposure (seconds)	108.03 (46.32)	95.22 (42.35)
Average Puff Duration (seconds)	3.52 (1.20)	2.83 (0.83)
Total Number of Puffs	32.53 (15.09)	36.03 (17.71)

TABLE 7

Table 7. Results of Multilevel Models Examining Predictors of Immediate Physiological Responses and Future Intentions to Use

Variables	***Estimate***	**S.E.**	**p-value**
Δ Systolic BP			
Intercept	-10.862^	2.598	<0.001***
Waterpipe Type (EWP)	-4.372	3.040	0.160
Total Smoke Exposure	0.055	0.028	0.060
Sex	0.590	2.510	0.816
Age	-1.051	0.904	0.253
White	7.725	3.079	0.017*
Black	1.990	2.120	0.354
Asian	12.328	5.366	0.028*
Hispanic	12.723	0.926	<0.001***
Other	5.901	4.770	0.225
HONC	0.322	0.445	0.475
Δ Diastolic BP			
Intercept	-7.332^	11.785	0.539
Waterpipe Type (EWP)	-2.158	1.786	0.235
Total Smoke Exposure	0.017	0.021	0.424
Sex	2.699	2.201	0.229
Age	-0.415	0.567	0.470
White	12.547	2.622	<0.001***
Black	4.271	1.417	0.005**
Asian	14.670	3.743	<0.001***
Hispanic	17.642	0.815	<0.001***
Other	14.623	3.646	<0.001***
HONC	0.266	0.382	0.491
Δ Heart Rate			
Intercept	13.730^	2.580	<0.001***
Waterpipe Type (EWP)	-7.607	1.694	<0.001***
Total Smoke Exposure	0.065	0.021	0.004**
Sex	1.774	2.145	0.414

Age	-0.049	1.015	0.962
White	-11.039	2.598	<0.001***
Black	-13.127	2.043	<0.001***
Asian	-6.443	3.270	0.057
Hispanic	-7.303	0.830	<0.001***
Other	-16.343	3.054	<0.001***
HONC	0.005	0.476	0.991
Δ Carbon Monoxide			
Intercept	11.846^	1.138	<0.001***
Waterpipe Type (EWP)	-9.965	0.821	<0.001***
Total Smoke Exposure	0.092	0.019	<0.001***
Waterpipe Smoked X Smoke Exposure	-0.086	0.019	<0.001***
Sex	-2.225	0.727	0.004**
Age	0.092	0.286	0.751
White	-1.182	1.064	0.275
Black	-1.710	0.961	0.084
Asian	0.331	1.277	0.767
Hispanic	-1.274	0.305	0.002**
Other	4.806	1.624	0.006**
HONC	-0.114	0.147	0.442
Δ Forced Expiratory Volume			
Intercept	0.328^	0.121	0.011*
Waterpipe Type (EWP)	-0.259	0.111	0.026*
Total Smoke Exposure	0.001	0.001	0.681
Sex	-0.001	0.125	0.992
Age	-0.096	0.042	0.028*
White	-0.182	0.196	0.362
Black	-0.505	0.100	<0.001***
Asian	-0.189	0.235	0.427
Hispanic	-0.024	0.061	0.699

Other	-0.756	0.235	0.003**
HONC	0.008	0.025	0.767
Δ Estimated Lung Age			
Intercept	-1.931^	2.060	0.357
Waterpipe Type (EWP)	1.079	2.066	0.605
Total Smoke Exposure	0.024	0.017	0.165
Sex	-0.441	1.895	0.817
Age	0.484	0.627	0.446
White	3.127	2.745	0.263
Black	9.108	1.759	<0.001***
Asian	-0.437	2.414	0.857
Hispanic	1.243	0.680	0.076
Other	2.285	2.239	0.315
HONC	-0.103	0.320	0.749
Future Intentions of Use			
Intercept	36.056^	1.769	<0.001***
Waterpipe Type (EWP)	-0.523	0.927	0.576
Total Smoke Exposure	0.039	0.019	0.047*
Sex	-4.369	2.049	0.040*
Age	-0.247	0.769	0.750
White	-7.150	2.323	0.004**
Black	-1.954	1.992	0.334
Asian	-7.418	2.623	0.008**
Hispanic	-8.980	0.683	<0.001***
Other	-12.865	3.528	<0.001***
HONC	0.107	0.414	0.798

Note:
* p <.05
** p < .01
*** p < .001
^ random slope or intercept

TABLE 8

Table 8. Model Fit Statistics				
Variables	**AIC**	**AICC**	**BIC**	**-2 Res Log Likelihood**
Δ Systolic BP	524.6	525.1	529.4	518.6
Δ Diastolic BP	468.6	469.0	473.4	462.6
Δ Heart Rate	474.0	474.5	478.8	468.0
Δ Carbon Monoxide	369.5	369.9	374.2	363.5
Δ Forced Expiratory Volume	135.7	136.1	140.4	129.7
Δ Estimated Lung Age	485.9	486.3	490.6	479.9
Future Intentions of Use	428.6	429.0	433.4	422.6

