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EPIDEMIOLOGY OF NICOTINE USE AMONG ADOLESCENTS AND YOUNG ADULTS IN THE UNITED STATES: FINDINGS FROM THE PATH STUDY

A Dissertation in
Biobehavioral Health

by
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ABSTRACT

In 2014, electronic nicotine delivery systems (ENDS, also referred to as vaping or e-cigarette use) surpassed combustible cigarettes as the most commonly used tobacco product among youth. This is a critical public health concern as early onset of ENDS use has been linked to subsequent initiation of cigarettes and other tobacco products. Among adolescents and young adults who have used tobacco, the use of two or more products is also quite common. However, detailed information regarding specific patterns and trends in use within the context of increasingly popular ENDS is lacking. The current dissertation aimed to address this critical gap in three ways. First, chapter one reviews the distinguishing features of a variety of vaping devices, as well as the correlates and consequences associated with their use among adolescents and young adults. Next, chapters two and three empirically examine national patterns and age-trends in the use of ENDS and other nicotine delivery systems. Finally, sociodemographic differences in these patterns and trends, as well as the association between nicotine and marijuana use, are examined.

The first empirical study examined nuanced age-trends in recent combustible cigarette, ENDS, and hookah use continuously from ages 14 to 24. Age-varying associations between marijuana use and each tobacco product were also examined. Data were from Wave 3 of the Population Assessment of Tobacco and Health (PATH) Study. The prevalence of past 30-day cigarette, ENDS, hookah, and marijuana use followed distinct age-trends. Cigarette and ENDS use were also significantly related to recent marijuana use across most ages. The association between ENDS and marijuana use was
strongest at ages 14 and 15, whereas the association between cigarette and marijuana use was strongest at age 17. Age-varying prevalences, as well as the age-varying association between ENDS and marijuana, differed by sex and race/ethnicity.

The second empirical study examined patterns and transitions in lifetime nicotine use among young adults ages 18 to 24 using latent class and latent transition analysis (LCA, LTA). Data were from Wave 1 and Wave 2 of the PATH Study. LCA demonstrated that young adults were best represented by five distinct patterns of use: ENDS Only (2%), Hookah Only (10%), Cigarettes Only (19%), Combustibles Only (23%), and Poly, No Smokeless (45%). Differences in latent class membership emerged based on sex and race/ethnicity; the proportion of males and NH white young adults were highest in the ENDS only, Combustibles Only, and Poly, No Smokeless classes. Young adults who had ever used marijuana were also more prevalent within the Combustibles Only and Poly, No Smokeless classes. Young adults in the Combustibles Only class at Wave 1 had a 31% chance of starting to use ENDS by Wave 2. Young adults in the Poly, No Hookah class at Wave 1 had an 11% chance of starting to use hookah by Wave 2.

Overall, this dissertation highlights the importance of research examining ENDS, polytobacco, and marijuana use among young people. Innovative statistical techniques provided added insight into who is at risk for using specific nicotine delivery systems at what age, as well as the factors contributing to polytobacco use and co-use with other drugs. Detailed information of this kind is necessary in order to prevent nicotine addiction and the associated health consequences, and to reduce overall burden of nicotine-related illnesses on the United States.
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CHAPTER 1:
Electronic Nicotine Delivery System Use among Adolescents and Young Adults: Trends, Perceived Risks, and Associations with Combustible Product Use

Cigarette smoking is consistently named the leading preventable cause of disease, disability, and death in the United States. (US Department of Health and Human Services, 2014). Substantial progress has been made to reduce the prevalence of cigarette smoking in the US, however, an estimated 15.5% of Americans currently smoke and approximately 480,000 individuals are impacted by smoking related illnesses each year (Jamal et al., 2016). The majority of established cigarette smokers begin experimenting with nicotine during adolescence or young adulthood; 99% of smokers report first use prior to age 26 (Bonnie, Stratton, & Kwan (eds.), 2015; Chassin, Presson, Rose, & Sherman, 1996; Lynch & Bonnie, 1994). Early age of smoking onset is related to an increased number of cigarettes smoked per day (Taioli & Wynder, 2010) and increased risk for nicotine dependence in later adulthood (Lanza & Vasilenko, 2015). As such, it is imperative to understand nicotine use among young people in order to prevent and reduce the overall impact of smoking related illness in the United States.

Prevalence of past-month cigarette smoking among high school students peaked at nearly 40% in 1976, declining slightly through the 1980s, and rising again in the 1990s (Johnston et al., 2019; Schulenberg et al., 2017). However, rates of combustible cigarette smoking have declined consistently and substantially among adolescents since 1998 (Jamal et al., 2016, 2017; Johnston et al., 2019). In 2018, approximately 2% of middle school students and 8% of high school students endorsed smoking cigarettes in the past
month (Gentzke et al., 2019). Similarly, young adult cigarette smoking has declined consistently since the 1990s, with rates of past-month smoking reaching approximately 10% among 18-24 year olds in 2017 (Wang, Asman, et al., 2018). Declines in cigarette smoking among adolescents and adults have been widely attributed to public health efforts aimed at tobacco control. Examples of successful efforts include: strict federal regulation of advertising, promotion, and sale of tobacco products to minors, substantial increases in federal taxes on cigarettes, and the introduction of warning labels on cigarette packages (Centers for Disease Control and Prevention, 2000; Johnston et al., 2019).

Despite declines in combustible cigarette smoking among young people, experimentation with and current use of alternative tobacco products, specifically electronic nicotine delivery systems (ENDS), are increasing at an alarming rate (Arrazola et al., 2015; Singh et al., 2016). ENDS are the most commonly used nicotine delivery system among US adolescents today (Johnston et al., 2019; Schulenberg et al., 2017). According to the National Youth Tobacco Survey, approximately 21% of high school aged adolescents (i.e., 3.05 million students) reported current use of ENDS in 2018 (Cullen et al., 2018). This dramatic increase in use led the U.S. Surgeon General to declare adolescent ENDS use an epidemic in December, 2018. ENDS use among youth is an emergent public health crisis as early exposure to nicotine may contribute to the development of nicotine dependence, the uptake of cigarette smoking and other tobacco product use (Huh & Leventhal, 2016; Lanza, Russell, & Braymiller, 2017; Leventhal et al., 2015; Primack, Soneji, Stoolmiller, Fine, & Sargent, 2015; Soneji et al., 2017), and
sustained nicotine use later in life (Barrington-Trimis et al., 2016; Dierker & Mermelstein, 2010).

Of further concern is the dearth of knowledge regarding the long term health consequences associated with acute and chronic ENDS use. Emerging evidence also indicates that ENDS use is linked to a number of adverse cardiovascular outcomes (Alzahrani, Pena, Temesgen, & Glantz, 2018; Bhatta & Glantz, 2019; Ndunda & Muutu, 2019; Skotsimara et al., 2019; Vindhyal, Ndunta, Munguti, Vindhyal, & Okut, 2019), suggesting that ENDS are not an inherently safe alternative to combustible cigarette smoking. Further research is warranted to understand the long term health consequences of chronic ENDS use, especially among those who initiate during adolescence and young adulthood. Current understanding of the health consequences is discussed below. Understanding trends in ENDS use among young people, reasons for ENDS use onset, and associations with subsequent combustible product use are critical for improving tobacco control policies and combatting this epidemic.

In this chapter, trends in the use of ENDS and other nicotine delivery systems will be described, followed by a discussion of the defining characteristics of various ENDS devices. Next, the physical, mental, and behavioral health consequences associated with ENDS use are outlined and the effects of early nicotine exposure are reviewed. Finally, the importance of understanding ENDS in the context of marijuana use and other contemporary substance use behaviors is discussed.

1.1 Trends in Adolescent and Young Adult Nicotine Use

Adolescence and young adulthood are often noted as periods of increased risk for substance use behavior. Adolescence is considered a particularly vulnerable period of
development due to increases in sensation seeking and risk taking behavior (Arnett, 1992; Spear, 2000), as well as normative changes in brain maturation and the changing relationship between sensitivity to reward and impulse control (Lydon, Wilson, Child, & Geier, 2014; Somerville, Jones, & Casey, 2010; Spear, 2000). Young adults are also at high risk for substance use due to changes in social roles and expectations (Evans-Polce, Maggs, Staff, & Lanza, 2017), identity exploration (Arnett, 2005), as well the increasing normativity of substance use behavior (Arnett, 2005; Schulenberg & Maggs, 2002).

Although both periods of development are associated with increased risk for tobacco use and other substance use behaviors, rates of use vary considerably across the lifespan, as do motives for specific product use and the associated risk factors and consequences (US Department of Health and Human Services, 2014).

Trends in contemporary nicotine use among young people in the United States have been examined extensively using data from large, nationally representative surveys such as the National Youth Tobacco Survey, Monitoring the Future, and the Population Assessment of Tobacco and Health (PATH) Study. Considerable evidence suggests that adolescent use of combustible tobacco products (e.g., cigarettes, cigars, pipe tobacco) are declining, yet experimentation with and regular use of ENDS remain quite high (Arrazola et al., 2015; Barnett, Forrest, Porter, & Curbow, 2014; Cobb, Ward, Maziak, Shihadeh, & Eissenberg, 2010; Cobb, Byron, Abrams, & Shields, 2010; Johnston, O’Malley, Miech, Bachman, & Schulenberg, 2016; Primack, Walsh, Bryce, & Eissenberg, 2009; Singh et al., 2016). Statistically significant increases in the prevalence of past-month ENDS use among middle and high school aged adolescents were observed each year from 2011 to 2014 (Arrazola et al., 2015; Jamal et al., 2017; Singh et al., 2016; Wang, et al., 2018). In
2014, rates of ENDS use surpassed combustible cigarette use within this age group, when prevalence spiked to 13.4% among high schoolers and 3.9% among middle schoolers (Arrazola et al., 2015; Wang, et al., 2018b).

Prevalence of past-month ENDS use among adolescents declined slightly between 2014 and 2017 (Wang, et al., 2018b), however, rates seem to be rising again in recent years. According to the National Youth Tobacco Survey, 20.8% of high school aged adolescents (i.e., 3.05 million students) reported current use of ENDS in 2018 (Cullen et al., 2018). This corresponds to a 78% increase in ENDS use within this age group from 2017 to 2018. Past-month ENDS use has been consistently higher than combustible cigarette use among both middle and high school adolescents since 2014. In 2017, 7.6% of high school students and 2.1% of middle school students reported smoking combustible cigarettes in the past month (Wang, et al., 2018).

Trends in ENDS use among young adults ages 18-24 are somewhat less clear. Data from the National Adult Tobacco Survey suggest that rates of current ENDS use among young adults (ages 18-24) are considerably lower than rates among high school aged adolescents (ages 14-17). However, when compared to adults ages 25 and older, young adults consistently report higher rates of every day or some day ENDS use (5.2% among 18-24 year olds in 2017; 3.6% among 25-44 year olds; 2.4% among 45-64 year olds; Wang, et al., 2018a). Additional evidence suggests that young adulthood may represent a time of increased incidence of ENDS use (i.e., ENDS use onset, initiation) rather than a period characterized by current, established ENDS use (Perry et al., 2018).

Combustible cigarette smoking continues to be the most prevalent form of current tobacco use among young adults, with 10.4% reporting current use (Wang, et al., 2018a).
However, rates of current cigarette smoking among young adults have consistently declined over the past decade, whereas rates of current ENDS use have remained close to 5% within this age group since 2014 (Hu et al., 2016; Wang, et al., 2018a). Further research is warranted to understand patterns and trends in young adult ENDS use in the context of other tobacco products, specifically with regard to age of onset and current use.

### 1.1a Gender and Racial/Ethnic Differences in Nicotine Use

There is a large body of evidence suggesting differences in the use of specific tobacco products by both sex and race/ethnicity. Between 2010 and 2015, male adolescents demonstrated higher rates of cigarette, cigar, smokeless tobacco, and ENDS use compared to females (Arrazola et al., 2015; Camenga et al., 2014; L. Johnston, O’Malley, Miech, Bachman, & Schulenberg, 2016; Rigotti, Lee, & Wechsler, 2000; Singh et al., 2016). Sex differences in hookah use, however, remain inconclusive. For example, a number of studies have shown that male adolescents are more likely to regularly or currently use hookah relative to females (Barnett, Curbow, Weitz, Johnson, & Smith-Simone, 2009; Singh et al., 2016; Sterling & Mermelstein, 2011), but rates of lifetime hookah use have been shown to be higher for females compared to males in 2014 (Arrazola et al., 2015).

Rates of tobacco use tend to be higher for non-Hispanic (NH) white adolescents compared to NH Black and Hispanic adolescents (Rigotti et al., 2000), particularly for products such as cigarettes and smokeless tobacco (Arrazola et al., 2015; Singh et al., 2016). However, racial/ethnic differences in the use of emerging products, such as ENDS and hookah, are also unclear. Some studies suggest that rates of hookah use are similar
between white and Hispanic adolescents (Arrazola et al., 2015; Barnett et al., 2009), but data from 2015 suggest that Hispanics are using hookah at a higher rate (Singh et al., 2016). Discrepancies in the use of ENDS among whites and Hispanics are similar; some findings suggest that white adolescents use ENDS at a higher rate than Hispanics (Camenga et al., 2014; Singh et al., 2016), while others suggest Hispanic adolescents are using at higher rates, particularly during early adolescence (Arrazola et al., 2015; Lanza, Russell, & Braymiller, 2017).

1.1b Polytobacco Use

The gaining popularity of ENDS may also lead to an increased prevalence of multi-product use during adolescence and young adulthood, as the growing market and increasing variety of these emerging products may contribute to greater opportunities for multi-product use within this population. In 2002 and 2004, 6.9% of adolescents in a nationally representative sample reported using multiple nicotine products (Bombard, Rock, Pederson, & Asman, 2008) and in 2015, this number increased to 13% (Singh et al., 2016). As novel delivery systems specifically marketed to adolescents and young adults continue to enter the market, prevalence of multi-product use in this population is likely to continue to rise along with subsequent increases in nicotine and toxicant exposure, as well as increased risk for the development of nicotine dependence.

Rates of polytobacco use are quite high among adults. Recent findings from wave one (W1) of the Population Assessment of Tobacco and Health (PATH) Study indicate that nearly 40% of adult tobacco users report the use of multiple tobacco products (Kasza et al., 2017). Of that 40%, nearly a quarter report the use of both combustible cigarettes and electronic nicotine delivery systems (ENDS) (Kasza et al., 2017). This particular
combination is also prevalent in the National Adult Tobacco Survey, with 30% of adults reporting the use of cigarettes and ENDS in 2012 to 2014 (Sung, Wang, Yao, Lightwood, & Max, 2018). Data from the National Survey on Drug Use and Health (NSDUH) and the Tobacco Use Supplements in the Population Survey (TUS-CPS) suggest that young adults aged 18 to 24/25 are the most likely to concurrently use two or more products compared to adolescents (US Department of Health and Human Services, 2014) and to adults ages 25 and older (Backinger et al., 2008).

The abovementioned research documents age-trends in terms of binned age variables, such that all adolescents 12 to 17 years old are compared to all young adults (18 to 24/25 years old) and all adults (25/26 and older), even though nicotine use behaviors likely vary continuously across development. Therefore, innovative statistical analyses are crucial in order to identify specific ages that may be at heightened risk for product use and co-use, as well as the development of nicotine dependence symptoms. Understanding very specific age trends in use and associated consequences is critical for the development and targeting of sustainable prevention and intervention efforts, as well as tobacco control policies.

Recent empirical evidence demonstrates that when compared to females, male adolescents have twice the odds of being multi-products users relative to non-users (Gilreath et al., 2015). Survey data from the CDC’s 2014 National Youth Tobacco Survey (NYTS; Office on Smoking and Health, 2015) similarly suggest that 15.3% of males and 10% of females currently used two or more tobacco products. Multi-product use also seems to differ by race/ethnicity. In 2014, 15.1% of White, 12.6% of Hispanic, and 5.4% of Black adolescents reported currently using two or more tobacco products.
1.2 What are Electronic Nicotine Delivery Systems (ENDS)?

The term ENDS refers to a variety of battery-powered nicotine delivery systems that heat a solution containing propylene glycol, vegetable glycerin, and other potentially harmful constituents into an aerosol to be inhaled by the user (Cahn & Siegel, 2011; Callahan-Lyon, 2014; Grana, Benowitz, & Glantz, 2014; Stanford Medicine, 2019). The vast majority of these solutions, also known as e-liquids, vape juice, or e-juices, also contain nicotine and various flavorants. Four generations of ENDS have evolved since the first electronic cigarettes were introduced, with an estimated four hundred and sixty different brands of electronic devices on the U.S. market today (Zhu et al., 2014). Throughout the literature, ENDS are commonly referred to as electronic cigarettes, e-cigarettes, or vaping devices; other street names include vapes, vape pens, vaporizers, hookah pens, e-hookah, mods, pod-mods, and tanks. However, these terms are often not synonymous and actually represent subtly different delivery systems. Qualitative evidence suggests that young ENDS users do utilize a variety of terms to describe various ENDS sub-types. Most notably, users often agree that e-cigarettes are “completely different” from devices like vape pens and e-hookahs (Wagoner et al., 2016). Inconsistent terminology poses many challenges for the measurement of ENDS use, the estimation of population prevalence rates, and the development of evidence-based tobacco control policies regarding ENDS devices.

