

Abstract

The Role of E-cigarette Use in Smoking Cessation and E-cigarette Dependence

Introduction. E-cigarettes have grown in popularity and use over the past decade. A major contributor to this rise is their implied suitability as a smoking cessation tool – but questions remain regarding the safety of e-cigarette use and the relationship between e-cigarette use and smoking cessation. Specifically, 1) are e-cigarettes associated with similar odds of successful attempts to quit smoking among individuals who smoke, when compared FDA-approved methods (i.e., nicotine replacement therapy, prescription medication) and 2) is e-cigarette use associated with e-cigarette dependence? **Methods.** Data from 288 cigarette smokers and e-cigarette users in the United States (U.S.) were collected via an online survey and were used to examine e-cigarette use behaviors, e-cigarette dependence, and smoking quit attempts. **Results.** Individuals trying to quit cigarettes had higher odds of successfully quitting if they used e-cigarettes to quit when compared to FDA-approved methods (OR = 7.82, 95% CI = 1.55 – 39.37). Also, e-cigarette use was associated with e-cigarette dependence, with higher quantity of use (i.e., average number of uses per day) being linked to higher e-cigarette dependence, ($R^2 = .309$, adjusted $R^2 = .222$, $p < .001$). **Conclusion.** E-cigarettes may be effective smoking cessation tools and have therapeutic value for individuals for whom traditional smoking cessation aids have been ineffective. The findings also suggest that e-cigarette use is associated with e-cigarette dependence, potentially placing e-cigarette users at risk of developing e-cigarette-related health problems due to difficulty discontinuing use. The study helps clarify e-cigarettes suitability as a smoking cessation aid and addresses potential health ramifications associated with e-cigarette use.

The Role of E-cigarette Use in Smoking Cessation and E-cigarette Dependence

by

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Dedication

To Arthur Shepherd Estey.

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Chapter I: Introduction

Overview

Cigarette smoking remains one of the most dangerous yet preventable causes of morbidity and mortality in the United States (U.S.). By inhaling tobacco smoke, smokers expose themselves to hazardous compounds that can access several vital organs and lead to notable cardiovascular, pulmonary, and oncological health problems (American Cancer Society, 2015). The 2014 Surgeon General’s report on smoking claims that 21 million premature deaths were caused in the U.S. by smoking and exposure to secondhand smoke over the past half-century (USDHHS, 2014). The report also indicates that cigarettes are responsible for over 480,000 deaths a year in the U.S. In 2019, 20.8% of the U.S. adult population reported tobacco product use, with 14.0% of U.S. adults reporting combustible cigarette use, suggesting that cigarettes are the most commonly used tobacco product (Cornelius et al., 2020).

Over the past decade, the popularity and use of electronic nicotine delivery systems (ENDS), referred to as “vaporizers” or “vapes”, and more commonly known as “electronic cigarettes” (e-cigarettes) has increased substantially in the U.S. (McMillen, 2015; Glasser et al., 2017), and pose a potential threat to public health. E-cigarettes are small, handheld devices that use a battery-powered coil to heat and vaporize a propylene glycol and glycerin-based liquid (known as “e-liquid”) into aerosol form, which is then inhaled (Palazzolo, 2013). E-liquid

can contain a variety of flavorings (e.g., mint, bubblegum, mango), and can be sold containing varying doses of nicotine. E-cigarettes are easy to use and can be easily customized to fit an individual's preferred nicotine intake, emitted cloud size, and vapor consumption. They can be similar to cigarettes in terms of size, shape, and portability, and appear to have fewer health risks when compared to cigarettes (NASEM, 2018).

These advantages have made e-cigarettes more popular in the U.S. In 2019, 3.2% of U.S. adults reported current e-cigarette use (Villaroel, Cha, & Vahratian, 2020), over double the percentage reported in 2011 (1.3%; King, Patel, Nguyen & Dube, 2015). Among youths, e-cigarette use has increased at a notably high rate. In 2020, 38.9% of high-school students reported using e-cigarettes 20 or more out of the past 30 days, a stark contrast to the 13.4% of high school students reporting past-30 days e-cigarette use in 2014 (Jamal et al., 2018, Wang et al., 2020). Based on the especially rapid increases in e-cigarette use among youth, the U.S. Food and Drug Administration (FDA) enforced stringent regulatory measures (e.g., banning the sale of flavored e-cigarettes to youths in stores, curbing marketing efforts directed towards teenagers) to curb e-cigarette use by those under the age of 18 (FDA, 2018).

Risks of E-cigarette Use

An initial underestimation of the harmful effects of cigarettes led to decades of research, public health education, treatment development and healthcare-related expenditures.

Exposure to tar, carcinogens and other harmful substances contained in cigarettes continues to be costly, and recently resulted in \$170 billion a year in direct medical costs, with an additional \$130 billion per year in economic losses (Xu et al., 2015, Federal Trade Commission, 2019).

E-cigarettes also expose its users to foreign, potentially harmful substances. They contain heavy metals, microparticles, and carbonyls (e.g., formaldehyde) that may lead to physical symptoms and illnesses that require medical care (NASEM, 2018). Though the safety of e-cigarettes has yet to be firmly established (e.g., Callahan-Lyon, 2014), Farsalinos & Polosa (2014) discussed the relative safety of e-cigarettes (compared to cigarettes) in a comprehensive review of the risks and potentially harmful effects of e-cigarette use. They noted the significantly lower relative risk of physical harm posed by e-cigarettes when compared to cigarettes, citing the lack of combustion and associated lack of harmful chemicals as a fundamentally positive aspect of e-cigarettes. They emphasize the gains in tobacco harm reduction presented by e-cigarettes, and how those gains outweigh the risks presented by e-cigarette use. Farsalinos (2018) later concluded that the levels of harmful substances in e-cigarettes range from 6 to 880 times lower compared to cigarettes. See Balfour and colleagues (2021) for a comprehensive review of the risks and benefits of e-cigarette use.

Though preliminary evidence suggests the relative safety of e-cigarettes when compared to cigarettes, evidence for e-cigarette safety remains unconvincing, both for the overall population and specific, vulnerable subgroups. For example, reviews of research on the links between e-cigarettes and both health during pregnancy and perinatal outcomes highlight the limited nature of existing research, and note how limited evidence prevents any firm conclusions to be drawn (Calder et al, 2021; DeVito et al, 2021). One major methodological challenge in e-cigarette research is the wide variety of available e-cigarette products. In 2014,

Zhu and colleagues reported the existence of over 450 e-cigarette brands, and over 7500 types of e-liquid. Given the range of possible variations by product, it is difficult to draw conclusions regarding safety that are generalizable to all e-cigarettes. For example, though e-liquids with higher numbers of chemicals (e.g., vegetable glycerin, vanillin) are more likely to be toxic when compared to e-liquids with fewer chemicals (Sassano et al., 2018), overall e-liquid toxicity is difficult to estimate and predict given the thousands of different e-liquid varieties available for consumption.

The CDC launched a 2019 investigation into a multistate outbreak of severe pulmonary diseases, consequent emergency room visits, and deaths related to e-cigarette use. Findings suggest a strong link between vitamin E acetate (an additive found in some tetrahydrocannabinol (THC)-containing e-cigarettes) and e-cigarette-related lung injuries (CDC, 2020), suggesting that some e-cigarette products may be more harmful than others. The lack of existing product regulation and manufacturing guidelines makes overall e-cigarette safety hard to determine. Other toxicant contributors beyond e-liquid include increased power or voltage of e-cigarette devices, suggesting that safer, improved e-cigarette manufacturing and design may reduce the health risks associated with e-cigarette use (Ward, Yaman, & Ebbert, 2020). Should the impact of prolonged e-cigarette use resemble or mimic the impact of cigarettes, the U.S. population could face the resurgence of a public health crisis that has been the focus of over half a century of research and treatment efforts. The risk is amplified by the presence of nicotine (i.e., the addictive substance strongly tied to sustained tobacco use) in e-cigarettes, which could lead to prolonged use and the development of e-cigarette dependence.

E-cigarettes and Cigarette Smoking Cessation

Because use of cigarettes is associated with increased risk of negative health effects, smoking cessation remains a public health goal worthy of pursuit. An examination of trends in smoking-related mortality among adults who smoke in the U.S. revealed a notably higher risk of death among adults who smoke compared to persons who never smoked. For example, between 2000 and 2010, the relative risk of death from lung cancer was 25.66x for women who smoke and 24.97x for men who smoke compared to women and men who do not smoke, respectively. In other words, men and women who smoked had 25 times greater risk of dying from lung cancer compared to men and women who didn't smoke. Similarly, the relative risk of death from chronic obstructive pulmonary disease (COPD) was 22.35 for women who smoke and 25.61 for men who smoke. The increased relative risk of death exists across other cigarette-smoking related causes (e.g., stroke, heart disease) for both men and women, with all causes combined leading to a 2.80 relative risk of death among men who smoke, and 2.76 relative risk of death among women who smoke, compared to men and women who do not smoke (Thun et al., 2013).

The higher risk of death related to smoking can be mitigated by smoking cessation. The 2014 Surgeon General's report on the health consequences of smoking highlighted the worthwhile benefits of smoking cessation: reduced cardiovascular risks after ceasing cigarette use for one year, risk of stroke comparable to a non-smoker after two to five years of smoking cessation, and lower risk of different types of cancer (e.g., mouth, lung, esophagus) after five to ten years of abstinence from smoking (USDHS, 2014). Smoking cessation can also be linked to

modest improvements in mental health (i.e., reduction of mixed anxiety and depressive symptoms, improved psychological quality of life, improvement in symptoms of stress; Taylor et al., 2021).

Given the stark contrast between the harmful effects and risks of smoking and the established benefits of smoking cessation, one could reasonably expect individuals who smoke cigarettes to try and quit their cigarette use. In 2018, the past-year quit attempt prevalence was 55.1% among adult U.S. smokers, but only 7.5% of those who attempted to quit were successful (Creamer et al., 2019). In other words, most U.S. adults who smoke attempt to quit, but very few are successful. The low quit rate persists despite an ever-expanding range of interventions for smoking cessation that includes acupuncture, hypnotherapy, monetary incentives, behavioral counseling, exercise, and pharmacological interventions (see Cochrane – Tobacco Addiction at <https://tobacco.cochrane.org/our-reviews> for a full list and associated reviews).

The FDA has approved several smoking cessation treatments to help individuals who smoke discontinue their cigarette use. Included are two prescription cessation medications that do not include nicotine: varenicline tartrate (Chantix) and bupropion hydrochloride (Zyban), and a range of nicotine replacement therapies (NRTs; e.g., nicotine gum, lozenges, nasal sprays, transdermal patches; FDA, 2017). Despite the availability and ease of use of FDA-approved methods for smoking cessation, the overall quit rate among U.S. adults who smoke remains low.

Caraballo and colleagues (2017) used data on 15, 943 U.S. adults who smoked cigarettes and attempted to quit cigarette use collected via a nationally representative longitudinal (2014-2016) survey to examine quit method usage and prevalence. Nearly three-quarters (74.7%) of past-three month quit attempters reported using multiple quit methods. There was lower use of FDA-approved prescription medications (12.2%) and NRT (25.4%) in past-three month quit attempts when compared to quitting cigarettes all at once (65.3%) or gradually reducing cigarette use (62.0%).

Of the remaining quarter of the sample, only reporting use of one quit method, less than 10% reported use of either FDA-approved prescription medication or NRT, whereas over 80% denied using any smoking cessation aids during their quit attempt. These findings suggest that FDA-approved smoking cessation aids are infrequently used by quit attempters, despite evidence to their effectiveness over quitting without aid (Anthenelli et al., 2016; Barua et al., 2018). Finding suitable smoking cessation aids that are safe, effective, and more frequently used by individuals trying to discontinue cigarette use thus remains a worthwhile goal.

E-cigarettes' similarities to cigarettes makes them an attractive option for adults who smoke and are looking to reduce or replace their cigarette use. In fact, the increase in e-cigarette use is due in part to the perceived suitability of e-cigarettes as a cigarette cessation aid (Zhu, Zhuang, Wong, Cummins, & Tedeschi, 2017). However, the suitability of e-cigarettes as a smoking cessation aid is unclear, and research examining the impact of e-cigarette use on smoking cessation has produced mixed results.

Some studies note the lack of advantages e-cigarettes provide compared to other smoking cessation methods, specifying that e-cigarette users were no more likely to quit smoking than non-e-cigarette users who used other smoking cessation methods (e.g., transdermal nicotine patches; Harrel et al, 2014; Weaver et al, 2018; Pierce et al, 2020). Others have concluded that e-cigarettes help to reduce but not to discontinue cigarette use (Bullen et al., 2013; Pokhrel, Herzog, Muranaka, Regmi, & Fagan, 2015), a pattern of use that then place users of both cigarettes and e-cigarettes (dual-users) at risk of developing problems associated with dual-use, such as increased risk of myocardial infarctions (Alzahrani, Pena, Temesgen & Glantz, 2018). Some research highlights the association of e-cigarettes with *less* tobacco abstinence among smokers, regardless of motivation to quit (Al-Delaimy et al, 2015; Rigotti, 2018), or higher odds of smoking relapse among both prior and current e-cigarette users who quit cigarettes when compared to never e-cigarette users (Dai & Leventhal, 2019), whereas other findings emphasize long term e-cigarette use for smoking cessation (Brown, Beard, Kotz, Michie, & West, 2014; Zhuang, Cummins, Sun & Zhu, 2016; Glasser et al, 2021). Data collected from a cohort of young adults (19-23) surveyed for four years suggested that e-cigarettes were useful for smoking cessation among highly nicotine-dependent young adults who smoke, but also *increased* cigarette use among non-nicotine-dependent young adults who smoke (Selya et al., 2018).

Systematic reviews and meta-analyses examining e-cigarette use for smoking cessation mirror the mixed evidence found in individual studies. Ghosh & Drummond (2017) reviewed four randomized clinical trials (RCT) and four cohort studies from 2013 to 2016 that examined the efficacy of e-cigarettes for smoking cessation among adult cigarette smokers

with varying levels of motivation to quit smoking. They found that e-cigarettes were no more or less effective than NRT and e-cigarette use among smokers was associated with a reduction in cigarettes. In a systematic review and meta-analysis of 18 observational studies and two RCTs regarding e-cigarette use for smoking cessation, Kalkhoran & Glantz (2016) concluded that the odds of e-cigarette users quitting cigarette smoking were 28% less than e-cigarette non-users. In contrast, Lam & West (2015) reviewed four RCTs that measured self-reported (and in some cases biochemically confirmed via carbon monoxide levels) smoking cessation, smoking reduction, and levels of desire for/withdrawal from smoking. They found that e-cigarettes could be considered an effective means of smoking cessation, though they emphasized that they did not take e-cigarette safety into consideration.

E-cigarettes, Nicotine, and Dependence

Nicotine is the main addictive component in cigarettes and plays a large role in sustaining tobacco use (Browne & Todd, 2018). Nicotine triggers the release of neurotransmitters (e.g., dopamine) which contribute to a rewarding and self-reinforcing effect with every intake of nicotine (Tan, Tang, & Hao, 2009). Discontinuation of nicotine use not only ceases the rewarding effects, but also leads to the rapid onset of several withdrawal symptoms, including but not limited to: irritability, anxiety, depressed mood, difficulty concentrating, increased appetite, insomnia, and restlessness (APA, 2013). These withdrawal symptoms are rapidly alleviated with re-exposure to nicotine. The onset of craving and motivations to smoke prompts the continued use and eventual dependence on cigarettes to deliver nicotine (McLaughlin, Dani, & De Biasi, 2015). Though several, non-physical barriers to smoking cessation such as enjoyment of cigarettes, use of cigarettes in response to boredom and stress,

and both pro-smoking social networks and environments have also been identified, nicotine dependence remains a notable barrier to smoking cessation that can be addressed via short-term health behavior interventions (Twyman et al., 2014). The FDA recently launched a major initiative to lower the nicotine content in cigarettes (FDA, 2018), highlighting the focus on nicotine as the primary driver of harmful smoking-related behavior. Part of e-cigarettes' appeal to smokers looking to quit cigarette use is that the e-liquid consumed can contain nicotine, but without the same presence of toxic substances and carcinogens typically found in cigarettes, therefore providing an allegedly "safer" source of nicotine.

Given nicotine's addictive nature and its presence in e-cigarettes, potential problems arise if e-cigarette use leads to e-cigarette dependence, which could then result in prolonged e-cigarette use. Consequently, if users dependent on e-cigarettes are unable to cease their use, they may be at higher risk than users not dependent on e-cigarettes for developing e-cigarette-related health problems. The average nicotine concentration in e-cigarettes has doubled in recent years, from 2.10% in 2013 to 4.34% in 2018 (Romberg et al., 2019). Additionally, the same study found that e-cigarettes containing higher nicotine concentrations (5% or greater) are sold far more frequently than their lower-nicotine (or no-nicotine) counterparts. E-cigarettes with 5% or higher nicotine concentrations accounted for 31.8% of dollar sales in 2017 and doubled to *two thirds* of dollar sales over the course of one year (66.4% in 2018). In contrast, no-nicotine e-cigarettes accounted for under 1% of dollar market share across the 2013-2018 period, highlighting the immense popularity of nicotine in e-cigarette products (Romberg et al., 2019). The rise of nicotine in e-cigarette products has

ushered in adaptations of existing dependence measures to better define and capture e-cigarette dependence.

The Penn State Electronic Cigarette Dependence Index (PSECDI; Foulds et al., 2015) was developed to objectively measure e-cigarette dependence. Foulds et al. (2015) used a cross-sectional online survey of 3,608 adult e-cigarette users who quit smoking cigarettes to validate the PSECDI. They examined the relationship between e-cigarette dependence and reported e-liquid nicotine concentration. Non-nicotine e-cigarette users had significantly lower e-cigarette dependence scores than users using 1-12 milligrams(mg)/milliliter(mL) of nicotine liquid ($p < 0.001$), who in turn had significantly lower e-cigarette dependence than users using > 13 mg/mL nicotine liquid ($p < 0.001$). Higher nicotine consumption was associated with higher e-cigarette dependence, but e-cigarette dependence also existed among non-nicotine e-cigarette users. The sample was restricted to former smokers; therefore, there was no analysis of e-cigarette dependence among cigarette smokers also using e-cigarettes and not planning to quit cigarette use.

Though nicotine plays a role in e-cigarette dependence (Schroeder & Hoffman, 2014), nicotine may be less impactful with regard to dependence for e-cigarettes than for cigarettes (Browne, 2018). In a study of 13,311 U.S. adult respondents to the Population Assessment of Tobacco and Health (PATH) study that compared e-cigarette dependence to dependence on cigarettes, Shiffman & Sembower (2020) found that the level of e-cigarette dependence was significantly lower than cigarette dependence among dual users (i.e., individuals who concurrently used both e-cigarettes and cigarettes). Between-subject analyses of individuals

who use e-cigarettes vs. individuals who smoke cigarettes similarly suggested that the level of dependence was lower among e-cigarette users when compared to individuals who smoked cigarettes. Given that both products deliver nicotine with varying effectiveness, e-cigarettes may allow individuals who switch from cigarettes to e-cigarettes to reduce their nicotine dependence. By reducing their nicotine dependence, they can reduce the amount of e-cigarette or cigarette use, and consequently lower the risk of developing use-related health problems. Dependence theory suggests that non-biological (e.g., psychological, sociocultural) factors also interact and lead to the development of sustained substance use (Teesson, Hall, Proudfoot, & Degenhardt, 2002). Understanding how the presence of nicotine is associated with e-cigarette dependence remains an area of research worth exploring.

Summary

The use of e-cigarettes has increased substantially in the U.S. over the past decade, but the long-term effects of e-cigarette use on public health remain unknown. Though switching to e-cigarettes may help reduce the public health risks posed by cigarettes, prolonged e-cigarette use might have its own negative health consequences, especially to those unable to discontinue usage for reasons similar to difficulty discontinuing use of cigarette such as dependence. E-cigarettes are analogous to cigarettes; they are handheld devices, emit visual indicators when used, are portable and accessible, and efficiently deliver nicotine. Conversely, e-cigarettes are tobacco-free, and contain fewer of the harmful substances commonly found in cigarettes. Likely perceived as a safe alternative to cigarettes, e-cigarettes can be used by cigarette smokers as a smoking cessation aid.

However, evidence regarding e-cigarettes' effectiveness as a smoking cessation aid and as related to e-cigarette dependence remains inconclusive. Explanatory factors include 1) prevalent lack of knowledge among e-cigarette users about whether their device contains nicotine or not, 2) lack of effective tools available to measure the details of e-cigarette use, and 3) only modest correlations between self-reported e-cigarette use and objective use measures (i.e., e-cigarette "puff" counters; Pearson et al., 2017; Pepper, Farrelly, & Watson, 2018; Yingst et al., 2018). The association between e-cigarette use and cigarette smoking cessation is unclear, and prolonged e-cigarette use driven by e-cigarette dependence may be unsafe, as long-term users may be exposed to health risks that are not fully understood. The aim of the current study was to provide a more comprehensive account of e-cigarettes as a smoking cessation aid than found in previous literature. To do so, we explored the use of e-cigarettes for smoking cessation by comparing their effectiveness to other smoking cessation methods. We also examined the associations between e-cigarette use and e-cigarette dependence and explored the relationship between e-cigarette dependence and e-cigarette nicotine concentration.

The current study consisted of a retrospective cross-sectional survey of past-year cigarette and e-cigarette users recruited via online panel. The survey included self-report measures capturing cigarette and e-cigarette usage, cigarette quit attempts, e-cigarette dependence, and nicotine consumption in e-cigarettes. This research design allowed data from past-year cigarette smokers, e-cigarette users, and dual-users of cigarettes and e-cigarettes to be used in statistical analyses, with the acknowledgment that different analytic samples were used for different aims (e.g., data from individuals who reported cigarette smoking but not e-cigarette

use were not compatible with analyses related to e-cigarette dependence, and thus were not included in those analyses). The primary aims were twofold: 1) to compare differences in self-reported effectiveness of e-cigarettes versus other smoking cessation aids for smoking cessation among cigarette smokers whose most recent quit attempt began within the past year and has lasted six months or more, and 2) to explore how the quantity/frequency of e-cigarette use and e-cigarette nicotine concentration each relate to e-cigarette dependence. Our additional aim was to examine the associations between cigarette dependence and quit attempt outcomes among dual-users and cigarette smokers attempting to stop smoking cigarettes. See below for a more detailed description of each aim.

Specific Aims

Primary Aim 1: Examine e-cigarette effectiveness as a cigarette smoking cessation aid. We compared self-reported successful quit attempts among i) cigarette smokers using e-cigarettes versus cigarette smokers using any FDA-approved methods (e.g., nicotine gum, nicotine inhaler, transdermal nicotine patch, varenicline) to quit smoking, and ii) e-cigarettes versus no additional aid to quit smoking. We hypothesized that participants using e-cigarettes to quit were significantly more likely to quit successfully when compared to individuals who smoke using FDA-approved smoking cessation methods. We also hypothesized that participants using e-cigarettes to quit were significantly more likely to quit successfully when compared to participants quitting unaided.

Primary Aim 2: Explore links between e-cigarette use and e-cigarette dependence. We examined the relationships among current e-cigarette users (a group

composed of both individuals who only used e-cigarettes and did not also use cigarettes, and individuals who both smoked cigarettes and used e-cigarettes, known as dual-users) between e-cigarette dependence and a) frequency and quantity of e-cigarette use, and b) e-liquid nicotine concentration. We hypothesized that a) both frequency and quantity of e-cigarette use would be associated with e-cigarette dependence index scores among current e-cigarette users, and b) e-liquid nicotine concentration would be associated with e-cigarette dependence index scores among e-cigarette users.

Exploratory Aim: Better understand today's e-cigarette user. We examined differences in demographics and cigarette dependence scores among persons using e-cigarettes versus other methods to quit smoking.