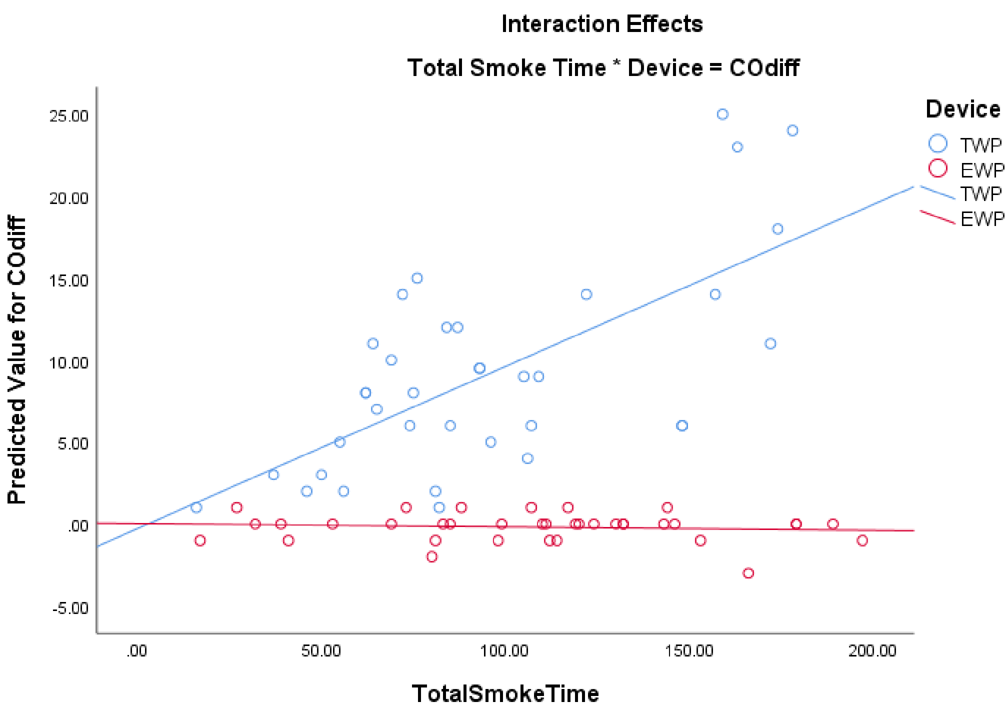
TABLE 9

Table 9. Intraclass Correlations and Percentage of Variance Accounted for in Models				
	ICC Intercept Only Model	**ICC Main Effects Model (without covariates)**	**ICC Full Model (with covariates)**	**Pseudo R^2 (Percent variance explained by the covariates)***
Outcome Variable				
Systolic BP	0.001	0.002	0.001	-1.00 (0.0%)
Diastolic BP	0.193	0.198	0.166	0.139 (13.9%)
Heart Rate	0.191	0.332	0.330	-0.727 (0.0%)
Carbon Monoxide	0.119	0.025	0.015	0.874 (87.4%)
FEV	0.115	0.178	0.213	-0.852 (0.0%)
Estimated Lung Age	0.002	0.046	0.006	-2.00 (0.0%)
Future Intentions of Use	0.593	0.631	0.635	-0.071 (0.0%)

*Higher pseudo R^2 values reflect a better model fit [83]. A negative pseudo R-squared should be interpreted as zero percent variance being explained by the model.

FIGURE 1

Figure 1. Interaction Plot for Δ Carbon Monoxide



APPENDIX A. EWP Questionnaire Reliability and Validity

A. Pilot Study EWP Questionnaire (PEWQ)

For the pilot study EWP questionnaire (PEWQ), the Cronbach's alpha was 0.802, which indicated a high level of internal consistency within the questionnaire. The results showed that the removal of Item 6 (How likely would you be to speak negatively about your experience with the electronic waterpipe?) and Item 13 (How willing would you be to speak negatively about your experience with the electronic waterpipe?) would result in a higher Cronbach's alpha (0.850 and 0.848 respectively). The Corrected Item-Total Correlation values were extremely low, -0.272 and -0.284 respectively. After full consideration of the question content, its purpose in the questionnaire, and the aforementioned values, it was determined that Item 6 and 13 would be removed for the full dissertation study (for Paper #3).