With each generation of electronic devices, the delivery of nicotine into the users’ lungs and bloodstream has become more and more efficient (i.e., higher nicotine yield per puff). These devices also differ in the level of nicotine and other toxins present in the e-
liquid (Gillman, Kistler, Stewart, & Paolantonio, 2016; Jensen, Luo, Pankow, Strongin, & Peyton, 2015). Thus, certain characteristics and distinguishing features of each delivery system may impact their potential for abuse by design. As new nicotine delivery systems become readily available and increasingly popular among young people, additional research is necessary to understand the specific devices that are being used, the abuse liability of each product, as well as the long-term health effects associated with their use.

1.2a The History of ENDS: “Cigalikes”, Vape Pens, and Mods

Disposable e-cigarettes, or “cigalikes” (e.g., NJOY, E-lites, Blu), were among the first ENDS to hit the U.S. market in 2007. First generation models were designed to look like combustible cigarettes in their shape, size, and color; the devices were often marketed as a safe alternative to combustible cigarette smoking (CDC Office on Smoking and Health, 2018; National Academies of Sciences, Engineering, and Medicine, 2018; Stanford Medicine, 2019; Truth Initiative, 2018). Cigalikes consist of a liquid-containing cartridge that is attached to a heating element with a small battery that cannot be recharged. First generation devices are closed systems, meaning that the cartridge cannot be refilled with e-liquid by the user. Later iterations of cigalikes featured limited flavor options and small, rechargeable batteries. The uptake of disposable e-cigarettes/cigalikes has not been very widespread among adolescents and young adults; evidence suggests that later generation models are much more popular among young people today (Barrington-Trimis et al., 2018). Future research is necessary to fully understand this preference, however, cigalikes deliver nicotine to the lungs less efficiently than later generation models and are less customizable in their temperature/power settings and e-
liquids. The appealing characteristics of later generation models are thought to be driving differences in specific type of ENDS use among young people and will be discussed in further detail below.

Second generation ENDS—often referred to as vape pens, e-cigarette pens, e-hookah, hookah pens, etc.—were commercially available in the U.S. by 2010. Second generation ENDS are distinguishable from first generation devices in three ways: larger batteries, open systems, and an increased variety of flavored e-liquids. Most notably, second generation devices have larger, rechargeable batteries (Truth Initiative, 2018). Consequently, the heating element is able to reach much higher temperatures, resulting in the production of denser vapor and more efficient delivery of nicotine into the lungs. Denser vapor also enables users to perform “vape tricks” such as producing very large clouds of exhaled vapor (“cloud chasing”) and making various shapes and patterns (Pepper et al., 2017; Wagoner et al., 2016). Vape tricks have emerged as a popular reason for experimenting with vape pens, e-hookahs, and other later generation ENDS among young people (Kong, Morean, Cavallo, Camenga, & Krishnan-Sarin, 2015).

The majority of second generation models also moved to an open system, meaning that liquid-containing cartridges were able to be refilled with e-liquids by the user. The advent of open systems led to a dramatic increase in the availability and popularity of flavored e-liquids. An estimated 7,500 different flavors are on the market today (Zhu et al., 2014), with fruit and candy flavored e-liquids being popular among young ENDS users, particularly underage adolescents. Evidence suggests that adolescents and young adults consider the wide variety of appealing flavors to be another prominent reason for ENDS use (Harrell, M. B. et al., 2017; Morean et al., 2018).
Refillable e-liquids for open-tank systems are also available in a wide variety of nicotine concentrations that are often mislabeled or poorly reported on product packaging (Stratton, Kwan, & Eaton (eds.), 2018). This poses additional measurement challenges when estimating ENDS users’ exposure to nicotine by way of later generation devices.

By 2013, many major tobacco companies (e.g., Altria Inc., British American Tobacco, Imperial Tobacco) had acquired e-cigarette manufacturers or had begun to develop their own line of ENDS products (Grana et al., 2014). These companies quickly capitalized on the appeal of flavored e-liquids and denser vapors by developing third generation models that are more customizable with very large lithium batteries. Third generation devices are the largest in size and are commonly referred to as mods, vape mods, box mods, and tank systems. These models are open systems, are available in various shapes and sizes, and often have customizable heating elements and batteries with adjustable voltage (Truth Initiative, 2018). Mods with larger and lower resistance coils, as well as higher voltage batteries have the ability to increase the electric current that passes through the heating element. As a result, users are able to further control the temperature of e-liquid aerosols in order to achieve larger vape clouds and more salient flavors. These modifications also result in increased puff volume and

![Figure 1.1. Illustration of first, second, and third generation electronic nicotine delivery systems (courtesy: Truth Initiative, 2018 and the National Academy of Science, Engineering, and Medicine)](image-url)
duration, as well as deeper lung hits (i.e., inhaling vapor directly into the lungs, rather than pulling vapor into the mouth first). Such changes in vaping topography likely contribute to an increased abuse liability for third generation devices, particularly for experienced users (Grana et al., 2014). Modifying the heating element and adjusting the power output of third generation ENDS devices has also been associated with dangerous malfunctions such as overheating and spontaneous explosions, which can result in user injury (Kumetz, Hurst, Cudnik, & Rudinsky, 2016). Image 1 provides an illustration of the differences between first, second, and third generation ENDS.

1.2b Current Generation of ENDS: Pod-Based Mods

The most recent generation of ENDS are considered pod-based mods or pod mods (e.g., JUUL, Suorin, Aspire/Breeze, Phix). Pod mods are smaller, more streamlined devices that consist of an e-liquid containing cartridge that snaps into a rechargeable battery. These devices became commercially available in the US during 2015. Many pod mods resemble USB drives in their shape and size (Barrington-Trimis & Leventhal, 2018; Truth Initiative, 2018) and are available in a variety of flavors such as mango, cool mint, and fruit medley. It is speculated that the recent dramatic spike in adolescent ENDS use can be attributed to the introduction of fourth generation pod mods like JUUL (Kavuluru, Han, & Hahn, 2019). Two specific characteristics of pod mods set these devices apart from earlier generations of ENDS. First, pod mods contain e-liquid solutions with nicotine salts rather than freebase nicotine. The addition of benzoic acid to the e-liquid results in a salt-based nicotine solution with a much lower pH compared to earlier e-liquids. A solution with a lower pH lessens the aversion to the inherent flavor of nicotine and lessens the harsh burn and other negative sensations associated with inhaling
high concentrations of nicotine (Barrington-Trimis & Leventhal, 2018).

Second, pod-mods contain much more nicotine per mL compared to earlier generations of ENDS. Earlier generations of e-liquids often contained between 1-3% nicotine, with 3% solutions marketed as a high concentration intended for those who typically smoke two packs of cigarettes per day. However, pod mods like JUUL have much higher concentrations, containing upwards of 6.5% nicotine or 56 mg/mL (Goniewicz, Boykan, Messina, Eliscu, & Tolentino, 2018; Jackler & Ramamurthi, 2019). Analysis of urinary biomarkers of nicotine exposure suggest that pod mod users receive between 0.77 and 0.85 mg of nicotine/10 puffs (Goniewicz, Boykan, Messina, Eliscu, & Tolentino, 2018). This is much higher than nicotine exposure received through earlier generations of e-cigarettes (0.02–0.51 mg/10 puffs) and is likely attributable to the salt-based solution (Goniewicz, Kuma, Gawron, Knysak, & Kosmider, 2013). By design, salt-based solutions with higher concentrations of nicotine likely contribute to an increase in abuse liability for current pod mod devices. Increased addictiveness in combination with a sleek design that is easy to conceal and an abundance of flavor options may also be contributing to the recent dramatic spike in adolescent and young adult ENDS use (Barrington-Trimis & Leventhal, 2018). Further, young people often report that ENDS are a less harmful, safer, and healthier alternative to combustible
cigarettes and other tobacco products (Ambrose et al., 2014; Kong, Morean, Cavallo, Camenga, & Krishnan-Sarin, 2015). Lower perceived risk associated with ENDS use is another factor that is likely contributing to the ENDS epidemic among adolescents and young adults. In recent years, the Food and Drug Administration (FDA) has taken formal action to combat the increase in ENDS use among youth. On May 10, 2016, e-cigarettes, vaporizers, and other ENDS were officially deemed tobacco products, making these devices subject to regulation by the FDA. Most notably, this ruling prohibited the sale of ENDS to minors and introduced an all-inclusive compliance policy that aims to federally regulate and enforce the manufacture, labeling, advertisement, and sale of ENDS. In March, 2019, the FDA proposed a modification to this policy that, if enacted, would further restrict the sale of flavored ENDS products (with the exception of tobacco, mint, and menthol flavors) due to their attractiveness to minors. These tobacco regulatory policy changes have occurred in response to the growing body of evidence suggesting significant increases in ENDS use and preference for flavored products among youth, as well as concerns regarding the health consequences associated with ENDS use and early exposure to nicotine.

1.3 Physical, Mental, & Behavioral Health Consequences Associated with ENDS Use

1.3a Health Impact of ENDS Use

The long-term health consequences related to combustible cigarette smoking are well documented (US Department of Health and Human Services, 2014). As ENDS have only penetrated the US market recently, considerably less is known about the long-term health effects associated with their use. Available evidence suggests that e-cigarette solvents and aerosols may contain fewer toxicants than combustible cigarette smoke
(Callahan-Lyon, 2014), and that established adult smokers who substitute and replace combustible cigarettes with ENDS may indeed experience reductions in biomarkers of nicotine exposure (e.g., NNAL), carcinogen exposure, and smoking urges (D’Ruiz, Graff, & Robinson, 2016). However, ENDS solutions (i.e., e-liquids) and aerosols contain many chemical compounds that have been recognized as harmful and potentially harmful constituents (HPHCs) by the FDA (US Department of Health and Human Services, 2012); thus, ENDS are not inherently safe alternatives to combustible products.

HPHCs are chemical compounds that have established addictive, carcinogenic, cardiovascular, respiratory, and/or reproductive and developmentally toxic effects. Carcinogens are chemicals or exposures that are capable of causing cancer in living tissue by making changes to a cell’s DNA (American Cancer Society, 2016). Cardiovascular toxicants adversely impact the heart and blood vessels, as well as organs and tissues involved in the production and circulation of blood (e.g., bone marrow, lymph nodes). Cardiovascular toxicity is related to diseases including, but not limited to, hypertension, arteriosclerosis, heart attack and heart failure (National Comprehensive Cancer Network, 2019). Reproductive toxicants impact the ability of an organism to successfully reproduce, and developmental toxicants are prenatal exposures or chemicals that have the potential to impact pre- and postnatal development (England et al., 2017; United Nations, 2013).

In 2012, the FDA released a list of HPHCs that are specific to tobacco smoke and tobacco products more broadly (US Department of Health and Human Services, 2012). Many common e-liquids and aerosols contain 25 or more HPHCs (Stanford Medicine, 2019). Examples include, but are not limited to: (1) lead, a carcinogen, cardiovascular
toxicant (CT), and reproductive/developmental toxicant (R/DT) often found in older paints, pipes, or faucets, (2) formaldehyde, a carcinogen and R/DT also found in embalming fluid, (3) acetone, a R/DT toxicant also found in nail polish remover, and (4) benzene, a carcinogen, CT, and R/DT commonly used in the production of plastics, rubber, lubricants, and many other materials (American Cancer Society, 2016). Benzene is abundant in combustible cigarette smoke and exposure is estimated to be up 10 times higher among smokers compared to nonsmokers (Vulimiri, Pratt, Kulkarni, Beedanagari, & Mahadevan, 2017). Evidence suggests that levels of exposure to benzene by way of ENDS are comparable to those expected from combustible cigarette smoke (Pankow et al., 2017). Acetaldehyde is another known carcinogen and respiratory toxicant with addictive properties that is found in cigarette smoke as well as e-liquids and aerosols (Gillman et al., 2016; Stanford Medicine, 2019). Acetaldehyde an additive that increases the reinforcing properties of nicotine, thus increasing its addictive potential (Talhout, Opperhuizen, & Van Amsterdam, 2007).

Given the number of HPHCs found in e-liquids and ENDS aerosols, recent research has aimed to investigate the association between ENDS use and a number of adverse health outcomes. Four studies to date have linked established ENDS use to an increased risk of myocardial infarction (i.e., heart attack); limited studies have also linked ENDS use to an increased risk of stroke, coronary artery disease, and arterial stiffness, as well as anxiety, depression, and other emotional problems (Alzahrani, Pena, Temesgen, & Glantz, 2018; Bhatta & Glantz, 2019; Ndunda & Muutu, 2019; Skotsimara et al., 2019; Vindhyal, Ndunda, Munguti, Vindhyal, & Okut, 2019). In 2018, Alzaharani, Pena, Temesgen, & Glantz examined the association between never, former, and current e-
cigarette use and myocardial infarction (MI) using data from 69,725 adults in the 2014 and 2016 cohorts of the National Health Interview Survey. Compared to never e-cigarette users, odds of MI were 1.79 times higher given daily e-cigarette use (AOR=1.79; 95% CI =1.20, 2.66, p=0.004); no statistically significant differences emerged for former or non-daily e-cigarette users (Alzahrai et al., 2018). Models adjusted for concurrent and former cigarette use, as well as sociodemographic variables and cardiac health history, suggesting that the association between daily e-cigarette use and risk of MI is independent of these factors.

Preliminary analyses using other nationally representative datasets (PATH, Behavioral Risk Factor Surveillance System) have produced similar results. Odds of MI were between 1.5 and 2 times higher among regular or some day e-cigarette users compared to never e-cigarette users (Bhatta & Glantz, 2019; Ndunda & Muutu, 2019; Vindhyal et al., 2019). Ndunda & Muutu (2019) also found that regular use of e-cigarettes was associated with an increased risk of stroke (OR 1.71; 95% CI =1.64, 1.8) and coronary artery disease (OR= 1.4; 95% CI = 1.35, 1.46).

Authors speculate that HPHCs in e-liquids and aerosols cause damage to blood vessels and promote blood clotting, in turn increasing risk for adverse cardiovascular events (Alzahrai et al., 2018). However, preclinical and experimental research is necessary in order to determine the biological mechanisms underlying the increased risk of adverse cardiac events. It should also be noted that much of the work linking ENDS use to cardiovascular events is preliminary; only one of four studies (Alzahrai et al., 2018) has undergone peer-review. Additional research has been presented at the 2019 meetings of the American College of Cardiology, the International Stroke Conference,
and the Society for Research on Nicotine and Tobacco. This work is also cross-sectional and focuses exclusively on adult e-cigarette users. Thus, findings are may not be generalizable to adolescent populations. Additional longitudinal research is necessary in order to unpack the effects of chronic exposure to HPHCs via e-liquids throughout the lifespan.

1.3b Effects of Early Nicotine Exposure

Nicotine is another key HPHC found in most e-liquids that is a known developmental toxicant and addictive compound. The long-term effects of nicotine exposure have been widely documented, with both prenatal exposure and early onset of use being linked to several neurocognitive and emotional deficits, as well as drug use disorders during adolescence and later in life (England et al., 2017; Fried, Watkinson, & Gray, 2006; Holliday et al., 2016). Nicotine binds to nicotinic acetylcholine (nAChR) receptors in the brain. As these receptors are functional prenatally, exposure to nicotine in the womb has the potential to impact the fetal brain, in addition to changing the trajectory of brain development postnatally and across the lifespan. Taken together, the literature suggests that nicotine has strong developmental effects that may ultimately impede functioning across multiple domains throughout the lifespan (see England et al., 2017 for a more comprehensive review of the developmental effects of nicotine).

Initiation of nicotine use during childhood and early adolescence is also associated with lasting cognitive, emotional, and behavioral deficits. When compared to non-smokers, adolescent daily cigarette smokers exhibit performance deficits on neurocognitive tasks assessing working memory, sustained and divided attention, verbal memory, and executive planning that persist into adulthood (England et al., 2017; Fried et
Earlier age of onset predicts larger performance deficits, suggesting that repeated and prolonged exposure to nicotine is particularly detrimental (England et al., 2017). Early onset of cigarette smoking is also often comorbid with mental health disorders such as schizophrenia, ADHD, depression, anxiety, and bipolar, among others (Benowitz, 2009; England et al., 2017). Evidence suggests a bidirectional relationship between smoking behavior and mental health; certain risk factors for smoking during adolescence also increase risk of mental health disorders and “addiction could result in or exacerbate symptoms of these disorders” (England et al., 2017; Hall et al., 2015).

Further, early exposure to nicotine is associated with lasting changes in smoking behavior and the development of nicotine dependence. Everett and colleagues (1999) found that earlier age of smoking onset is associated with a higher likelihood of current frequent smoking (defined as smoking on 20 or more days in the last 30 days), current daily smoking, and ever daily smoking during late adolescence and young adulthood. Earlier age of onset is also associated with smoking more cigarettes per day (Everett et al., 1999) and symptoms of nicotine dependence in adulthood. Lanza & Vasilenko (2015) used logistic time-varying effect models to examine rates of adult nicotine dependence as a continuous function of age of daily smoking onset. Data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) suggest that rates of adult nicotine dependence are highest for those who begin smoking daily during middle childhood through early adolescence.