Significance

A lack of consensus regarding the role of e-cigarette use for smoking cessation highlights the need for additional research efforts on e-cigarette use. Though e-cigarette proponents advocate for its use to reduce or cease smoking, the long-term effects of prolonged e-cigarette use remain unknown. Promoting e-cigarettes as a smoking cessation aid may encourage their use and place current and former cigarette smokers at risk of developing e-cigarette use-related health problems.

The first aim, comparing quit rates among current and former smokers using e-cigarettes versus other smoking cessation methods, provided information to clarify e-cigarettes' suitability for smoking cessation and inform future decisions in the realms of public health,

policymaking, and clinical work regarding the addition of e-cigarettes to the pre-existing set of approved smoking cessation aids available to the public. The second aim, examining e-cigarette dependence among e-cigarette users, provided information on whether e-cigarette users can cease their use, should long-term e-cigarette use be proven to be harmful. Given the costly impact nicotine addiction and dependence have had on the U.S. population over the past century, it is critical that potential negative impacts of e-cigarettes be fully understood before approving their widespread use. Our exploratory aim examined differences in demographic characteristics and cigarette dependence among people trying to quit smoking using e-cigarettes versus other smoking cessation aids. It yielded a better understanding of who currently uses e-cigarettes for smoking cessation, and helped establish whether different cigarette dependence levels were associated with the use of e-cigarettes versus other smoking cessation aids.

Innovation

Few studies have examined e-cigarette use via a national U.S. sample. Established, large-scale national surveys of tobacco use (i.e., PATH study, NESARC) have only begun collecting limited data on e-cigarette use within the past several years, and other prior studies on e-cigarettes collected data from samples in health-related settings or drawn from pro e-cigarette websites and forums. This study collected data from a sample of U.S. cigarette and e-cigarette users representative of the adult U.S. population by race and gender. Using nationwide online panels helps to avoid biases usually found in studies conducted in healthcare-related settings (where participants might try to present themselves favorably) and in studies using pro e-cigarette resources (e.g., vape shops, websites) in which users may display a positive bias towards e-cigarettes.

Demographic information collected from our participants provided a clearer picture of today's e-cigarette user. Our study compared rates of quitting cigarettes using e-cigarettes to those found among smokers using effective NRTs (Hartmann-Boyce, Chepkin, Ye, Bullen, & Lancaster, 2018) and FDA-approved pharmaceutical aids. Our comparison to validated cessation methods allowed for a more robust measurement of effectiveness when compared to using treatment as usual or placebos. We included unaided quitting as a comparison group. Quitting unaided is a common type of smoking cessation and is generally under-recognized in smoking cessation research (Chapman & MacKenzie, 2010; Caraballo, 2017).

This study contextualized e-cigarette use and nicotine consumption within the multifaceted nature of dependence. Dependence, though generally referred to as a single construct, results from individual-level factors (e.g., genetic, environmental, cognitive) interacting together. Our study examined whether the presence of nicotine is a factor related to e-cigarette dependence and worthy of further study. The study extended research regarding the safety as e-cigarettes by focusing less on the direct impacts of prolonged e-cigarette use, and more on factors that may result in prolonged e-cigarette use.

Chapter II: Methods

Research Design

This study involved creating and administering a cross-sectional online survey to collect data from participants who reported regularly smoking cigarettes or using e-cigarettes in the past year. The survey consisted of items capturing demographic characteristics and five domains related to cigarette and e-cigarette use: smoking history, smoking cessation attempts, smoking cessation methods, e-cigarette use history, and e-cigarette dependence (described in detail below). Participants completed one of three possible item sets, depending on their answers to screening questions, which categorized them as “e-cigarette user”, “cigarette smoker”, or “dual user” (i.e., e-cigarette user and cigarette smoker). The same survey was presented to all eligible participants, though not all items were applicable to every participant, thus participants were not presented with non-applicable items (e.g., individuals who denied cigarette smoking were not presented further with cigarette-related items).

Data were collected from cigarette smokers and dual users via self-report of smoking history, e-cigarette use history, and quit attempts. Participants who reported a quit attempt also provided information regarding quit methods used, allowing us to compare the proportions of smokers who quit using e-cigarettes, versus FDA-approved methods, versus smokers who quit unaided. E-cigarette users and dual users completed similar self-reports, and completed the PSECDI. The relationships between e-cigarette use, e-cigarette dependence, and e-

cigarette nicotine concentration were examined. See **Appendix – Figure 1** for a summary of the research design.

General Procedures

Qualtrics – Survey Creation. The cross-sectional online survey was created and disseminated to research participants through Qualtrics XM's encrypted data transmission and storage software. Qualtrics (accessible at <https://qualtrics.com>) is a data collection and management service that provides access to an online sample of participants based on demographic and other characteristics specified by the user. With user-based recruitment specifications, Qualtrics targets potential participants through an aggregation of third-party market research panels, each with their own recruitment strategies (e.g., email, banner ads, radio) and compensation structures (e.g., sweepstakes entries, gift cards). Though this approach decreases reliance on a single recruitment source and avoids single-source related biases, the user does not have direct control/access to recruitment methods and compensation strategies, thus resulting in a more opaque recruitment process.

Survey and data collection platforms like Qualtrics are designed to protect participant data. Panelists recruited through Qualtrics willingly provide personal health information (PHI), such as names, addresses, and telephone numbers in order to verify their identity. Though our survey did not collect PHI, there is always the risk that a panelist could have been linked to their participation in this survey through participation data gathered by Qualtrics. HITECH (Health Information Technology for Economic and Clinical Health Act) updated HIPAA

rules to ensure that data are properly protected, and best security practices followed.

Qualtrics safeguards all customer data and uses secure data centers to ensure the highest protection as per HITECH requirements.

Participants completed the questions in a randomly presented order to balance participant fatigue. To help identify careless responses in our survey data, we followed recommendations set forth by Meade & Craig (2012) to include an instructed response item (e.g., “Respond with ‘strongly agree’ for this item”). Individuals who smoked cigarettes were asked about their favorite cigarette brand, and were instructed to select “Karelia” from a list of cigarette brands. Individuals using e-cigarettes were asked about their favorite e-cigarette flavor, and were instructed to select “mango” from a list of e-cigarette flavors. Survey time-to-completion was verified for each participant to identify outliers (e.g., 8 minutes for a 15-minute survey). National phone and online smoking cessation resources (e.g., CDC phone quit line, BeTobaccoFree.gov) were displayed upon survey completion.

Qualtrics – Recruitment and Compensation. Once created, the survey was advertised by Qualtrics to potential research participants based on guidelines provided by the author. Specifically, the survey was to be disseminated to any potential participant within the U.S. who was over the age of 18 and who spoke and read English. Participants were provided with a general description of the research project (i.e., a survey looking at smoking and e-cigarette use), but were not informed what the survey was specifically measuring. The author also designated biological/assigned sex and race/ethnicity quota constraints to make the study

sample mirror the overall U.S. adult population. The biological/assigned sex quotas were an even split of 50% male and 50% female participants. The race/ethnicity quotas were 66% Non-Hispanic White participants, 12% Non-Hispanic Black participants, 12% Hispanic participants, with the remaining 10% being non-specified.

Recruitment and data collection occurred between February 2020 and March 2020. A pilot study was first conducted based on 25 participants (10% of planned total sample size) to verify survey integrity, proper functioning of survey pathways, estimated time to completion, and conduct a final review of items for clarity. Review of the data led to a minor change in one question for clarity (i.e., instructing respondents to select the smoking cessation method they found most helpful instead of selecting all smoking cessation methods used), and rectification of technical issues that prevented some respondents from being assigned the appropriate questions. Collection of main study data began shortly after.

All participants were recruited by Qualtrics from various sources, including website intercept recruitment, member referrals, targeted email lists, gaming sites, customer loyalty web portals, permission-based networks, and social media. Eligible participants who had previously expressed interest in survey participation were e-mailed an invitation to the survey by Qualtrics (see **Appendix – Figure 2**). The typical survey invitation was simple and generic. It provided a hyperlink which took the respondent to the survey, and mentioned the incentive offered. Participant materials (e.g., project title, informed consent form, external survey) were submitted to and reviewed by the Western Institutional Review Board (WIRB) prior to data collection. WIRB designated the study as exempt from continued review for the

following reason: “This is survey research conducted through Qualtrics. No identifiers will be collected or used as part of this research.”

Participants completed an informed consent form (see **Appendix – Figure 3**) and were asked to answer questions to determine eligibility. Because participants were recruited from a variety of sources and panels, compensation varied by participant (e.g., airline members were rewarded with airline miles, retail shoppers were compensated with points for their favorite retail store). Upon completing the survey, participants received the compensation they agreed to before entering the survey. Given the unique participant identification number tied to each research participant, Qualtrics limited each ID to one survey attempt, thus preventing multiple attempts/survey completions by the same participant.

Participant Screening.

Inclusion criteria. The inclusion criteria included: reporting being 18 years of age or older, living in the U.S., and reporting current/recent (past-year) cigarette or e-cigarette use. To determine current cigarette use, participants were asked to report their current cigarette smoking status. Participants were deemed eligible if they reported any current/past-year use of either cigarettes or e-cigarettes (see **Appendix – Figure 4**). Those reporting occasional, most days, or daily use were considered “current smokers/e-cigarette users” in all analyses. Those reporting having discontinued use of cigarettes/e-cigarettes within the past year were considered “former smokers/e-cigarette users.”

Exclusion criteria. Exclusion criteria included: reporting being younger than 18 years of age, not having smoked cigarettes nor used e-cigarettes in the past year, not residing in the U.S., and not speaking or reading English.

Measures

Demographics. Participants were asked to provide demographics including age (continuous), biological/assigned sex (categorical; Male, Female), gender (categorical; Woman, Gender-variant/non-binary, Man, Transgender woman, Transgender man, Other, Prefer not to answer), sexual orientation (categorical; Bisexual, Gay or lesbian, Heterosexual, Other, Prefer not to answer), race/ethnicity (categorical; American Indian or Alaskan Native, Asian, Black or African American, Hispanic or Latino, Native Hawaiian or Other Pacific Islander, White, Other, Prefer not to answer), education level (categorical; Some high school, High school graduate, Some College, Trade/technical/vocational training, Associate's degree, Bachelor's degree, Some graduate training, Master's degree, Doctorate degree, Other, Prefer not to answer), current marital status (categorical; Single, Married, Divorced, Widowed, Living with partner, Separated, Other, Prefer not to answer), employment status (categorical; Employed full-time, Employed part-time, Unemployed (currently looking for work), Unemployed (not currently looking for work), Student, Retired, Self-employed, Unable to work) and yearly income (categorical; Below \$10,000, \$10,000 - \$50,000, \$50,000 - \$100,000, \$100,000 - \$150,000, Above \$150,000).

Cigarette Use. Participants who reported current cigarette use were asked how many days per week, on average, they smoked over the past year (categorical; Less than one day per week, 1 to 2 days per week, 3 to 5 days per week, 6-7 days per week, every day) and how many cigarettes per day they usually smoke (categorical; 0-4 cigarettes per day, 5-9 cigarettes per day, 10-14 cigarettes per day, 15-19 cigarettes per day, 20-29 cigarettes per day, 30+ cigarettes per day).

Participants who reported former cigarette use were asked how many days per week, on average, they smoked over the past year before they quit smoking (categorical; Less than one day per week, 1 to 2 days per week, 3 to 5 days per week, 6-7 days per week, every day) and how many cigarettes per day they usually smoked before they quit smoking (categorical; 0-4 cigarettes per day, 5-9 cigarettes per day, 10-14 cigarettes per day, 15-19 cigarettes per day, 20-29 cigarettes per day, 30+ cigarettes per day).

Cigarette Dependence.

Penn State Cigarette Dependence Index (PSCDI). The PSCDI is a 10-item measure that captures cigarette dependence. Items vary in the range of possible scoring options (i.e., some items are scored on a 0-1 scale, other items are scored on a 0-5 scale). The index score is calculated by adding the individual items score into a total. The total index score ranges from 0 to 20, with 0-3 indicative of no dependence, 4-8 indicating low dependence, 9-13 indicating medium dependence, and 13+ indicative of high dependence. The measure was developed by Foulds et al. (2012) to address weaknesses in commonly-used measures of nicotine dependence, such as the Fagerström Test for Nicotine Dependence (FTND; Heatherton et al., 1991) and the Hooked on Nicotine Checklist (HONC; DiFranza et al., 2002). These weaknesses included: 1) lack of validity for DSM-5 criteria for Tobacco Use Disorder (TUD), 2) scoring that was incompatible with current patterns of smoking among daily smokers, and 3) ceiling effects among adult heavy smokers.

The PSCDI contains items that map on to four of the 11 DSM-5 criteria for TUD (substance is taken in larger amounts or over a longer period than intended, craving or strong desire, persistent desire or unsuccessful efforts to curb use, and withdrawal). These items allow the PSCDI to detect mild to moderate TUD, in contrast to the FTND, which does not map on as well to DSM-5 criteria.

The FTND is a 6-item measure with a possible score of 0-10, with higher scores indicative of higher dependence. Given that the FTND item measuring cigarette consumption attributes a score of 0 to anyone reporting less than 11 cigarettes per day, the FTND does not adequately match the more recent pattern of fewer cigarettes smoked per day. It may also underestimate nicotine dependence in Black and Latinx individuals who smoke daily and who traditionally report fewer cigarettes smoked per day than White individuals who smoke daily (Schoenborn et al., 2013). The PSCDI allows for a more granular approach to measuring cigarette consumption, and acknowledges that <11 cigarettes smoked per day may still be indicative of dependence.

Finally, the HONC is a 10-item measure (scores range from 0-10, with higher scores indicative of higher dependence) designed primarily to detect dependence in adolescents. Given that adult smokers would likely have smoked longer than adolescents and report more symptoms of dependence, the HONC cannot adequately differentiate levels of dependence among moderate/heavy smokers, and should only be used to measure dependence in adults whose cigarette consumption is low (Wellman et al., 2010).

The 10-item PSCDI is thus a combination of items from aforementioned scales that remain predictive of dependence, and newly composed items to make sure the other aspects of dependence (e.g., withdrawal, difficulty quitting, craving, consumption) are covered. The PSCDI is comprised of two items from the FTND (cigarette consumption item converted to continuous scale, time to first cigarette item converted to continuous scale), five items from the HONC (continued smoking due to difficulty quitting, presence of strong craving, difficulty not smoking in prohibited area, irritability linked to cessation, nervousness/anxiety linked to cessation), two items assessing nighttime cigarette use after waking, and one item assessing urges to use. Foulds and colleagues (2015) pilot tested the PSCDI in a smoking cessation trial involving 225 smokers and found that lower PSCDI scores (lower dependence) predicted higher quit rates, which is consistent with past research linking lower dependence with better cessation outcomes (Ussher, Kakar, Hajek, & West, 2016).

Cigarette Quit Attempts. Participants were asked how many cigarette quit attempts they had made over the past year, the start date of their most recent quit attempt, and whether their most recent quit attempt was successful (i.e., they have not smoked since their most recent quit date). Participants with a past-year quit attempt were asked to select all quit methods used during their most recent quit attempt from a list that included: e-cigarettes, FDA-approved quit methods listed individually (Buproban/Zyban (bupropion), Chantix (varenicline), Nicotrol Inhaler, Nicotrol NS (nicotine spray pump), Nicorelief/Nicorette/Thrive (nicotine gum or lozenge), Nicoderm CQ (transdermal nicotine patch), and no aid (“cold turkey”). They were able to select as many options as they wanted,

and were then asked to both indicate which method was most helpful during their most recent attempt, and to rate how helpful it was.

E-cigarette Use. Eligible participants endorsing e-cigarette use were asked to specify the type of device used via a visual reference (see **Appendix – Figure 5**) for the types of devices being studied. Participants who reported current e-cigarette use were asked how many days per week, on average, they used e-cigarettes over the past year (categorical: Less than one day per week, 1 to 2 days per week, 3 to 5 days per week, 6-7 days per week, every day), and how many times per day they usually used their e-cigarette (with one use being defined as 15 puffs or 10 minutes; categorical: 0-4 times per day, 5-9 times per day, 10-14 times per day, 15-19 times per day, 20-29 times per day, 30+ times per day).

Participants who reported former e-cigarette use were asked how many days per week on average they used e-cigarettes over the past year before they discontinued e-cigarette use (categorical: Less than one day per week, 1 to 2 days per week, 3 to 5 days per week, 6-7 days per week, every day), and how many times per day they usually used their e-cigarette before they discontinued e-cigarette use (with one use being defined as 15 puffs or 10 minutes; categorical: 0-4 times per day, 5-9 times per day, 10-14 times per day, 15-19 times per day, 20-29 times per day, 30+ times per day).

E-cigarette Nicotine Content and Concentration. Participants reported whether they typically use e-liquid containing nicotine (yes/no). Those who endorsed having e-liquid

containing nicotine were asked to report their typically-used e-liquid nicotine concentration (0, 3, 6, 12, 18, 24, 30+ mg/ml, or “I do not know”; Morean et al., 2018).

E-cigarette Dependence.

Penn State E-Cigarette Dependence Index (PSECDI). The PSECDI (see **Appendix – Figure 6**) is a 10-item e-cigarette dependence measure developed by Foulds et al. (2015), based on their previously developed 10-item PSCDI (described above). Foulds et al. (2011) began adapting the PSCDI to measure e-cigarette use, and, based on pilot data and feedback from face-to-face interviews with 108 e-cigarette users, made notable modifications to only one item from the original measure to better assess e-cigarette use frequency (i.e., “How many times per day do you usually use your e-cigarette – assume one “time” consists of around 15 puffs, or lasts around 10 minutes?” instead of “How many cigarettes per day do you usually smoke?”). E-cigarettes are not generally consumed as a whole and then discarded (as cigarettes are). E-cigarette users found it possible to estimate the amount of e-cigarette use by quantifying one “use” as 15 puffs, or use lasting 10 minutes. In a study of 259 e-cigarette users and 1165 observations of e-cigarette use, Yingst et al. (2018) concluded that the PSECDI self-report measure of frequency of use is a significant predictor of actual puffs taken per day (with the two measures being moderately positively correlated). All other PSECDI items were adapted directly from the PSCDI, with minor changes to the wording to reflect the focus on e-cigarette instead of cigarette dependence (e.g., “Do you sometimes awaken at night to use your e-cigarette device” instead of “Do you sometimes awaken at night to have a cigarette”).

Data Analytic Plan

Sample Size and Power Analysis. All power analyses below were conducted using G*Power 3.1.9.2 (Faul et al., 2009). Primary Aim 1 examined the odds of smokers successfully quitting cigarettes while using e-cigarettes versus FDA-approved methods to quit. Based on findings from a previous study looking at e-cigarettes for smoking cessation (Brown et al., 2014), the author estimated 19.1% of e-cigarette users, and 8.4% of smokers using NRT, will have successfully quit cigarettes within the past year. Brown and colleagues (2014) also found that e-cigarette users were 1.63 (95% CI: 1.17 – 2.27) times more likely than quitters using NRT to successfully quit smoking cigarettes. Using these estimates as parameters to calculate the sample size required to achieve 80% power at $\alpha = 0.05$, the required number of participants was 178.

Primary Aim 2a examined the relationship between e-cigarette dependence scores and e-cigarette use (frequency and quantity). Detecting a large effect (Cohen's $f^2=0.35$) with 80% power using a multiple linear regression (fixed effects; $\alpha = 0.05$) required 31 e-cigarette users to participate. Primary Aim 2b examined the relationship between the e-cigarette dependence index score and e-cigarette nicotine concentration. Detecting a large effect (Cohen's $f^2 = 0.35$) with 80% power using simple linear regression (fixed effects; $\alpha = 0.05$) required 46 participants. The author estimated that 97% of e-cigarette users used nicotine (Etter & Bullen, 2011; Foulds et al., 2015), suggesting the author needed 48 e-cigarette users for Primary Aim 2b, 46 of whom would use nicotine.

In summary, the a-priori analyses suggested that our survey would have to reach a minimum of 178 smokers and 46 e-cigarette users to allow for adequately powered and interpretable

data for Primary Aims 1 and 2. We estimated that 9.2% of smokers would also use e-cigarettes, suggesting our sample would include 16 dual users (Pulvers et al., 2015).

Statistical Analysis

Preliminary analyses. Outcomes were statistically described and assessed for normality via visual inspection and Shapiro-Wilk Tests. Demographic variables for the overall sample were reported. The sample was divided into three groups (e-cigarette users only, smokers only, dual product users), and demographic variables were compared across the three groups. Additional demographic variable comparisons were conducted for Primary Aims 1 and 2, based on the participant groups of each aim. Demographic variables differing significantly across participant groups of an aim were included as covariates in the primary outcome analyses for that aim, and the results of both unadjusted and adjusted analyses are presented in the Results section. Post-hoc comparisons were performed when appropriate. Tests were considered significant at $p < 0.05$.

Primary Aim 1: Examine e-cigarette effectiveness as a smoking cessation aid. For Primary Aim 1, participants with at least one quit attempt in the past year were considered “Quit attempters” and were placed into groups based on the method used during the most recent quit attempt (e-cigarettes only, FDA-approved methods only, unaided only). Responders reporting sustained cessation and whose most recent quit attempt began six months prior to the survey were considered “successful quitters.” The six-month mark was chosen as a marker of prolonged abstinence recommended by the Society for Research on Nicotine and Tobacco in 2003 and again in 2020 (Hughes et al., 2003; Piper et al., 2020).

Group members were categorized as successful or non-successful quitters. The primary outcome for Aim 1 was the odds ratio of smokers successfully quitting while using e-cigarettes versus FDA-approved methods to quit. This ratio was calculated in a simple logistic regression.

Primary Aim 1 Hypothesis: Smokers had significantly higher odds of quitting cigarettes while using e-cigarettes to quit, than smokers using FDA-approved methods as a smoking cessation aid. Outcome parameters: Odds ratios with 95% confidence intervals (Exp(B); CI), and significance level (p). A secondary simple logistic regression analysis including unaided quitters as a quit method was run for comparative purposes.

Primary Aim 2: Explore links between e-cigarette use and e-cigarette dependence. For Primary Aim 2a, e-cigarette users and dual users provided their e-cigarette use history and completed the PSECDI to assess e-cigarette dependence (Foulds et al., 2015). Quantity of daily average e-cigarette use was defined as number of minutes spent using e-cigarettes per day averaged across days of e-cigarette use in a week. Frequency of e-cigarette use was defined as the average number of days of e-cigarettes use in a week. Both averages were examined in relation to e-cigarette dependence scores (ranging from 0 to 13+; Foulds et al., 2015). The primary outcome for Aim 2a was the proportion of variance in e-cigarette dependence index scores associated with both quantity and frequency of e-cigarette use. A multiple linear regression was run to model the relationship between the two independent variables: daily average e-cigarette use and daily average frequency of e-cigarette use, and the outcome variable: e-cigarette dependence index scores. Both independent variables were entered into the model simultaneously.

Primary Aim 2a Hypothesis: Both quantity and frequency of e-cigarette use were associated with a significant proportion of the variance in e-cigarette dependence index scores. Outcome parameters: adjusted coefficient of determination (Adjusted R^2), F-value (F), degrees of freedom (df), significance level (p), and effect size (Cohen's f^2). Secondary outcomes included beta coefficients (b) for each independent variable (Field, 2009).

For Primary Aim 2b, e-liquid nicotine concentration was obtained by asking participants to provide their e-liquid's nicotine concentration (in milligrams per milliliter; mg/ml). The primary outcome for Aim 2b was the proportion of variance in e-cigarette dependence index scores associated with e-liquid nicotine concentration. A simple linear regression was run to examine the association between nicotine concentration and e-cigarette dependence index scores.

Primary Aim 2b Hypothesis: E-liquid nicotine concentration was associated with a significant proportion of variance in e-cigarette dependence index scores. Outcome parameters: adjusted coefficient of determination (Adjusted R^2), F-value (F), degrees of freedom (df), significance level (p), and effect size (Cohen's f^2).