B. Dissertation Study EWP Questionnaire (mPEWQ)

For the dissertation study, the modified PEWQ (with Items 6 and 13 removed) was used. Additionally, the modified PEWQ was mirrored and questions asking about EWP were now asked about TWP. For the purposes of this discussion, the PEWQ related to EWP will be deemed Q1 and the PEWQ related to TWP will be labelled Q2. Internal reliability tests were conducted independently on each questionnaire (Q1 and Q2). For Q1, the Cronbach's alpha was 0.939, which demonstrated a high level of internal consistency. The output showed that if Item 8 (How willing are you to research and collect information and details about the electronic waterpipe?) was removed, Cronbach's alpha would increase to 0.941. The Corrected Item-Total Correlation value was 0.530. To determine whether an item in Q1 was valid or not, a correlation analysis was conducted. The correlation between one item in a questionnaire and the summed total for the questionnaire was assessed using the significance level of 5% ($p < 0.05$). It was determined that all items were significantly correlated with the summed total, and therefore, accurately measured what they were intended to measure. After deliberation, it was decided that removing the Item 8 would not significantly change the reliability or the validity of the questionnaire and will be kept as part of the questionnaire.

For Q2, the Cronbach's alpha was 0.695, which showed a moderate level of consistency among items. Results explained that if Item 3 (How likely would you be to research and collect information about the traditional waterpipe?), and Item 6 (How willing are you to use a traditional waterpipe?) were removed that the alpha would improve to 0.698 and 0.767, respectively. The Corrected Item-Total Correlation values were low, 1.98 and -0.383 respectively. To determine whether an item in Q2 was valid or not, a correlation analysis was conducted. The correlation between one item in a questionnaire and the summed total for the questionnaire was assessed using the significance level of 5% ($p < 0.05$). Results showed that all but one item (Item 6) in the TWP-related questionnaire was significantly correlated ($p < 0.05$) and it can be concluded that they are valid items within the questionnaire. However, the correlation coefficient for Item 6 (How willing are you to use a traditional waterpipe?) was $r=-0.317$ ($p=0.060$) showing that it did not measure what it was supposed to measure. After evaluating these results, the investigators have concluded that Item 3 should be kept in future applications of Q2. However, Item 6 should be removed from the Q2 as it is lacking reliability and validity. Overall, the use of Q2 in future studies is questionable as the internal reliability is not as great compared to previous applications of the questionnaire (as in Q1) and data does not meet an acceptable Cronbach's alpha level of > 0.08.

CHAPTER 5

Implications and Future Work

IMPLICATIONS AND FUTURE WORK

Young adults are highly susceptible to social and environmental influences to use tobacco, which can lead to experimentation with a range of tobacco products [17]. Although there have been expanding efforts to decrease combustible traditional waterpipe (TWP) smoking, it remains a popular tobacco product in this population. Traditionally, there have been no alternatives for TWP smokers; however, e-waterpipes (EWP) have recently emerged as an alternative non-combustible product. The EWP is relatively new to the marketplace; therefore, this dissertation serves as the first known exploration of the EWP. The overall purpose of the dissertation was to build a platform for researchers and policymakers to identify and analyze the EWP.

Since there are no publications regarding the EWP, it can be assumed that researchers and regulatory agencies have yet to consider the potential benefits, harm or overall influence of EWP as a nicotine delivery system. As previously shown in the literature regarding e-cigarettes, several manuscripts were published, prior to experimental research being conducted, that describe the device, its mechanisms, perspectives, and implications of use. This dissertation provided the literature with an introduction to the EWP to address the same concerns regarding the EWP and e-bowl, including a technical description, a list of current e-bowls publically available, implications of use, and recommended future directions for research. The first manuscript of this dissertation highlights a crucial need for more investigation into the use of EWP, as well as the need for comprehensive EWP and e-head regulation. This is the first known peer-reviewed paper assessing the e-bowl and EWP.

Prior to this dissertation, there were no known research studies describing smokers' perceptions of EWP use or their future intentions of using the waterpipe. This dissertation utilized data from the first known pilot study as the initial step in exploring the EWP in an experimental setting. For the second manuscript, a secondary data analysis described first-time EWP smokers' perceived health outcomes, willingness and likelihood of future use, and first-time experiences with EWP. Findings from this study suggest that EWP may gain popularity and become socially acceptable in a way similar to TWP and e-cigarettes. This research may help explain the likelihood of transitioning from combustible to non-combustible waterpipe. However, more research is necessary to understand the complex nature of decision-making and behavior change. Specifically, prevention and intervention research could focus the likelihood of a combustible smoker transitioning to a lower risk product. These findings also suggest that the public become aware of the health risks associated with electronic smoking devices, in addition to traditional tobacco products. Public health messaging aimed at reducing or eliminating the use of any combustible or non-combustible nicotine/tobacco product should be considered.

Preceding this dissertation, there were no known systematic, experimental studies comparing the effect of smoking EWP and TWP on immediate physiological responses such as lung and cardiovascular function and carbon monoxide (CO) exposure. The present study provided evidence that the EWP may exposure users to less CO than when smoking a TWP. Further research is necessary to better understand these findings. With increasingly high rates of young adult TWP smokers and the associated health risks, it is essential to identify alternative products that may reduce harm. Future research is necessary to understand the health effects of EWP and to provide critical data on potential harm reduction and potential benefits of advocating switching products.