It should be noted that the vast majority of work assessing the effects of early nicotine exposure on physical, mental, and behavioral health has been conducted in the
context of cigarette smoking. However, as the concentration of nicotine in commercially available ENDS products is comparable to combustible cigarettes—or considerably higher in the case of pod mods like JUUL—findings on the effects of nicotine exposure likely generalize. As the landscape of commercially available nicotine products continues to change, additional research is necessary to understand potential differences by product. This is particularly important given the dramatic uptick in adolescent use of products like JUUL that more efficiently deliver nicotine to the lungs, circulatory system, and brain. Efficient delivery systems with high concentrations of nicotine, coupled with the absence of many adverse sensory experiences associated with inhaling high concentrations of nicotine, likely increase the abuse liability for these products and promote the development of nicotine dependence, continued use, and prolonged nicotine exposure (Barrington-Trimis & Leventhal, 2018; Goniewicz et al., 2018).

1.3c The Development of Nicotine Dependence: A Developmental Perspective

Nicotine dependence is a drug use disorder characterized by several physiological, psychological, and behavioral symptoms that can emerge following the onset of nicotine use (U.S. Department of Health and Human Services, 1988). The pharmacodynamics of nicotine and the neurobiological underpinnings of nicotine dependence have been well studied (see Benowitz, 1988, 2008). Nicotine acts on nAChRs which are highly abundant in the mesolimbic dopaminergic system (i.e, ventral tegmental area, hippocampus, nucleus accumbens, and frontal cortex); this system is particularly important for the hedonic and positively reinforcing properties of many drugs of abuse (Benowitz, 2008; D’Souza & Markou, 2011; Hyman, Malenka, & Nestler, 2006). Nicotine is an agonist, meaning it mimics the action of acetylcholine, binding to
nAChRs in the mesolimbic dopaminergic system and producing similar downstream effects. Binding of nicotine in these brain regions enhances the release of neurotransmitters such as acetylcholine, dopamine, glutamate, serotonin, and norepinephrine (among others), contributing to the positively reinforcing properties that play a role in the development of dependence and future smoking behaviors (Benowitz, 1988).

Specifically, the nAChR α4β2 receptor subtype is thought to play an important role in the development of nicotine dependence (Benowitz, 2009). The α4 receptor subunit plays a role in the user’s sensitivity to the rewarding and pleasurable effects of nicotine and the development of tolerance, whereas the β2 subunit is thought to play a specific role in self-administration and the behavioral responses to nicotine (Benowitz, 2009). Nicotine also binds to specific receptors that inhibit the action of monoamine oxidase (MAOA or MAOB), enzymes that break down neurotransmitters such as dopamine in the synapse. This indirectly results in an abundance of dopamine in the synapse, continued activation of post-synaptic neurons, and increased signaling in the mesolimbic dopaminergic system (Benowitz, 2009). Chronic activation of these neurons due to repeated exposure to nicotine contributes to long-lasting changes in nAChR receptor function (Benowitz, 2009; Govind, Vezina, & Green, 2009).

Adolescence is a period of development that is particularly sensitive to changes in the mesolimbic dopaminergic system and enhanced dopamine signaling throughout the brain, making drugs of abuse quite salient for this age group. Normative adolescent brain development is characterized by early functioning reward regions (i.e., mesolimbic dopamine system) and slower development of regions associated with impulse control,
decision making, and executive functioning (Somerville, Jones, & Casey, 2010; Spear, 2000). Thus, the adolescent brain has often been compared to a car with “all gas and no brakes” or “starting the engine without yet having a skilled driver behind the wheel” (Payne, 2012; Steinberg, 2005). This imbalance in brain development contributes to a heightened sensitivity to the pleasurable and rewarding effects of nicotine and the often quick progression from onset, to experimentation, and to more regular smoking behavior during adolescence.

It should be noted that biological changes contributing to the development of nicotine dependence do not happen after one instance of nicotine use. Repeated exposure to nicotine—thus repeated activation of the mesolimbic dopamine system—strengthens association between the experience of pleasure and drug-taking behavior and contributes to the biological and psychological symptoms of dependence. Nicotine use and the development of dependence has often been conceptualized as a progression from first use of nicotine, to patterns of experimentation and irregular use, culminating in habitual daily, or almost daily use that is largely driven by nicotine dependence (see review in Mayhew, Flay, & Mott, 2000).

There has been some debate regarding the timing of dependence onset within this seemingly sequential framework. It was once thought that the development of nicotine dependence during adolescence was a slow process, occurring years after one’s first smoking experience and only in the context of established, daily use (Leventhal & Cleary, 1980). However, there is evidence to suggest that the development of nicotine dependence symptoms during adolescence can occur quickly after initiation, even prior to the onset of daily nicotine use (DiFranza et al., 2000; Gervais, O’Loughlin,
Further, there is evidence for a bidirectional relationship between smoking behavior and nicotine dependence during adolescence and young adulthood in particular (i.e., escalation in smoking behavior leads to the development of nicotine dependence, while nicotine dependence also contributes to the progression of smoking behavior). Still, current smoking behavior has been shown to more strongly predict later nicotine dependence rather than current level of nicotine dependence predicting later smoking behavior (Doubeni, Reed, & DiFranza, 2010; Selya, Rose, Dierker, Hedeker, & Mermelstein, 2018).

Again, much of the work regarding the development of nicotine dependence during adolescence has been conducted in the context of cigarette smoking. The pharmacological role of nicotine and the biological mechanisms underlying the development of addiction are similar across tobacco products broadly. However, continued research is necessary to determine if the psychological and behavioral symptoms of nicotine dependence are shared between ENDS, cigarettes, and other tobacco products. Emerging research suggests that adolescent and adult ENDS users experience dependence symptoms that are unique to e-cigarettes and ENDS devices (Case et al., 2018). Continued research is necessary to understand the development of nicotine dependence among exclusive ENDS users.

In conclusion, the literature to date does not support public perceptions and widespread industry claims that ENDS are a safe and harmless alternative to cigarette smoking or an effective smoking cessation aid. ENDS use as a harm reduction strategy among established, adult cigarette smokers may indeed lead to reductions in biomarkers.
of nicotine and carcinogen exposure, as well as reductions in combustible cigarette use overall (D’Ruiz et al., 2016; Fagerström & Bridgman, 2014). However, detrimental physical, mental, and behavioral health outcomes may result from continued ENDS use. Early exposure to nicotine by way of ENDS is also of particular concern, as early nicotine use onset has been associated increased risk for the development of dependence as well as the uptake of cigarette smoking and other nicotine products. Continued research regarding what devices are being used by whom, and in what context is necessary to inform tobacco control policies and prevention/ intervention strategies.

1.4 Co-use of Nicotine and Marijuana

Of further concern is the ability for ENDS—particularly third and fourth generation devices—to be used with cannabis products. Nicotine, marijuana, and alcohol are the substances most likely to be abused across the lifespan (Mohler-Kuo, Eun Lee, & Wechsler, 2003; Nichter, Nichter, Carkoglu, & Lloyd-Richardson, 2010; Wechsler, Dowdall, Maenner, Gledhill-Hoyt, & Lee, 1998) and patterns of co-use have been widely documented (Agrawal, Budney, & Lynskey, 2012; Cohn et al., 2015; Primack et al., 2012). Co-use of nicotine and marijuana, particularly the use of both substances on the same occasion, is associated with greater frequency of marijuana use and increases in marijuana-related consequences (e.g., missing school, getting into trouble, driving under the influence of marijuana; Tucker et al., 2019). However, little is known about comprehensive patterns of nicotine and marijuana co-use specifically in the context of emerging delivery systems and increasingly popular ENDS products.

According to Monitoring the Future, rates of past-month ENDS use and marijuana use have been consistently higher than combustible cigarette use among young people
since 2014 (Johnston et al., 2019). Current data suggest that 22% of high school seniors and 22% of young adults ages 18-25 endorse past-month marijuana use (Center for Behavioral Health Statistics and Quality, 2018; Johnston et al., 2019). Vaping cannabis products has become an increasingly popular method of delivery among adolescents, with 44% of lifetime cannabis users reporting ever vaping in 2016 (Knapp et al., 2019). Some evidence suggests that adolescents reporting ENDS use in their lifetime are more likely to report vaping cannabis products (Morean, Kong, Camenga, Cavallo, & Krishnan-Sarin, 2015), especially among those who initiated ENDS use at an earlier age (Lee, Crosier, Borodovsky, Sargent, & Budney, 2016). Adult ENDS users also report higher rates of vaping cannabis in the lifetime and in the past month (Jones, Hill, Pardini, & Meier, 2016; Morean, Lipshie, Josephson, & Foster, 2017), however, less is known about young adults in particular. Further research is necessary in order to understand the association between ENDS use and marijuana use among adolescents and young adults, specifically with regard to age-specific risk factors for co-use and vaping of both substances.

It is speculated that device-level characteristics shared by ENDS and certain cannabis delivery systems may be facilitating concurrent use of nicotine and marijuana. For example, devices similar to ENDS – particularly vaporizers, vape pens and pod mods—have been increasingly marketed for use with THC/CBD liquids and other cannabis products such as hash oil. Companies such as PAX and MarkTen have developed vaporizers for cannabis herbs, waxes, oils, and extracts that closely resemble JUUL devices in their shape, size, and function (see Figure 3). Adolescents and young adults also report modifying third and fourth generation ENDS for use with THC or CBD e-liquids, hash oils, and in some cases, dried cannabis. Lifetime and current marijuana
users endorse several reasons for vaping cannabis that are quite similar to reported reasons for ENDS use. Reasons for vaping cannabis include: better taste, lower perceived risk of harm, ease of concealment, and better smell (Morean et al., 2017). Similar motivating factors likely impact the desire to vape both nicotine and cannabis products, however, there is a lack of research investigating specific motivations for use among adolescent and young adult co-users.

![Illustration of JUUL pod mod device, MarkTen Elite, and PAX Era](courtesy: CDC)

**Figure 1.3.** Illustration of JUUL pod mod device, MarkTen Elite, and PAX Era (courtesy: CDC)

Hookah/waterpipes and bongs are also similar delivery systems, however, they are not interchangeable devices; hookah/waterpipes are most commonly used to smoke tobacco, whereas bongs are most commonly used to smoke marijuana. Both devices are designed to pull smoke through a base filled with water as the user inhales through a hose or mouthpiece. Young adults, particularly college students, report similar motivations for hookah/waterpipe and marijuana use, with the most popular reasons for use being socializing/partying, relaxation, and lower perceived risk of harm/addiction (Braun, Glassman, Wohlwend, Whewell, & Reindl, 2012; Lee, Neighbors, & Woods, 2007; Patrick et al., 2011; Smith-Simone, Maziak, Ward, & Eissenberg, 2008). Parallels in
device-level characteristics and similarities in the perceived risks and expectancies associated with ENDS, hookah/waterpipe, and marijuana use may impact the concurrent use of both nicotine and cannabis products.

Understanding adolescent and young adult nicotine use and the relation to other substance use behaviors is imperative in order to improve tobacco control and intervention strategies, as well as reduce the impact of substance use and smoking related illness on the United States. Given the recent rise in ENDS use among young people, as well as state-level changes in the legalization of recreational marijuana, it is increasingly important to understand risk factors and consequences associated with co-use of nicotine and marijuana. As outlined above, early exposure to nicotine is related to numerous long-term behavioral, mental, and physical health consequences. Marijuana use during adolescence and young adulthood is also related to many negative consequences such as increased risk of internalizing and externalizing behaviors, marijuana use disorder symptoms, missing school/work, and driving under the influence of marijuana, among others (Litt, Kilmer, Tapert, & Lee, 2016; Patrick, Bray, & Berglund, 2016; Tucker et al., 2019). Therefore, prevention/intervention programming and public policy efforts targeting early substance use need to consider the unique challenges and risks associated with increasingly popular nicotine and cannabis delivery systems, particularly vaping devices.

### 1.5 An Empirical Examination of Nicotine and Marijuana Use among Adolescents and Young Adults: Findings from the PATH Study

Advances in national longitudinal tobacco surveillance data, such as the PATH Study, provide new opportunities to document population-level tobacco use behaviors
and concurrent use with other substances. The remaining chapters of this dissertation aim to capitalize on these rich, national data in order examine patterns and trends in the use of ENDS, other tobacco products, and marijuana among adolescents and young adults in the United States. Innovative statistical techniques provide added insight into who is at risk for using specific tobacco products at each age, as well as the factors contributing to polytobacco use and co-use with marijuana.

In Chapter 2, age-varying prevalence of recent cigarette, ENDS, hookah, and marijuana use are estimated across ages 14 to 24 using time-varying effect modeling. Differences in these age-trends are examined by sex and race/ethnicity. Age-varying associations between recent marijuana use and the use of each tobacco product are also estimated; sex and race/ethnicity are examined as moderators. Contemporary data are from Wave 3 (W3) of the PATH Study.

In Chapter 3, patterns of lifetime tobacco use are examined among young adults ages 18-24 in Wave 1 (W1) of the PATH Study and transitions in these patterns from W1 to Wave 2 (W2) are estimated using latent transition analysis. Sex, race/ethnicity, and lifetime use of marijuana are examined as covariates in order to investigate demographic differences in latent class membership. To close, Chapter 4 integrates the findings from both empirical studies and implications are considered within the context of the rapidly changing landscape of ENDS and marijuana use in the United States.
CHAPTER 2: Age-varying Associations between Nicotine and Marijuana Use among 14 to 24 year-olds in the United States

According to Monitoring the Future, rates of past-month marijuana use have been consistently higher than combustible cigarette use among young people since 2014 (Johnston et al., 2019). Current data suggest that 22% of high school seniors and 22% of young adults ages 18-25 endorse using marijuana in the past 30 days (Center for Behavioral Health Statistics and Quality, 2018; Johnston et al., 2019). Marijuana use during adolescence and young adulthood is related to an increased risk for several negative health outcomes including internalizing and externalizing behaviors, marijuana and other substance use disorder symptoms, as well as accidental injury (Litt, Kilmer, Tapert, & Lee, 2016; Tucker et al., 2019). Use among young people is also associated with behavioral consequences such as impaired driving, poor academic and job performance, and higher rates of missing school/work (Brook, Adams, Balka, & Johnson, 2019; Litt et al., 2016).

As of May, 2019, 10 states have legalized recreational marijuana use among individuals over 21 years-old and 23 states allow limited use of medical marijuana. Some evidence suggests that changes in marijuana legislation have been associated with increases in marijuana use initiation among underage individuals, as well as increased odds of marijuana use and dependence among those 21 and older (Wen, Hockenberry, & Cummings, 2015). Data from the 2017 National Survey on Drug Use and Health also indicate that underage marijuana use is higher in states that have legalized recreational use (Center for Behavioral Health Statistics and Quality, 2018). As state-level marijuana
laws continue to change, it is increasingly important to understand factors that influence marijuana use behaviors among young people in order to prevent negative consequences associated with early and chronic use.

Evidence suggests that marijuana use during adolescence and young adulthood is often associated with concurrent nicotine use; patterns of co-use of marijuana, nicotine, and alcohol use across the lifespan have been widely documented (Cohn et al., 2015, Mohler-Kuo, Eun Lee, & Wechsler, 2003; Nichter, Nichter, Carkoglu, & Lloyd-Richardson, 2010; Wechsler, Dowdall, Maenner, Gledhill-Hoyt, & Lee, 1998). For example, high school seniors who currently use marijuana are more likely to report recent hookah use compared to those who do not use marijuana (Palamar, Zhou, Sherman, & Weitzman, 2014); young adult cigarette smokers are also more likely to report recent marijuana use compared to non-smokers (Sutfin et al., 2012). Current nicotine use, therefore, may be a risk factor for current marijuana use among young people in the US. However, little is known about comprehensive patterns of nicotine and marijuana co-use specifically in the context of increasingly popular electronic nicotine delivery systems (ENDS).

In 2014, ENDS surpassed combustible cigarettes as the most commonly used nicotine delivery system among US adolescents (Johnston et al., 2019; Singh et al., 2016), and prevalence of ENDS use increased by 78% from 2017 to 2018 (Cullen et al., 2018). Rates of current ENDS use and marijuana use among adolescents and young adults remain higher than combustible cigarette smoking today (Johnston et al., 2019). It is theorized that characteristics of certain nicotine and marijuana delivery systems may facilitate concurrent use, as similar—or often the same—materials can be used to
consume both substances (Enofe, Berg, & Nehl, 2014; Sutfin, Song, Reboussin, & Wolfson, 2014).

ENDS are battery-powered devices that heat a solution containing nicotine, propylene glycol, vegetable glycerin, and other potentially harmful constituents into an aerosol to be inhaled by the user (Cahn & Siegel, 2011; Callahan-Lyon, 2014; Grana, Benowitz, & Glantz, 2014; Standford Medicine, 2019). Devices similar to ENDS have been increasingly marketed for use with THC/CBD liquids and other cannabis products. Companies such as PAX and MarkTen have developed vaporizers for use with cannabis herbs, waxes, oils, and extracts. These marijuana vaping devices closely resemble ENDS in their shape, size, and function. Hookah/waterpipes and bongs are also similar delivery systems for nicotine and marijuana respectively; both devices are designed to pull smoke through a base filled with water as the user inhales through a hose or mouthpiece. It is speculated that parallels in device-level characteristics and similarities in the perceived risks and expectancies associated with ENDS, hookah/waterpipe, and marijuana use may impact the concurrent use of both nicotine and cannabis products.