Exploratory Aim: Examine differences in demographics and cigarette dependence among smokers trying to quit using e-cigarettes versus other methods. For the Exploratory Aim analyses, demographic variables and PSCDI scores (measuring cigarette dependence) were collected from both cigarette smokers and dual users with at least one past-year quit attempt, and were compared between smokers using e-cigarettes versus other methods to quit smoking. The differences in categorical demographic characteristics were

determined via chi-square analyses examining differences in proportions of quit attempters using e-cigarettes versus other methods across demographic variables (e.g., race/ethnicity, biological sex, education). Differences in age (continuous demographic characteristic) were determined via independent samples *t*-test to compare mean ages between quit attempters using e-cigarettes versus other smoking cessation aids. Similarly, cigarette dependence was examined via independent samples *t*-test to compare mean PSCDI scores between quit attempters grouped by smoking cessation method used.

Chapter III: Results

Data collection

Data collection occurred between February 2020 and March 2020, and was conducted in three stages. First, pilot data from 25 respondents were collected and analyzed to determine feasibility and functionality of the survey. Review of the data led to a minor change in one question for clarity (i.e., instructing respondents to select the smoking cessation method they found most helpful instead of selecting all smoking cessation methods used), and rectification of technical issues that prevented some respondents from being assigned the appropriate questions. Pilot data were omitted from consequent analyses to preserve consistency of survey questions and responses.

Collection of main study data, the second stage of recruitment, began shortly after. Responses from 248 participants were collected per study protocol, and recruitment was stopped. Visual inspection and frequency data revealed fewer than expected cigarette quit attempters, prompting the third stage of recruitment: 40 additional participants who 1) reported e-cigarette use (current/former) and 2) reported a cigarette quit attempt, resulting in 313 total participants. Geographically, the four major regions in the U.S. were represented: Northeast = 68, Midwest = 81, South = 113, and West = 48 (with 3 participants registered as being outside of U.S. at time of survey). Data from the 25 pilot respondents were omitted from consequent analyses, yielding a final sample of 288 participants.

A significant number of potential survey completers were screened out or excluded from the study. Participants who were screened out or excluded were not compensated for their participation, were not able to complete the survey, and did not have their responses saved or analyzed. Only participants who successfully completed the survey were compensated, and only their data was retained and analyzed.

Participants were first presented the informed consent form, followed by two questions that established the participant's status as a cigarette smoker or e-cigarette user. Any participant who did not provide informed consent ($n = 84$) or was neither cigarette smoker nor e-cigarette user ($n = 179$), was not allowed to continue with the survey and was immediately brought to the "End-of-survey" page, which informed them that their response was recorded and were thanked them for their time. Participants were then asked to provide demographic information (e.g., age, sex, gender, income). Race and gender quotas were established to approximate a sample representative by race and gender of the adult U.S. population (e.g., 50% male and 50% female, ~60% White, 13% Black). Participants under the age of 18 ($n = 1$), or who selected a race or gender group that had already been filled (e.g., identifying as White when the quota for White participants was met; $n = 902$) were not allowed to continue with the survey and were immediately brought to the "End-of-survey" page, which informed them that their response was recorded and were thanked them for their time. Participants who failed any one of the attention check questions embedded in the survey ($n = 569$) were immediately brought to the "End-of-survey" page, which informed them that their response was recorded and thanked them for their time. Three participants who completed the survey in under 111 seconds (i.e., less than 2 minutes) were compensated for completing the study but their responses were not included in consequent analyses. Participants who failed either

the attention check or time check were considered as “failed quality check” ($n = 572$). Ultimately, 313 participants across all three study stages (pilot study, main recruitment, recruitment of additional cigarette quit attempters) completed the study and were compensated, with the 25 pilot study respondents being omitted from main analyses, resulting in a final analytic sample size of 288 respondents (see **Appendix –Figure 7**).

Demographics

See Table 1 for demographic information of the overall sample by type of user (cigarette smoker, e-cigarette user, dual user). The analytic study sample consisted of predominantly White (66.7%), middle-aged ($M = 42.7$, $SD = 14.3$) heterosexual (84.4%) men and women (49.3% female). Slightly over half (55%) of the sample reported “some high school,” “high school graduate,” or “some college” as the highest level of education they’ve achieved. Similarly, slightly over half (55%) of respondents were either married or living with their partner. Three-quarters (78%) of respondents reported a household income between \$10,000 and \$100,000, and 58% of respondents reported some type of employment (full-time, part-time, self-employed).

Table 1.
Demographic Characteristics Overall and by Type of Cigarette/E-cigarette User ($n = 288$).

	Total n (%)	Type of User n (%)			<i>p</i>
		Cigarette Smoker	E-cigarette User	Dual User	
Total Sample	288 (100)	191 (66.3)	11 (3.8)	86 (29.9)	

Age¹, M (SD)	42.7 (14.3)	47.0 (14.2)	23.5 (4.7)	35.7 (9.6)	<.001
Biological Sex					.608
Female	142 (49.3)	94 (49.2)	7 (63.6)	41 (47.7)	
Male	146 (50.7)	97 (50.8)	4 (36.4)	45 (30.8)	
Gender					
Cisgender Woman	139 (49.1)	94 (49.5)	5 (62.5)	40 (47.1)	.695
Cisgender Man	144 (50.9)	96 (50.5)	3 (37.5)	45 (52.9)	
Sexual Orientation					.101
Bisexual	23 (8.0)	15 (7.9)	2 (18.2)	6 (26.1)	
Gay or Lesbian	15 (5.2)	9 (4.7)	0 (0.0)	6 (7.0)	
Heterosexual	243 (84.4)	165 (86.4)	8 (72.7)	70 (81.4)	
Other	6 (2.1)	1 (0.5)	1 (9.1)	4 (4.7)	
Race/Ethnicity					<.001
Asian	10 (3.5)	7 (3.7)	0 (0)	3 (3.5)	
Black or African American	35 (12.2)	22 (11.5)	2 (18.2)	11 (12.8)	
Hispanic or Latinx	34 (11.8)	8 (4.2)	5 (45.5)	21 (24.4)	
White	192 (66.7)	142 (74.3)	2 (18.2)	48 (55.8)	
Other	17 (5.9)	12 (6.3)	2 (18.2)	3 (3.5)	
Level of Education					<.001
Some high school	11 (3.8)	11 (5.8)	0 (0)	0 (0)	
High school graduate	74 (25.7)	59 (30.9)	4 (36.4)	11 (12.8)	
Some college	74 (25.7)	53 (27.7)	2 (18.2)	19 (22.1)	
Trade/vocational school	21 (7.3)	16 (8.4)	1 (9.1)	4 (4.7)	
Associate's degree	30 (10.4)	21 (11)	1 (9.1)	8 (9.3)	
Bachelor's degree	47 (16.3)	20 (10.5)	0 (0)	27 (31.4)	
Other	31 (10.8)	11 (5.8)	3 (27.3)	17 (19.8)	
Marital Status					.001
Single	81 (28.1)	45 (23.6)	7 (63.6)	29 (33.7)	
Married	115 (39.9)	71 (37.2)	1 (9.1)	43 (50)	
Divorced	29 (10.1)	28 (14.7)	0 (0)	1 (1.2)	
Living with partner	43 (14.9)	32 (16.8)	2 (18.2)	9 (10.5)	
Other	20 (6.9)	15 (7.9)	1 (9.1)	4 (4.7)	
Current Household Income					<.001
Below \$10,000	25 (8.7)	19 (9.9)	3 (27.3)	3 (3.5)	
\$10,000 - \$49,999	138 (47.9)	106 (55.5)	4 (36.4)	28 (32.6)	
\$50,000 - \$99,999	87 (30.2)	50 (26.2)	4 (36.4)	33 (38.4)	
\$100,000 - \$150,000	21 (7.3)	9 (4.7)	0 (0)	12 (14)	
Above \$150,000	17 (5.9)	7 (3.7)	0 (0)	10 (11.6)	
Current Employment Status					<.001
Employed full-time	126 (43.8)	64 (33.5)	4 (36.4)	58 (67.4)	

Employed part-time*	26 (9)	21 (11)	2 (18.2)	3 (3.5)
Unemployed (looking for work)	29 (10.1)	22 (11.5)	1 (9.1)	6 (7)
Unemployed (not looking for work)	31 (10.8)	20 (10.5)	2 (18.2)	9 (10.5)
Retired	34 (11.8)	31 (16.2)	0 (0)	3 (3.5)
Self-employed	16 (5.6)	12 (6.3)	1 (9.1)	3 (3.5)
Unable to work	26 (9)	21 (11)	1 (9.1)	4 (4.7)

Notes: Fields with 10 or fewer counts after were collapsed into new categories when possible. Consequent fields with fewer than ten counts were omitted from analyses. **Gender:** included in our sample but omitted from preliminary analyses were 1 Gender non-binary/non-conformant individual (E-cigarette user) and 3 Transgender Males (1 cigarette smoker, 2 e-cigarette users). **Sexual Orientation:** “Other” and “Prefer not to answer” were collapsed into “Other” category. **Race/Ethnicity:** American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Other, and Prefer not to Answer were collapsed into “Other” category. **Level of Education:** Master’s degree, Doctorate degree, and “Prefer not to answer” were collapsed into the “Other” category. **Marital Status:** Widowed, Separated, Prefer Not to Answer, and Other were collapsed into “Other” category. **Current Employment Status:** Student was collapsed into the “Unemployed (not looking for work) category.

¹ Age is reported as Mean (Standard Deviation).

The overall sample consisted of 66.3% cigarette-only users, 3.8% e-cigarette-only users, and 29.9% dual users (See **Appendix – Supplemental Table 1** for frequency and quantity of current cigarette and e-cigarette use). In other words, two-thirds of respondents only smoked cigarettes, just under one third used both e-cigarettes and cigarettes, and comparatively few respondents only used e-cigarettes. User groups did not differ in biological sex, gender, or sexual orientation. Age, race/ethnicity, level of education, marital status, current household income, and current employment status all differed by type of user (see Table 1). All comparisons detailed below were based on the cigarette/e-cigarette group as compared to the overall sample.

Age. E-cigarette-only users were significantly younger than both dual users and cigarette-only users. Dual users were also significantly younger than cigarette-only users.

Race/Ethnicity. Cigarette-only users were more likely to be White when compared to the overall sample. E-cigarette-only users and dual users were more likely to be Hispanic or Latinx when compared to the overall sample.

Education. Cigarette-only users were more likely to have no education beyond high school, and less likely to be respondents with a Bachelor's degree or with some graduate training. Dual users were less likely to have no education beyond high school, and more likely to have a Bachelor's degree.

Marital Status. Cigarette-only users were less likely to be single, and more likely to be divorced. E-cigarette-only users were less likely to be married and more likely to be single. Dual users were more likely to be married, and less likely to be divorced.

Employment Status. Cigarette-only users were more likely to be retired, and less likely to be employed full time. In contrast, dual users were more likely to be employed full time, and less likely to be retired.

Current Income. Cigarette-only users were more likely to earn between \$10,000 and \$50,000 annual income, and less likely to earn between \$100,000 and \$150,000, or above \$150,000 annual income. E-cigarette-only users were more likely to report less than \$10,000 annual income. Dual users were more likely to earn between \$100,000 and \$150,000, or above \$150,000 annual income. Dual users were less likely to earn less than \$10,000, or between \$10,000 and \$50,000 annual income.

Primary Aim 1: Examine e-cigarette effectiveness as a cigarette smoking cessation aid

A binary logistic regression was run to determine whether persons using e-cigarettes to quit smoking cigarettes have higher odds of quitting (with quitting defined as self-reported abstinence 6+ months after start of most recent past-year quit attempt) than those using FDA-approved methods to quit smoking cigarettes. See **Appendix – Figures 8 and 9** for number of lifetime and past-year quit attempts among quit attempters.

No differences in demographic characteristics by quit attempt outcome were found (see Table 2), thus no covariates were entered into the model. The “Quit Attempt Method” variable was entered as one block into the model. The “FDA-Approved Method” was the reference variable for the three remaining methods (“E-cigarettes,” “Combination of methods,” and “no aid ‘cold turkey’”).

Table 2.

Demographic Characteristics by Quit Attempt Outcome After 6 months (n = 171).

	Total n (%)	Quit Attempt Outcome After 6 months n (%)		p
		No Success	Success	
Total Sample	171 (100)	148 (87.0)	23 (13.0)	
Age¹, M (SD)	41.3 (13.1)	41.4 (13.0)	40.7 (14.0)	.820
Biological Sex				.990
Female	82 (48.0)	71 (48.0)	11 (47.8)	
Male	89 (52.0)	77 (52.0)	12 (52.2)	
Sexual Orientation				.389
Bisexual, gay or lesbian	18 (10.5)	14 (77.8)	4 (22.2)	
Heterosexual	149 (87.1)	131 (88.5)	18 (78.3)	
Other/Prefer not to say	4 (2.3)	3 (2.0)	1 (4.3)	

Race/Ethnicity				.831
Black or African American	23 (13.5)	19 (12.8)	4 (17.4)	
Hispanic or Latinx	21 (12.3)	19 (12.8)	2 (8.7)	
White	115 (67.3)	99 (66.9)	16 (69.6)	
Other ¹	12 (7.0)	11 (7.4)	1 (4.3)	
Level of Education				.729
Some high school or high school graduate	46 (26.9)	41 (27.7)	5 (21.7)	
Some college	39 (22.8)	33 (22.3)	6 (26.1)	
Trade/vocational school or Associate's degree	28 (16.4)	25 (16.9)	3 (13.0)	
Bachelor's degree	36 (21.1)	29 (19.6)	7 (30.4)	
Other ²	22 (12.9)	20 (13.5)	2 (8.7)	
Marital Status				.636
Single	41 (24)	37 (25)	4 (17.4)	
Married	76 (44.4)	65 (43.9)	11 (47.8)	
Divorced	17 (9.9)	16 (10.8)	1 (4.3)	
Living with partner	24 (14)	19 (12.8)	5 (21.7)	
Other ³	13 (7.6)	11 (7.4)	2 (8.7)	
Current Household Income				.273
Below \$50,000	91 (53.2)	80 (54.1)	11 (47.8)	
\$50,000 - \$100,000	52 (30.4)	42 (28.4)	10 (43.5)	
Above \$100,000	28 (16.4)	26 (17.6)	2 (8.7)	
Current Employment Status				.211
Employed	109 (63.7)	91 (61.5)	18 (78.3)	
Unemployed	26 (15.2)	25 (16.9)	1 (4.3)	
Other ⁴	36 (21.1)	32 (21.6)	4 (17.4)	

Notes: Fields with 5 or fewer counts were further collapsed into new categories when possible. **Sexual Orientation:** "Other" and "Prefer not to answer" were collapsed into "Other" category. **Race/Ethnicity:** American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Other, and Prefer not to Answer were collapsed into "Other" category. **Level of Education:** Master's degree, Doctorate degree, and "Prefer not to answer" were collapsed into "Other" category. **Marital Status:** Widowed, Separated, Prefer Not to Answer, and Other were collapsed into "Other" category. **Current Employment Status:** Student, Retired, Unable to Work were collapsed into the "Other" category, whereas Self-Employed was collapsed into the "Employed" category.

¹ Age reported as Mean (Standard Deviation)

Of the 171 cigarette quit attempters, 29 attempted to quit using only FDA-approved methods, 30 attempted to quit using only e-cigarettes, 48 attempted to quit using a combination of FDA-approved methods and e-cigarettes, and 64 attempted to quit without aids (See Table

3). The majority of individuals who both smoked cigarettes and used e-cigarettes (dual-users) did *not* attempt to quit smoking cigarettes (56 out of 86 dual-users). Overall, out of each 10 quit attempts, approximately 9 attempts did not last beyond six months, as 86.5% of all quit attempters across methods resumed cigarette smoking within six months of starting their most recent quit attempt. This 9:1 ratio was also reflected among persons using FDA-approved methods to quit, as 92.6% of quit attempters resumed smoking within 6 months. Similarly, 89.6% of quit attempters using a combination of methods resumed smoking within 6 months, as did 92.2% of quit attempters quitting with no aid.

Table 3.

Binary Logistic Regression Results – Quit Attempt Outcome after 6 Months by Quit Method (n =171).

Quit Attempt Method	Frequency n (%)		B	S.E.	Wald	Df	Sig.	Exp(B)	95% CI
	Unsuccessful 148 (86.5)	Successful 23 (13.5)							
FDA-Approved Method	27 (92.6)	2 (7.4)	-	-	14.39	3	.002	-	-
E-cigarettes	19(63.3)	11 (36.7)	2.06	.83	6.21	1	.013	7.82	1.55 – 39.37
Combination	43 (89.6)	5 (10.4)	.45	.87	.27	1	.605	1.57	.28 – 8.67
No aid (“cold turkey”)	59 (92.2)	5 (7.8)	.135	.87	.02	1	.877	1.14	.21 – 6.27
Constant			-2.60	.73	12.61	1	.000	.074	

Key: FDA: Food and Drug Administration. **Combination:** Group composed of quit attempters reporting both e-cigarettes and FDA-approved methods as smoking cessation tools in their most recent quit attempt.

Notes: Quit rates for e-cigarette only, combination, and no aid (“cold turkey”) groups were compared to the baseline, FDA-Approved Method group.

Regarding odds of quit attempt success by quit attempt method, neither “combination” (OR = 1.57, 95% CI = 0.28 – 8.67) nor “no aid” (cold turkey; OR = 1.14, 95% CI = 0.21 – 6.27) quit attempt methods were linked to greater odds of a successful quit attempt when compared to FDA-approved methods. In contrast, the odds of unsuccessful to successful quit attempters

using e-cigarettes to quit was 2:1. Persons who smoked and used e-cigarettes to quit had almost *eight* times greater odds (OR = 7.82, 95% CI = 1.55 – 39.37) of a successful cigarette quit attempt when compared to persons who smoked and used FDA-approved methods to quit.

Primary Aim 2a: Examine the relationship between e-cigarette dependence index score and e-cigarette use (frequency and quantity)

58.9% of all e-cigarette users (including dual users) endorsed moderate or high levels of e-cigarette dependence (9 or higher on a scale of 20), and e-cigarette dependence levels did not vary by demographic characteristics (see Table 4). See **Appendix – Supplemental Tables 2 and 3** for demographic characteristics by full range of e-cigarette dependence levels (None, Low, Medium, High) and by average e-cigarette dependence index score.

Table 4.

Collapsed Demographic Characteristics by Collapsed E-cigarette Dependence Level (None/Low, Med/High; n = 90).

	Total n (%)	E-cigarette Dependence Level n (%)		<i>p</i>
		None/Low	Med/High	
Total Sample	90	37 (41.1)	53 (58.9)	
Age, M (SD)	34.6 (10.0)	34.35 (10.5)	34.9 (9.8)	.811
Biological Sex				.134
Female	45 (50.0)	15 (40.5)	30 (56.6)	
Male	45 (50.0)	22 (59.5)	23 (43.4)	
Gender				.074
Cisgender Woman	43 (48.9)	13 (37.1)	30 (56.6)	
Cisgender Man	45 (51.1)	22 (62.9)	23 (43.4)	
Sexual Orientation				.127
Bisexual, gay or lesbian	14 (15.6)	8 (21.6)	6 (11.3)	
Heterosexual	72 (80)	26 (70.3)	46 (86.8)	
Other/Prefer not to say	4 (4.4)	3 (8.1)	1 (1.9)	

Race/Ethnicity				.709
Black or African American	10 (11.1)	3 (8.1)	7 (13.2)	
Hispanic or Latinx	25 (27.8)	11 (29.7)	14 (26.4)	
White	48 (53.3)	19 (51.4)	29 (54.7)	
Other	7 (7.8)	4 (10.8)	3 (5.7)	
Level of Education				.517
Some high school or high school graduate	14 (15.6)	8 (21.6)	6 (11.3)	
Some college	19 (21.1)	8 (21.6)	11 (20.8)	
Trade/vocational school or Associate's degree	12 (13.3)	4 (10.8)	8 (15.1)	
Bachelor's degree	26 (28.9)	8 (21.6)	18 (34.0)	
Some graduate training	19 (21.1)	9 (24.3)	10 (18.9)	
Marital Status				.548
Single	33 (36.7)	16 (43.2)	17 (32.1)	
Married	42 (46.7)	14 (37.8)	28 (52.8)	
Living with partner	10 (11.1)	5 (13.5)	5 (9.4)	
Other	5 (5.6)	2 (5.4)	3 (5.7)	
Current Household Income				.873
Below \$50,000	33 (36.7)	14 (37.8)	19 (35.8)	
\$50,000 - \$100,000	35 (38.9)	15 (40.5)	20 (37.7)	
Above \$100,000	22 (24.4)	8 (21.6)	14 (26.4)	
Current Employment Status				.223
Employed	67 (74.4)	29 (78.4)	38 (71.7)	
Unemployed	11 (12.2)	2 (5.4)	9 (17.0)	
Other	12 (13.3)	6 (16.2)	6 (11.3)	

Notes:

¹ "Other" Race/Ethnicity category includes American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Other, and Prefer not to Answer.

² "Some graduate training" Level of Education category includes Some graduate training, Master's Degree, Doctorate Degree.

² "Other" Marital Status category includes Separated, Widowed, Divorced, and Prefer not to answer.

³ "Other" Current Employment Status includes Student, Retired, and Self-Employed.

⁴ Age reported as Mean (Standard Deviation).

A multiple linear regression was run to examine the link between e-cigarette dependence index scores among current e-cigarette users and both average days per week that e-cigarettes were used, and average number of e-cigarette uses per day (see **Appendix – Supplemental Table 4** and **Appendix – Figures 10 and 11** for frequency and quantity of cigarette and e-cigarette use). Assumptions of multiple linear regression were met: 1) a linear relationship between e-cigarette dependence index scores and both independent variables as verified by

scatterplot (see **Appendix – Figures 12 and 13**) 2) multivariate normality as verified by standardized residual histogram and P-P plot (see **Appendix – Figure 14**), 3) no multicollinearity as verified by Variance Inflation Factor < 2 for all variables, and 4) homoscedasticity as verified by standardized residual scatterplot (see **Appendix – Figure 15**), and 5) no autocorrelation as verified by Durbin-Watson $d = 1.975$.

We found that average number of days of e-cigarette use per week varied by race/ethnicity, specifically among White e-cigarette users (e-cigarette users using 6-7 days per week were *more* likely to be White when compared to overall sample, and e-cigarette users using 1-2 days per week were *less* likely to be White when compared to overall sample; see Table 5). Average number of e-cigarette uses per day used varied by marital status, specifically among e-cigarette users living with their partner (e-cigarette users with 20+ uses per day were more likely to be living with their partner when compared to overall sample; see Table 6). Dummy coding was conducted for all four categorical variables (race/ethnicity, marital status, average days of e-cigarette use per week, and average e-cigarette uses per day). Baseline categories for dummy coding included “White” for race/ethnicity, “Married” for marital status, “1-2 days per week” for average days per week used, and “<10 per day” for average uses per day.

Table 5.

Collapsed Demographic Characteristics by Collapsed Average Number of Days of E-cigarette Use per Week (Past-Year; n = 90).