In summary, the three manuscripts detailed in this dissertation provide the first evaluation of the EWP, in relation to TWP, and its purpose was to set a foundation for future research and regulatory action regarding the novel device. After conducting the initial review (Chapter 2), it can be concluded that the e-head device should be regulated similarly to an e-cigarette. There would need to be few additions to the e-cigarette regulations already in place. For example, there should be restrictions surrounding the voltage available on an e-head to heat the e-liquid. A voltage that can vary from a low to high setting should be standard so that smokers do not burn their throats when trying the new device. The EWP, as a larger system that includes the e-head and the structure of a TWP, should not be sold to minors under the age of 18. There are policies already in place that require hookah distribution websites and tobacco store owners to ask for identification confirming their age. Those regulations should be extended to include e-heads online and in-person. Overall, placing additional requirements on the design and manufacturing of e-heads and on the distribution of the products are necessary.

REFERENCES

1. Hu SS, Neff L, Agaku IT, et al. Tobacco product use among adults - United States, 2013-2014. *MMWR Morb Mortal Wkly Rep*. 2016;65(27):685-691. doi:10.15585/mmwr.mm6527a1

2. Schulenberg J, Johnston L, O'Malley P, Bachman J, Miech R, Patrick M. Monitoring the Future national survey results on drug use, 1975-2017: Volume II, college students and adults ages 19-55. 2018. http://monitoringthefuture.org/pubs/monographs/mtf-vol2_2017.pdf. Accessed August 28, 2018.

3. U. S. Department of Health and Human Services. Research Priorities for FDA Center for Tobacco Products. https://prevention.nih.gov/tobacco-regulatory-science-program/research-priorities. Published 2017. Accessed October 27, 2017.

4. Weaver SR, Majeed BA, Pechacek TF, Nyman AL, Gregory KR, Eriksen MP. Use of electronic nicotine delivery systems and other tobacco products among USA adults, 2014: results from a national survey. *Int J Public Health*. 2016;61(2):177-188. doi:10.1007/s00038-015-0761-0

5. American Lung Association.Smoke-free Communities Project. Hookah Smoking. A Growing Threat to Public Health. 2011. http://www.lung.org/assets/documents/tobacco/hookah-policy-brief-updated.pdf. Accessed October 21, 2017.

6. Akl EA, Gaddam S, Gunukula SK, Honeine R, Jaoude PA, Irani J. The effects of waterpipe tobacco smoking on health outcomes: a systematic review. *Int J Epidemiol*. 2010;39(3):834-857. doi:10.1093/ije/dyq002

7. American Lung Association. An Emerging Deadly Trend: Waterpipe Tobacco Use. 2007. http://www.lungusa2.org/embargo/slati/Trendalert_Waterpipes.pdf. Accessed May 21, 2017.

8. Cobb CO, Sahmarani K, Eissenberg T, Shihadeh A. Acute toxicant exposure and cardiac autonomic dysfunction from smoking a single narghile waterpipe with tobacco and with a

"healthy" tobacco-free alternative. *Toxicol Lett*. 2012;215(1):70-75. doi:10.1016/j.toxlet.2012.09.026

9. Eissenberg T, Ward KD, Smith-Simone S, Maziak W. Waterpipe tobacco smoking on a U.S. college campus: prevalence and correlates. *J Adolesc Health Off Publ Soc Adolesc Med*. 2008;42(5):526-529. doi:10.1016/j.jadohealth.2007.10.004

10. Nosratzehi T, Arbabi-Kalati F, Alijani E, Tajdari H. Comparison of cotinine salivary levels in hookah smokers, passive smokers, and non-smokers. *Addict Health*. 2015;7(3-4):184.

11. Salameh P, Waked M, Aoun Z. Waterpipe smoking: construction and validation of the Lebanon Waterpipe Dependence Scale (LWDS-11). *Nicotine Tob Res*. 2008;10(1):149-158. doi:10.1080/14622200701767753

12. Aboaziza E, Eissenberg T. Waterpipe tobacco smoking: what is the evidence that it supports nicotine/tobacco dependence? *Tob Control*. 2015;24(Suppl 1):i44-i53. doi:10.1136/tobaccocontrol-2014-051910

13. Alzoubi KH, Khabour OF, Azab M, et al. CO exposure and puff topography are associated with Lebanese waterpipe dependence scale score. *Nicotine Tob Res Off J Soc Res Nicotine Tob*. 2013;15(10):1782-1786. doi:10.1093/ntr/ntt049

14. Kassim S, Al-Bakri A, Al'Absi M, Croucher R. Waterpipe tobacco dependence in U.K. male adult residents: a cross-sectional study. *Nicotine Tob Res Off J Soc Res Nicotine Tob*. 2014;16(3):316-325. doi:10.1093/ntr/ntt148

15. Dube SR, Pathak S, Nyman AL, Eriksen MP. Electronic cigarette and electronic hookah: a pilot study comparing two vaping products. *Prev Med Rep*. 2015;2:953-958. doi:10.1016/j.pmedr.2015.10.012

16. Farsalinos KE, Polosa R. Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review. *Ther Adv Drug Saf*. 2014;5(2):67-86. doi:10.1177/2042098614524430

17. U.S. Department of Health and Human Services. Centers for Disease Control and Prevention. Preventing tobacco use among youth and young adults: a report of the Surgeon General. 2012. https://www.surgeongeneral.gov/library/reports/preventing-youth-tobacco-use/index.html. Accessed June 26, 2017.