Early evidence suggests that there may be a link between ENDS use and marijuana use among adolescents and young adults. For example, in 2016 44% of lifetime cannabis users also reported using ENDS (Knapp et al., 2019). Additional evidence suggests that adolescents that have ENDS used in their lifetime are more likely to report vaping cannabis products (Morean et al., 2015), especially among those who initiated ENDS use at an earlier age (Lee, Crosier, Borodovsky, Sargent, & Budney, 2016). Adult ENDS users also report higher rates of vaping cannabis in the lifetime and in the past month (Jones et al., 2016; Morean et al., 2017), however, less is known about
young adults in particular. Further research is necessary in order to understand the association between ENDS use and marijuana use among adolescents and young adults, specifically with regard to age-specific risk factors for co-use and vaping of both substances.

Rates of nicotine and marijuana use behaviors have previously been examined by age (Arrazola et al., 2015; Brodbeck, Bachmann, Croudace, & Brown, n.d.; Chen & Jacobson, 2012; Singh et al., 2016), however, the majority of these studies focus on a small age range or use loosely binned age variables (e.g., middle schoolers ages 11-13, high schoolers ages 14-17, young adults ages 18-24), even though these behaviors likely vary continuously across development. The current study examines the age-varying prevalence of recent (e.g., past 30-day) combustible cigarette, ENDS, hookah, and marijuana use across adolescence and young adulthood using time-varying effect modeling (TVEM; Tan, Shiyko, Li, Li, & Dierker, 2012). The age-varying associations between recent marijuana and of recent cigarette, ENDS, and hookah use are also examined. TVEM is an innovative method that flexibly estimates regression coefficients. Rather than estimating a single regression coefficient that represents the overall association between hookah and marijuana use, TVEM estimates this coefficient as a function of continuous age. Coefficient functions are plotted, along with their corresponding 95% confidence intervals, to facilitate interpretation of age-varying effects. The use of TVEM has the potential to provide new insight into the particular ages that may be at heightened risk for current cigarette, ENDS, hookah, and marijuana use and co-use.
2.1 Method

2.1a Sample: Population Assessment of Tobacco and Health (PATH) Study

Participants are adolescents and young adults from Wave 3 (W3) of the Population Assessment of Tobacco and Health (PATH) Study. The PATH Study is a nationally representative, ongoing, longitudinal cohort study of 45,971 adolescents and adults ages twelve and older (Hyland et al., 2016). W3 data were collected from October 2015 through October 2016. PATH was designed to assess tobacco use and other substance use behaviors based on the host, vector, agent, and environmental (HAVE) conceptual model. The HAVE model posits that multiple factors or spheres of influence interact to impact substances use behaviors and related health outcomes. The host represents the substance user, the agent represents characteristics specific to the substances(s) being used, and the vector refers to factors that introduce, promote, and facilitate substance use (e.g., tobacco manufacturers, advertisements, product packaging). Environmental factors include all policy changes and social/cultural norms that impact substance use behaviors. The HAVE conceptual model has been widely used in Epidemiology to assess the transmission and impact of infectious diseases, but the model has been validated to assess tobacco control policies (Giovino, 2002) and the impact of ENDS in particular (Garcia-Cazarin, Mandal, Grana, Wanke, & Meissner, 2018).

PATH used a four-stage, stratified sampling design, incorporating address-based sampling methods to randomly select 150,000 households across the US. This resulted in a national sample of tobacco users and non-users. The design oversampled tobacco users, young adults ages 18 to 24, and African-Americans. Single-wave and longitudinal weight variables were created to adjust for stratification, clustering, and oversampling of certain
populations, as well as attrition. Data were collected in the home using Audio Computer-Assisted Self-Interviewing and Computer-Assisted Personal Interviewing systems. The use of such interviewing systems allowed images to be presented as examples of each nicotine delivery system being assessed. Biospecimens (urine, blood, buccal samples) were collected in a subgroup of participants at each wave. Sampling procedures and the protocol for data collection have been described in detail by Hyland et al., 2016 and in the user’s guide for the PATH restricted–use files (Hyland et al., 2016; United States Department of Health and Human Services, National Institutes of Health, & National Institute on Drug Abuse, 2019).

The current analyses were conducted using the W3 restricted-use files. A precise age variable is not available in the PATH public-use dataset, therefore, restricted data were necessary in order to model age-varying associations between past-month nicotine product (i.e., combustible cigarette, ENDS, hookah/waterpipe) and marijuana use (United States Department of Health and Human Services et al., 2019). The final analytic sample included adolescents and young adults ages 14 to 24 (N=16,196). Twelve and 13 year-old adolescents were excluded from the analytic sample due to low response rates for past-month nicotine and marijuana use. The institutional review board at The Pennsylvania State University has approved this study; a Restricted Data Use Agreement has been approved by the Inter-university Consortium for Political and Social Research (ICPSR) and The Pennsylvania State University Office of Sponsored Programs. Restricted-use files were accessed through the ICPSR Virtual Data Enclave in a secure office in which only those approved to work with the restricted-use files have access.
2.1b Measures

Outcome. Past 30-day use of marijuana was measured using three questionnaire items. Participants were first asked if they have smoked part or all of a traditional cigar, cigarillo, or filtered cigar with marijuana in it (i.e., a blunt) in the past 12 months. If yes, participants were asked if they had used marijuana, hash, THC, grass, pot or weed within the past 30 days. If participants did not report smoking a blunt, they were asked if they had used marijuana, hash, THC, grass, pot or weed in the past 12 months. If yes, they were asked if they had used in the past 30 days. A binary indicator of past-month marijuana use was created using information from all questionnaire items, with 1 indicating marijuana use in the past 30 days and 0 indicating no use in the past 30 days. In this case, a response of 0 could indicate (1) no use in the lifetime, or (2) use in the past year, but not the past 30 days.

Predictors. Past 30-day use of combustible cigarettes, ENDS, and hookah/waterpipe were examined as predictors of past 30-day marijuana use. ENDS use was defined as having used any electronic nicotine product in the past 30 days, including e-cigarettes, vape pens/e-hookahs/hookah pens, personal vaporizers and mods, e-cigars, or e-pipes. Binary indicators of past-month use were created for each nicotine delivery system (cigarettes, ENDS, hookah/waterpipe) based on several questionnaire items. Participants were first asked if they had ever seen or heard of each delivery system (with the exception of combustible cigarettes); if yes, participants were then asked if they had used the product in their lifetime. Participants were only asked if they had used each product in the past 30 days if they endorsed having seen/heard of the product and also endorsed using the product in their lifetime. Information from each of these items was
used to create binary indicators of past-month combustible cigarette, ENDS, and hookah/waterpipe use, with 1 indicating use in the past 30 days and 0 indicating no use in the past 30 days. A response of 0 could indicate (1) no use in the lifetime, (2) use in the lifetime, but not the past 30 days, or (3) the participant had never seen or heard of the product before the study.

**Time variable.** Prevalence of past-month nicotine and marijuana use, as well as the associations between combustible cigarette, ENDS, hookah/waterpipe, and marijuana use were estimated as functions of continuous age, from ages 14-24. Age at the time of interview was reported to the nearest year and incorporated into all models as the measure of time. As stated above, 12 and 13 year-old adolescents were excluded from the analytic sample due to low response rates for past-month nicotine and marijuana use.

**Covariates and Moderators.** Census region was collected via address-based sampling methods. Four binary, mutually exclusive categories were created indicating residence in the Northeast, Midwest, South, and West. One binary indicator of past-month cigars/cigarillos/filtered cigars (i.e., cigar products) and past-month chewing tobacco/snuff/dip (i.e., smokeless tobacco) use was created to control for other tobacco product use. Census region was included as a time-invariant covariate; other tobacco product use was included as a time-varying covariate.

Biological sex, race, and ethnicity were measured by self-report. Race and ethnicity were assessed using separate items, such that individuals had the opportunity to endorse belonging to multiple racial/ethnic groups (e.g., white and Hispanic, Black and Hispanic, white and Black, and so on). Mutually exclusive racial/ethnic categories were created using information from all race and ethnicity variables, resulting in dummy coded
variables indicating Non-Hispanic white, Non-Hispanic Black, Hispanic, and multi-racial/other. The multi-racial/other category was comprised of individuals of Asian, American Indian, and Native Hawaiian or Native Pacific Islander decent, as well as those reporting multiple races; this group has been excluded from all analyses examining differences by racial/ethnic groups due to limited statistical power resulting from small sample size. Descriptive statistics are presented in Table 2.1.

Table 2.1. Descriptive statistics for the final analytic sample, adolescents and young adults ages 14-24, W3 of the PATH Study (N=16,196).

<table>
<thead>
<tr>
<th>Demographics</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>48.9%</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>56.5%</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>13.9%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>22.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Past 30-day Substance Use</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarettes</td>
<td>18.1%</td>
</tr>
<tr>
<td>ENDS</td>
<td>13.1%</td>
</tr>
<tr>
<td>Hookah</td>
<td>6.2%</td>
</tr>
<tr>
<td>Marijuana</td>
<td>16.5%</td>
</tr>
</tbody>
</table>

Note. The analytic sample includes adolescents and young adults. Percentages are rounded to the nearest whole number.

2.1c Overall Analytic Plan

Analyses proceeded in several steps. TVEM (Tan et al., 2012) was used to estimate the age-varying prevalence of recent (past 30-day) combustible cigarette, ENDS, hookah/waterpipe, and marijuana use as a function of continuous age. Next, the age-varying effects of recent cigarette, ENDS, and hookah use on recent marijuana use were estimated. Finally, dynamic (age-varying) moderation by sex and race/ethnicity was
examined to assess differences in prevalence and age-varying associations across population subgroups. All models were run in SAS 9.4 using the Weighted TVEM macro (Dziak, Li, & Wagner, 2017).

2.1d Intercept-only Models: Estimating Age-varying Prevalence (Aim 1)

First, weighted logistic TVEM was used to estimate the prevalence of past 30-day cigarette, ENDS, hookah, and marijuana use as a function of continuous age in four separate intercept-only models. Rates of use were first examined in the full analytic sample and follow up analyses included age-varying interaction terms for sex and race/ethnicity to assess differences in complex age-trends by population subgroup. W3 sample weights were applied in all models to ensure nationally representative estimates. The B-spline method was used to estimate all intercept-only models and model selection was conducted in several steps.

Age-varying prevalence estimates for past 30-day combustible cigarette, ENDS, hookah, and marijuana use were estimated four times, with each coefficient function specified to have 3, 2, 1, and then 0 knots. For each behavior, models were then compared using Akaike information criterion (AIC) and Bayesian information criterion (BIC) in order to determine the optimal number of knots for each coefficient function. Models with the lowest AIC and BIC values were selected, as lower values reflect optimal balance between model fit and parsimony. In TVEM, the number of knots specified in a given model represents the complexity of the function that is estimated. Models with more knots estimate increasingly more complex functions, whereas models with fewer knots estimate smoother curves. In instances where the AIC and BIC were not
in agreement regarding the optimal number of knots, BIC was given more weight and a more parsimonious model was favored.

As an example, the age-varying prevalence of past 30-day ENDS use was estimated first with 3 knots, followed by 2, 1, and finally 0 knots. AIC and BIC values were then compared for each model. This processes was repeated for cigarette, hookah, and marijuana use. Model fit statistics for each intercept only model are presented in Appendix A. The equation for an age-varying, intercept-only weighted logistic TVEM model estimating past 30-day ENDS use is presented in Equation 1; corresponding SAS syntax is presented in figure 2.1.

(Eq. 1) \[
\ln \left( \frac{p(p_{30\text{dENDS}})}{1-p(p_{30\text{dENDS}})} \right) = \beta_0(\text{age})
\]

2.1e Age-varying Associations with Marijuana Use (Aim 2)

The age-varying main effects of past-month cigarette, ENDS, and hookah use were estimated in one weighted logistic TVEM model. The B-spline method was used and final model selection was conducted systematically. Each predictor (i.e., cigarette, ENDS, hookah use) was specified as having 3 knots, followed by 2, 1, and finally 0 knots. First, the knots were varied for the intercept coefficient while all other predictors were held constant. For example, the intercept coefficient was specified to have 3 knots, while the coefficients for cigarette, ENDS, and hookah use were each specified to have 0 knots.

```sas
%WeightedTVEM(data = mydata, 
time = age, 
dv = p30dENDS, 
tvary_effect = int, 
 knots = 3/* 2 1 0 */,
 dist = binary, 
 cluster = PERSONID, 
 weight = R03_Y_PWGT, 
);
```

Figure 2.1. Sample SAS syntax for an intercept-only model in weighted logistic TVEM
knots. Once the optimal number of knots was selected for the intercept coefficient using AIC and BIC, the knots were then varied in a similar manner for each predictor sequentially. The optimal number of knots was selected for each coefficient using AIC and BIC. Again, in instances where the AIC and BIC were not in agreement regarding the optimal number of knots, BIC was given more weight and a more parsimonious model was favored. Model fit statistics are presented in Appendix A.

Time-invariant covariates were included in the model to control for sex, race/ethnicity, and geographic region – these coefficients were not specified as age-varying. The equation for an age-varying, weighted logistic TVEM model estimating the effect of past 30-day nicotine use on past 30-day marijuana use is presented in equation 2; corresponding SAS syntax is presented in figure 2.2.

```
%WeightedTVEM(data = mydata,
    time = age,
    dv = p30dMarijuana,
    tvary_effect = int p30dCIG p30dENDS p30dHookah other_prod_use,
    invar_effect = female black hisp Midwest south west,
    knots= 3 /* 2 1 0 */
            3 /* 2 1 0 */
            3 /* 2 1 0 */
            3 /* 2 1 0 */,
    dist = binary,
    cluster = PERSONID,
    weight = R03_Y_PWGT,
);   
```

*Figure 2.2. Sample SAS syntax for the main effects model in weighted logistic TVEM.*
Finally, age-varying interaction terms were included for sex and race/ethnicity to assess population subgroup differences in these age-varying associations. Model selection was conducted systematically, as outlined above. Each predictor (i.e., cigarette, ENDS, hookah use) and its interaction (i.e., Cigarette*Female, ENDS *Female, Hookah *Female) was specified as having 3 knots, followed by 2, 1, and finally 0 knots. Knots were varied for each coefficient one at a time until the optimal number of knots was selected for each coefficient. Model fit statistics for the interaction models are presented in Appendix B.

2.2 Results

To facilitate interpretation, results from all weighted logistic TVEM models are presented as figures in which coefficient functions are presented across continuous age. Intercept-only models for past-month cigarette, ENDS, hookah, and marijuana use are presented as age-varying prevalence estimates with 95% confidence intervals. The associations between marijuana use and recent cigarette, ENDS, and hookah use are presented as age-varying odds ratios with 95% confidence intervals. Ages at which the 95% confidence intervals do not include 1.0 indicate statistical significance at the p < 0.05 level.
2.2a Age-varying Prevalence Estimates (Aim 1)

Figure 2.3 presents age-varying prevalence estimates for past-month cigarette, ENDS, hookah, and marijuana use for adolescents and young adults ages 14 to 24. Prevalence of cigarette use is presented in black, ENDS in blue, hookah in purple, and marijuana in green. Solid lines represent age-specific prevalence estimates and dashed lines represent upper and lower limits for the 95% confidence interval. Ages at which the 95% confidence intervals for each delivery system do not overlap provide a conservative estimate of significant differences in prevalence.

Past 30-day use of cigarettes, ENDS, hookah, and marijuana generally increased during adolescence and peaked during young adulthood. Across all ages, rates of hookah

![Prevalence of Past 30 Day Substance Use](image)

*Figure 2.3. Age-varying prevalence of past 30-day combustible cigarette, ENDS, hookah, and marijuana use across adolescence and young adulthood, ages 14-24. N=16,217; Year = 2015 to 2016; Cigarettes are pictured in black, ENDS in blue, hookah in purple, and marijuana in green.*
use were significantly lower than cigarette, ENDS, and marijuana use. Prevalence of hookah use increased slowly during mid adolescence and peaked at 10.7% at age 21 (CI = 9.6%, 12.0%).

Rates of cigarette, ENDS, and marijuana use were similar at age 14, however, age-varying prevalence estimates followed different age-trends for each delivery system. Prevalence of past-month cigarette use was lowest at age 14 (prevalence = 1.9%; 95% CI = 1.4%, 2.6%); a steep increase in prevalence was observed between ages 15 (2.9%; CI = 2.4%, 3.4%) and 20 (25.4%; CI = 23.9%, 26.8%). Cigarette use continued to increase across ages 21 – 24, but at a slower rate; prevalence peaked at age 24 (31.7%; CI = 28.9%, 34.8%).

Past-month ENDS use was also lowest at age 14 (2.6%; CI = 2.0%, 3.4%); a steep increase in prevalence was observed between ages 16 (5.8%; CI = 5.0%, 6.8%) and 18.5 (20.5%; CI = 19.0%, 22.2%). Prevalence of past-month ENDS use peaked around 21% at age 18.5, followed by a slight decrease in prevalence through age 21. ENDS use plateaued at approximately 16% for ages 21 – 24. A cross-over effect emerged between rates of cigarette use compared to ENDS use compared to cigarette use at age 15 and between ages 20 – 24. Prevalence of past-month ENDS use was significantly higher than cigarette use among 15 year olds, however, past-month cigarette use was significantly higher than ENDS use among 20 – 24 year olds.