	Total n (%)	Average Days/Week Used n (%)			<i>p</i>
		1-2 days	3-5 days	6-7 days	

Total Sample	90	23 (25.6)	29 (32.2)	38 (42.2)	
Age⁵, M (SD)	34.6 (10.0)	35.3 (8.6)	31.5 (8.6)	36.7 (11.4)	
Biological Sex					.211
Female	45 (50.0)	8 (34.8)	15 (51.7)	22 (57.9)	
Male	45 (50.0)	15 (65.2)	14 (48.3)	16 (42.1)	
Gender					.215
Cisgender Female	43 (48.9)	8 (34.8)	13 (48.1)	22 (57.9)	
Cisgender Male	45 (51.1)	15 (65.2)	14 (51.9)	16 (42.1)	
Sexual Orientation					.495
Bisexual, gay or lesbian	14 (15.6)	3 (13)	4 (4.4)	7 (7.8)	
Heterosexual	72 (80)	18 (78.3)	23 (79.3)	31 (81.6)	
Other/Prefer not to say	4 (4.4)	2 (8.7)	2 (6.9)	0 (0)	
Race/Ethnicity					.010
Black or African American	10 (11.1)	1 (4.3)	6 (20.7)	3 (7.9)	
Hispanic or Latinx	25 (27.8)	11 (47.8)	5 (17.2)	9 (23.7)	
White	48 (53.3)	8 (34.8)	14 (48.3)	26 (68.4)	
Other ¹	7 (7.8)	3 (13.0)	4 (13.8)	0 (0)	
Level of Education					.986
Some high school or high school graduate	14 (15.6)	4 (17.4)	4 (13.8)	6 (15.8)	
Some college	19 (21.1)	5 (21.7)	7 (24.1)	7 (18.4)	
Trade/vocational school or Associate's degree	12 (13.3)	4 (17.4)	4 (13.8)	4 (10.5)	
Bachelor's degree	26 (28.9)	6 (26.1)	9 (31.0)	11 (28.9)	
Some graduate training ²	19 (21.1)	4 (17.4)	5 (17.2)	10 (26.3)	
Marital Status					.612
Single	33 (36.7)	9 (39.1)	14 (48.3)	10 (26.3)	
Married	42 (46.7)	11 (47.8)	11 (37.9)	20 (52.6)	
Living with partner	10 (11.1)	2 (8.7)	2 (6.9)	6 (15.8)	
Other ³	5 (5.6)	1 (4.3)	2 (6.9)	2 (5.3)	
Current Household Income					.895
Below \$50,000	33 (36.7)	9 (39.1)	12 (41.4)	12 (31.6)	
\$50,000 - \$100,000	35 (38.9)	8 (34.8)	10 (34.5)	17 (44.7)	
Above \$100,000	22 (24.4)	6 (26.1)	7 (24.1)	9 (23.7)	
Current Employment Status					.773
Employed	67 (74.4)	19 (82.6)	20 (69.0)	28 (73.7)	
Unemployed	11 (12.2)	2 (8.7)	5 (17.2)	4 (10.5)	
Other ⁴	12 (13.3)	2 (8.7)	4 (13.8)	6 (15.8)	

Notes:

¹ "Other" Race/Ethnicity category includes American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Other, and Prefer not to Answer.

² "Some graduate training" Level of Education category includes Some graduate training, Master's Degree, Doctorate Degree.

³ "Other" Marital Status category includes Separated, Widowed, Divorced, and Prefer not to answer.

⁴ "Other" Current Employment Status includes Student, Retired, and Self-Employed.

⁵ Age reported as Mean (Standard Deviation).

Table 6.

*Collapsed Demographic Characteristics by Collapsed Average Number E-cigarette**Uses per Day (Past-Year; n = 90).*

	Total n (%)	Average E-cigarette Uses per Day n (%)			<i>p</i>
		<10 per day	10-19 per day	>20 per day	
Total Sample	90	48 (53.3)	30 (33.3)	12 (13.3)	
Age⁵, M (SD)	34.6 (10.0)	35.3 (10.4)	32.7 (8.6)	36.9 (11.9)	
Biological Sex					.377
Female	45 (50.0)	27 (56.3)	12 (40.0)	6 (50.0)	
Male	45 (50.0)	21 (43.8)	18 (60.0)	6 (50.0)	
Gender					.455
Cisgender Female	43 (48.9)	26 (54.2)	11 (39.3)	6 (50.0)	
Cisgender Male	45 (51.1)	22 (45.8)	17 (60.7)	6 (50.0)	
Sexual Orientation					.399
Bisexual, gay or lesbian	14 (15.6)	10 (20.8)	2 (6.7)	2 (16.7)	
Heterosexual	72 (80)	35 (72.9)	27 (90.0)	10 (83.3)	
Other/Prefer not to say	4 (4.4)	3 (6.3)	1 (3.3)	0 (0)	
Race/Ethnicity					.345
Black or African American	10 (11.1)	6 (12.5)	4 (13.3)	0 (0)	
Hispanic or Latinx	25 (27.8)	16 (33.3)	5 (16.7)	4 (33.3)	
White	48 (53.3)	21 (43.8)	19 (63.3)	8 (66.7)	
Other ¹	7 (7.8)	5 (10.4)	2 (6.7)	0 (0)	
Level of Education					.315
Some high school or high school graduate	14 (15.6)	5 (10.4)	6 (20.0)	3 (25.0)	
Some college	19 (21.1)	15 (31.3)	2 (6.7)	2 (16.7)	
Trade/vocational school or Associate's degree	12 (13.3)	7 (14.6)	3 (10.0)	2 (16.7)	
Bachelor's degree	26 (28.9)	12 (25.0)	11 (36.7)	3 (25.0)	
Some graduate training ²	19 (21.1)	9 (18.8)	8 (26.7)	2 (16.7)	
Marital Status					.022
Single	33 (36.7)	19 (39.6)	12 (40.0)	2 (16.7)	
Married	42 (46.7)	22 (45.8)	16 (53.3)	4 (33.3)	
Living with partner	10 (11.1)	5 (10.4)	0 (0)	5 (41.7)	
Other ³	5 (5.6)	2 (4.2)	2 (6.7)	1 (8.3)	
Current Household Income					.472
Below \$50,000	33 (36.7)	21 (43.8)	7 (23.3)	5 (41.7)	

\$50,000 - \$100,000	35 (38.9)	17 (35.4)	14 (46.7)	4 (33.3)	
Above \$100,000	22 (24.4)	10 (20.8)	9 (30.0)	3 (25.0)	
Current Employment Status					.928
Employed	67 (74.4)	36 (75.0)	23 (76.7)	8 (66.7)	
Unemployed	11 (12.2)	5 (10.4)	4 (13.3)	2 (16.7)	
Other ⁴	12 (13.3)	7 (14.6)	3 (25.0)	2 (16.7)	

Notes:

¹“Other” Race/Ethnicity category includes American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Other, and Prefer not to Answer.

²“Some graduate training” Level of Education category includes Some graduate training, Master’s Degree, Doctorate Degree.

³“Other” Marital Status category includes Separated, Widowed, Divorced and Prefer not to answer.

⁴“Other” Current Employment Status includes Student, Retired, and Self-Employed.

⁴ Age reported as Mean (Standard Deviation).

The two demographic covariates (i.e., race/ethnicity and marital status) were entered first in one block, followed by the average days per week used and average number of uses per day in a second block. Using the Enter method combined with bootstrapping (1000 samples), we found a non-significant regression equation for the first model (only including demographic covariates); $F(6, 83) = .740, p = .619, R^2 = .051, \text{adjusted } R^2 = -.018$. The regression was significant for the second model (including both demographic covariates and both independent variables; $F(10, 79) = 3.537, p < .001, R^2 = .309, \text{adjusted } R^2 = .222$. Our initial analyses suggested that a model including both average number of days of e-cigarette use and average number of uses per day could detect an association between e-cigarette use and e-cigarette dependence index scores (on a 20-point scale, where a higher score denotes higher dependence). In other words, a greater average number of days per week of e-cigarette use and a greater average number of e-cigarette uses per day were associated with greater e-cigarette dependence index scores.

To determine the independent associations of average days per week used and average number of uses per day on e-cigarette dependence index scores, a second multiple linear regression was calculated using the Enter method, combined with bootstrapping (1000 samples). Level of education and marital status were entered first, average days per week used entered second, and average number of uses per day entered third. Similar to the first model (including only demographic variables), the second model, including demographic variables and average days per week used, did not account for a significant proportion of variance in e-cigarette dependence index scores; $F(8, 81) = 1.685, p = .115, R^2 = .143,$ adjusted $R^2 = .058$. In contrast, the third model, adding average uses per day, accounted for a significantly higher proportion of the variance in e-cigarette dependence index scores than the first two models, $F(10, 79) = 3.537, p < .001, R^2 = .309$ adjusted $R^2 = .222$.

A comparison of linear, bootstrapped coefficients for both independent variables (average days per week used and average uses per day) indicated that while both independent variables were positively correlated with e-cigarette dependence index scores, average uses per day was more strongly associated with e-cigarette dependence index scores than average days per week used (see Table 6).

Table 6.

Summary of Multiple Linear Regression Analysis Examining the Association between Frequency and Quantity of E-cigarette Use and E-cigarette Dependence.

	B	Std. error	Std β	t	Sig	95% CI for β		VIF
						Lower	Upper	

Constant	6.29	1.14		5.30	<.001	4.06	8.56	
Frequency (Avg. Days/Week)¹								
3-5 days/week	1.85	1.25	.18	1.48	.14	-.69	4.14	1.74
6-7 days/week	2.07	1.20	.22	1.67	.10	-.29	4.50	1.92
Quantity (Avg. Uses/Day)²								
10-19 uses/day	3.25	1.02	.32	3.13	<.01	1.0	5.07	1.22
20+ uses/day	5.74	1.80	.41	3.73	<.001	2.21	9.07	1.40

Notes:

¹ Reference group for Frequency was “1-2 days/week.”

² Reference group for Quantity was “<10 uses/day.”

Frequency. When compared to the baseline category “1-2 days/week” (which was the lowest frequency category), no category denoting increased frequency of use was associated with a significant increase in e-cigarette dependence index scores. When compared to less than daily use (lowest frequency), daily use (highest frequency) was associated with a non-significant, 2.07 point increase in e-cigarette dependence index scores.

Quantity. When compared to the baseline category “<10 uses/day” (which was the lowest collapsed quantity category), both categories denoting higher quantity used were associated with significantly higher e-cigarette dependence index scores. When compared to baseline use, (<10 uses/day), e-cigarette users reporting “10-19 uses/day” scored 3.25 points higher on the e-cigarette dependence index score (20-point scale). The largest difference was seen between the baseline category (lowest quantity) and the “>20 uses/day” category (highest quantity), where e-cigarette users who endorsed the highest amount of use per day scored 5.74 points higher on the e-cigarette dependence index scale when compared to those with the lowest amount of use.

Primary Aim 2b: Examine the relationship between the e-cigarette dependence index score and e-cigarette nicotine concentration

50% of e-cigarette users reported no/low levels (0-6 mg/mL) of e-cigarette nicotine concentration. 31.1% reported medium (12-24 mg/mL) and 18.9% reported high (30+ mg/mL) levels of e-cigarette nicotine concentration (see Table 7). See **Appendix – Figures 15 and 16** for more detailed data on type of device and range of nicotine concentrations used).

Table 7.

Demographic Characteristics of Current E-cigarette Users by E-cigarette Nicotine

Concentration (n = 90).

	Total n (%)	E-cigarette Nicotine Concentration n (%)			<i>p</i>
		None/Low (0-6 mg/mL)	Medium (12-24 mg/mL)	High (30+ mg/mL)	
Total Sample	90	45 (50.0)	28 (31.1)	17 (18.9)	
Age⁵, M (SD)	34.6 (10.0)	37.0 (10.8)	32.6 (7.9)	31.8 (9.9)	
Biological Sex					.553
Female	45 (50.0)	25 (55.6)	12 (42.9)	8 (47.1)	
Male	45 (50.0)	20 (44.4)	16 (57.1)	9 (52.9)	
Sexual Orientation					.804
Bisexual, gay or lesbian	14 (15.6)	6 (13.3)	5 (17.9)	3 (17.6)	
Heterosexual	72 (80)	37 (82.2)	21 (75.0)	14 (82.4)	
Other/Prefer not to say	4 (4.4)	2 (4.4)	2 (4.1)	0 (0)	
Race/Ethnicity					.235
Black or African American	10 (11.1)	3 (6.7)	6 (21.4)	1 (5.9)	
Hispanic or Latinx	25 (27.8)	13 (28.9)	6 (21.4)	6 (35.5)	
White	48 (53.3)	24 (53.3)	16 (57.1)	8 (47.1)	
Other ¹	7 (7.8)	5 (11.1)	0 (0)	2 (11.8)	
Level of Education					.047
Some high school or high school graduate	14 (15.6)	7 (15.6)	4 (14.3)	3 (17.6)	

Some college	19 (21.1)	10 (22.2)	7 (25.0)	2 (11.8)	
Trade/vocational school or Associate's degree	12 (13.3)	11 (24.4)	0 (0)	1 (5.9)	
Bachelor's degree	26 (28.9)	11 (24.4)	11 (39.3)	4 (23.5)	
Some graduate training ²	19 (21.1)	6 (13.3)	6 (21.4)	7 (41.2)	
Marital Status					
Single	33 (36.7)	14 (31.1)	12 (42.9)	7 (41.2)	.550
Married	42 (46.7)	20 (44.4)	14 (50.0)	8 (47.1)	
Living with partner	10 (11.1)	7 (15.6)	2 (7.1)	1 (5.9)	
Other ³	5 (5.6)	4 (8.9)	0 (0)	1 (5.9)	
Current Household Income					
Below \$50,000	33 (36.7)	19 (42.2)	9 (32.1)	5 (29.4)	.634
\$50,000 - \$100,000	35 (38.9)	18 (40.0)	10 (35.7)	7 (41.2)	
Above \$100,000	22 (24.4)	8 (17.8)	9 (32.1)	5 (29.4)	
Current Employment Status					.774
Employed	67 (74.4)	32 (71.1)	22 (78.6)	13 (76.5)	
Unemployed	11 (12.2)	5 (11.1)	4 (14.3)	2 (11.8)	
Other ⁴	12 (13.3)	8 (17.8)	2 (7.1)	2 (11.8)	

Notes:

¹ "Other" Race/Ethnicity category includes American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Other, and Prefer not to Answer.

² "Some graduate training" Level of Education category includes Some graduate training, Master's Degree, Doctorate Degree.

³ "Other" Marital Status category includes Separated, Widowed, and Prefer not to answer.

⁴ "Other" Current Employment Status includes Student, Retired, and Self-Employed.

⁴ Age reported as Mean (Standard Deviation).

A multiple linear regression was run to examine the link between e-cigarette dependence index scores and e-liquid nicotine concentration among current e-cigarette users (see **Appendix – Figure 17** for type of e-cigarette device used by e-cigarette users and dual users). Assumptions of multiple linear regression were met: 1) a linear relationship between e-cigarette dependence index score and e-liquid nicotine concentration (see **Appendix – Figure 18**), 2) multivariate normality as verified by standardized residual histogram and P-P plot (see **Appendix – Figure 19**), 3), no multicollinearity as verified by Variance Inflation Factor < 2.1 for all variables, and 4) homoscedasticity as verified by standardized residual

scatterplot (see **Appendix – Figure 20**), and 5) no autocorrelation as verified by Durbin-Watson $d = 1.779$.

We found that nicotine concentration varied by level of education. Specifically, individuals using no/low nicotine concentration (0-6 mg/mL) e-liquid were more likely to have trade/vocational training or an Associate’s degree when compared to the overall sample. In contrast, individuals using high levels of nicotine concentration (30+ mg/mL) e-liquid were more likely to have some graduate-level training when compared to the overall sample. Dummy coding was conducted for level of education, with the baseline category being “Some high school or high school graduate.” Dummy coding was also conducted for nicotine concentration, with the baseline category being “No/Low Concentration (0-6 mg/mL)”. Using the Enter method combined with bootstrapping (1000 samples), level of education was entered into the model first as a covariate, and nicotine concentration was entered second. We found non-significant regression equation for the both models; $F(4, 85) = .164, p = 0.956, R^2 = .008, \text{adjusted } R^2 = -.039$, and $F(6, 83) = 1.145, p = .344, R^2 = .076, \text{adjusted } R^2 = .010$. Our analyses suggested that e-cigarette nicotine concentration did not account for a significant proportion of variance in e-cigarette dependence index scores (see Table 8).

Table 8.

Summary of Multiple Linear Regression Examining the Association Between Collapsed (No/Low, Med, High) E-cigarette Nicotine Concentration and E-cigarette Dependence.

	B	Std. error	Std β	t	Sig	95% CI for β	VIF
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						Lower	Upper	
Constant	8.57	1.37		5.79	<.001	5.92	11.17	
Nicotine Concentration)¹								
Med (12-24 mg/mL)	2.58	1.03	.25	2.14	<.05	.338	4.58	1.25
High (30+ mg/mL)	-.57	1.46	-.05	-.40	.69	-3.48	2.21	1.24

Notes: Reference category for Nicotine Concentration was “No/Low Concentration (0-6 mg/mL).”

A comparison of linear, bootstrapped coefficients of the independent variable categories revealed that medium levels of nicotine concentration (12-24 mg/mL) level were associated with significantly higher e-cigarette dependence index scores, when compared to no/low nicotine concentration (0-6 mg/mL). Medium levels of nicotine concentration appear to have a stronger association with e-cigarette dependence index scores when compared to higher (30+ mg/mL) nicotine concentration levels.

Exploratory Aim: Examine differences in demographics and cigarette dependence among smokers trying to quit using e-cigarettes versus other methods

Demographic information of cigarette quit attempters was examined to detect differences in demographic characteristics by quit attempt method (see Table 6). Among all quit attempters, 17.5% of quit attempters used only e-cigarettes to quit, compared to 82.5% of quit attempters using other methods (FDA-approved methods, combination of e-cigarettes and FDA-approved methods, no aid “cold turkey”).

Table 9.

Demographic characteristics of cigarette quit attempters by quit attempt method (n = 171)

Total Quit Attempt Method p

	Sample n (%)⁵	E-cigarette n (%)	Other¹ n (%)	
Total Sample	171 (100)	30 (17.5)	141 (82.5)	
Age (M, SD)	41.3 (13.1)	34.8 (9.15)	42.7 (13.4)	<.001
Biological Sex				.551
Female	82 (48.0)	16 (19.5)	66 (80.5)	
Male	89 (52.0)	14 (15.7)	75 (84.3)	
Sexual Orientation				.156
Bisexual, Gay or Lesbian	18 (10.5)	6 (33.3)	12 (66.7)	
Heterosexual	149 (87.1)	23 (15.4)	126 (84.6)	
Other/Prefer not to say	4 (2.3)	1 (25)	3 (75)	
Race/Ethnicity				.548
Black or African American	23 (13.5)	4 (17.4)	19 (82.6)	
Hispanic or Latino	21 (12.3)	2 (9.5)	19 (90.5)	
White	115 (67.3)	23 (20)	92 (80)	
Other ²	12 (7.0)	1 (8.3)	11 (91.7)	
Level of Education				<.01
Some high school or high school graduate	46 (26.9)	3 (6.5)	43 (93.5)	
Some college	39 (22.8)	7 (17.9)	32 (82.1)	
Trade/vocational school/Associates	28 (16.4)	2 (7.1)	26 (92.9)	
Bachelor's degree	36 (21.1)	12 (33.3)	24 (66.7)	
Some graduate training, Masters, or Doctorate	22 (12.9)	6 (27.3)	16 (72.7)	
Marital Status				.300
Single	41 (24.0)	10 (24.4)	31 (75.6)	
Married	76 (44.4)	12 (15.8)	64 (84.2)	
Divorced	17 (9.9)	1 (5.9)	16 (94.1)	
Living with partner	24 (14)	6 (25)	18 (75)	
Other ³	13 (7.6)	1 (7.7)	12 (92.3)	
Current Household Income				<.001
Below \$10,000	17 (9.9)	1 (5.9)	16 (94.1)	
\$10,000 - \$50,000	74 (43.3)	11 (14.9)	63 (85.1)	
\$50,000 - \$100,000	52 (30.4)	9 (17.3)	43 (82.7)	
\$100,000 - \$150,000	15 (8.8)	1 (6.7)	14 (93.3)	
Above \$150,000	13 (7.6)	8 (61.5)	5 (38.5)	
Current Employment Status				.175
Employed full-time	89 (52)	21 (23.6)	68 (76.4)	
Employed part-time	10 (5.8)	1 (10)	9 (90)	
Unemployed (looking for work)	14 (8.2)	1 (7.1)	13 (92.9)	
Unemployed (not looking for work)	12 (7.0)	1 (8.3)	11 (91.7)	

Retired	16 (9.4)	1 (6.3)	15 (93.8)
Unable to work	17 (9.9)	1 (5.9)	16 (94.1)
Other ⁴	13 (7.6)	4 (30.8)	9 (69.2)

Notes:

¹ “Other” Quit Attempt Method category includes FDA-approved methods, combination of e-cigarettes and FDA approved methods, and no-aid (“cold turkey”).

² “Other” Race/Ethnicity category includes American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Other, and Prefer not to Answer.

³ “Other” Marital Status category includes Separated, and Widowed.

⁴ “Other” Current Employment Status includes Student, and Self-Employed.

⁵ Age reported as Mean (Standard Deviation).

Quit attempters using e-cigarettes to quit were younger than quit attempters using other methods. Quit attempters using e-cigarettes to quit were more likely to have a Bachelor’s degree when compared to the overall sample whereas quit attempts using other methods were more likely to have stopped pursuing education after high school when compared to the overall sample. Quit attempters using only e-cigarettes to quit were more likely to have an income above \$150,000 when compared to the overall sample.

Current (smoking within past 6 months) and former (ceased smoking 6+ months prior to survey completion) cigarette dependence was collected from all participants who endorsed cigarette use or dual use over the past year (See **Appendix – Supplemental Table 4** for demographic characteristics by current cigarette dependence index score). E-cigarette-only users were not provided the PSCDI measure of cigarette dependence. Given the uneven group sizes of quit attempters using only e-cigarettes to quit versus quit attempters using other methods, a two-sample Welch’s *t*-test was conducted to compare mean cigarette dependence scores (PSCDI) between quit attempters group by smoking cessation method used. Results from the two-sample Welch’s *t*-test (see Table 10) did not suggest a difference

in mean cigarette dependence scores (current or former) by quit attempt method (e-cigarettes versus other methods).

Table 10.
Mean cigarette dependence score by quit attempt method (e-cigarette vs. other methods; n = 171).

	N	Mean (Standard Deviation)	95% Confidence Interval		P ⁴
			Lower	Upper	
Current Cigarette Dependence¹					.133
Total	154	11.58 (3.98)	10.94	12.21	
E-cigarette	20	10.2 (4.29)	8.19	12.21	
Other Methods ²	134	11.79 (3.90)	11.12	12.45	.410
Former Cigarette Dependence³					
Total	17	11.76 (5.11)	9.13	14.40	
E-cigarette	10	12.6 (5.80)	8.46	16.75	
Other Methods ²	7	10.6 (4.08)	6.80	14.34	

Notes:

¹ Current cigarette dependence was measured via the Penn State Cigarette Dependence Index (PSCDI), with scores ranging from 0 (no dependence) to 13+ (high dependence).

² “Other” Quit Attempt Method category includes FDA-approved methods, combination of e-cigarettes and FDA approved methods, and no-aid (“cold turkey”).

³ Former cigarette dependence was measured via a modified version of the Penn State Cigarette Dependence Index (PSCDI), with scores ranging from 0 (no dependence) to 13+ (high dependence), where the question tense was altered from present (e.g., “Do you sometimes awaken at night to have a cigarette?”) to past (e.g., “Did you sometimes awaken at night to have a cigarette?”).

⁴ *p*-values reflect comparison of mean cigarette dependence scores (current or former) between quit attempters using e-cigarettes versus quit attempters using other methods to quit.

A separate, Kruskal-Wallis H test was then conducted to compare current and former mean cigarette dependence scores across the complete set of four specific quit attempt methods (i.e., e-cigarettes only, FDA-approved methods only, combination of methods, no aid “cold turkey”). The Kruskal-Wallis H test was selected due to uneven group sizes (see Table 11). The Kruskal-Wallis H test did not reveal any significant differences in current ($\chi^2(3) = 6.41$,

$p = .093$) or former ($\chi^2(3) = 2.2.1, p = .550$) cigarette dependence scores by specific quit attempt method.

Table 11.

Mean ranks of current and former cigarette dependence scores by quit attempt methods (e-cigarettes, FDA-approved methods, combination of quit methods, no aid).