18. Lerner CA, Sundar IK, Watson RM, et al. Environmental health hazards of e-cigarettes and their components: oxidants and copper in e-cigarette aerosols. *Environ Pollut Barking Essex 1987*. 2015;198:100-107. doi:10.1016/j.envpol.2014.12.033

19. Salter J. Atomizer vs. Cartomizer vs. Clearomizer. Cig Buyer.com. http://www.cigbuyer.com/atomizer-vs-cartomizer-vs-clearomizer/. Published 2014. Accessed October 30, 2017.

20. Hookahjunkie.com. Fantasia Hookah E-Bowl. Hookah Junkie. https://hookahjunkie.com/products/fantasia-hookah-flavors-e-bowl. Published April 16, 2018. Accessed April 18, 2018.

21. Smoke Free, Inc. Electronic Hookah. http://www.smokefreeonline.com/ehookah-kit. Published April 16, 2018. Accessed April 18, 2018.

22. Square Smoke. Square E-Head. Square E-Head. https://www.squaresmoke.com/products/square-e-head. Published April 16, 2018. Accessed April 18, 2018.

23. TheHookah.com. Kelvin H1 E-Bowl. https://www.thehookah.com/products/kelvin-h1-e-bowl. Published April 17, 2018. Accessed April 18, 2018.

24. Harrell PT, Marquinez NS, Correa JB, et al. Expectancies for cigarettes, e-cigarettes, and nicotine replacement therapies among e-cigarette users (aka vapers). *Nicotine Tob Res*. 2015;17(2):193-200. doi:10.1093/ntr/ntu149

25. Pearson J, Richardson A, Niaura R, Vallone D, Abrams D. E-cigarette awareness, use, and harm perceptions in US adults. *Am J Public Health*. 2012;102(9):1758-1766. doi:10.2105/AJPH.2011.300526

26. Cobb C, Ward KD, Maziak W, Shihadeh AL, Eissenberg T. Waterpipe Tobacco Smoking: An Emerging Health Crisis in the United States. *Am J Health Behav*. 2010;34(3):275-285. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3215592/.

27. McRobbie H, Phillips A, Goniewicz ML, et al. Effects of switching to electronic cigarettes with and without concurrent smoking on exposure to nicotine, carbon monoxide, and acrolein. *Cancer Prev Res Phila Pa*. 2015;8(9):873-878. doi:10.1158/1940-6207.CAPR-15-0058

28. Ashurst JV, Urquhart M, Cook MD. Carbon monoxide poisoning secondary to hookah smoking. *J Am Osteopath Assoc*. 2012;112(10):686-688. doi:10.7556/jaoa.2012.112.10.686

29. Blank MD, Cobb CO, Kilgalen B, et al. Acute effects of waterpipe tobacco smoking: A double-blind, placebo-control study. *Drug Alcohol Depend*. 2011;116(1–3):102-109. doi:10.1016/j.drugalcdep.2010.11.026

30. Goniewicz ML, Knysak J, Gawron M, et al. Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tob Control*. 2014;23(2):133-139. doi:10.1136/tobaccocontrol-2012-050859

31. Offermann F. Chemical emissions from e-cigarettes: direct and indirect (passive) exposures. *Build Environ*. 2015;93(Part 1):101-105. doi:10.1016/j.buildenv.2015.03.012

32. Polosa R, Morjaria JB, Caponnetto P, et al. Effectiveness and tolerability of electronic cigarette in real-life: a 24-month prospective observational study. *Intern Emerg Med*. 2014;9(5):537-546. doi:10.1007/s11739-013-0977-z

33. Farsalinos KE, Tsiapras D, Kyrzopoulos S, Savvopoulou M, Voudris V. Acute effects of using an electronic nicotine-delivery device (electronic cigarette) on myocardial function: comparison with the effects of regular cigarettes. *BMC Cardiovasc Disord*. 2014;14:78. doi:10.1186/1471-2261-14-78

34. Vardavas CI, Anagnostopoulos N, Kougias M, Evangelopoulou V, Connolly GN, Behrakis PK. Short-term pulmonary effects of using an electronic cigarette: impact on respiratory

flow resistance, impedance, and exhaled nitric oxide. *Chest*. 2012;141(6):1400-1406. doi:10.1378/chest.11-2443

35. Allen JG, Flanigan SS, LeBlanc M, et al. Flavoring chemicals in e-cigarettes: diacetyl, 2,3-pentanedione, and acetoin in a sample of 51 products, including fruit-, candy-, and cocktail-flavored e-cigarettes. *Environ Health Perspect*. 2016;124(6):733-739. doi:10.1289/ehp.1510185

36. Centers for Disease Control and Prevention. Smoking and Tobacco Use; Fact Sheet: Hookahs. Smoking and Tobacco Use. http://www.cdc.gov/tobacco/data_statistics/fact_sheets/tobacco_industry/hookahs/. Published 2016. Accessed May 8, 2018.