Age-varying prevalence of past-month marijuana use was strikingly similar to the prevalence of ENDS use among adolescents ages 14 – 18. Marijuana use was lowest at age 14 (2.8%; CI = 2.2%, 3.7%), followed by a steep increase in prevalence from ages 16 (6.1%; CI = 5.3%, 7.1%) to 18.5 (24.0%; CI = 22.3%, 25.8%). After age 19,
prevalence of past-month marijuana use decreased slightly through age 21 (21.4%; CI = 19.7%, 23.2%), increased through age 23 (23.7%; CI = 21.7%, 25.9%), and then decreased again at age 24 (21.0%; CI = 18.5%, 23.8%). Prevalence of past-month marijuana use was significantly higher than ENDS use between ages 19 and 24.

Significant differences also emerged for past-month marijuana use compared to cigarette use at multiple ages. Rates of marijuana use were significantly higher than cigarette use among adolescents ages 14-15 and 17-19. There was no significant difference in rates of past-month marijuana and cigarette use at age 16. Prevalence of past-month cigarette use was significantly higher than marijuana use during young adulthood.

2.2b Disparities in Age-Varying Prevalence of Nicotine and Marijuana Use

Figure 2.4 presents sex differences in the age-varying prevalence of past-month cigarette (A), ENDS (B), hookah (C), and marijuana (D) use for adolescents and young adults ages 14 to 24. Solid lines represent age-specific prevalence estimates for males and females and dashed lines represent 95% confidence intervals; males and females are differentiated by color. Ages at which the 95% confidence intervals do not overlap provide a conservative estimate of significant differences in prevalence between males and females.

For all nicotine products, prevalence was similar during adolescence, however, males reported higher rates of use compared to females in young adulthood. From ages 19 to 23, the proportion of males reporting past-month cigarette use was approximately 10% higher than females (see figure 2.4A). Prevalence of past-month ENDS use diverged between males and females at age 18; rates of use were 5 – 10% higher among males compared to females (see figure 2.4B). Past-month use of hookah was significantly
higher among males at age 22 (see figure 2.4C). Interestingly, a crossover effect was observed for past-month marijuana use. Females endorsed using marijuana at higher rates than males at ages 16 and 17, however males used at higher rates across ages 19 – 24 (see figure 2.4D).

Figure 2.5 presents racial/ethnic differences in the age-varying prevalence of past-month cigarette (A), ENDS (B), hookah (C), and marijuana (D) use. Solid lines represent age-specific prevalence estimates and dashed lines represent 95% confidence intervals. NH white, NH Black, and Hispanics are differentiated by color. Ages at which the 95% confidence intervals do not overlap provide a conservative estimate of significant differences in prevalence by race/ethnicity.

Across ages 14 – 20, prevalence of past-month cigarette use was higher among NH white individuals compared to NH Blacks and Hispanics. Prevalence of cigarette use was also higher among Hispanic individuals compared to NH Blacks from age 17 – 23 (see Figure 2.5A). Similarly, rates of past-month ENDS use were higher among NH whites compared to NH Blacks and Hispanics across ages 15 – 18; rates of ENDS use were higher among both NH whites and Hispanics compared to NH Blacks from age 18 – 22 (see Figure 2.5B).

A crossover effect was observed for past-month hookah use among Hispanic and NH Black individuals. Hispanic individuals endorsed higher rates of hookah use than their non-Hispanic white and non-Hispanic Black counterparts between ages 18 and 20. However, non-Hispanic Black individuals used hookah at a higher rate than their Hispanic and non-Hispanic white counterparts at ages 23-24 (see Figure 2.5C). Finally, prevalence of past-month marijuana use was higher among NH Black and NH white
individuals compared to Hispanics at ages 18 and 19; prevalence was higher among NH Black individuals compared to both NH whites and Hispanics at 23 (see Figure 2.5D).
Figure 2.4. Sex differences in the age-varying prevalence of past 30-day cigarette (A), ENDS (B), hookah (C), and marijuana (D) use. Solid lines represent age-varying prevalence estimates; dashed lines represent the 95% confidence interval.
Figure 2.5. Racial/ethnic differences in the age-varying prevalence of past 30-day cigarette (A), ENDS (B), hookah (C), and marijuana (D) use. Solid lines represent age-varying prevalence estimates; dashed lines represent the 95% confidence interval.
2.2c Age-varying Associations with Marijuana Use (Aim 2)

Figure 2.6 presents the association between past-month cigarette use and marijuana use across ages 14 – 24. Solid lines represent age-varying odds ratios and dashed lines represent the upper and lower limits of the 95% confidence interval. Ages at which the 95% confidence intervals do not include 1.0 indicate increased odds of using marijuana given recent cigarette, ENDS, or hookah use. Past-month cigarette use was associated with increased odds of using marijuana for ages 15 – 24. This association was strongest at age 17 (OR = 5.9; 95% CI = 3.9, 8.9) and weakest, but still statistically significant, at ages 15 (OR = 3.5; 95% CI = 1.8, 6.6) and 22 (OR = 2.8; 95% CI = 2.2, 3.5).

Figure 2.6. Age-varying association between past-month cigarette use and past-month marijuana use. Solid lines represent age-varying odds ratios; dashed lines represent the 95% confidence interval.
Figure 2.7 presents the association between past-month ENDS use and marijuana use across ages 14 – 24. Past-month ENDS use was associated with increased odds of using marijuana in the past month for ages 14 – 23. Adolescents using ENDS at age 14 had approximately 8 times higher odds of also using marijuana (OR = 7.8; 95% CI = 3.1, 19.7). The strength of the association decreased, but remained significant, through age 23; past-month ENDS use was associated with approximately 2 times higher odds of marijuana use at age 18 – 24.

**Figure 2.7.** Age-varying association between past-month ENDS use and past-month marijuana use. Solid lines represent age-varying odds ratios; dashed lines represent the 95% confidence interval.
Figure 2.8 presents the association between past-month hookah use and marijuana use across ages 14 – 24. Past-month hookah use was associated with increased odds of using marijuana at ages 21 (OR = 1.6; 95% CI = 1.13, 2.19) and 22 (OR = 1.5; 95% CI = 1.04, 2.1). The association was not statistically significant at any other age.

![Graph](image)

*Figure 2.8. Age-varying association between past-month hookah use and past-month marijuana use. Solid lines represent age-varying odds ratios; dashed lines represent the 95% confidence interval.*

2.2d Age-varying Moderation by Sex and Race/Ethnicity

Finally, age-varying interaction terms for sex and race/ethnicity examined demographic differences in the associations between nicotine and marijuana use. Figure 2.9 presents sex differences in the age-varying odds ratios for past-month marijuana use given cigarette (A), ENDS (B), and hookah use (C). Solid lines represent age-varying
odds ratios for females; dashed lines represent age-varying odds ratios for males. There were no age periods during which the Sex*Cigarette, Sex*ENDS, or Sex*Hookah interaction terms were significant.

Figure 2.10 presents racial/ethnic differences in the age-varying odds ratios for past-month marijuana use given cigarette (A), ENDS (B), and hookah use (C). There were no age periods during which the interaction terms for cigarette and hookah use were significant. The association between ENDS and marijuana use was moderated by race/ethnicity; boxes indicate age periods during which the interaction terms were significant. Compared to white individuals, non-Hispanic Black individuals had significantly increased odds of reporting marijuana use in the past month given ENDS use at ages 14 and 15 (see Fig. 2.10, red box). Hispanic individuals also demonstrated significantly increased odds of reporting marijuana use in the past month given ENDS use at ages 15-18 (see Fig. 2.10, black box).
Figure 2.9: Sex differences in the age-varying association between past 30-day cigarette (A), ENDS (B), and hookah (C) use. Solid lines represent males and dashed lines represent females.
Figure 2.10: Racial/ethnic differences in the age-varying association between past 30-day cigarette (A), ENDS (B), and hookah (C) use. Solid lines represent NH whites, thick dashed lines represent NH Blacks, and thin dashed lines represent Hispanics.
2.3 Discussion

This study examined how recent nicotine, marijuana use, and their associations vary across age among adolescents and young adults using weighted logistic TVEM. Contemporary data are from W3 of the PATH Study, collected from October 2015 through October 2016. Consistent with prior research, results from this study demonstrate that prevalence of past-month nicotine and marijuana use generally increase from adolescence into young adulthood, regardless of delivery system. However, TVEMs extend these findings by providing a more nuanced examination of developmental trends for each substance use behavior, as well as the age-varying associations between nicotine and marijuana use.

A key finding of this study is that steep increases in the prevalence of past-month cigarette, ENDS, and marijuana use were observed between ages 16 and 19. This indicates that age 16 might be a critical age for the onset of these behaviors. Further, the prevalence of past-month ENDS and marijuana use followed similar developmental trends during adolescence, but differed during young adulthood. Age-varying prevalence estimates overlap considerably from age 14 to 17, only diverging after age 18 when rates of recent marijuana use were significantly higher than ENDS use through age 24. Existing evidence from various national samples of adolescents and young adults (e.g., Monitoring the Future, National Youth/Adult Tobacco Survey) suggest that rates of current ENDS and marijuana use are higher than current cigarette smoking today, particularly among underage adolescents and non-college attending young adults (Arrazola et al., 2015; Johnston et al., 2019; Singh et al., 2016). Intercept-only models in this study, however, demonstrate that past-month ENDS and marijuana use were only
significantly higher than cigarette use among 15 year olds. Past-month marijuana use, but not ENDS use, was also significantly higher than cigarette use among 17 and 18 year olds. Rates of past-month cigarette smoking were higher than marijuana and ENDS use for young adults, particularly those aged 21 and 24.

Findings from this study also suggest that specific population subgroups may be at increased risk for nicotine and marijuana use at certain ages. Consistent with prior research, young adult males reported higher rates of past-month cigarette, ENDS, and marijuana use compared to females between ages 18 or 19 and 24; males also used hookah in the past month at a higher rate at age 22. Interestingly, a crossover effect was observed for past-month marijuana use among males and females. Females endorsed using marijuana at higher rates than males at ages 16 and 17, however males used at higher rates across ages 19 – 24.

Several interesting differences in the age-varying prevalence of past-month cigarette, ENDS, hookah, and marijuana also emerged by race/ethnicity. Most importantly, another crossover effect was observed for past-month hookah use among Hispanic and NH Black individuals. Hispanic individuals endorsed higher rates of hookah use than their non-Hispanic white and non-Hispanic Black counterparts between ages 18 and 20. However, non-Hispanic Black individuals used hookah at a higher rate than their Hispanic and non-Hispanic white counterparts at ages 23-24. Future research is warranted to understand who is most at risk for nicotine and marijuana use, potential drivers of age-specific disparities in use, and the differential impact of these behaviors on various negative consequences and health outcomes (e.g., substance use disorders, poor
academic and job performance) for individuals of different sexes and racial/ethnic backgrounds.

Another important finding from this study is that both cigarette and ENDS use in the past 30 days are associated with increased odds of recent marijuana use across most ages. Interestingly, ENDS use in the past month was significantly associated with increased odds of recent marijuana use for ages 14 – 23 and the association was strongest at age 14. Cigarette use in the past month was not significantly associated with recent marijuana use at age 14, but was associated with increased odds of marijuana use between ages 15 – 24; this association was strongest at ages 17 and 24. Past-month hookah use was only associated with a slight increase in odds of marijuana use at ages 21 and 22. These findings suggest that recent use of ENDS and other vaping devices may be a particularly important indicator of concurrent marijuana use for young adolescents (i.e., age 14), whereas cigarette use remains a stronger indicator of other substance use for individuals ages 16 and older. Longitudinal research is necessary in order to examine how the association between cigarette, ENDS, and marijuana use may change over historical time, especially as 14 year olds in this cohort age into late adolescence and young adulthood.

2.3a Limitations and Future Directions

Despite the importance of these findings, several limitations must be considered in the interpretation of the results as presented. As previously alluded to, this study focused on cross-sectional prevalence estimates and associations between cigarette, ENDS, hookah and marijuana use as a function of age. As such, developmental and cohort/generational effects may be confounded. Future research should incorporate
contemporary waves of data and use longitudinal methods to disentangle historical time versus developmental effects. Relatedly, data from W3 are the most recently available, however, these data were collected in October 2015 through October 2016. Replication of cross-sectional age-trends using newer waves of data has the potential to shed light on the rapidly changing landscape of commercially available nicotine and marijuana delivery systems.

Longitudinal analyses are also critical in order to understand the impact of novel delivery systems on the prevalence and concurrent use of both substances over time. Longitudinal analyses would also allow researchers to understand temporal associations between cigarette, ENDS, hookah, and marijuana use, and better infer possible causal pathways. The current study is unable to examine transitions in substance use behaviors, specifically whether or not cigarette, ENDS, or hookah use leads to the uptake of marijuana use.

Another limitation of the current study is the inability to distinguish the specific marijuana delivery system used by the respondent due to the wording of the questionnaire item in the PATH Study. The variable for past-month marijuana use is based on reported use of any cannabis product (e.g., dried marijuana, concentrates, waxes, THC, hash oils) in a number of different delivery systems (e.g., blunts, vaping device, hookah). Future research should incorporate more detailed information regarding marijuana delivery system in order to comprehensively test the theory that shared characteristics of certain nicotine and marijuana delivery systems may be facilitating concurrent use of both substances.
Finally, the current measure of past-month cigarette, ENDS, hookah, and marijuana use is not based on any threshold of established use. As such, these indicators of past-month use could represent both experimentation (i.e., users who recently tried for the first time), and more established/current use (i.e., users who tried for the first time a while ago, but also used within the past month). This decision was made due to the scarcity of evidence regarding appropriate thresholds of established use for non-cigarette nicotine delivery systems like ENDS and hookah, particularly during adolescence. Future research is warranted to understand what is considered established use with regard to novel and increasingly popular nicotine delivery systems, and further, to tease apart the relationship marijuana and nicotine use among more established users.

2.3b Conclusions

This study provides important information regarding (1) developmental trends in recent cigarette, ENDS, hookah, and marijuana use, (2) age-specific disparities in use by sex and race/ethnicity, (3) age-varying associations between specific nicotine delivery system use and recent use of marijuana, and (4) age-specific moderation of these associations by sex and race/ethnicity. Important findings suggest that recent cigarette and ENDS use are both significantly associated with increased odds of marijuana use across most ages. Other factors above and beyond the shared characteristics of novel nicotine and marijuana delivery systems (e.g., vaping devices, bongs, and waterpipes) may be contributing to concurrent use. Even so, use of ENDS may be a particularly important indicator of concurrent nicotine and marijuana use for young adolescents (ages 14, 15), whereas cigarette use may be a more important indicator of concurrent use during young adulthood (age 24).
CHAPTER 3: Patterns of Nicotine Use among Young Adults Over Time: Findings from the PATH Study

Polytobacco use is increasingly common among adolescents and adults today. In 2004, approximately 7% of adolescents in a nationally representative sample reported using more than one tobacco product (Bombard et al., 2008) and prevalence of polytobacco use increased to 13% in 2015 (Singh et al., 2016). Rates of polytobacco use are also quite high among adults. Recent findings from wave one (W1) of the Population Assessment of Tobacco and Health (PATH) Study indicate that nearly 40% of adult tobacco users report the use of multiple tobacco products (Kasza et al., 2017). Of that 40%, nearly a quarter report the use of both combustible cigarettes and electronic nicotine delivery systems (ENDS) (Kasza et al., 2017). This particular combination is also prevalent in the National Adult Tobacco Survey, with 30% of adults reporting the use of cigarettes and ENDS in 2012 to 2014 (Sung et al., 2018).

Research has shown that young adults ages 18 to 24/25 are more likely to concurrently use two or more tobacco products compared to adolescents (US Department of Health and Human Services, 2014) and adults ages 25 and older (Backinger et al., 2008; Kasza et al., 2017). However, a critical gap in the literature remains regarding specific patterns of polytobacco use among young adults in particular, especially within the context of ENDS. As the use of ENDS is becoming more pervasive among young people in the United States today (Arrazola et al., 2015; Singh et al., 2016), the landscape of polytobacco use among adolescents and young adults is also likely to change. As such, research examining contemporary patterns of polytobacco use is increasingly important.
The use of multiple tobacco products has been linked to higher rates of nicotine dependence symptoms (Sung et al., 2018), as well as other substance use behaviors (Creamer, Portillo, Clendennen, & Perry, 2016) and substance use disorders (Cavazos-Rehg, Krauss, Spitznagel, Grucza, & Bierut, 2014). Further, increased exposure to the harmful constituents of e-liquids, tobacco smoke, and smokeless tobacco products have been linked to adverse health outcomes, including higher rates of several tobacco-related cancers and heart disease (Backinger et al., 2008; Bhatta & Glantz, 2019; Ferrence, Slade, Room, & Pope, 2000; Ndunda & Muutu, 2019; Vindhyal et al., 2019). It is critical to understand who is at risk for polytobacco use, as well as which combinations or patterns of product use are linked to negative outcomes like nicotine dependence and other substance use.