	N	Mean Rank	Kruskal-Wallis-H (χ^2)	Degrees of Freedom	Asymptotic Significance
Current Cigarette Dependence					
E-cigarettes	20	62.0	6.41	3	.093
FDA-Approved Methods	26	87.4			
Combination of Quit Methods	46	86.1			
No Aid	62	72.0			
Former Cigarette Dependence			2.11	3	.550
E-cigarettes	10	10.4			
FDA-Approved Methods	3	6.0			
Combination of Quit Methods	2	7.0			
No Aid	2	8.75			

Chapter IV: Discussion

This cross-sectional survey study examined the relationships between e-cigarette use and both (i) cigarette smoking cessation and (ii) e-cigarette dependence among a sample of adult online survey panelists in the U.S. This study also explored differences in both demographics and cigarette dependence among cigarette quit attempters using e-cigarettes versus other methods to quit smoking. Regarding e-cigarette use for smoking cessation, cigarette smokers using e-cigarettes to quit had significantly higher odds of having a successful quit attempt lasting over 6 months when compared to (i) cigarette smokers using FDA-approved smoking cessation methods and (ii) cigarette smokers using no aid (i.e., quitting “cold turkey”). Regarding e-cigarette use and its associations with e-cigarette dependence, the quantity of e-cigarette use was associated with e-cigarette dependence; with higher quantities of use related to higher levels of e-cigarette dependence. Neither e-liquid nicotine concentration nor frequency of e-cigarette use were significantly associated with e-cigarette dependence. Regarding demographic differences and differences in cigarette dependence level by cigarette quit attempt method (e-cigarettes versus other methods), participants using e-cigarettes versus participants using other methods to quit smoking cigarettes varied significantly in terms of age, level of education, and income level. No significant differences were found in cigarette dependence based on quit attempt method.

Primary Aim 1: Examine e-cigarette effectiveness as a cigarette smoking cessation aid

Of the 171 cigarette quit attempts captured in this study, only 23 (13.5%) were successful, consistent with the low success rate that persists among U.S. adults attempting to cease their cigarette use (6.3% in 2009, 7.5% in 2018; Creamer, 2019). Three of the four quit methods examined in this study had similarly low quit success rates: 1) FDA-approved methods (7.4%), 2) combined use of e-cigarettes and FDA-approved methods (10.4%), and 3) no aid / “cold turkey” (7.8%). In contrast, individuals using only e-cigarettes for smoking cessation had a significantly higher successful quit rate (36.7%) and had approximately *eight* times higher odds of quitting when compared to individuals trying to quit using FDA-approved cessation methods or using no aid (“cold turkey”).

Previous findings regarding e-cigarettes for cigarette smoking cessation remain mixed. A systematic review and consequent meta-analysis of 12 studies (RCTs or cohort studies) by El Dib and colleagues (2017) concluded that evidence pointing to the possible efficacy of e-cigarettes for smoking cessation could only be rated at very-low to low certainty, limiting the utility of study findings. A more recent systematic review and meta-analysis of 12 RCTs suggested that e-cigarettes containing nicotine were more effective for smoking cessation than both e-cigarettes without nicotine and nicotine replacement therapy but echoed previous concerns with the quality of evidence and number of available studies, making a conclusive argument regarding e-cigarette efficacy for smoking cessation difficult (Grabovac et al., 2020). Our study’s findings that e-cigarette use for smoking cessation was associated with significantly higher odds of successful smoking cessation when compared to other quit methods is consistent with the trend of evidence pointing towards e-cigarettes’ utility as a

smoking cessation aid, and congruent with the consensus that frequent e-cigarette use is associated with a higher likelihood of successfully quitting cigarettes (NASEM, 2018).

E-cigarettes may be more effective than FDA-approved methods as a smoking cessation tool, though the small number of quit attempters who used e-cigarettes to quit ($n = 30$) suggests a conservative interpretation of this study's findings, as the 30 respondents captured in this study may not be representative of the larger population of those attempting to quit cigarettes by using e-cigarettes. Though the cross-sectional nature of this study does not allow for conclusions to be drawn regarding quit method efficacy in smoking cessation, reasons why e-cigarettes may be useful for cigarette smoking cessation are worth exploring further. The design and characteristics of an e-cigarette allow for similar tactile and sensory experiences to cigarettes. They emit a similar visual indicator of use (i.e., vapor instead of smoke), can come in similar shapes and designs, are used in the same (or near-identical) ways, and are easier to use in areas where cigarettes are prohibited or more easily detected. They also allow for social (e.g., participating in a "smoke break") and habitual (e.g., "smoking" after a cup of coffee) continuity during a quit attempt, reducing the reliance on cigarettes for access to social and habitual experiences.

Given the option of replacing cigarette use with a 1) possibly less harmful, 2) equally effective, and 3) more accessible way of delivering nicotine, it is possible that quit attempters using only e-cigarettes to quit found it easier to discontinue cigarette use than those not using e-cigarettes. FDA-approved methods have fewer similarities to cigarettes when compared to

e-cigarettes. NRTs also deliver nicotine, but the nicotine is delivered in less familiar ways (e.g., via lozenge or transdermally instead of through inhalation). Furthermore, cigarettes deliver a notably higher amount of nicotine over the shortest period of time when compared to other NRTs, leaving cigarettes as the most efficient nicotine delivery system (Hatsukami et al., 2009). Both NRTs and other pharmacological interventions (i.e., varenicline and bupropion) lack some of the sensory, behavioral, and social characteristics offered by e-cigarettes, possibly making them a less appealing alternative to cigarettes than e-cigarettes (which mimic nicotine delivery through cigarettes most closely), resulting in higher likelihood of continued cigarette smoking.

It is also possible that demographic characteristics of e-cigarette users increased their odds of successfully quitting compared to non-e-cigarette users. Quit attempters using only e-cigarettes were younger and had both higher levels of education and income when compared to quit attempters using other methods. Access to higher education and income may be linked to access to increased resources to quit, which were not captured in this study. A range of non-pharmacological cessation resources exist, including group therapy, behavioral counseling, strong support networks, exercise interventions, hypnotherapy, and incentive-based methods (see Fiore et al., 2009 and Hartmann-Boyce et al., 2021 for reviews of smoking cessation interventions). Other cessation methods may have supplemented e-cigarette use and contributed to higher odds of successfully quitting.

We did not expect the difference in likelihood of a successful quit attempt between e-cigarettes and FDA-approved methods to be so large. Previous findings related to increased likelihood of successfully quitting using e-cigarettes versus other methods suggest that the likelihood of successfully quitting would be between one and a half to five times higher for e-cigarette users (Brown, 2014; Zhuang, 2016; Glasser, 2021). Our result is inconsistent with previous research and may be driven by a small group size ($n=30$). Increasing the sample in future studies may decrease the range of calculated 95% confidence intervals, and provide more precise estimates of the true likelihood of a successful quit attempt using e-cigarettes versus FDA-approved methods.

Consistent with previous literature regarding quit attempt methods was our finding that the most frequently used quit attempt method was no aid / “cold turkey” (37.4%). Data from the 2014 PATH study (Rodu & Plurphanswat, 2017) suggested that among current and former smokers with a past-year quit attempt, 45% to 47% did not use a quit method during their attempt. The same study revealed that the most frequently used single quit attempt method was “friends and family” (37%), followed by e-cigarettes (32%; Rodu & Plurphanswat, 2017). These data are consistent with an unchanging trend of low pharmacological treatment use among smokers attempting to quit (Shiffman et al, 2008; Soulakova & Crockett, 2017). Given that pharmacological interventions (especially bupropion and NRT) do retain effectiveness as smoking cessation tools, it is possible that increased use of pharmacological treatments during cigarette quit attempts may improve quit success rates (Lemmens, Oenema, Knut, & Brug, 2008). Despite the unclear role of e-cigarettes in smoking cessation, some evidence exists regarding e-cigarettes as a useful smoking cessation aid (Harrel, 2014;

Weaver, 2018; Hajek et al., 2019; Pierce et al., 2020). It is possible that the use of e-cigarettes as a smoking cessation aid increased the odds of a successful quit attempt when compared to no use of aid, given that e-cigarettes could provide nicotine replacement, maintenance of behavioral/social habits, and lower levels of craving/distress.

Primary Aim 2a: Examine the relationship between e-cigarette dependence scores and e-cigarette use (frequency and quantity)

Over half (58%) of current e-cigarette users in this study endorsed medium or high levels of e-cigarette dependence. Given that short-term e-cigarette use poses health risks, and the health effects of prolonged e-cigarette use remain unknown (Bold, Krishnan-Sarin, & Stoney, 2018), understanding the links between e-cigarette use and e-cigarette dependence remains critical. Should long-term e-cigarette use have negative health consequences (e.g., cardiovascular disease, pulmonary disorders, cancer), e-cigarette users dependent on e-cigarettes may have difficulty discontinuing their use, placing them at higher risk of developing health problems.

When measured together, frequency and quantity of use represent “intensity” or “heaviness” of use, one of the ten recommended constructs used to measure e-cigarette dependence (Bold et al., 2018). Should frequency and quantity of e-cigarette use predict e-cigarette dependence, they could be used as low-cost, fast, and easily implementable screening questionnaires/instruments that clinicians could rely on to detect users at risk of developing or endorsing e-cigarette dependence. This study’s findings regarding the associations of both frequency and quantity of e-cigarette use with e-cigarette dependence levels suggest that

frequency of e-cigarette use, measured by average number of days per week e-cigarettes were used, was weakly associated with e-cigarette dependence. In contrast, quantity of e-cigarette use, measured by average number of uses per day on days when e-cigarettes were used, was more strongly linked to e-cigarette dependence, with higher quantity of e-cigarette use linked to higher levels of e-cigarette dependence.

The association between quantity of e-cigarette use and level of e-cigarette dependence's directionality is difficult to ascertain given the cross-sectional nature of the study. Though e-cigarette dependence was conceptualized as most likely a *consequence* of high quantity and frequency of use, it is possible that the etiological relationship is reversed; individuals dependent on e-cigarettes will consequently use e-cigarettes frequently and in high quantities (e.g., to relieve cravings). In all likelihood, the relationship between e-cigarette dependence and frequency/quantity of use is bidirectional, with factors related to dependence (e.g., tolerance, withdrawal) influencing "heaviness" or "intensity" of use, while external factors including environmental stressors and ease/availability of use promote use patterns that result in dependence (Piper, McCarthy, Baker, 2006). Due to the similarities between cigarettes and e-cigarettes, it is possible that nicotine dependence and e-cigarette dependence manifest and are measured similarly as well. However, recent research has noted that while similarities between nicotine dependence and e-cigarette dependence exist, they are not identical, and product-specific dependency remains worthy of study (Rest, Mermelstein, & Hedeker, 2021).

Cigarettes per day (CPD) is an item measuring quantity of use commonly seen in a range of nicotine dependence measures (e.g., Fagerström Test Questionnaire (FTQ), FTND, Nicotine Dependence Syndrome Scale (NDSS)), and has modest ($r = .22$ to $.48$) correlations with dependence index scores (Donny et al., 2008). This study's results suggest that number of e-cigarette uses per day, which attempts to mirror items measuring cigarettes per day, appears to also be linked to e-cigarette dependence. Uses per day thus appears to be a concept developed to measure nicotine dependence that translates well into the measurement of e-cigarette dependence.

Frequency of use appears less translatable. This study's findings suggest a weak association between frequency of use (average days used per week) and e-cigarette dependence. When measuring the link between frequency and nicotine dependence, commonly used nicotine dependence measures present a wider range of frequency measures (i.e., smoking days per week, smoking days per month, daily vs. non-daily smoking), and has lower (but still modest) correlation with nicotine dependence ($r = .22$ to $.25$; Donny, 2008). Regarding e-cigarettes, it is possible that frequency measures (days of use per week) are more weakly tied to e-cigarette dependence than frequency measures are to nicotine dependence.

Participants in this sample reporting cigarette use smoked predominantly on a daily or near-daily basis. In comparison, though daily or near-daily e-cigarette use was most prominent among dual users as well (only 11 participants were e-cigarette-only users, making cigarette only-to-e-cigarette only comparisons difficult), the proportions of non-daily to daily/near-daily dual users were far more balanced, suggesting that frequencies of use among

individuals smoking cigarettes vs. using e-cigarettes do not mirror of one another. With the weak association suggested by this study's findings, frequency of e-cigarette use (as defined as average number of days used per week) may be better replaced with a different range of frequency (e.g., days used per month), or with a different item entirely (e.g., time to first use upon awakening).

Primary Aim 2b: Examine the relationship between the e-cigarette dependence index score and e-cigarette nicotine concentration

Half of the current e-cigarette users reported no or low (0-6 mg/mL) nicotine concentration in their e-liquid. Approximately one-third of e-cigarette users reported moderate (12-24 mg/mL) levels of e-liquid nicotine concentration, and the remaining 20% reported high (30+ mg/mL) nicotine concentration. These proportions suggest that using e-liquid with little to no nicotine is a popular choice among e-cigarette users. Given the strong association between nicotine and tobacco dependence (Benowitz, 2009), one could hypothesize a similar association between nicotine and e-cigarette dependence (where nicotine consumption via e-liquid could lead to e-cigarette dependence). Should the widespread use of low concentration/no nicotine e-liquid suggested by this sample be mirrored in the overall e-cigarette user population, e-cigarette users may be at lower risk of becoming dependent compared to individuals who smoke and become tobacco-dependent through nicotine use, and thus be less likely to develop health problems related to prolonged e-cigarette use.

E-liquid nicotine concentration was hypothesized to be linked to e-cigarette dependence, with higher levels of nicotine concentration expected to be related to higher levels of e-cigarette dependence (and lower nicotine concentration being related to lower dependence). Results from this study suggested that e-liquid nicotine concentration had a weak association with e-cigarette dependence levels among current e-cigarette users. These findings were surprising given 1) previous findings of e-liquid nicotine concentration being positively correlated with e-cigarette dependence scores (Foulds et al., 2015), and 2) the expectation that because e-cigarettes and cigarettes share many similarities, the relationship between nicotine and e-cigarette dependence would mirror the relationship between nicotine and tobacco dependence.

One possible explanation is that despite being similar to cigarettes in shape, size, method of use, and purpose, e-cigarettes have enough differences that make the relationship between nicotine and tobacco dependence an inappropriate parallel. For example, nicotine delivered via e-cigarettes is generally absorbed into the bloodstream at a significantly slower rate when compared to nicotine delivered via cigarettes (Yingst et al., 2019). Also, the ways e-cigarettes are used also vary from cigarettes. A phenomenon known as “pre-puffing,” which is the act of taking a smaller e-cigarette puff to prime the heat element, thereby facilitating maximal activation during the longer, “primary” puff, does not exist with cigarettes. Also, a puff taken from a cigarette generally lasts two seconds, whereas an e-cigarette puff lasts around four seconds, and one instance of “use” of a traditional cigarette lasts for seven to 10 puffs (at which point the cigarette is considered consumed), whereas e-cigarettes can be used for 20-30 puffs at a time with ease (Behar, Hua, & Talbot, 2015). Given that nicotine is

delivered somewhat differently via cigarettes versus e-cigarettes, it is possible that the PSECDI e-cigarette dependence measure (adapted from the PSCDI, a cigarette dependence measure) is measuring a construct of dependence that does not take the differences between the two products sufficiently into account. However, this possibility seems unlikely, as a validation study of the E-cigarette Dependence Scale (EDS), had strong convergent validity with the PSECDI and used e-liquid nicotine concentration to verify a test-criterion relationship (Morean et al., 2018), which suggests that further research on the relationship between e-liquid nicotine concentration and dependence is needed.

E-cigarette nicotine concentration also varies *widely* across type of device and e-liquid used. With over 450 different e-cigarette brands and 7500 types of e-liquid (Zhu, 2014), a standardized approach to implementing, labeling, regulating, and researching e-liquid nicotine concentration remains challenging. Some nicotine concentrations are labeled quantitatively (e.g., “6 mg”), whereas others are labeled qualitatively (e.g., “high”). Standardization issues clearly arise in the context of qualitative descriptors (i.e., what determines “high” vs. “low”), but even quantitatively, there is variation in the units of measurement (i.e., “mg,” “mg/mL,” “percent by volume”).

Variations in labeling mirror variations in labeled vs. actual e-liquid nicotine concentration. Etter, Zather, & Svensson (2013) reported that the measured concentration of e-liquid nicotine concentration from 10 different brands from the U.S. and Western Europe ranged from 6 to 29 mg/mL, and that the actual concentration varied from 85% to 107% of the

concentration listed on the label. In the U.S., one study found that nicotine levels deviated from labeled nicotine strength by more than 20% in nine of 32 tested samples, while another study found that nicotine concentrations in over 30 different e-liquid types were 5.8% to 41.7% lower than what was labeled (Goniewicz et al., 2015; Lisko et al., 2015). See Chapter 4: Nicotine from Public Health Consequences of E-cigarettes (NASEM, 2018) for a complete overview of nicotine concentration in e-cigarettes.

This study asked two rudimentary questions to measure presence and magnitude of e-liquid nicotine concentration. These questions may have inadequately captured the notable variability in labeling, measurement, and actual concentration of the nicotine concentrations used by the participants, thus making the linear relationship between nicotine concentration and e-cigarette dependence harder to detect. This high variability in e-liquid nicotine concentration may also have affected participants' ability to report an accurate concentration level, especially given the specialized tools that would be required for an e-cigarette user to biochemically verify the nicotine concentration in their e-liquid and compare it to the listed concentration level.

Exploratory Aim: Examine differences in demographics and cigarette dependence among smokers trying to quit using e-cigarettes versus other methods

This study examined whether quit attempters using e-cigarettes to quit versus quit attempters using any other method (i.e., FDA-approved methods, combination of e-cigarettes and FDA-approved methods, no aid “cold turkey”) varied across a range of demographic characteristics. Quit attempters using only e-cigarettes were predominantly younger, had a

higher level of education, and reported a higher income than quit attempters using other methods. Little research has been done to study demographic differences by quit attempt method, but one study of e-cigarette use and smoking cessation in U.S., college-aged adults found that quit attempters who used e-cigarettes were younger than quit attempters who did not use e-cigarettes, while the two attempter groups did not vary by race or sex (Mantey et al., 2017).

A broader examination of e-cigarette users' demographic characteristics from the 2018-2019 Current Population Survey, a nationally-representative survey that includes items for tobacco use, indicated that e-cigarette use in the U.S. is more prevalent among men, and among individuals who self-identified as 1) non-Hispanic White, 2) American Indian/Alaska Native, or 3) multiracial (Mayer, Reyes-Guzman, Grana, 2020). They found that prevalence of e-cigarette use rose in conjunction with education level (less than high school, to high school, to some college). This trend continued until reaching respondents with a college degree, among whom e-cigarette use was less prevalent than among those with less than a high school education. Also, e-cigarette users who reported never smoking were younger than e-cigarette users who reported current or former smoking (i.e., dual users; Mayer et al., 2020)).

The lower age of e-cigarette-only quit attempters compared to quit attempters using other methods may be attributable to the advent of e-cigarettes as a new technology that has recently emerged over the past decade. Compared to younger populations, older individuals tend to avoid novelty, preferring familiarity and predictability (Lawton et al., 1992, McCrae

et al., 2000). Traditional cigarettes offer a reliable and remarkably consistent experience, whereas e-cigarettes offer near-limitless customization in power, heat source, shape, size, nicotine concentration, and flavor. The variability may be attractive to younger individuals seeking different sensations and more control over their quit attempts, whereas it may alienate individuals looking for more traditional cessation tools that are regulated and have been available for longer periods of time. Of particular attraction to younger individuals are e-cigarette flavors. Flavor is a primary driver of e-cigarette use among adolescents and younger adults (ages 18-24; Patel et al., 2016), and may provide a more pleasurable smoking cessation experience. Aside from menthol cigarettes, all flavored cigarettes have been banned in the U.S. since 2009, whereas e-cigarette flavors remain legal, albeit with some restrictions; e-liquid cartridges that are particularly attractive for use among youth are limited to tobacco and menthol flavors, and can no longer contain other flavors (e.g., mint, bubblegum, waffles; FDA, 2020).

Our results suggested that higher income (>\$150,000) was associated with higher likelihood of quit attempts using only e-cigarettes when compared to lower income. Individuals of lower socioeconomic status (SES; living below the poverty level) are equally as likely to attempt to quit smoking as individuals not of lower SES (i.e., living at or above poverty level; 66.6% vs. 69.9%). However, individuals of lower SES are less likely to successfully quit when compared to individuals not of lower SES (34.5% vs. 57.5%; USDHHS, 2014). This study's findings suggest a possible reason for this disparity. Using income as a proxy for SES, if individuals of higher SES are more likely to use e-cigarettes to quit cigarettes than those of lower SES, and e-cigarettes are associated with higher successful quit rates,

individuals of higher SES will be more likely to quit successfully than individuals of lower SES.

E-cigarettes require the purchase of a “starter” kit that can range from \$15 to \$50 (Loomis et al., 2016), and typically costs more than a pack of cigarettes (average cost ranges from \$4.62 to \$10.67; Orzechowski & Walker, 2017). E-cigarettes may thus have a high “barrier to entry” which is cost-prohibitive to individuals with low SES. Interestingly, a cost-effectiveness study comparing e-cigarettes to traditional NRTs in the United Kingdom (U.K.) suggested that e-cigarettes (£105, \$146) were more cost-effective than traditional NRTs (£201, \$278) over a 12-month period (Li et al., 2020). These findings suggest that the high initial cost of e-cigarettes may dissuade individuals of low SES from using them as a smoking cessation aid, despite e-cigarettes likely being more cost-effective over the long term. Providing more education regarding cost-effectiveness may help bridge the gap between e-cigarette use for smoking cessation among low vs. high SES individuals.

Similarly, high educational attainment (Bachelor’s degree) was associated with higher likelihood of quit attempts using only e-cigarettes when compared to individuals with lower educational attainment. Individuals of low educational attainment (no high school diploma) are equally as likely to attempt to quit smoking as individuals with higher educational attainment (college degree or higher; 39.0% vs. 44.0%). However, individuals of lower educational attainment are less likely to successfully quit when compared to individuals of higher educational attainment (43.5% vs. 73.9%; USDHHS, 2014). Little is known at this time regarding the association between educational attainment and quit attempts with e-cigarettes, and this question is worthy of future study.

This study also examined differences in cigarette dependence index scores among individuals using e-cigarettes versus other methods to quit smoking and found that mean cigarette dependence index scores did not vary based on which quit method individuals used. These findings suggest that the choice of quit method is not related to level of dependence on cigarettes at the time of a quit attempt, and that individuals looking to quit are not selecting their quit attempt methods based on their level of dependence on tobacco.

Clinical Implications

Several clinical implications arise from this study's findings. The main implication of this study is that e-cigarettes may have some worth as a cigarette smoking cessation aid. Because individuals who used e-cigarettes as a smoking cessation aid during their quit attempt had higher odds of quitting cigarettes than individuals using other methods (particularly, FDA-approved methods), e-cigarettes may facilitate smoking cessation in a way that other smoking cessation methods do not. Studies with larger sample sizes may provide a more precise estimate of the higher odds of quitting cigarettes linked to e-cigarette use. Further experimental research in the form of RCTs would also be needed to ascertain effectiveness of e-cigarettes for cigarette smoking cessation when compared to other methods. If this research yields evidence that points to e-cigarettes as an effective smoking cessation tool, then clinicians could recommend e-cigarettes to patients who have struggled to discontinue cigarette use using FDA-approved methods. By offering patients a novel smoking cessation tool, clinicians may facilitate a successful cigarette quit attempt that other smoking cessation aids would have been unhelpful for. A successful quit attempt would thereby reduce the

patient's risk of developing cigarette-related health problems, and also reduce the financial burden associated with treating said cigarette-related health conditions.