37. Ward KD, Hammal F, VanderWeg MW, et al. Are Waterpipe Users Interested in Quitting? *Nicotine Tob Res*. 2005;7(1):149-156. doi:10.1080/14622200412331328402

38. Noonan D, Patirck ME. Factors associated with perceptions of hookah addictiveness and harmfulness among young adults. *Subst Abuse Off Publ Assoc Med Educ Res Subst Abuse*. 2013;34(1):83-85. doi:10.1080/08897077.2012.718251

39. Abughosh S, Wu I-H, Peters RJ, Essien EJ, Crutchley R. Predictors of persistent waterpipe smoking among university students in the United States. *Epidemiol Open Access*. 2011;1(1). doi:10.4172/2161-1165.1000102

40. Heinz AJ, Giedgowd GE, Crane NA, et al. A comprehensive examination of hookah smoking in college students: use patterns and contexts, social norms and attitudes, harm perception, psychological correlates and co-occurring substance use. *Addict Behav*. 2013;38(11):2751-2760. doi:10.1016/j.addbeh.2013.07.009

41. Braun RE, Glassman T, Wohlwend J, Whewell A, Reindl DM. Hookah use among college students from a midwest university. *J Community Health N Y*. 2012;37(2):294-298. doi:http://dx.doi.org.ezaccess.libraries.psu.edu/10.1007/s10900-011-9444-9

42. Eissenberg T, Ward KD, Smith-Simone S, Maziak W. Waterpipe tobacco smoking on a U.S. college campus: prevalence and correlates. *J Adolesc Health*. 2008;42(5):526-529. doi:10.1016/j.jadohealth.2007.10.004

43. Barnett TE, Shensa A, Kim KH, Cook RL, Nuzzo E, Primack BA. The predictive utility of attitudes toward hookah tobacco smoking. *Am J Health Behav*. 2013;37(4):433-439. doi:10.5993/AJHB.37.4.1

44. Kim K-H, Kabir E, Jahan SA. Waterpipe tobacco smoking and its human health impacts. *J Hazard Mater*. 2016;317:229-236. doi:10.1016/j.jhazmat.2016.05.075

45. Romijnders KAGJ, van Osch L, de Vries H, Talhout R. Perceptions and reasons regarding e-cigarette use among users and non-users: a narrative literature review. *Int J Environ Res Public Health*. 2018;15(6):1190. doi:10.3390/ijerph15061190

46. Bailey SR, Bryson SW, Killen JD. Predicting successful 24-hr quit attempt in a smoking cessation intervention. *Nicotine Tob Res*. 2011;13(11):1092-1097. doi:10.1093/ntr/ntr151

47. Foulds J, Veldheer S, Yingst J, et al. Development of a questionnaire for assessing dependence on electronic cigarettes among a large sample of ex-smoking e-cigarette users. *Nicotine Tob Res*. 2015;17(2):186-192. doi:10.1093/ntr/ntu204

48. Square. Square E-Head. Square Smoke. https://www.squaresmoke.com/products/square-e-head. Published July 2, 2018. Accessed July 2, 2018.

49. Mantey DS, Harrell MB, Case K, Crook B, Kelder SH, Perry CL. Subjective experiences at first use of cigarette, e-cigarettes, hookah, and cigar products among Texas adolescents. *Drug Alcohol Depend*. 2017;173:10-16. doi:10.1016/j.drugalcdep.2016.12.010

50. Soulakova JN, Pham T, Owens VL, Crockett LJ. Prevalence and factors associated with use of hookah tobacco among young adults in the U.S. *Addict Behav*. 2018;85:21-25. doi:10.1016/j.addbeh.2018.05.007

51. Haider MR, Salloum RG, Islam F, Ortiz KS, Kates FR, Maziak W. Factors associated with smoking frequency among current waterpipe smokers in the United States: Findings from

the National College Health Assessment II. *Drug Alcohol Depend*. 2015;153:359-363. doi:10.1016/j.drugalcdep.2015.05.015

52. Villanti AC, Cobb CO, Cohn AM, Williams VF, Rath JM. Correlates of hookah use and predictors of hookah trial in U.S. young adults. *Am J Prev Med*. 2015;48(6):742-746. doi:10.1016/j.amepre.2015.01.010

53. Ramôa CP, Shihadeh A, Salman R, Eissenberg T. Group waterpipe tobacco smoking increases smoke toxicant concentration. *Nicotine Tob Res*. 2016;18(5):770-776. doi:10.1093/ntr/ntv271

54. von Rappard J, Schönenberger M, Bärlocher L. Carbon monoxide poisoning following use of a water pipe/hookah. *Dtsch Ärztebl Int*. 2014;111(40):674-679. doi:10.3238/arztebl.2014.0674

55. Nosratzehi T, Arbabi-Kalati F, Alijani E, Tajdari H. Comparison of cotinine salivary levels in hookah smokers, passive smokers, and non-smokers. *Addict Health*. 2015;7(3-4):184-191. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4741239/.