Person-centered statistical techniques such as latent class analysis (LCA; Collins & Lanza, 2010) allow researchers to capture heterogeneity in patterns of behavior within a given population. Specifically, LCA is able to identify common population subgroups that are characterized by unique combinations of substance use behaviors and assesses their prevalence within the population. LCA can also provide insight into which patterns of behavior are associated with a variety of sociodemographic factors and negative health outcomes; such information has the potential to improve the development of effective prevention and intervention efforts and public policies (Lanza & Rhoades, 2013). Latent transition analysis (LTA) is a longitudinal extension of LCA that allows researchers to characterize movement into and out of these population subgroups over time (Collins & Lanza, 2010). This is particularly useful in understanding the progression from single
product use to more diverse—and potentially more harmful—patterns of polytobacco use among young people.

Several studies have used person-centered approaches like LCA and LTA to understand polytobacco use and other substance use behaviors among adolescents (Gilreath et al., 2015; Harrell, Naqvi, Plunk, Ji, & Martins, 2017; Huh & Leventhal, 2016; Morean et al., 2016). However, these approaches have rarely been utilized in the study of young adult polytobacco use, particularly in the wake of the ENDS epidemic today. The purpose of this study was to address this critical gap in the literature in three ways. The goal of Aim 1 was to identify patterns of nicotine use among young adults ages 18 to 24 in the PATH Study. To that end, a latent class model was estimated based on lifetime use of five nicotine delivery systems at W1: combustible cigarettes, ENDS, hookah, cigars/cigarillos/filtered cigars, and smokeless tobacco. The goal of Aim 2 was to understand differences in these patterns of nicotine use based on sex, race/ethnicity, lifetime marijuana use, and nicotine dependence. A three-step approach for LCA with covariates was used to examine differences in these latent classes based on the aforementioned factors. Finally, the goal of Aim 3 was to examine changes in these patterns of nicotine use over time. A latent transition model estimated potential shifts in patterns of nicotine use from W1 to W2 of the PATH Study.

3.1 Method

3.1a Sample: The Population Assessment of Tobacco and Health (PATH) Study

Participants are young adults ages 18-24 from W1 and W2 of the PATH Study. The PATH Study is a nationally representative, longitudinal cohort study of adolescents and adults ages twelve and older (Hyland et al., 2016). W1 data were collected in 2013-
2014; 32,320 adults (49.5% female; 71.9% white; 15.4% Black; 10.2% other; 17.1% Hispanic; 28.2% 18-24 years old) were assessed. W2 data were collected in 2014-2015; 28,362 adults (50.5% female; 71.4% white; 15.7% Black; 10.3% other; 17.8% Hispanic; 28.8% 18-24 years old) were assessed. 26,447 of the individuals assessed in W2 were also assessed in W1. PATH was designed to assess tobacco use and other substance use behaviors based on the host, vector, agent, and environmental (HAVE) conceptual model. This is a common epidemiological framework that has been validated to assess tobacco control policies (Giovino, 2002) and the impact of ENDS more broadly (Garcia-Cazarin et al., 2018).

PATH randomly selected 150,000 households in the United States using a four-stage, stratified, address-based sampling design. The design oversampled tobacco users, young adults ages 18 to 24, and African-Americans. Data were collected in the home using Audio Computer-Assisted Self-Interviewing and Computer-Assisted Personal Interviewing systems. Sampling procedures and the protocol for data collection have been described in detail by Hyland et al., 2016 and in the user’s guides for the PATH public-use and restricted–use files (Hyland et al., 2016; United States Department of Health and Human Services et al., 2019).

The analytic sample for the current project includes young adults ages 18 to 24 who reported using at least one nicotine product in their lifetime. Subsetting the data in this way eliminated a large group of non-users in the latent class and latent transition models, allowing for a better examination of more typical patterns and transitions in product use among young adults who use nicotine. The final analytic sample included 6,399 young adults (47% Female; 53% non-Hispanic (NH) white, 14% NH Black, 24%
Hispanic, 9% NH multi-racial/other).

3.1b Indicators of Latent Class Membership

Lifetime (ever) use of five tobacco products were examined as indicators of latent class membership: combustible cigarettes, ENDS, hookah, cigars/cigarillos/filtered cigars (referred to as cigar products), and chewing tobacco/snuff/dip (referred to as smokeless tobacco). Indicators were created using information from several questionnaire items regarding general awareness of each product, as well as the use of each product in the lifetime. Participants were first asked: “Have you ever seen or heard of [product] before this study?” If yes, participants were then asked: “Have you ever used [product] such as [examples], even one or two times?” Response categories for each indicator were coded such that 1 = ever use of the nicotine delivery system and 2 = never used the delivery system in the lifetime, or had never seen or heard of the delivery system before the study.

The questionnaire item assessing ENDS use in W1 specifically referred to the use of first generation e-cigarettes (i.e., cigalikes such as NJOY, Blu). This item was updated in W2 to assess ENDS use more broadly; the W2 ENDS item referred to the use of e-cigarettes, e-cigars, e-pipes, e-hookahs, personal vaporizers, vape pens and hookah pens. Lifetime use of cigars, cigarillos, and filtered cigars were combined into one indicator of cigar product use due to the similarities between these products and the low rate of endorsement for each individual product. Similarly, use of chew, snuff, and dip, were combined into one indicator of smokeless tobacco use.

3.1c Covariates

Sociodemographic information including biological sex, race, and ethnicity were measured via self-report. Based on information regarding race and ethnicity (assessed
using separate questionnaire items), individuals were assigned to mutually exclusive racial/ethnic groups including NH white, NH Black, Hispanic, and non-Hispanic NH multi-racial/other. The NH multi-racial/other group included individuals of Asian, American Indian, and Native Hawaiian or Native Pacific Islander origins, as well as individuals who endorsed multiple categories for race. All demographic covariates were dummy coded such that 1 = yes and 0 = no; in the case of biological sex, 1 = female and 0 = male.

Lifetime use of marijuana was also examined. Participants were first asked if they had ever smoked part or all of a traditional cigar, cigarillo, or filtered cigar with marijuana in it (i.e., a blunt). If yes, lifetime (ever) use of marijuana was coded as 1. If no, participants were then asked if they had ever used marijuana, hash, THC, grass, pot, or weed. If yes, lifetime use of marijuana was coded as 1. If participants responded no to both questionnaire items, ever use of marijuana was coded as 0.
Nicotine dependence was assessed using ten items from the Wisconsin Inventory of Smoking Motives (WISDM; Piasecki, Piper, Baker, & Hunt-Carter, 2011; Piper et al., 2004) and the Nicotine Dependence Syndrome Scale (NDSS; Shiffman, Waters, & Hickcox, 2004). 24 nicotine dependence items are assessed in PATH. These items have been adapted from existing cigarette-specific nicotine dependence measures (WISDM, NDSS, DSM-IV Diagnostic Criteria) in order to assess dependence more broadly among a variety of tobacco users. Strong et al., (2017) used differential item functioning analyses to examine the validity of all 24 adapted measures in assessing and comparing nicotine dependence symptoms across all delivery systems and tobacco users. Findings suggest that 16 of the 24 items assessed in PATH are able to broadly and accurately assess nicotine dependence.

Buu, Hu, Piper, and Lin (2018) expanded on these findings and ultimately supported ten items for the assessment of nicotine dependence symptoms across delivery systems: eight WISDM items and two NDSS items. The ten items recommended by Buu, Hu, Piper, and Lin (2018) were averaged and rescaled to create a continuous measure of nicotine dependence ranging from 0 – 4, with 0 indicating no dependence symptoms reported and 4 indicating the highest level of dependence. Specific questionnaire items used to create the dependence measure for the current study are included in Appendix C. A binary measure assessing the experience of one or more nicotine dependence symptoms was also created, coded such that individuals endorsing any nicotine dependence symptom = 1 and individuals who did not endorse any symptoms = 0. Descriptive statistics are presented in Table 3.1.
Table 3.1. Frequencies and percentages [n (%)] for indicators of nicotine use, demographic characteristics, and covariates among young adults ages 18-24 in W1 and W2 of the PATH Study.

<table>
<thead>
<tr>
<th></th>
<th>W1 Overall N</th>
<th>W1; n (%)</th>
<th>W2 Overall N</th>
<th>W2; n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nicotine Use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combustible Cigarettes</td>
<td>6,397</td>
<td>5,172 (81%)</td>
<td>6,138</td>
<td>5,308 (83%)</td>
</tr>
<tr>
<td>ENDS</td>
<td>6,390</td>
<td>3,399 (53%)</td>
<td>5,673</td>
<td>3,990 (62%)</td>
</tr>
<tr>
<td>Hookah</td>
<td>6,396</td>
<td>4,423 (69%)</td>
<td>5,952</td>
<td>4,683 (73%)</td>
</tr>
<tr>
<td>Cigar Products</td>
<td>6,321</td>
<td>4,445 (69%)</td>
<td>5,881</td>
<td>4,668 (73%)</td>
</tr>
<tr>
<td>Smokeless Tobacco</td>
<td>6,379</td>
<td>1,429 (22%)</td>
<td>5,260</td>
<td>1,506 (24%)</td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>6,396</td>
<td>2,981 (47%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NH white</td>
<td>6,363</td>
<td>3,383 (53%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NH Black</td>
<td>6,363</td>
<td>886 (14%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>6,363</td>
<td>1,208 (24%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-racial/Other</td>
<td>6,363</td>
<td>922 (9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other W1 Covariates</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marijuana use</td>
<td>6,356</td>
<td>4,101 (64%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANY Dependence Symptoms</td>
<td>6,308</td>
<td>3,167 (49%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dependence Scale Score</td>
<td>6,308</td>
<td>Mean = 0.7; SD = 1.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note. Analytic Sample N = 6,399; sample consisted of young adults that have used nicotine in the lifetime.

3.1d Overall Analytic Plan

Statistical analyses proceeded in several steps. First, latent class analysis (LCA) was used to estimate patterns of nicotine use among young adults ages 18 to 24 at W1. Next, the “Bolck, Croon, and Hagenaars” (BCH) approach (Bolck, Croon, & Hagenaars, 2004) was used to examine differences in class membership based on several covariates including sex, race/ethnicity, lifetime use of marijuana, and nicotine dependence. Finally, latent transition analysis (LTA) was used to estimate transitions in patterns of nicotine use over time.

2.1e Estimating Patterns of Nicotine Use, W1 LCA (Aim 1)

PROC LCA (SAS Version 9.4; Lanza, Dziak, Huang, Wagner, & Collins, 2015) was used to estimate latent classes based on the lifetime use of five nicotine products:
combustible cigarettes, ENDS, hookah, cigar products, and smokeless tobacco. Models with one to five latent classes were estimated and compared in order to determine the

```sas
proc lca data=analysis;
  nclass 5;
  items evr_cig1 evr_ends1 evr_hook1 evr_cigar1 evr_smkls1;
  categories 2 2 2 2 2;
  seed 861551;
  nstarts 100;
run;
```

Fig. 3.1. Sample syntax for PROC LCA in SAS

optimal number of classes. Identification of each candidate model was confirmed using 100 sets of random starting values. Models with six or more classes could not be estimated due to limited degrees of freedom. The best fitting model was chosen based on Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and entropy. For both AIC and BIC, lower values indicate optimal balance between fit and parsimony. Entropy is an indicator of the level of certainty in model classification; values near 1.00 indicate high certainty. The interpretability of the item-response probability estimates for each solution were also examined carefully before selecting a final model to ensure that all latent classes were distinct and meaningful. Item-response probabilities reflect the degree to which each indicator is endorsed by members of each latent class. Example SAS syntax for a basic LCA model with 5 classes is presented in Figure 3.1.

3.1 If Estimating Differences in Class Membership, W1 (Aim 2)

After the optimal latent class model was selected, class membership probabilities, item-response probabilities, and posterior probabilities from the optimal model were saved in a SAS data file using the OUTPARAM and OUTPOST statements in PROC LCA. Posterior probabilities refer to the probability that each individual is classified in a
given class. The LCA Distal BCH SAS Macro (Dziak, Bray, & Wagner, 2017) was then used to estimate the proportion of individuals within each latent class corresponding to each covariate attribute. Binary covariates for sex, race/ethnicity, lifetime marijuana use, and nicotine dependence were examined. A continuous indicator of nicotine dependence (scale score, ten nicotine dependence items) was also examined. An omnibus Wald test was used to test significant differences in class membership based on each covariate; follow-up pairwise comparisons tested significant differences in the proportion or mean level of each covariate between each pair of classes (e.g., class 1 versus class 2, class 1 versus class 3, etc.) based on each covariate. Example SAS syntax for the BCH macro is presented in Figure 3.2.

3.1g Estimating Transitions in Patterns of Use – Latent Transition Analysis (Aim 3)

Finally, transitions in patterns of nicotine use were estimated from W1 to W2. Before examining a latent transition model, PROC LCA was used to verify a 5 class solution based on the same five indicators of lifetime nicotine use assessed at W2. Identification was confirmed and model selection followed the same processes as outlined in Aim 1; AIC, BIC, entropy, and the interpretability of all solutions were examined to determine the best fitting LCA model. Any between the latent class solutions
at W1 and W2 were examined.

Next, PROC LTA (SAS, Version 9.4; Lanza, Dziak, Huang, Wagner, & Collins, 2015) was used to estimate a latent transition model based on indicators of lifetime nicotine use at each wave (combustible cigarettes, ENDS, hookah, cigar products, and smokeless tobacco). Latent transition models with two through seven latent classes were estimated. Measurement invariance was imposed across times to ensure that transitions in latent class membership was meaningful. The optimal LTA model was selected based on AIC, BIC, the interpretability of each candidate model, and consistency with the model selected for the W1 LCA. Example SAS syntax for an LTA model is presented in Figure 3.3.

```
PROC LTA data=analysis;
 nstatus 5;
 ntimes 5;
 items evr_cig1 evr_ends1 evr_hook1 evr_cigar1 evr_smkls1 evr_cig2 evr_ends2 evr_hook2 evr_cigar2 evr_smkls2;
 categories 2 2 2 2 2 2 2 2 2 ;
 measurement times;
 seed 32456;
 run;
```

Fig. 3.3. Sample syntax for PROC LTA in SAS

### 3.2 Results

#### 3.2a Latent Class Model, W1 (Aim 1)

Based on AIC, BIC, entropy, and a careful interpretation of the W1 latent class solutions, a five-class model was selected. Model fit statistics for the W1 candidate models are presented in Table 3.2. Next, the five latent classes were interpreted and labeled based on item-response probability estimates. Item-response probabilities range
from 0 to 1, reflecting the degree to which each indicator is endorsed by members of each latent class.

Table 3.2. Model Fit Statistics, W1 Latent Class Model

<table>
<thead>
<tr>
<th>Classes</th>
<th>Log Likelihood</th>
<th>G^2</th>
<th>AIC</th>
<th>BIC</th>
<th>df</th>
<th>Entropy</th>
<th>% Seeds</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-18729.49</td>
<td>2800.26</td>
<td>2810.26</td>
<td>2844.08</td>
<td>26</td>
<td>1.00</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>-17703.98</td>
<td>749.23</td>
<td>771.23</td>
<td>845.64</td>
<td>20</td>
<td>0.59</td>
<td>100%</td>
</tr>
<tr>
<td>3</td>
<td>-17512.00</td>
<td>365.28</td>
<td>399.28</td>
<td>514.26</td>
<td>14</td>
<td>0.65</td>
<td>99%</td>
</tr>
<tr>
<td>4</td>
<td>-17453.40</td>
<td>248.09</td>
<td>294.09</td>
<td>449.66</td>
<td>8</td>
<td>0.73</td>
<td>46%</td>
</tr>
<tr>
<td>5</td>
<td>-17398.86</td>
<td>139.00</td>
<td>197.00</td>
<td>393.16</td>
<td>2</td>
<td>0.79</td>
<td>61%</td>
</tr>
</tbody>
</table>

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; analytic sample = 6,399.

Class prevalences and item-response probabilities for each latent class are presented in Table 3.3. Latent classes have been ordered from least to most prevalent. Classes one through three were distinguished by exclusive use of one nicotine delivery system. Class 1 represented 2% of the sample and was labeled ENDS Only. This class was characterized by a high probability of ever using ENDS, but a low probability of using all other delivery systems. Class 2 represented 10% of the sample and was labeled Hookah Only; young adults in this class had a high probability of ever using hookah, but a low probability of using all other delivery systems. Class 3 (19% of the sample) was labeled Cigarettes Only and was characterized by a high probability of ever using combustible cigarettes, but a low probability of using other delivery systems.

Classes 4 and 5 were characterized by the use of multiple nicotine delivery systems. Class 4 (23%) was labeled Combustibles Only; young adults in this class were characterized by a high probability of ever using cigarettes, hookah, and cigar products, but a low probability of using ENDS and smokeless tobacco. Class 5 (45%) was labeled Poly, No Smokeless; young adults in this class were characterized by a high probability of
ever using cigarettes, hookah, ENDS, and cigar products, but a low probability of using smokeless tobacco.

3.2b Differences in Latent Class Membership (Aim 2)

Next, the BCH approach was used to examine differences in latent class membership based on sex, race/ethnicity, lifetime marijuana use, and nicotine dependence. Omnibus test statistics and the percentage of young adults within each class corresponding to each covariate attribute are presented in Table 3.4. Omnibus Wald tests revealed significant differences in class membership based on all covariates of interest (p < 0.01).