The benefits of e-cigarette use for smoking cessation would have to be weighed with the cost and potential risks of e-cigarette use (e.g., e-cigarette dependence, harmful effects of short/long-term e-cigarette use), especially if individuals are unable to discontinue e-cigarette use after quitting cigarettes, and ultimately replacing one source of nicotine with another. This phenomenon would be consistent with the philosophy of harm reduction, which acknowledges the continued use of nicotine as inevitable, and aims to reduce adverse health consequences related to its use. However, e-cigarettes present a harm reduction-based solution to cigarette smoking insofar as e-cigarettes are not equally (or more) harmful than cigarettes. It wasn't until several decades after the onset of cigarette smoking in the U.S. that the health risks of cigarette smoking were well-understood, and this delay contributed to incalculable losses (both economically and in human lives lost). The health risks of prolonged e-cigarette use are not well-understood and prevent firm conclusions to be made regarding their safety.

Ideally, individuals who use e-cigarettes to quit smoking cigarettes would discontinue e-cigarette use as well, as complete abstinence from nicotine would provide the lowest risk of developing nicotine-related health problems. E-cigarette cessation may be more feasible given the flexibility in e-liquid nicotine content, allowing for users to titrate the amount of nicotine in e-liquid down to 0% over time. Ultimately, very few methods to stop cigarettes

are completely risk-free, and individuals looking to quit cigarette use should collaborate with healthcare providers to discuss potential costs and benefits to e-cigarette use for smoking cessation.

This study found that one third of cigarette quit attempters who used e-cigarettes as a smoking cessation aid successfully quit. If e-cigarette use for smoking cessation enabled the success of one third of all cigarette quit attempts, cigarette smoking prevalence in the U.S. would decrease drastically, from ~15% to ~10%. This decrease would lead to improvements in overall health and a reduction in mortality rate for the ~5% of the U.S. adult population that ceased smoking cigarettes through e-cigarettes. Relevantly, a third of the study participants attempted to quit unaided (“cold turkey”), which was the most popular quit method. This finding speaks to the importance of making new smoking cessation aids that are more effective or more appealing to quit attempters, thereby increasing their likelihood of use in a quit attempt and possibly increasing the odds of a successful quit attempt. Of course, the benefits of new smoking cessation aids must be weighed against risks associated with their use. E-cigarettes may be less harmful than cigarettes, but they are not harmless. If initiation of e-cigarette use is related to smoking cessation, e-cigarettes should be discontinued upon successful smoking cessation. Palmer and colleagues (2021) explored desire to quit e-cigarettes among current e-cigarette users, and noted that the majority of e-cigarette users expressed current or eventual interest in discontinuation. However, ceasing e-cigarette use may be difficult for individuals who develop e-cigarette dependence.

This study found that quantity of e-cigarette use (uses on days used) was associated with e-cigarette dependence. Clinicians with patients who use e-cigarettes can ask about quantity of

e-cigarette use to help assess the risk of their patient being dependent on e-cigarettes (especially if they report over 10 uses per day on days used), without the use of a screening tool or dependence measure. Depending on quantity used, clinicians can engage in conversations with their patients and provide education regarding their risk of e-cigarette dependence based on the quantity reported. In contrast, information on either e-liquid nicotine concentration or frequency of e-cigarette use is less useful in assessing risk for e-cigarette dependence. However, findings measuring correlation between e-cigarette measures (e.g., quantity, nicotine concentration) in e-cigarette users imply low internal consistency among the general population. These findings suggest that e-cigarette users have difficulty reliably assessing and reporting their use, or that existing measures do not reliably assess facets of e-cigarette use (though it is likely a combination of both; Parker, Pearson & Villanti, 2019). Asking about quantity of e-cigarette use and e-liquid nicotine concentration may help patients become more informed about their e-cigarette use, and raise awareness of the health risks associated with it.

Though general trends in demographics appear to be emerging among e-cigarette users compared to non-e-cigarette users (e.g., younger, generally more versus less educated), it is important to continue identifying today's e-cigarette user, specifically in the context of smoking cessation. Should e-cigarettes be effective smoking cessation tools, demographic information can be used to identify what makes e-cigarette use for smoking cessation attractive for those most likely to use them. Conversely, demographic information can also be used to identify demographic groups that have *lower* odds of using e-cigarettes for smoking cessation, and to address obstacles barring them from using a potentially effective

smoking cessation tool. For example, 64% of dual-users reported a current household income of \$50,000 or higher, whereas only 34.6% of cigarette smokers reported incomes of \$50,000+. The difference could be attributable to dual-users earning higher incomes, and thus having more financial resources to devote to healthcare/their well-being Or perhaps dual-users live in areas with higher costs-of-living, thus requiring higher incomes. Dual-users may also be part of larger households, thus leading to higher household incomes. There are several potential explanations for this one demographic difference, and demographic differences extend beyond just current household income, suggesting the need for further exploration of demographic differences by type of e-cigarette and cigarette use.

Strengths and Limitations

Regarding strengths of this study, the study design provided low levels of burden on the participant, requiring at most 15 minutes to complete, in total anonymity, with no travel/transportation costs or requirements. The online nature of the survey allowed it to be disseminated to participants throughout the U.S., allowing for data to be collected from a sample more representative of the general population when compared to local recruitment methods. Few exclusion criteria allowed for the recruitment of virtually any English-speaking U.S. adult who used cigarettes or e-cigarettes in the past year, reducing the odds of selection bias in participant selection. Together, the study was cost-effective: requiring only 1) set-up costs for survey design, and 2) per-participant recruitment costs (including dissemination and participant compensation), while providing valuable cigarette and e-cigarette use data from the general population.

The data collected also allowed for a granular look at number of cigarette/e-cigarette users, the demographic makeup of the users, their use behaviors, quit attempts and quit attempt outcomes, and smoking cessation methods used in said quit attempts. The data allow for further hypotheses to be generated regarding e-cigarettes' role in smoking cessation and help clarify the link between e-cigarette use and e-cigarette dependence.

Regarding limitations, this study's cross-sectional nature prevented any conclusions to be made regarding the direct impact of e-cigarettes on smoking cessation over time. A randomized clinical trial with established treatment arms comparing e-cigarettes to evidence-based, FDA-approved smoking cessation methods among cigarette smokers looking to quit would better answer the question regarding e-cigarettes' effectiveness for smoking cessation and the relationship of e-cigarette dependence to cessation outcomes. Participants were asked to recall and report aspects of their past-year cigarette and e-cigarette use. Being unable to verify the accuracy of their recollections makes it difficult to estimate self-report errors or deception – a common factor in online nicotine research (Heffner et al., 2021).

The survey results may also be impacted by time-based response bias. The survey was disseminated over a total period of 6 days (i.e., the sample size limit was met on the 6th day), leading to a time-bias through which only participants with quicker response times were included and potential participants with quicker response times may differ from potential participants with lower response times. For example, quicker respondents may have been more motivated to complete surveys, more compensation-driven, or more interested in our subject matter, all of which possibly leading to biased results. Conversely, our limited sample size and quota restrictions prevented several potential participants from completing the

survey, leading to a non-response bias. In particular, our sample consisted predominantly of White men. Though this sample was constructed by design to meet race/gender quotas, this sample composition reduces the number of conclusions that can be drawn regarding non-White, non-male populations. The study also did not address possible confounding effects of motivation to quit. It is possible that individuals who smoked and attempted to quit using e-cigarettes were more motivated to quit than those using FDA-approved methods, and could explain the difference in successful quit attempts found in this study.

The majority of current e-cigarette users were dual-users, and only 11 individuals were e-cigarette-only users. Given the small number of e-cigarette-only users, we were unable to compare associations between e-cigarette use and e-cigarette dependence across the two types of e-cigarette users (e-cigarette-only versus dual). As noted earlier, future studies with larger sample sizes would have a number of benefits including being able to examine e-cigarette-only users versus dual users.

Yingst et al. (2018) noted that e-cigarette use can be overreported based on the type of question used to determine quantity of e-cigarette use, suggesting a potential inflation in e-cigarette dependence scores. Specifically, they asked participants to report both the number of daily puffs taken, and the number of daily uses of e-cigarettes (with one instance of e-cigarette use defined as 15 puffs per time used). They discovered that users self-reported a greater number of uses than was indicated by the reported number of puffs taken daily. Given that a participant may overreport their e-cigarette use when asked to provide the number of

daily uses versus the number of daily puffs taken, the phrasing of the PSECDI's first item (ascertaining number of e-cigarette uses) may inadvertently inflate e-cigarette dependence scores.

Participants were asked to provide the nicotine concentration of their e-liquid, but not the volume of e-liquid consumed on a daily basis. Though measuring the amount of e-liquid consumed daily would allow the calculation of daily average nicotine consumption (thereby providing a more accurate account of nicotine consumed), e-liquid consumption has no standardized measure, and is rarely tracked accurately (i.e., does not account for changes in use patterns, sharing with other users). E-liquid nicotine concentration is standardized (mg/ml), can be found on the e-liquid container or via online product brochures, and has been used in prior research (e.g., Foulds et al., 2015; Morean et al., 2018).

The remote completion of the self-report survey prevented the author from presenting the survey in a controlled environment or verifying proper informed consent and understanding of survey completion procedures. Researchers were unable to ensure active and non-distracted participation, though this limitation was mitigated via attention checks and survey time limits.

Only Qualtrics respondents residing in the U.S. were recruited, rendering our data less applicable to international populations. Countries vary in e-cigarette regulation, methodology of use, and marketing, making generalization of findings more difficult. For example, in

contrast to the U.S., Canada does not allow the marketing or sale of e-cigarettes containing nicotine (Hammond et al., 2015). Whereas U.S. health officials do not promote or encourage e-cigarettes for smoking cessation, the U.K. Royal College of Physicians emphatically encourages e-cigarette use to discontinue smoking (Amos et al., 2016). Finally, the U.S. allows for online marketing and sale of e-cigarette products, whereas China recently banned online marketing and sale of e-cigarettes, thereby decreasing their availability (Xiao, 2021).

Additionally, Qualtrics respondents are not fully representative of U.S. adults (e.g., some groups are excluded from participation such as prison populations, inpatients, and individuals without internet access) which limits the generalizability of our findings. No biochemical assessments (e.g., carbon monoxide levels, cotinine levels) were available to verify current smoking or abstinence, which may have allowed inaccurate reporting of smoking and e-cigarette use to influence our results. Further, the variable nature of e-cigarette devices and use patterns makes standardized measurements of use difficult to establish.

The survey did not measure other key variables related to cigarette smoking, e-cigarette use, or quit attempts such as comorbid medical conditions, psychological distress, stress and mood. For example, individuals with higher levels of psychological distress are more likely to smoke than individuals with none or low levels of psychological distress, and are also less likely to quit successfully (Forman-Hoffman et al., 2017; Streck et al., 2018). Future research would benefit from incorporating these variables into studies that attempt to better understand e-cigarettes' effectiveness as a smoking cessation aid.

Finally, the primary aim of the study was to look at quit attempt outcomes, defined as total abstinence after a 6-month period, and data related to possible decreases in cigarette smoking during quit attempts were not captured. E-cigarettes may be better suited as a harm-reduction tool, as it replicates physical, psychological, and social factors of cigarettes that represent an adequate substitute for individuals looking to decrease their cigarette use, but are having trouble discontinuing completely (Notley, Ward, Dawkins & Holland, 2018). Future research is warranted to establish e-cigarettes' role as a smoking *reduction* tool instead of a smoking cessation aid.

Conclusion

This study examined differences in successful quit attempts among individuals who smoke cigarettes by type of smoking cessation method used (e-cigarettes, FDA-approved methods, no aid “cold turkey”). Findings suggested that quit attempters using e-cigarettes to quit had higher odds of successfully quitting cigarettes when compared to quit attempters using other methods, providing evidence for e-cigarettes' role as a viable smoking cessation tool. This study also found an association between e-cigarette use and e-cigarette dependence, suggesting that individuals engaged in heavy e-cigarette use are at risk of becoming dependent on e-cigarettes. The utility of e-cigarettes for smoking cessation is tempered by the possibility of developing e-cigarette dependence, and thus being more vulnerable to the potential harms of long-term e-cigarette use. Further research is warranted on e-cigarettes' effectiveness as a smoking cessation aid, and whether the harms mitigated by smoking cessation are replaced by the potential effects of prolonged e-cigarette use.

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Appendices

Appendix A. Figures

Figure 1: Summary of the Research Design.

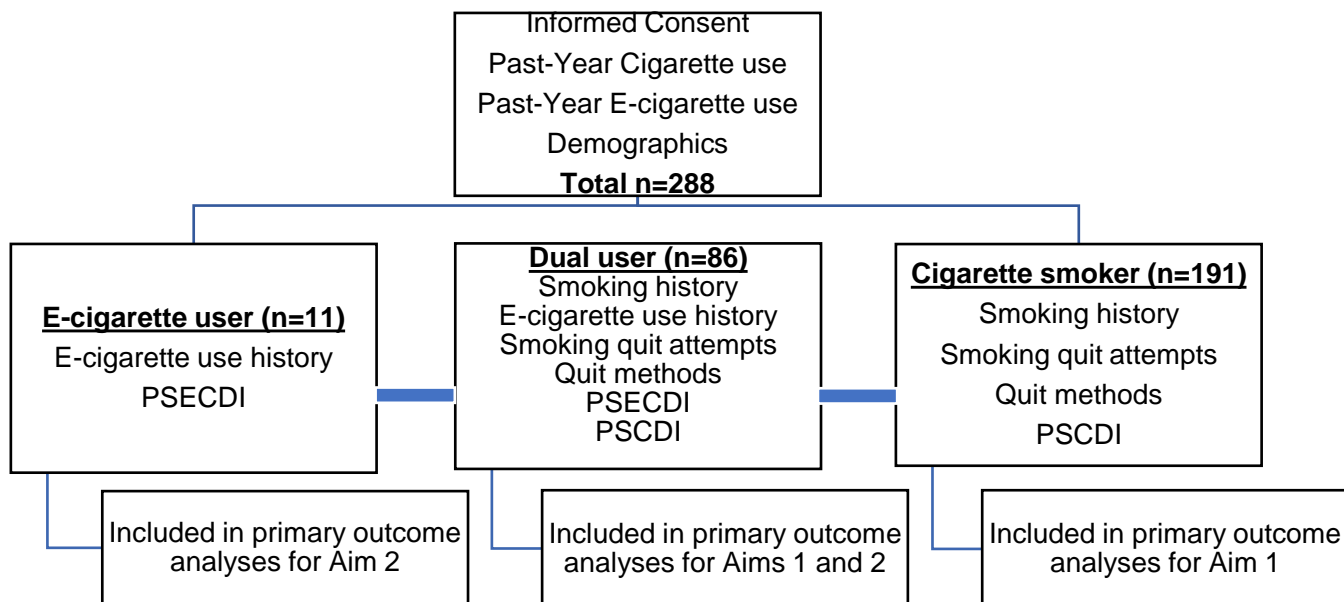


Figure 2: Qualtrics Survey Invitation.

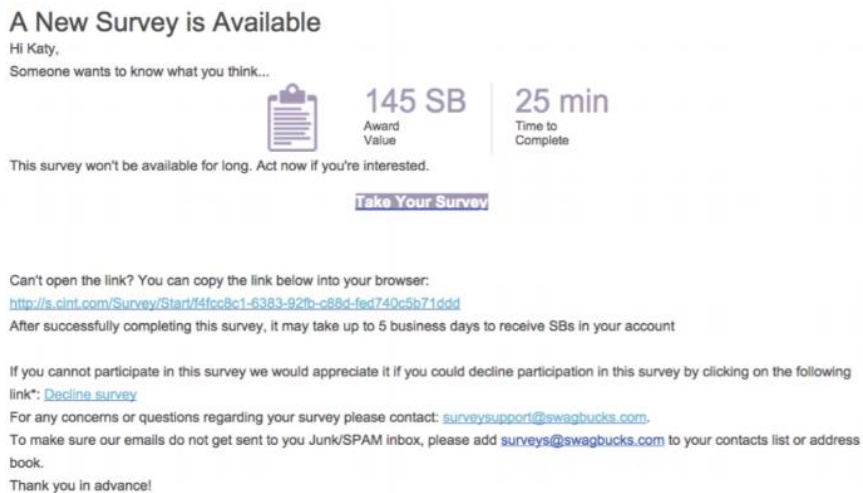


Figure 3: Informed Consent Form.

Consent Form

You are invited to participate in this web-based research project on smoking and e-cigarette use. This is a research project being conducted by researchers at Yeshiva University/Einstein, and data collected will only be used for research purposes.

Your participation in this research study is voluntary. You may choose not to participate. If you decide to participate in this research survey, you may withdraw at any time. If you decide not to participate in this study or if you withdraw from participating at any time, you will not be penalized. The procedure involves filling an online survey that will take approximately 15 minutes. Your responses will be confidential and, research staff do not collect identifying information such as your name, email address or IP address. [Amazon MTurk Disclaimer].

We will do our best to keep your information confidential. All data is stored in a password protected electronic format. To help protect your confidentiality, the surveys will not contain information that will personally identify you. The results of this study will be used for scholarly purposes only and may be shared with Yeshiva University representatives.

You will receive no direct benefits from participating in this study, other than compensation offered after successful completion of the survey per Amazon MTurk Worker/Requester policies.

The potential risks or discomfort associated with your participation in the study are minimal. Some questions ask about cigarette use, and past attempts to quit smoking, and may be distressing to you as you think about your experiences.

You will be asked to answer a set of screening questions to determine your eligibility for the study. Ineligible participants will be unable to complete the survey, and will not qualify for compensation.

If you have any questions about the research study, please contact study staff [contact info]. This research has been reviewed according to Yeshiva University and Einstein IRB procedures for research involving human subjects.

ELECTRONIC CONSENT: Please select your choice below.

Clicking on the "I Consent" button below indicates that:

- 1) You have read and understood the above information**
- 2) You voluntarily agree to participate**
- 3) You are at least 18 years of age.**

If you do not wish to participate in the research study, please decline participation by clicking on the "I Do Not Consent" button.

I Consent

I Do Not Consent

Figure 4: Eligibility Questions.

Please select the statement that best describes your cigarette use

- I have never been a cigarette smoker
- I am a former smoker, meaning that I used to smoke cigarettes, but I successfully quit over a year ago
- I recently quit smoking, meaning that I used to smoke cigarettes, but I successfully quit less than a year ago
- I smoke occasionally, meaning at least once a month
- I smoke cigarettes most days, but not daily
- I smoke cigarettes daily

Please select the statement that best describes your e-cigarette use. For the purposes of this study, the term "e-cigarettes" refers to all types of battery-powered electronic cigarette devices (e.g., cig-a-likes, e-cigs, vapes, tanks, vape pens)

- I have never been an e-cigarette user
- I am a former e-cigarette user, meaning that I used to use e-cigarettes, but I successfully quit over a year ago
- I recently quit e-cigarettes, meaning that I used to use e-cigarettes, but I successfully quit less than a year ago
- I use e-cigarettes occasionally, meaning at least once a month
- I use e-cigarettes most days, but not daily
- I use e-cigarettes daily

Figure 5: Visual representation of electronic nicotine delivery devices (CDC, 2018).



Figure 6: Penn State Electronic Cigarette Dependence Index (PSECDI; Foulds et al., 2015).

Penn State Electronic Cigarette Dependence Index
<p>1. How many times per day do you usually use your electronic cigarette* (assume that one "time" consists of around 15 puffs or lasts around 10 minutes) _____ times</p> <p>(Scoring: 0-4 times/day = 0, 5-9 = 1, 10-14 = 2, 15-19 = 3, 20-29 = 4, 30+ = 5)</p>
<p>2. On days that you can use your electronic cigarette freely, how soon after you wake up do you first use your electronic cigarette?* _____ minutes</p> <p>(Scoring: < 5 minutes = 5, 6-15 = 4, 16-30 = 3, 31-60 = 2, 61-120 = 1, 121+ = 0)</p>
<p>3. Do you sometimes awaken at night to use your electronic cigarette? *</p> <p>(Scoring: Yes = 1, No = 0)</p>
<p>4. If yes, how many nights per week do you typically awaken to use your electronic cigarette ? *</p> <p>(Scoring: 0-1 nights = 0, 2-3 nights = 1, 4+ nights = 2)</p>
<p>5. Do you use your electronic cigarette now because it is really hard to quit (using e-cigs)? *</p> <p>(Scoring: Yes = 1, No = 0)</p>
<p>6. Do you ever have strong cravings to use your electronic cigarette? *</p> <p>(Scoring: Yes = 1, No = 0)</p>
<p>7. Over the past week, how strong have the urges to use your electronic cigarette been? *</p> <p>(Scoring: None/Slight = 0, Moderate/Strong= 1, Very Strong/Extremely Strong = 2)</p>
<p>8. Is it hard to keep from using your electronic cigarette in places where you are not supposed to? *</p> <p>(Scoring: Yes = 1, No = 0)</p>
<p>When you haven't used an electronic cigarette for a while or when you tried to stop using....</p>
<p>9. Did you feel more irritable because you couldn't use your electronic cigarette? *</p> <p>(Scoring: Yes = 1, No = 0)</p>
<p>10. Did you feel nervous, restless, or anxious because you couldn't use your electronic cigarette? *</p> <p>(Scoring: Yes = 1, No = 0)</p>
<p>11. What is the concentration of nicotine in the liquid that you usually use in your electronic cigarette?</p> <p>(answers can be accepted in either % nicotine or mg/ml. This does not contribute to the score but is often relevant to assessing dependence. Many e-cig users are unclear about the concentration).</p>
<p>Scoring: 0-3= not dependent, 4-8 low dependence, 9-12 medium dependence, 13+ = high dependence</p> <p>*From FTND/HIS, *From Bover, *From Hooked on Nicotine Checklist, *From Fiddler</p>

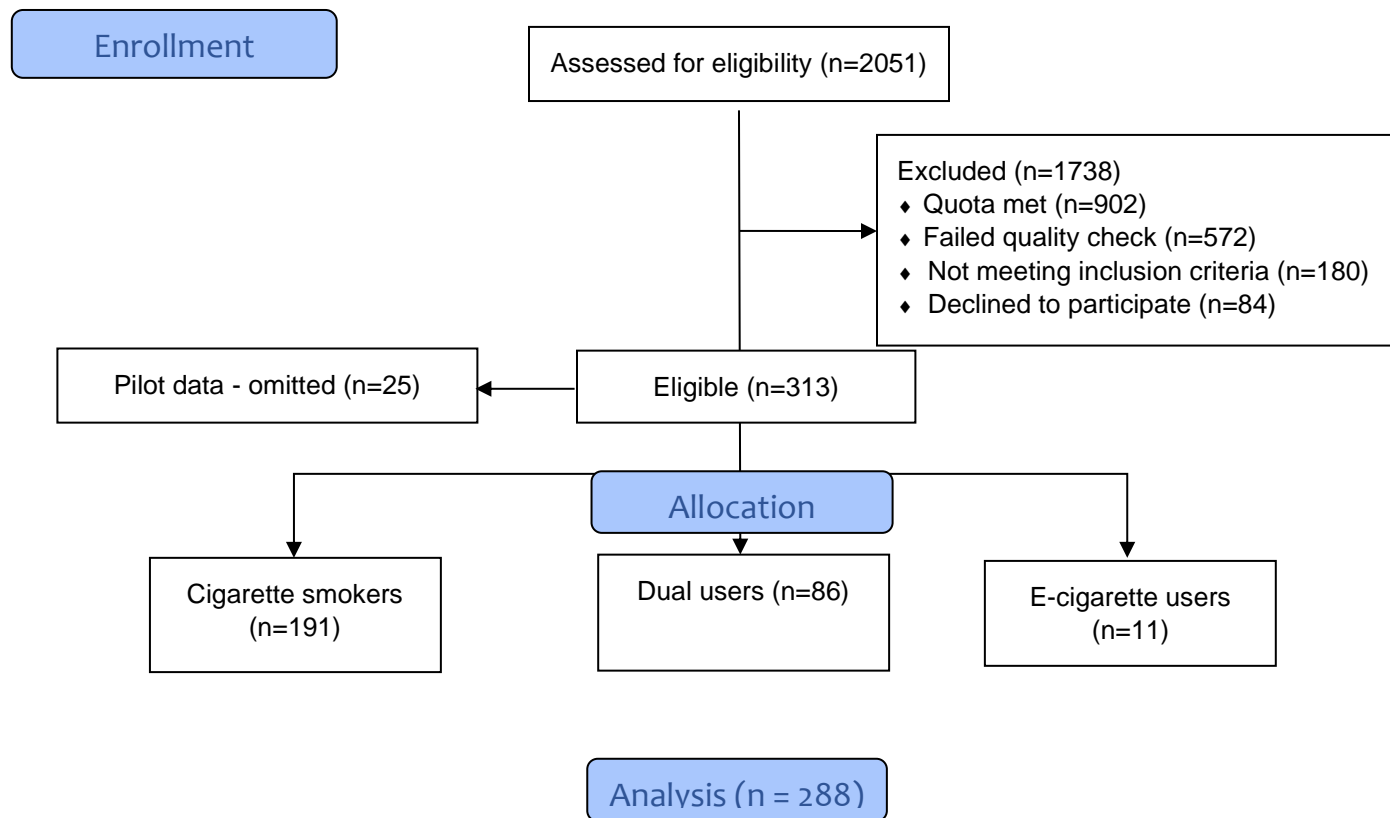
Figure 7: Study Recruitment Flow Diagram

Figure 8: Lifetime Quit Attempts Among Current Cigarette Smokers and Dual Users (n = 271).