56. Neergaard JM, Singh P, Job J, Montgomery S. Waterpipe smoking and nicotine exposure: a review of the current evidence. *Nicotine Tob Res*. 2007;9(10):987-994. doi:10.1080/14622200701591591

57. Portico. Tobacco Use Disorder: Assessment and Diagnosis. https://www.porticonetwork.ca/treatments/disorders-qr/tobacco-use-disorder/tobacco-use-disorder-assessment-diagnosis. Published January 1, 2019. Accessed January 2, 2019.

58. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (5th ed.). 2013.

59. Schroeder MJ, Hoffman AC. Electronic cigarettes and nicotine clinical pharmacology. *Tob Control*. 2014;23(suppl 2):ii30-ii35. doi:10.1136/tobaccocontrol-2013-051469

60. Farsalinos KE, Spyrou A, Stefopoulos C, et al. Nicotine absorption from electronic cigarette use: comparison between experienced consumers (vapers) and naïve users (smokers). *Sci Rep*. 2015;5. doi:10.1038/srep11269

61. Cobb CO, Sahmarani K, Eissenberg T, Shihadeh A. Acute toxicant exposure and cardiac autonomic dysfunction from smoking a single narghile waterpipe with tobacco and with a "healthy" tobacco-free alternative. *Toxicol Lett*. 2012;215(1):70-75. doi:10.1016/j.toxlet.2012.09.026

62. Sears M. Smoking, asthma, chronic airflow obstruction and COPD | European Respiratory Society. *European Respiratory Journal*. 2015;45:586-588. doi:10.1183/09031936.00231414

63. Flouris AD, Chorti MS, Poulianiti KP, et al. Acute impact of active and passive electronic cigarette smoking on serum cotinine and lung function. *Inhal Toxicol*. 2013;25(2):91-101. doi:10.3109/08958378.2012.758197

64. Ferrari M, Zanasi A, Nardi E, et al. Short-term effects of a nicotine-free e-cigarette compared to a traditional cigarette in smokers and non-smokers. *BMC Pulm Med*. 2015;15. doi:10.1186/s12890-015-0106-z

65. Deane K, Stevermer JJ. Help smokers quit: Tell them their "lung age." *J Fam Pract*. 2008;57(9):584-586. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3183917/.

66. Stroup AM, Branstetter SA. An introduction to the electronic waterpipe. *Addict Behav*. September 2018. doi:10.1016/j.addbeh.2018.09.034

67. Qu Y, Kim K-H, Szulejko JE. The effect of flavor content in e-liquids on e-cigarette emissions of carbonyl compounds. *Environ Res*. 2018;166:324-333. doi:10.1016/j.envres.2018.06.013

68. Dinakar C, O'Connor GT. The health effects of electronic cigarettes. *N Engl J Med*. 2016;375(14):1372-1381. doi:10.1056/NEJMra1502466

69. European Lung Foundation. E-cigarettes linked to increased arterial stiffness, blood pressure and heart rate in humans -- ScienceDaily. https://www.sciencedaily.com/releases/2017/09/170910232512.htm. Published 2017. Accessed November 30, 2018.

70. Qasim H, Karim ZA, Rivera JO, Khasawneh FT, Alshbool FZ. Impact of electronic cigarettes on the cardiovascular system. *J Am Heart Assoc Cardiovasc Cerebrovasc Dis*. 2017;6(9). doi:10.1161/JAHA.117.006353

71. Shi Y, Warner DO. Surgery as a teachable moment for smoking cessation. *Anesthesiology*. 2010;112(1):102-107. doi:10.1097/ALN.0b013e3181c61cf9

72. Tonnesen P, Norregaard J, Mikkelsen K, Jorgensen S, Nilsson F. A double-blind trial of a nicotine inhaler for smoking cessation. *JAMA*. 1993;269(10):1268-1271.

73. Centers for Disease Control and Prevention. Smoking and Tobacco Use: Data and Statistics. Smoking and Tobacco Use. http://www.cdc.gov/tobacco/data_statistics/. Published 2017. Accessed May 19, 2017.

74. DiFranza JR, Savageau JA, Fletcher K, et al. Measuring the loss of autonomy over nicotine use in adolescents: the DANDY (Development and Assessment of Nicotine Dependence in Youths) study. *Arch Pediatr Adolesc Med*. 2002;156(4):397-403.