Table 3.3 Class prevalences and item-response probabilities for the W1 latent class model.

<table>
<thead>
<tr>
<th>Class Prevalences</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENDS Only</td>
<td>2%</td>
<td>10%</td>
<td>19%</td>
<td>23%</td>
<td>45%</td>
</tr>
<tr>
<td>Hookah Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarettes Only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y 0.16</td>
<td>0.03</td>
<td>1.00</td>
<td>0.69</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>N 0.84</td>
<td>0.97</td>
<td>0.00</td>
<td>0.31</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>ENDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y 0.71</td>
<td>0.10</td>
<td>0.36</td>
<td>0.15</td>
<td>0.88</td>
<td></td>
</tr>
<tr>
<td>N 0.29</td>
<td>0.90</td>
<td>0.64</td>
<td>0.85</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>Hookah</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y 0.01</td>
<td>1.00</td>
<td>0.49</td>
<td>0.60</td>
<td>0.79</td>
<td></td>
</tr>
<tr>
<td>N 0.99</td>
<td>0.00</td>
<td>0.51</td>
<td>0.40</td>
<td>0.21</td>
<td></td>
</tr>
<tr>
<td>Cigar Products</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y 0.00</td>
<td>0.10</td>
<td>0.06</td>
<td>0.99</td>
<td>0.97</td>
<td></td>
</tr>
<tr>
<td>N 1.00</td>
<td>0.90</td>
<td>0.94</td>
<td>0.00</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Smokeless Tobacco</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y 0.32</td>
<td>0.01</td>
<td>0.06</td>
<td>0.13</td>
<td>0.38</td>
<td></td>
</tr>
<tr>
<td>N 0.68</td>
<td>0.99</td>
<td>0.94</td>
<td>0.87</td>
<td>0.62</td>
<td></td>
</tr>
</tbody>
</table>

Note. Item response probabilities were rounded to the nearest hundredth; those above 0.5 were bolded to indicate a high probability of endorsing use of each nicotine delivery system.
Figure 3.4 depicts the percentage of females, NH white, NH Black, and Hispanic individuals estimated to be in the ENDS Only class, the Hookah Only class, and the Cigarettes Only class. The majority of young adults in the ENDS Only class were males (63% male, 37% female) and NH white (52% NH white, 12% NH Black, and 13% Hispanic). Young adults in the ENDS Only class also had a 26% chance of ever using marijuana and a 20% chance of endorsing one or more nicotine dependence symptoms.

| Table 3.4. Percentage of young adults in each class corresponding to each covariate attribute. |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Omnibus  | Within-Class Percentage | 1 ENDS Only | 2 Hookah Only | 3 Cig. Only | 4 Combust. Only | 5 Poly, No Smkls. |
| Test Stat., df | Demographics |  |  |  |  |  |
|  | Female |  |  |  |  |  |
| 318.62, 4* | 37% | 67% | 64% | 48% | 35% |
|  | NH white |  |  |  |  |  |
| 122.84, 4* | 52% | 40% | 49% | 45% | 62% |
|  | NH Black |  |  |  |  |  |
| 166.50, 4* | 12% | 17% | 11% | 27% | 8% |
|  | Hispanic |  |  |  |  |  |
| 69.39, 4* | 23% | 32% | 31% | 22% | 20% |
|  | NH other |  |  |  |  |  |
| 15.78, 4* | 13% | 12% | 9% | 6% | 10% |
|  | Other Covariates |  |  |  |  |  |
|  | Marijuana use |  |  |  |  |  |
| 710.84, 4* | 26% | 34% | 42% | 66% | 82% |
|  | ANY Dependence Symptoms |  |  |  |  |  |
| 832.40, 4* | 20% | 10% | 41% | 27% | 76% |
|  | Dependence Scale Score |  |  |  |  |  |
| 1942.61, 4* | 0.30 | 0.05 | 0.55 | 0.22 | 1.20 |
|  |  | (0.07) | (0.01) | (0.03) | (0.03) | (0.03) |

Note. * = p < 0.01

- \(^a\) = All pairwise comparisons of the proportion of females in each class were significantly different (p < 0.01) except for Class 2 versus Class 3 and Class 1 versus Class 5.
- \(^b\) = Significant differences in the proportion of NH white individuals in Classes 2, 3, 4 versus Class 5 and Class 2 versus Class 3 (p < 0.01).
- \(^c\) = Significant differences in the proportion of NH Black individuals in Classes 1, 2, 3, 5 versus Class 4 and Class 3, 5 versus 2 (p < 0.01).
- \(^d\) = Significant differences in the proportion of Hispanic individuals in Classes 4, 5 versus Class 2 and Classes 4, 5 versus 3 (p < 0.01).
- \(^e\) = All pairwise comparisons of the proportion of individuals who have ever used marijuana in each class were significantly different (p < 0.01) except for Class 1 versus Class 2.
- \(^f\) = All pairwise comparisons of the proportion of individuals who reported one or more nicotine dependence symptoms were significantly different (p < 0.01) except for Class 1 versus Class 4.
- \(^g\) = All pairwise comparisons of the mean level of nicotine dependence symptoms were significantly different (p < 0.01) except for Class 1 versus Class 4.
Young adults in the Hookah Only class, however, were mostly female (33% male, 67% female). Members of this class were 40% NH white, 17% NH Black, and 32% Hispanic. Young adults in the Hookah Only class had a 34% chance of ever using marijuana and a 10% chance of endorsing one or more nicotine dependence symptoms. Young adults in the Cigarettes Only class were also mostly female (36% male, 64% female). Approximately half of this class was represented by NH white individuals (49% NH white, 11% NH Black, and 31% Hispanic). Young adults in the Cigarettes Only class had a 42% chance of ever using marijuana and a 41% chance of reporting one or more nicotine dependence symptoms.

Figure 3.5 depicts the percentage of young adults estimated to be in the Combustibles Only and Poly, No Smokeless classes corresponding to each covariate attribute. The majority of young adults in the Combustibles Only class were male (52% male, 48% female). Members of this class were 45% NH white, 27% NH Black, and 22% Hispanic. Young adults in the Combustibles Only class had a striking 66% chance of ever using marijuana and a 27% chance of reporting one or more nicotine dependence symptoms.

The majority of young adults in the Poly, No Smokeless class were also male (65% male, 35% female) and NH white (62% NH white, 8% NH Black, 20% Hispanic). Young adults in the Combustibles Only class had an even higher 82% chance of ever using marijuana and a 76% chance of reporting one or more nicotine dependence symptoms.

Pairwise comparisons revealed statistically significant differences in the percentage of young adults in each latent class given each covariate attribute. For
example, the proportion of females in the Cigarettes Only and Hookah Only classes were significantly higher than the proportion of females in the Combustibles Only, ENDS Only, and Poly, No Smokeless classes. The proportion of females was also higher in the Combustibles Only class compared to the ENDS Only and Poly, No Smokeless classes.

The proportion of NH white young adults was significantly higher in the Poly, No Smokeless class compared to the Hookah Only, Cigarettes Only, and Combustibles Only classes. Prevalence of NH whites was also significantly higher in the Cigarettes Only class compared to the Hookah Only class.

The proportion of NH Black young adults was significantly higher in the Combustibles Only class compared to any other class. Interestingly, prevalence of NH Blacks was also higher in the Hookah Only class compared to the Cigarettes Only and Poly, No Smokeless classes. Finally, the proportion of Hispanic young adults was significantly higher in the Cigarettes Only and Hookah Only classes compared to the Combustibles Only and Poly, No Smokeless classes.

Taken together, these results provide insight into the demographic makeup of each latent class, as well as the proportion of individuals that report marijuana use and nicotine dependence symptoms. Findings indicate that males and NH white young adults make up a greater proportion of ENDS Only, Combustibles Only, and Poly, No Smokeless Classes. Marijuana users are also more prevalent in the Combustibles Only and Poly, No Smokeless Classes.
### Class 1: ENDS Only

<table>
<thead>
<tr>
<th>Category</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>37%</td>
</tr>
<tr>
<td>NH white</td>
<td>52%</td>
</tr>
<tr>
<td>NH Black</td>
<td>12%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>13%</td>
</tr>
<tr>
<td>Marijuana Use</td>
<td>26%</td>
</tr>
<tr>
<td>Any Nicotine Dependence</td>
<td>20%</td>
</tr>
</tbody>
</table>

### Class 2: Hookah Only

<table>
<thead>
<tr>
<th>Category</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>67%</td>
</tr>
<tr>
<td>NH white</td>
<td>40%</td>
</tr>
<tr>
<td>NH Black</td>
<td>17%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>32%</td>
</tr>
<tr>
<td>Marijuana Use</td>
<td>34%</td>
</tr>
<tr>
<td>Any Nicotine Dependence</td>
<td>10%</td>
</tr>
</tbody>
</table>

### Class 3: Cigarettes Only

<table>
<thead>
<tr>
<th>Category</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>64%</td>
</tr>
<tr>
<td>NH white</td>
<td>49%</td>
</tr>
<tr>
<td>NH Black</td>
<td>11%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>31%</td>
</tr>
<tr>
<td>Marijuana Use</td>
<td>42%</td>
</tr>
<tr>
<td>Any Nicotine Dependence</td>
<td>41%</td>
</tr>
</tbody>
</table>

Fig. 3.4 Within-class demographics and percentages of individuals endorsing ever marijuana use and any nicotine dependence symptoms for the ENDS Only, Hookah Only, Cigarettes Only classes
<table>
<thead>
<tr>
<th>Class 4: Combustibles Only</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female</strong></td>
</tr>
<tr>
<td>NH white</td>
</tr>
<tr>
<td>NH Black</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Marijuana Use</td>
</tr>
<tr>
<td>Any Nicotine Dependence</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class 5: Poly, No Smokeless</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female</strong></td>
</tr>
<tr>
<td>NH white</td>
</tr>
<tr>
<td>NH Black</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Marijuana Use</td>
</tr>
<tr>
<td>Any Nicotine Dependence</td>
</tr>
</tbody>
</table>

Fig. 3.5 Within-class demographics and percentages of individuals endorsing ever marijuana use and any nicotine dependence symptoms for the Combustibles Only and Poly, No Smokeless Classes.
3.2c Latent Transition Model, W1 to W2 (Aim 2)

The final aim of this study was to examine changes in patterns of nicotine use over time. To that end, LTA was used to estimate potential shifts in patterns of nicotine use from W1 to W2. Prior to estimating the latent transition model, LCA was used to confirm that a five-class solution was optimal in W2. Model fit statistics for the W2 LCA candidate models are presented in Table 3.5. Based on AIC, BIC, entropy, and a careful interpretation of models with two to five latent classes, the five-class model was confirmed as the optimal solution.

<table>
<thead>
<tr>
<th>Classes</th>
<th>Log Likelihood</th>
<th>G²</th>
<th>AIC</th>
<th>BIC</th>
<th>df</th>
<th>Entropy</th>
<th>% Seeds</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-15108.23</td>
<td>2612.14</td>
<td>2622.14</td>
<td>2655.95</td>
<td>26</td>
<td>1.00</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>-14022.45</td>
<td>440.58</td>
<td>462.58</td>
<td>536.98</td>
<td>20</td>
<td>0.58</td>
<td>100%</td>
</tr>
<tr>
<td>3</td>
<td>-13887.08</td>
<td>169.84</td>
<td>203.84</td>
<td>318.83</td>
<td>14</td>
<td>0.64</td>
<td>100%</td>
</tr>
<tr>
<td>4</td>
<td>-13859.93</td>
<td>115.54</td>
<td>161.54</td>
<td>317.11</td>
<td>8</td>
<td>0.66</td>
<td>14%</td>
</tr>
<tr>
<td>5</td>
<td>-13839.21</td>
<td>74.10</td>
<td>132.10</td>
<td>328.25</td>
<td>2</td>
<td>0.70</td>
<td>23%</td>
</tr>
</tbody>
</table>

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; analytic sample = 6,399.

Careful examination of the W2 5-class model revealed a slight difference in latent class structure between the W1 and W2 5-class models. Most notably, the W2 model did not have a class that was characterized by exclusive combustible cigarette use. However, the absence of a Cigarettes Only class was not unexpected, as nicotine users are likely to transition out of single product use over time and polytobacco use is common during young adulthood (Backinger et al., 2008; Kasza et al., 2017; US Department of Health and Human Services, 2014). Instead, the W2 5-class model included a class that was characterized by a high probability of using cigarettes (item response probability = 0.9996) and a moderate probability of using hookah (item
response probability = 0.5575) in the past year. Four of the original W1 classes were retained in the W2 LCA model: ENDS Only, Hookah Only, Combustibles Only, and Poly, No Smokeless. Class prevalences and item-response probabilities for the 5-class solution at W2 are presented in Appendix C. Further differences in the latent class solutions for W1 and W2 and implications for the identification of the latent transition model are discussed in greater detail within the discussion section of this chapter.

Given the high degree of overlap in latent class interpretations for W1 and W2, a latent transition model was estimated in order to examine the incidence of transitions in lifetime nicotine use over time from W1 to W2. Measurement invariance was imposed across waves to ensure that the meaning of each latent class was consistent at both time points. Model fit statistics for the latent transition model are presented in Table 3.6. Based on the optimal latent class solutions for W1 and W2, as well as a careful interpretation of candidate models with two through seven latent classes, a five-class latent transition model was selected. Identification was confirmed by running the five-class model with 100 random seed values. Eight percent of the starting values converged on the five-class model as presented. A six-class model was also examined, however even fewer (5%) of the 100 seed values converged on the same solution.

<table>
<thead>
<tr>
<th>Classes</th>
<th>Log Likelihood</th>
<th>$G^2$</th>
<th>AIC</th>
<th>BIC</th>
<th>df</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>-29298.18</td>
<td>17301.87</td>
<td>17327.87</td>
<td>17415.8</td>
<td>1010</td>
</tr>
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<td>3</td>
<td>-27581.55</td>
<td>13868.61</td>
<td>13914.61</td>
<td>14070.18</td>
<td>1000</td>
</tr>
<tr>
<td>4</td>
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<td>11090.43</td>
<td>11160.43</td>
<td>11397.17</td>
<td>988</td>
</tr>
<tr>
<td>5</td>
<td>-25310.12</td>
<td>9691.84</td>
<td>9789.84</td>
<td>10121.27</td>
<td>974</td>
</tr>
<tr>
<td>6</td>
<td>-24267.35</td>
<td>7240.21</td>
<td>7370.21</td>
<td>7809.86</td>
<td>958</td>
</tr>
<tr>
<td>7</td>
<td>-23896.77</td>
<td>6499.05</td>
<td>6665.05</td>
<td>7226.46</td>
<td>940</td>
</tr>
</tbody>
</table>

Note. AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; analytic sample = 6,399.
Next, the five latent classes were interpreted and labeled based on item-response probability estimates. Similar to the parameter estimates in the LCA model, item-response probabilities range from 0 to 1 and reflect the degree to which each indicator is endorsed by members of each latent class. Item-response probabilities, class prevalences, and transition probabilities are presented in Table 3.7. Three classes that were present in the W1 and W2 latent class solutions were retained in the LTA model: Hookah Only, Combustibles Only, and Poly, No Smokeless.

Class 1 was labeled *Hookah Only*: young adults in this class had a high probability of endorsing exclusive hookah use in their lifetime and a low probability of using any other nicotine delivery system. Young adults in Class 2 were characterized by a high probability of ever using cigarettes, hookah, and cigar products, but a low probability of using ENDS and smokeless tobacco. As such, Class 2 was labeled *Combustibles Only*. Class 3 was labeled *Poly + Smokeless*: young adults in this class had a high probability of endorsing use of all five nicotine delivery systems in their lifetime. The Poly + Smokeless class was unique to the LTA model that pooled information across two times. Young adults in Class 4 were characterized by a high probability of using most nicotine delivery systems with the exception of hookah; Class 4 was labeled *Poly, No Hookah*. This class was also unique to the LTA model. Class 5 was labeled *Poly, No Smokeless*: young adults in this class had a high probability of using most nicotine delivery systems with the exception of smokeless tobacco.

Classes characterized by the use of four or more nicotine delivery systems were the most prevalent at both waves. The most common class at W1 was Poly, No Hookah (25%), followed by Poly, No Smokeless (24%), Poly + Smokeless (21%), Combustibles
Only (17%), and Hookah Only (14%). At W2, however, the most common class was Poly, No Smokeless (32%), followed by Poly + Smokeless (22%), Poly, No Hookah (21%), Combustibles Only (12%), and Hookah Only (12%).

The transition probability matrix presented at the bottom of Table 3.6 demonstrates the likelihood of transitioning from one latent class to another between W1 and W2. Rows represent class membership at W1 and columns represent class membership at W2.
membership at W2. Values along the diagonal of the matrix represent the likelihood of belonging to the same class at both waves. Values off the diagonal represent the likelihood of transitioning into a different class at W2.

Young adults in the Hookah Only class at W1 had an 89% chance of belonging to the same class at W2. These individuals also had a 6% chance of transitioning into the Combustibles Only class. In other words, young adults who exclusively used hookah at W1 had a 6% chance of starting to use cigarettes and cigar products by W2. Similarly, young adults in the Hookah Only class had a 5% chance of transitioning into the Poly, No Smokeless class (i.e., also using cigarettes, cigar products, and ENDS) at W2.