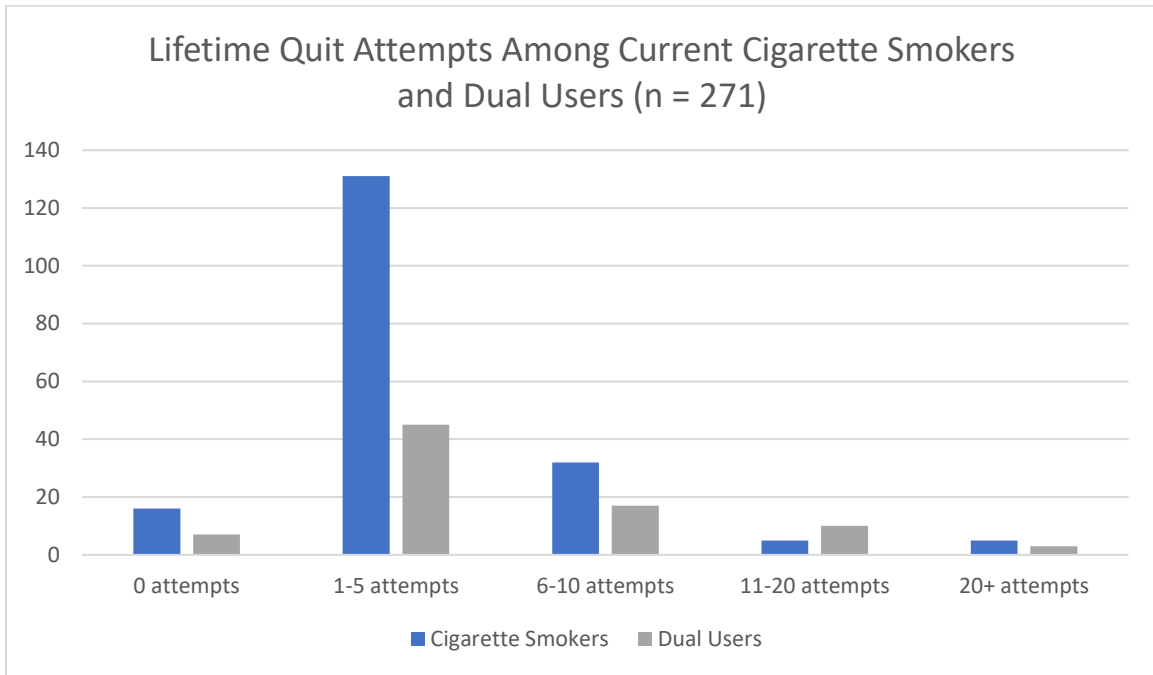


Figure 9. Past Year Quit Attempts Among Current Cigarette Smokers and Dual Users (n = 271)

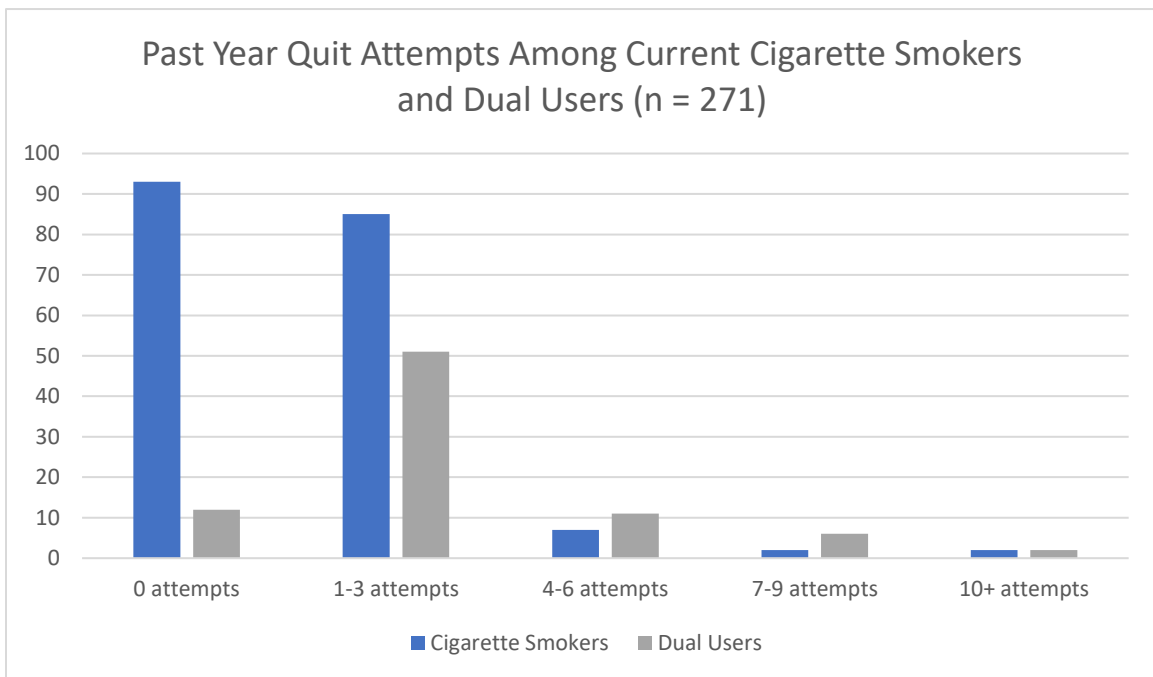


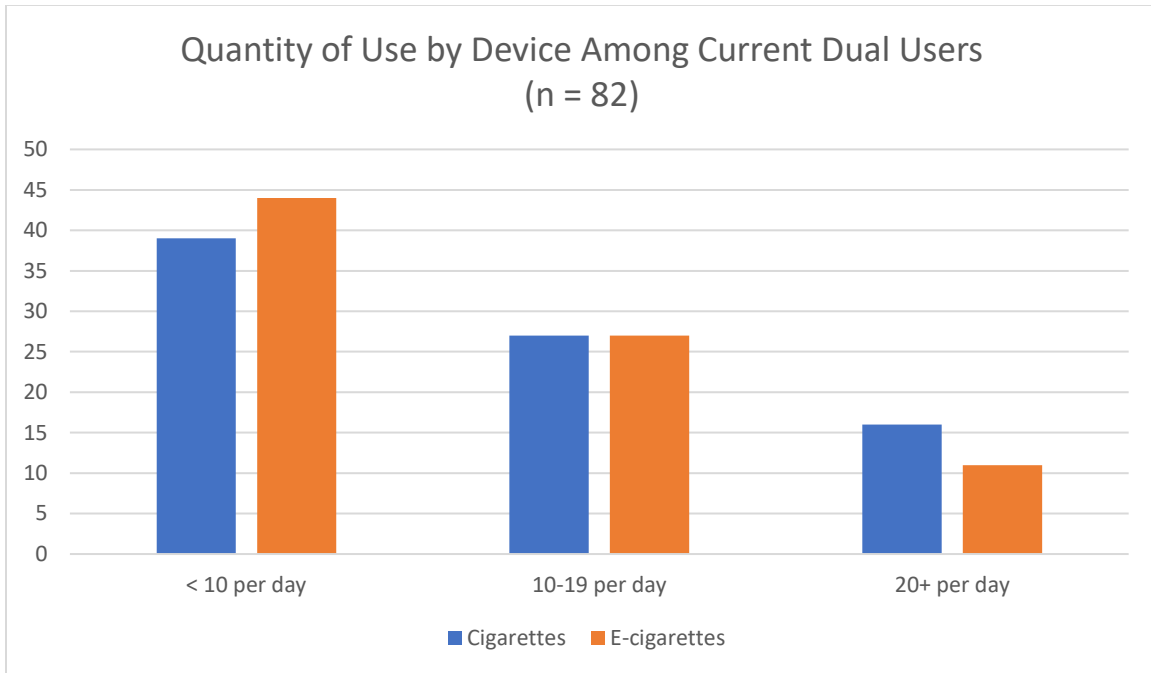
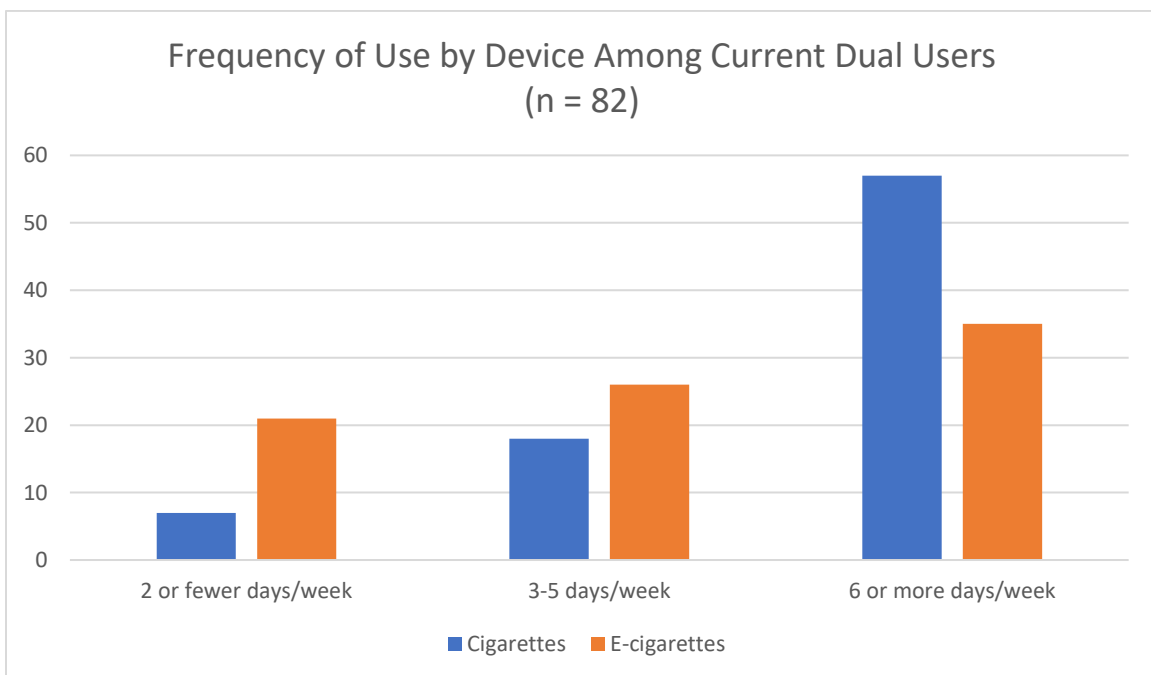
Figure 10: Quantity of Use by Device Among Current Dual Users (n = 82).**Figure 11: Frequency of Use by Device Among Current Dual Users (n = 82).**

Figure 12: Scatterplot of Total Current E-cigarette Dependence Score by Recoded E-cigarettes per day.

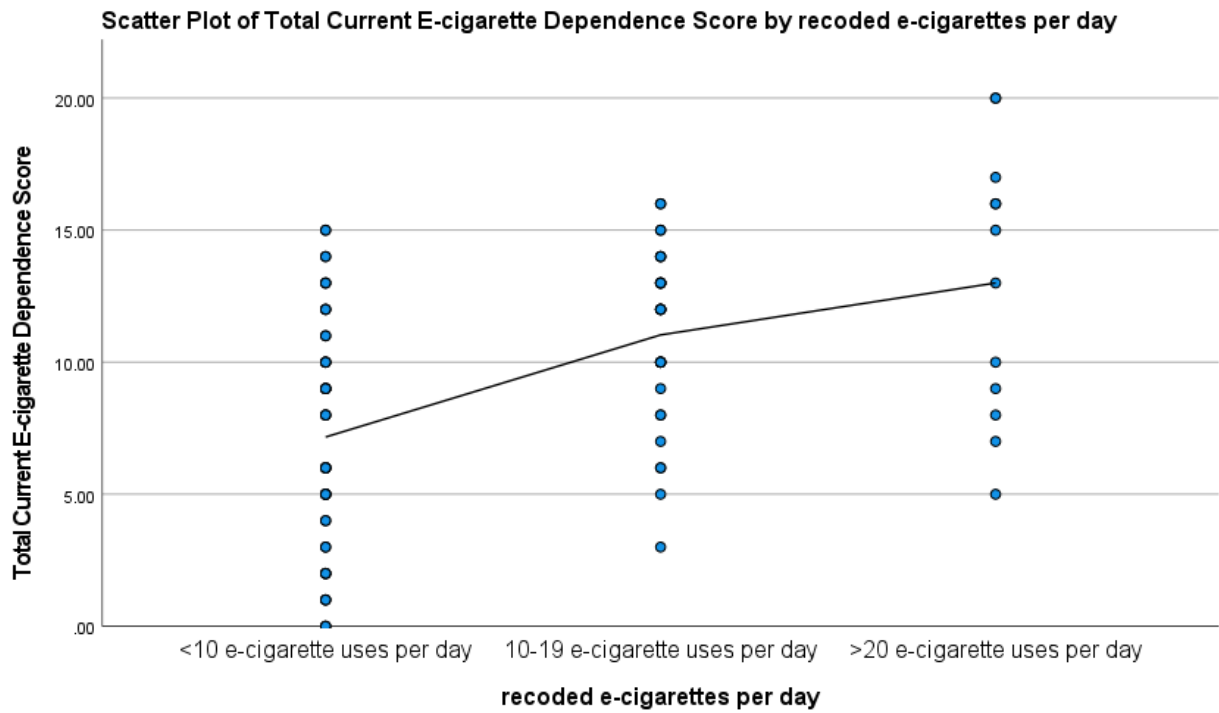


Figure 13: Scatterplot of Total Current E-cigarette Dependence Score by Recoded Cigarette Days per Week.

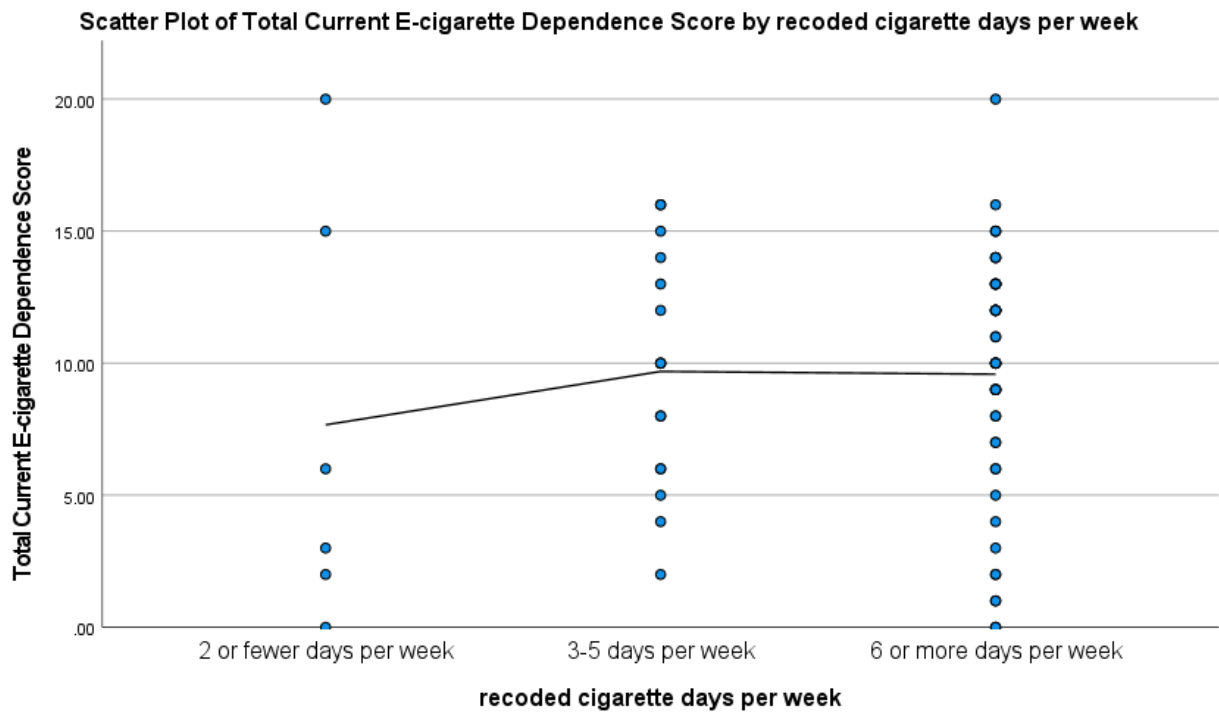


Figure 14

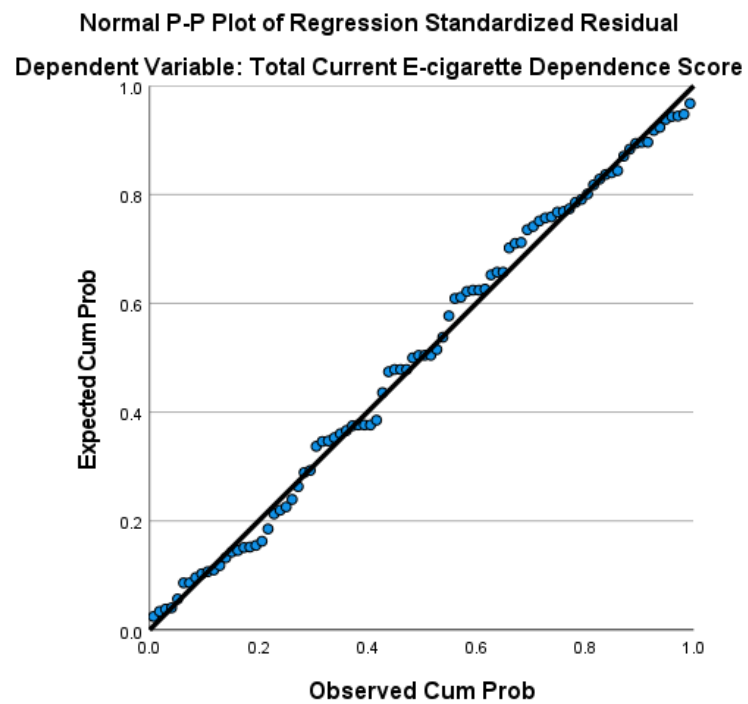
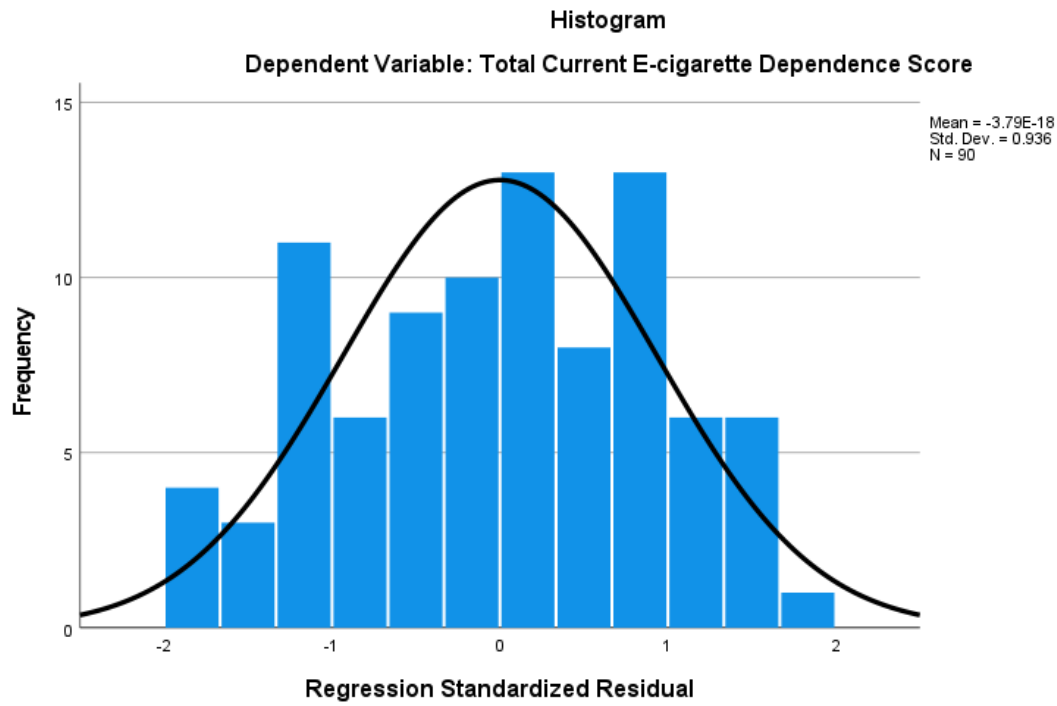


Figure 15: Scatterplot of Standardized Regression Residuals of Total Current E-cigarette Dependence Scores.