75. National Cancer Institute. Hooked on Nicotine Checklist (HONC). https://cancercontrol.cancer.gov/brp/tcrb/guide-measures/honc.html. Published 2012. Accessed November 27, 2018.

76. CoVita. Smokerlyzer. https://www.covita.net/smokerlyzer.html. Published 2018. Accessed November 27, 2018.

77. Vitalograph. Vitalograph - lung age. https://vitalograph.com/product/161420/lung-age. Published 2018. Accessed November 27, 2018.

78. Omron. Omron Upper Arm Blood Pressure Monitor With Printer. https://omronhealthcare.com/products/upper-arm-blood-pressure-monitor-with-printer-hem705cp/. Published 2018. Accessed November 27, 2018.

79. Faul F, Erdfelder E, Buchner A, Lang A-G. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods*. 2009;41(4):1149-1160. doi:10.3758/BRM.41.4.1149

80. SAS. Analytics, Business Intelligence and Data Management. https://www.sas.com/en_us/home.html. Published 2018. Accessed November 27, 2018.

81. O'Neill M. ANOVA and REML: A GUIDE TO LINEAR MIXED Guide to Linear Mixed Models in an Experimental Design Context. 2010. http://stats.net.au/dropbox/ANOVA%20&%20REML%20manual.pdf.

82. Grace-Martin K. The Intraclass Correlation Coefficient in Mixed Models. The Analysis Factor. https://www.theanalysisfactor.com/the-intraclass-correlation-coefficient-in-mixed-models/. Published August 22, 2013. Accessed December 2, 2018.

83. FAQ: What are pseudo R-squareds? https://stats.idre.ucla.edu/other/mult-pkg/faq/general/faq-what-are-pseudo-r-squareds/. Accessed December 4, 2018.

84. Beaumont R. Analyzing repeated measures with linear mixed models (random effects models). 2012. http://www.robin-beaumont.co.uk/virtualclassroom/contents.htm.

85. Grinberg A, Goodwin R. Prevalence and correlates of hookah use: a nationally representative sample of U.S. adults aged 18 to 40 years old. *American Journal of Drug and Alcohol*. 2016;42(5):567-576.

86. Tweeddale PM, Merchant S, Leslie M, Alexander F, McHardy GJ. Short term variability in FEV1: relation to pretest activity, level of FEV1, and smoking habits. *Thorax*. 1984;39(12):928-932. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC459955/.

87. Whittaker A, Sutton A, Beardsmore C. Are ethnic differences in lung function explained by chest size? *Arch Dis Child Fetal Neonatal Ed*. 2005;90(5):F423-F428. doi:10.1136/adc.2004.062497

88. Braun L. Race, ethnicity, and lung function: a brief history. *Can J Respir Ther*. 2015;51(4):99-101. doi:PMC26566381

89. Johnston R. Estimated Lung Age (ELA). PFTBlog. https://www.pftforum.com/blog/estimated-lung-age-ela/. Published November 27, 2016. Accessed November 29, 2018.

90. American Heart Association. Blood Pressure vs. Heart Rate (Pulse). https://www.heart.org/en/health-topics/high-blood-pressure/the-facts-about-high-blood-pressure/blood-pressure-vs-heart-rate-pulse. Published 2016. Accessed November 30, 2018.

91. Ross K, Gubner N, Tyndale R, Hawk L, Lerman C, George T. Racial differences in the relationship between rate of nicotine metabolism and nicotine intake from cigarette smoking. *Pharmacology Biochemistry and Behavior*. 2016;148:1-7.

92. Maas CJM, Hox JJ. Sufficient sample sizes for multilevel modeling. *Methodol Eur J Res Methods Behav Soc Sci*. 2005;1(3):86-92. doi:10.1027/1614-2241.1.3.86

93. Sechidis K, Sperrin M, Petherick ES, Luján M, Brown G. Dealing with under-reported variables: An information theoretic solution. *Int J Approx Reason*. 2017;85:159-177. doi:10.1016/j.ijar.2017.04.002

94. Lantini R, McGrath AC, Stein LAR, Barnett NP, Monti PM, Colby SM. Misreporting in a randomized clinical trial for smoking cessation in adolescents. *Addict Behav*. 2015;45:57-62. doi:10.1016/j.addbeh.2015.01.017

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SELECTED PUBLICATIONS

1. **Stroup, A.** & Branstetter, S.A. (2018). Effect of e-cigarette advertisement exposure on intention to use e-cigarettes in adolescents. *Addictive Behaviors, 82,* 1-6. https://doi.org/10.1016/j.addbeh.2018.02.021

2. **Stroup, A.** & Branstetter, S.A. (In press). An introduction to the novel e-waterpipe. *Addictive Behaviors.* https://doi.org/10.1016/j.addbeh.2018.02.021