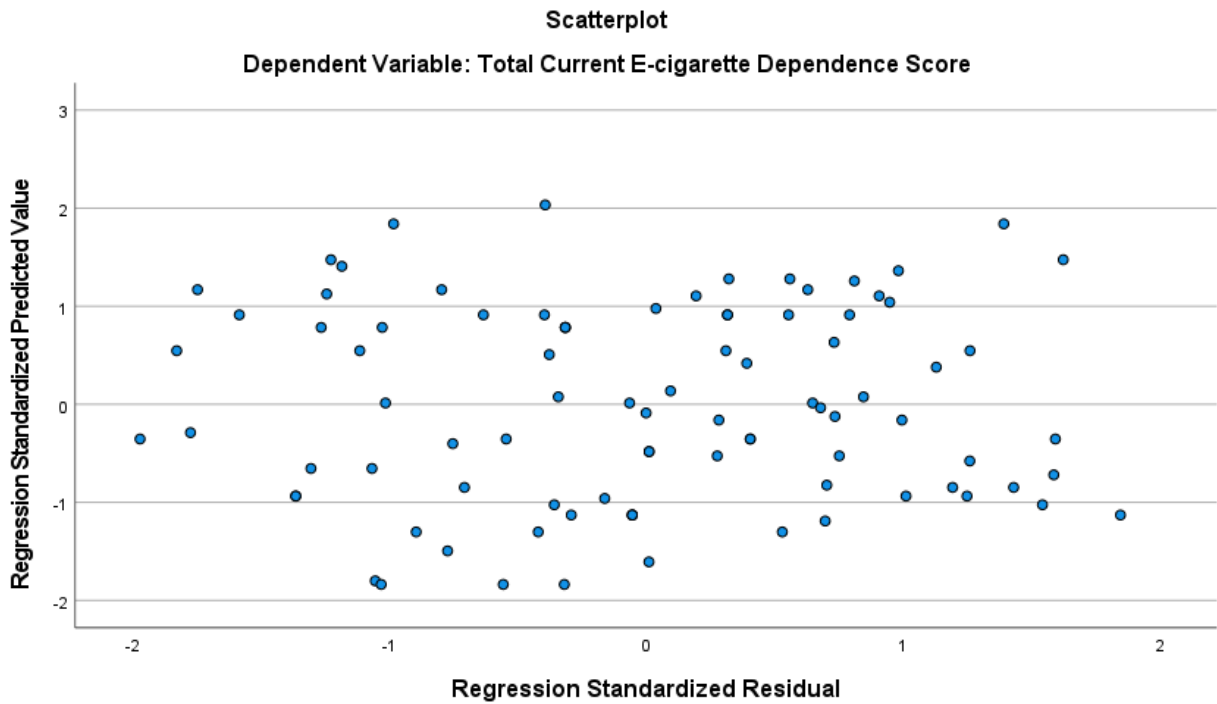
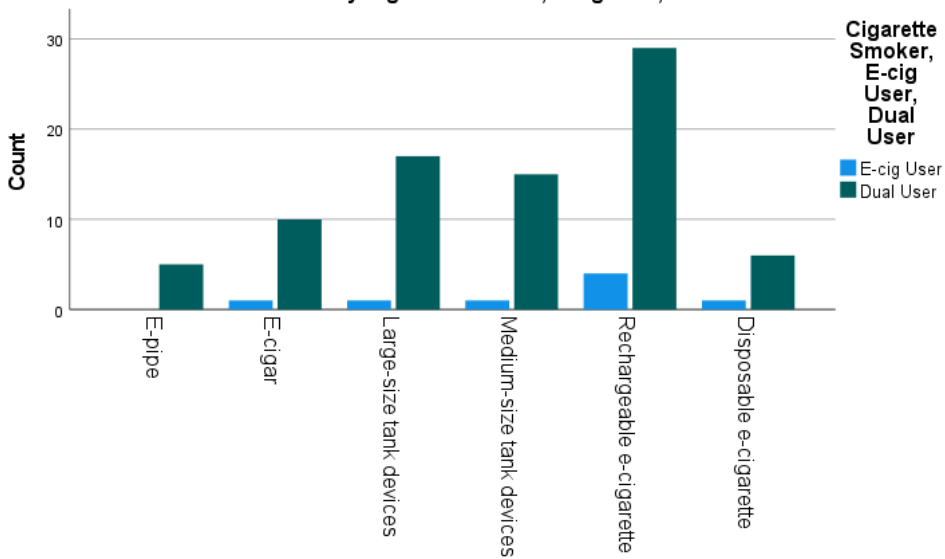


Figure 16: Type of Device Used Among E-cigarette Users and Dual Users (n = 97).

Clustered Bar Count of Which image best represents the type of e-cigarette device you most commonly use?
by Cigarette Smoker, E-cig User, Dual User



Which image best represents the type of e-cigarette device you ...

Figure 17: Nicotine Concentration Used Among E-cigarette Users and Dual Users (n = 97).

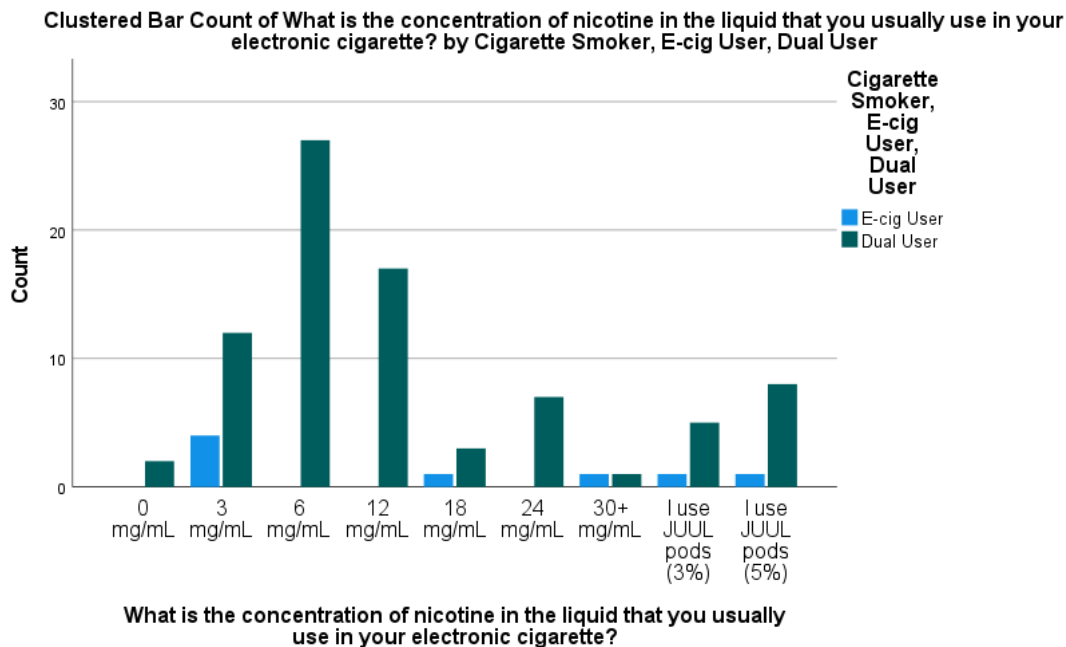


Figure 18: Scatterplot of Total Current E-cigarette Dependence Score by Current Level of E-cigarette Nicotine Concentration (Low/Mid/High).

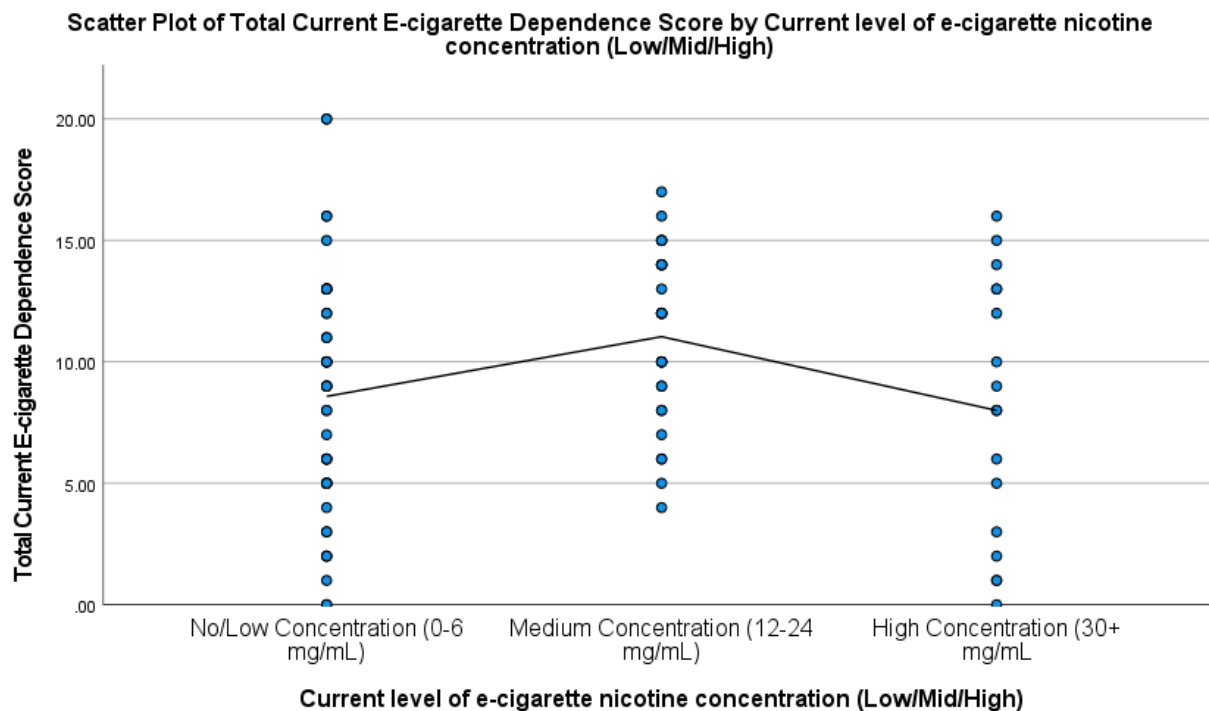


Figure 19

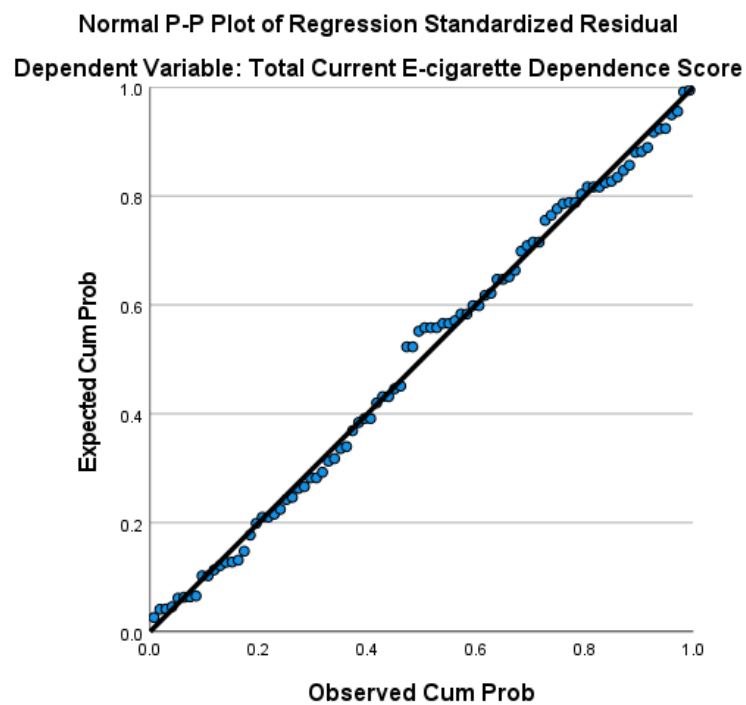
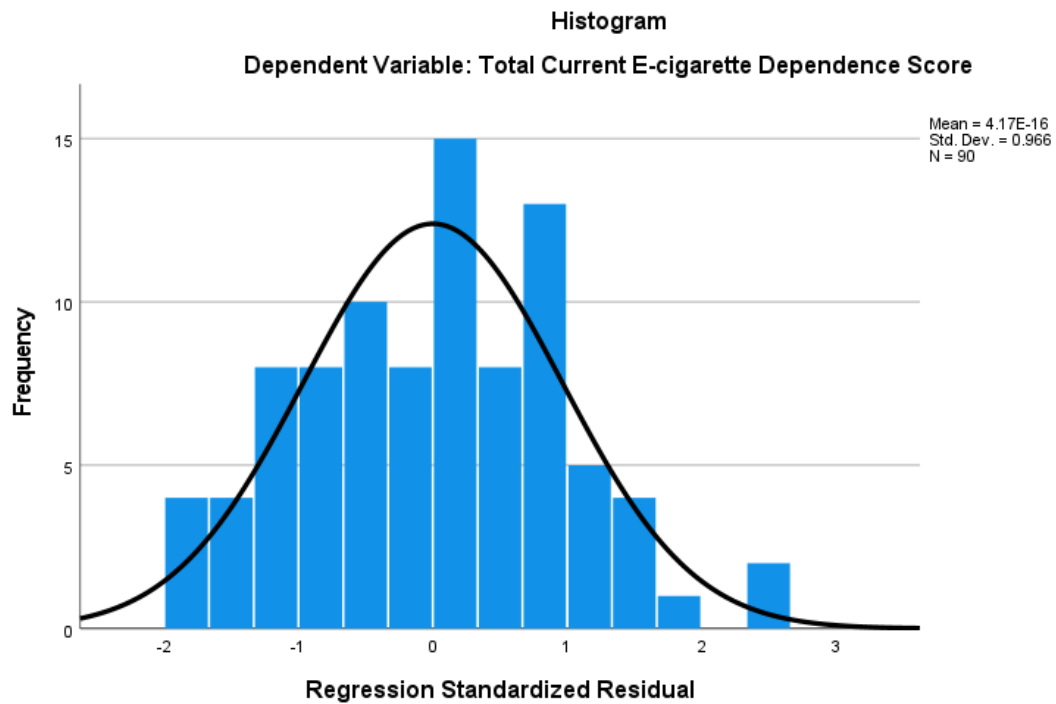
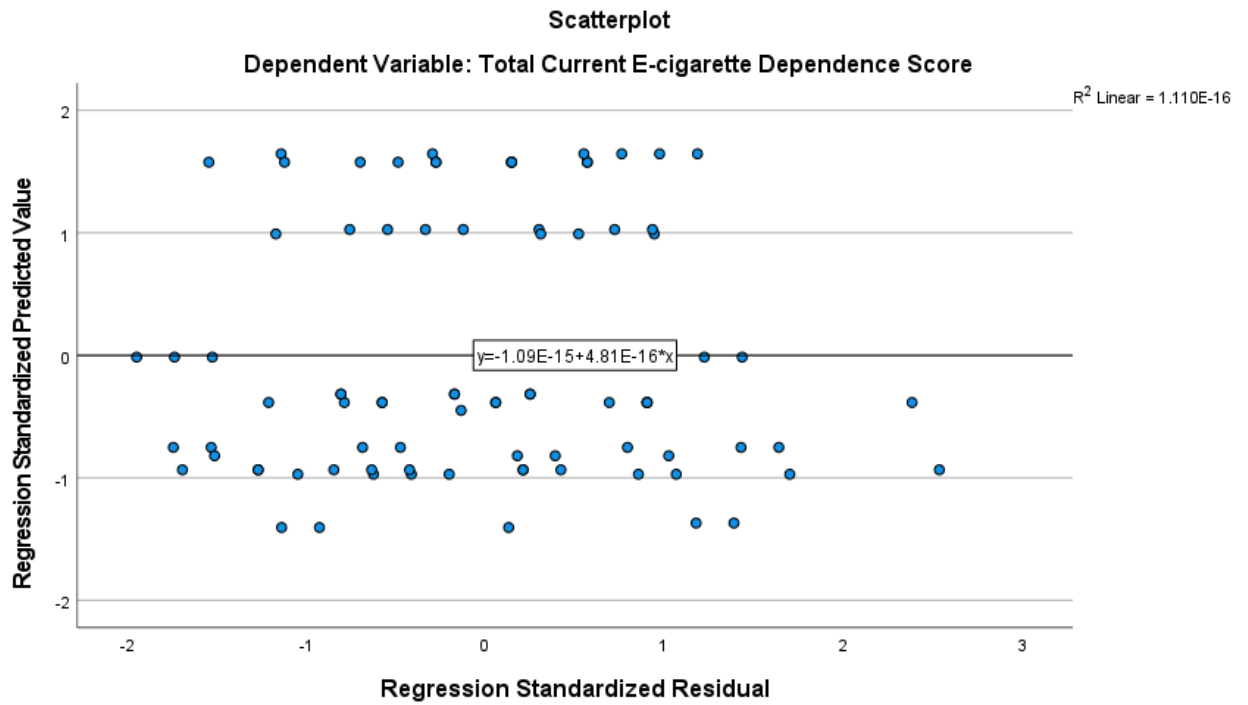


Figure 20: Regression Standardized Residual of Total Current E-cigarette Dependence Score



Appendix B. Tables

Supplemental Table 1: Frequency and Quantity of Current Cigarette and E-cigarette Use (n = 197)

	Total n (%)	Type of User n (%)	
		Cigarette Smoker	E-cigarette User
	197 (100)	189 (96.0)	8 (4.0)
Frequency (Avg. Days/Week)			
2 or fewer days/week	13	11 (84.6)	2 (15.4)
3-5 days per week	14	11 (78.6)	3 (21.4)
6 or more days per week	170	167 (98.2)	3 (1.8)
Quantity (Avg. Uses/Day)			
Less than 10 per day	73	69 (94.5)	4 (5.5)
10-19 per day	81	78 (96.3)	3 (3.7)
20 or more per day	43	42 (97.7)	1 (2.3)

Supplemental Table 2: Demographic Characteristics by E-cigarette Dependence Level (None, Low, Medium, High; n = 90)

	Total n (%)	E-cigarette Dependence Level n (%)				<i>p</i>
		None	Low	Med	High	
Total Sample	90	13 (14.4)	24 (26.7)	27 (30.0)	26 (28.9)	
Age, M (SD)	34.6 (10.0)	30.5 (7.5)	36.4 (11.4)	36.1 (9.7)	33.6 (9.9)	.285
Biological Sex						.207
Female	45 (50.0)	7 (53.8)	8 (33.3)	17 (63.0)	13 (50.0)	
Male	45 (50.0)	6 (46.2)	16 (66.7)	10 (37.0)	13 (50.0)	
Gender						.190
Cisgender Female	43 (48.9)	6 (46.2)	7 (31.8)	17 (63.0)	13 (50.0)	
Cisgender Male	45 (51.1)	7 (53.8)	15 (68.2)	10 (37.0)	13 (50.0)	
Sexual Orientation						.301
Bisexual, gay or lesbian	14 (15.6)	2 (15.4)	6 (25.0)	5 (18.5)	1 (3.8)	
Heterosexual	72 (80)	10 (76.9)	16 (66.7)	22 (81.5)	24 (92.3)	
Other/Prefer not to say	4 (4.4)	1 (25.0)	2 (50.0)	0 (0.0)	1 (25.0)	
Race/Ethnicity						.317
Black or African American	10 (11.1)	0 (0.0)	3 (12.5)	3 (11.1)	4 (15.4)	
Hispanic or Latinx	25 (27.8)	6 (46.2)	5 (20.0)	7 (25.9)	7 (26.9)	
White	48 (53.3)	4 (30.8)	15 (62.5)	15 (55.6)	14 (53.8)	
Other	7 (7.8)	3 (23.1)	1 (4.2)	2 (7.4)	1 (3.8)	
Level of Education						.746
Some high school or high school graduate	14 (15.6)	3 (23.1)	5 (20.8)	2 (7.4)	4 (15.4)	
Some college	19 (21.1)	3 (23.1)	5 (20.8)	6 (22.2)	5 (19.2)	
Trade/vocational school or Associate's degree	12 (13.3)	3 (23.1)	1 (4.2)	4 (14.8)	4 (15.4)	
Bachelor's degree	26 (28.9)	2 (15.4)	6 (25.0)	11 (40.7)	7 (26.9)	
Other	19 (21.1)	2 (15.4)	7 (29.2)	4 (14.8)	6 (23.1)	
Marital Status						.590

Single	33 (36.7)	8 (61.5)	8 (33.3)	9 (33.3)	8 (30.8)	
Married	42 (46.7)	4 (30.8)	10 (41.7)	15 (35.7)	13 (50.0)	
Divorced	1 (1.1)	0 (0)	0 (0)	1 (3.7)	0 (0)	
Living with partner	10 (11.1)	1 (7.7)	4 (16.7)	1 (3.7)	4 (15.4)	
Other	4 (4.4)	0 (0)	2 (8.3)	1 (3.7)	1 (3.8)	
Current Household Income						.985
Below \$50,000	33 (36.7)	6 (46.2)	8 (33.3)	10 (37.0)	9 (34.6)	
\$50,000 - \$100,000	35 (38.9)	5 (38.5)	10 (41.7)	10 (37.0)	10 (38.5)	
Above \$100,000	22 (24.4)	2 (15.4)	6 (25.0)	7 (25.9)	7 (26.9)	
Current Employment Status						.559
Employed	67 (74.4)	10 (77.9)	19 (79.2)	20 (74.1)	18 (69.2)	
Unemployed	11 (12.2)	0 (0)	2 (8.3)	5 (18.5)	4 (15.4)	
Other	12 (13.3)	3 (23.1)	3 (12.5)	2 (7.4)	4 (15.4)	

Supplemental Table 3: Demographic Characteristics by Current E-cigarette Dependence Index Score (n = 90)

	Total n (%)	E-cigarette Dependence Index Score		<i>F</i>	<i>p</i>
		Mean	Standard Deviation		
Total Sample	90 (100)	9.23	4.76		
Biological Sex				.419 ¹	.676
Female	45 (50.0)	9.44	4.91		
Male	45 (50.0)	9.02	4.64		
Sexual Orientation				1.83	.166
Bisexual, gay or lesbian	14 (15.6)	7.28	3.95		
Heterosexual	72 (80)	9.71	4.82		
Other/Prefer not to say	4 (4.4)	7.50	4.76		
Race/Ethnicity				1.31	.278
Black or African American	10 (11.1)	10.60	2.92		
Hispanic or Latinx	25 (27.8)	8.72	5.17		
White	48 (53.3)	9.63	4.63		
Other	7 (7.8)	6.43	4.79		
Level of Education				.164	.956
Some high school or high school graduate	14 (15.6)	8.57	4.80		
Some college	19 (21.1)	8.90	5.10		
Trade/vocational school or Associate's degree	12 (13.3)	9.17	5.41		
Bachelor's degree	26 (28.9)	9.73	4.14		
Other	19 (21.1)	9.42	5.17		
Marital Status				.326	.823
Single	33 (36.7)	8.64	5.07		
Married	42 (46.7)	9.74	4.48		
Living with partner	10 (11.1)	9.10	5.80		
Other	5 (5.6)	9.20	3.35		
Current Household Income				.640	.530
Below \$50,000	33 (36.7)	8.58	4.55		
\$50,000 - \$100,000	35 (38.9)	9.34	5.12		
Above \$100,000	22 (24.4)	10.05	4.76		
Current Employment Status				1.70	.189
Employed	67 (74.4)	8.99	4.78		
Unemployed	11 (12.2)	11.63	3.85		
Other	12 (13.3)	8.42	5.04		

¹ Test statistic reported is from *t*-test conducted due to comparison between two independent samples.

Supplemental Table 4: Demographic Characteristics by Current Cigarette Dependence Index Score (n = 259)

	Total n (%)	Cigarette Dependence Index Score		<i>F</i>	<i>p</i>
		Mean	Standard Deviation		
Total Sample	259 (100)	11.05	4.19		
Biological Sex				.961	.338
Female	125 (48.3)	11.31	3.90		
Male	134 (51.7)	10.81	4.45		
Sexual Orientation				2.827	.061
Bisexual, gay or lesbian	34 (13.1)	11.53	4.63		
Heterosexual	219 (84.6)	11.08	4.06		
Other/Prefer not to say	6 (2.3)	6.80	5.81		
Race/Ethnicity				5.138	<.01
Black or African American	31 (12.0)	11.68	3.11		
Hispanic or Latinx	26 (10.0)	12.54	3.78		
White	178 (68.7)	11.11	4.18		
Other ¹	24 (9.3)	8.25	4.84		
Level of Education				.842	.500
Some high school or high school graduate	80 (30.9)	11.46	4.52		
Some college	68 (26.2)	10.37	4.09		
Trade/vocational school or Associate's degree	47 (18.1)	11.02	4.01		
Bachelor's degree	39 (15.1)	11.62	3.77		
Other	25 (9.7)	10.80	4.41		
Marital Status				3.005	<.05
Single	71 (27.4)	10.03	4.12		
Married	106 (40.9)	11.16	4.40		
Living with partner	37 (14.3)	11.11	3.92		
Other ²	45 (17.4)	12.38	3.77		
Current Household Income				.305	.737
Below \$50,000	149 (57.5)	11.20	4.31		
\$50,000 - \$100,000	74 (28.6)	10.97	3.92		
Above \$100,000	36 (13.9)	10.61	4.30		
Current Employment Status				1.006	.367

Employed	149 (57.5)	10.75	4.27
Unemployed	51 (19.7)	11.33	3.64
Other	59 (22.8)	11.59	4.43

Notes:

¹Individuals in “Other” race/ethnicity category (including American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, Prefer not to say) had significantly lower cigarette dependence index scores when compared to individuals in all other race/ethnicity categories.

²Individuals in “Other” marital status category (including Separated, Divorced, Widowed, Prefer not to say) had significantly higher cigarette dependence index scores when compared to individuals in “Single” category.