Young adults in the Combustibles Only class at W1 had a 68% chance of remaining in the same class at W2. Interestingly, members of this class at W1 had a 31% chance of transitioning into the Poly, No Smokeless class at W2. In other words, young adults who had only ever used combustible products at W1 had a 31% chance of starting to use ENDS by W2. As expected, members of the Poly + Smokeless class at W1 had 100% chance of remaining in the same class at W2.

Young adults in the Poly, No Hookah class at W1 had an 87% chance of remaining in the same class at W2. These individuals had an 11% chance of transitioning to the Poly, No Smokeless class (i.e., adding hookah) and a 2% chance of transitioning to the Poly + Smokeless class (i.e., using all nicotine delivery systems) at W2. Finally, members of the Poly, No Smokeless class at W1 had a 97% chance of remaining in the same class and a 3% chance of also having used smokeless tobacco at W2.

Taken together, these findings provide insight into how young adults’ use of a variety of nicotine delivery systems progresses over one year. The most substantial
change over time was detected from the Combustibles Only class. A very high percentage (31%) of these individuals began using ENDS in the subsequent year.

3.3 Discussion

The purpose of this study was to (1) identify patterns of nicotine use among young adults ages 18 to 24, (2) understand differences in these patterns of use based on sex, race/ethnicity, lifetime marijuana use, and nicotine dependence, and (3) examine transitions in patterns of nicotine use over time. First, LCA was used to identify latent classes of nicotine use in W1 of the PATH Study based on lifetime use of five delivery systems: combustible cigarettes, ENDS, hookah, cigar products, and smokeless tobacco. Next the BCH approach was used to examine differences in these latent classes based on sociodemographic characteristics, marijuana use, and nicotine dependence symptoms. Finally, LTA was used to estimate transitions in patterns of nicotine use from W1 to W2 of the PATH Study.

Aim 1 revealed that young adults ages 18 to 24 in W1 of the PATH Study were characterized by five distinct patterns of nicotine use: ENDS Only (2%), Hookah Only (10%), Cigarettes Only (19%), Combustibles Only (23%), and Poly, No Smokeless (45%). Interestingly, the most common patterns of lifetime nicotine use involved the use of three or more delivery systems. The Combustibles Only and Poly, No Smokeless classes accounted for approximately 68% of the sample, whereas classes characterized by the exclusive use of one delivery system accounted for approximately 31%. This finding parallels existing research that suggests nearly half of current young adult tobacco users report concurrently using more than one nicotine delivery system (Agaku et al., 2014;
As the W1 latent class model presented in this study was based on patterns of *lifetime* nicotine use, variation in the recency, frequency (i.e., how often), and intensity (i.e., how much) of these nicotine use behaviors was not captured. As such, it is unclear if young adults in each class only tried the delivery system(s) once or twice, or if they are regular/established users. Future research should incorporate indicators of past 30-day use in order to capture more recent behavior, as well as indicators of frequency and intensity (e.g., daily/weekly use, number of puffs, number of cartridges/containers used, etc.).

Nevertheless, these findings demonstrate that patterns of polytobacco use are common by the time individuals reach age 18. The gaining popularity of ENDS among adolescents, coupled with increases in the abuse liability of pod mods such as JUUL (Barrington-Trimis & Leventhal, 2018), may lead to further increases prevalence of polytobacco use during young adulthood. As such, public policy and intervention efforts should focus on adolescents and should target experimentation and regular use of multiple delivery systems comprehensively.

Another key finding from Aim 1 was that the ENDS Only and Hookah Only classes were the least common among young adults at W1 of the PATH Study. It is important to note that W1 data were collected in 2013-2014, prior to the dramatic shift in ENDS use among young people. Further research is warranted to understand patterns of use in more contemporary waves of the PATH data. It is speculated that exclusive ENDS use might be more prevalent among young adults in recent years. However, it is likely
that poly-use classes would still be highly prevalent as initiation and experimentation with nicotine is most common prior to age 19 (Bonnie, Stratton, & Kwan, 2015).

Aim 2 revealed several important differences in latent class membership based on sex, race/ethnicity, lifetime marijuana use, and nicotine dependence. Most notably, the proportion of young adult males was significantly higher within classes characterized by the use of multiple nicotine delivery systems compared to classes characterized by the exclusive use of one. These findings align with prior research that suggests males are more likely to be polytobacco users (Agaku et al., 2014; Gilreath et al., 2015; Kasza et al., 2017; Soneji et al., 2016).

The proportion of NH whites was also significantly higher in the Poly, No Smokeless class compared to the proportion of NH whites in other classes. This finding differs from existing literature suggesting that NH white adults are less likely to report the use of multiple tobacco products compared to racial and ethnic minority groups (Kasza et al., 2017; King, Dube, & Tynan, 2012). There are two potential explanations for this difference. First, much of the existing literature on polytobacco use among adults focuses on current, established users rather than lifetime users. Second, pairwise comparisons in the BCH approach are testing differences in the within class proportions of NH white for Class 1 vs. 2, Class 1 vs. 3, etc., rather than comparing NH white to NH Black and Hispanic. Findings from a different approach (i.e., LCA with covariates rather than BCH approach) might align more closely with existing literature.

Taken together, differences in polytobacco use by sex and race/ethnicity suggest that certain population subgroups may be at increased risk for the development of nicotine dependence, other substance use behaviors, and the associated negative health
consequences. For example, the Poly, No Smokeless class was identified as being the “riskiest” in terms of lifetime marijuana use and nicotine dependence symptoms. Males and NH white young adults were most prevalent in this class, and as such, might be at a greater risk. These sociodemographic subgroups might benefit from prevention and intervention efforts targeting multiple forms of tobacco use.

Another key finding from Aim 2 was that the proportion of marijuana users in the Combustibles Only and Poly, No Smokeless classes were significantly higher than the proportion of marijuana users in other classes. Interestingly, the only pairwise comparison for lifetime marijuana use that was not statistically significant was between the Hookah Only and the ENDS Only classes. There are several potential explanations for this finding. First, the Combustible only and Poly, No Smokeless classes are the only classes characterized by cigar product use. The use of cigars is highly linked to blunt use among young adults (Delnevo, Bover-Manderski, & Hrywna, 2011); blunts refer to hollowed out cigars that are filled with marijuana. Relatedly, the current study utilized data that were collected prior to the dramatic increase in the popularity of ENDS (Arrazola et al., 2015) and vaping marijuana (Knapp et al., 2019). As such, marijuana users within this cohort may be using blunts rather than vaping cannabis products, contributing to these differences in latent class membership.

Finally, important findings from Aim 3 demonstrated that young adults who report lifetime use of cigarettes, hookah, and cigar products at W1 have a 31% chance of transitioning into the Poly, No Smokeless class at W2. In other words, these individuals have a relatively high chance of starting to use ENDS between W1 and W2. Based on these analyses, it is unclear if these young adults are introducing ENDS as a harm
reduction strategy, or if they are adding ENDS to their existing repertoire without reducing their use of other delivery systems. The former would result in a net decrease in nicotine exposure, while the later would result in a net increase. Future research should incorporate indictors of frequency and intensity of nicotine use to better understand the uptake of ENDS and the impact on nicotine exposure as well as symptoms of dependence.

3.3a Limitations and Future Directions

Despite the importance of these findings, several limitations must be considered in the interpretation of the results as presented. As mentioned above, data from W1 of the PATH study were collected in 2013-2014 and data from W2 were collected in 2014-2015. Future research should replicate these findings with more contemporary waves of PATH data as they are made available in order to examine the most up-to-date patterns of polytobacco use.

It is also important to note that although a five-class model was confirmed as most optimal at both W1 and W2, the solutions looked slightly different between years. Most notably, the W2 model did not have a Cigarettes Only class. One explanation is that young adults at W1 had transitioned into more diverse patterns of use by W2 and are therefore not well represented by a latent class characterized by exclusive combustible cigarette use. Another explanation is that there were more opportunities for polytobacco use at W2 given the rapidly changing landscape of commercially available products, and as such, young adults at W2 were better characterized by several distinct poly-use classes (e.g., Cigarettes + Hookah, Combustibles Only, Poly, No Smokeless).

Nonetheless, measurement differences between the optimal W1 and W2 latent
class solutions likely impacted the interpretation of the latent classes presented in the LTA model and merit further study. It is important to highlight that only three of the original classes present in the W1 and W2 latent class solutions were retained in the LTA model: Hookah Only, Combustibles Only, and Poly, No Smokeless. Two unique classes emerged in the LTA model that were not present at either wave independently: Poly + Smokeless and Poly, No Hookah. This resulted in a limited ability to infer about transitions from single- to poly-use between waves, as only one class was characterized by single product use. Future research is necessary in order to address this critical gap in the literature more comprehensively.

Interestingly, the most sizeable transition in use was observed among two classes that were identified in both the W1 and W2 five-class models. Members of the Combustibles Only class at W1 had a 31% chance of transitioning into the Poly, No Smokeless class at W2. However, the LTA model as presented should also be interpreted with caution, as inconsistencies in latent class structure across waves warrant further investigation. Future research should involve an in-depth exploration of measurement invariance between W1 and W2 before strong conclusions can be made regarding transitions in patterns of use over time. Further, as additional waves of data from the PATH study are released, it will be important to examine measurement invariance across a longer period of time amidst the backdrop of rapidly changing laws and norms related to tobacco products.

3.3b Conclusions

This study provides important information regarding common patterns of tobacco use among young adults in 2013/2014 and differences in these patterns of use based on
sex, race/ethnicity, lifetime marijuana use, and nicotine dependence. Transitions in common patterns of young adult tobacco use were also examined across one year. Important findings suggest that polytobacco use is common by young adulthood, and further, that sex and racial/ethnic disparities exist in these poly-use classes. Additionally, the most prevalent transition in use over time was detected among young adults who report lifetime use of cigarettes, hookah, and cigar products at W1. These individuals had a relatively high chance of starting to use ENDS in the subsequent year (i.e., transitioning into the Poly, No Smokeless class). However, findings from the LTA model are preliminary and further research is necessary in order to make more substantial conclusions about transitions in patterns of young adult tobacco use. Taken together, these findings suggest that polytobacco use is common by young adulthood, and early intervention is key in preventing nicotine dependence, as well as other health consequences associated with increased exposure to nicotine.
Chapter 4: Discussion and Future Directions

The purpose of this dissertation was threefold. First, chapter one aimed to describe electronic nicotine delivery systems (ENDS) and the correlates and consequences associated with their use among adolescents and young adults in the United States. Next, chapters two and three aimed to elucidate patterns and trends in ENDS use among young people within the context of other nicotine delivery systems. Finally, sociodemographic differences in these patterns and trends, as well as the association between nicotine and marijuana use, were examined in each chapter. The key points from each chapter are summarized below; important findings regarding disparities in use and the link between nicotine and marijuana use are also integrated and discussed.

As noted in chapter one, the term ENDS refers to a variety of battery-powered nicotine delivery systems that heat a solution containing many harmful and potentially harmful constituents into an aerosol that is inhaled by the user (Cahn & Siegel, 2011; Callahan-Lyon, 2014; Grana, Benowitz, & Glantz, 2014; Standford Medicine, 2019). Four generations of ENDS have evolved since the devices first hit the market in 2006-2007. First generation devices resemble combustible cigarettes in their shape and size. Second generation devices (i.e., vape pens, hookah pens) contain larger, rechargeable batteries and are able to be refilled with a variety of flavored e-liquids. Third generation devices (i.e., mods, vape mods, box mods) are available in various shapes and sizes, and often have customizable heating elements and batteries with adjustable voltage (Grana et al., 2014; Truth Initiative, 2018).
The current generation of ENDS (i.e., pod mods) resemble USB drives in their shape and size (Barrington-Trimis & Leventhal, 2018; Truth Initiative, 2018). Pod mods like JUUL contain far greater nicotine per mL compared to earlier generations of ENDS (Goniewicz et al., 2018). It is speculated that the recent dramatic spike in adolescent ENDS use can be attributed to the introduction of pod mods because of their high nicotine content, appealing flavor options, and small design that is easy to conceal (Barrington-Trimis & Leventhal, 2018; Kavuluru et al., 2019). This is concerning, because ENDS use among young people has been linked to the uptake of combustible cigarette smoking and other tobacco product use (Huh & Leventhal, 2016; Lanza, Russell, & Braymiller, 2017; Leventhal et al., 2015a; Primack, Soneji, Stoolmiller, Fine, & Sargent, 2015; Soneji et al., 2017).

Rates of past 30-day ENDS use surpassed combustible cigarette use among adolescents in 2014 (Arrazola et al., 2015); prevalence of ENDS use has remained considerably higher than cigarette use among individuals ages 12 to 17. Young adults ages 18 to 24, however, use ENDS at much lower rates and combustible cigarettes remain the most popular nicotine delivery system within this population (Wang, Asman, et al., 2018). However, much of the work examining nicotine use among adults focuses on current and established tobacco users. New evidence suggests that young adulthood may represent a time of increased initiation and experimentation with ENDS use rather than a period characterized by daily or weekly, established use (Perry et al., 2018).

Current trends in ENDS and other nicotine use behaviors have been examined by age categories (i.e., adolescents ages 14 to 17 compared to young adults ages 18 to 24) rather than examining how these behaviors change continuously across development.
Based on existing literature, it is understood that adolescents are particularly vulnerable to ENDS use. However, precise information about exactly what ages are the most vulnerable (i.e., exactly when these sharp increases in prevalence occur) could ultimately improve tobacco control efforts, protect young people from the development of addiction, and reduce the overall impact of nicotine use on the United States.

3.1 Elucidating Age-Related Trends in Nicotine and Marijuana Use

Chapter two examined these nuanced age-trends in nicotine use among adolescents and young adults ages 14 to 24. Time-varying effect modeling (TVEM) was used to examine the age-varying prevalence of past 30-day ENDS, combustible cigarette, hookah, and marijuana use in the most recent wave of data from the Population Assessment of Tobacco and Health (PATH) Study. Age-varying associations between marijuana use and the use of each nicotine delivery system were also examined.

Intercept-only TVEMs indicated that during 2015/2016, past 30-day use of both nicotine and marijuana generally increased from ages 14 to 24 and peaked during young adulthood. The use of ENDS, cigarettes, and marijuana varied strongly across continuous age and followed distinct trends. Interestingly, the age-trends for past 30-day ENDS use and marijuana use were nearly identical from ages 14 to 17; a sharp increase in the prevalence of both substances was observed after age 16. Among those over age 18, rates of marijuana use were consistently higher than ENDS and hookah use. Prevalence of past 30-day cigarette use also increased considerably following age 16; after age 20, rates were consistently higher than ENDS, hookah, and marijuana use.

This study revealed that in 2015/2016, a significant age-varying association between past 30-day ENDS and marijuana use. ENDS use was significantly related to
marijuana use for individuals ages 14 to 23. The strength of this association was strongest for 14 year-olds; odds of recent marijuana use were nearly 8 times higher among individuals who used ENDS at age 14. Interestingly, this association was moderated by race/ethnicity. Compared to whites, non-Hispanic Black individuals had significantly higher odds of reporting marijuana use in the past month given ENDS use at ages 14 and 15. Hispanic individuals also had higher odds of reporting marijuana use in the past month given ENDS use for ages 15 thorough 18. The relationship between ENDS and marijuana use was not moderated by sex.

A significant age-varying association also was found between past 30-day cigarette use and marijuana use for individuals ages 15 to 24. This association was strongest for 17 year-olds; odds of recent marijuana use were 5.5 times higher among individuals who used cigarettes at age 17. The relationship between cigarette and marijuana use was not moderated by race/ethnicity or sex. Overall, recent ENDS and cigarette use are linked to recent marijuana use across most ages. However, ENDS use might be a particularly important indicator of concurrent nicotine and marijuana use for young adolescents, whereas cigarette use might be more indicative of concurrent nicotine and marijuana use during young adulthood.

It is important to note that age and historical time are confounded in this study to a great extent. It may be tempting to interpret the findings from this study as being developmental in nature. However, given the speed with which the prevalence of ENDS use is changing, it is perhaps more likely that these age-trends during adolescence provide a glimpse of what’s to come as these individuals age into young adulthood. As such, it is increasingly important to understand patterns and trends in nicotine use among
young adults, specifically within the context of ENDS.

3.2 Patterns of Nicotine Use among Young Adults over Time

Chapter three examined patterns and transitions in nicotine use among young adults aged 18 to 24 in Wave 1 (W1) and Wave 2 (W2) of the PATH Study. Latent class analysis (LCA; Collins & Lanza, 2010) was used to estimate underlying patterns of use based on lifetime use of five nicotine delivery systems: combustible cigarettes, ENDS, hookah, cigars/cigarillos/filtered cigars, and smokeless tobacco. The “Bolck, Croon, and Hagenaars” (BCH) approach (Bolck et al., 2004) approach was used to examine differences in these latent classes based on sex, race/ethnicity, lifetime marijuana use, and nicotine dependence. Finally, latent transition analysis (LTA; Collins & Lanza, 2010) was used to estimate potential shifts in patterns of nicotine use from W1 to W2.

LCA demonstrated that young adults ages 18 to 24 were best represented by five distinct patterns of nicotine use: ENDS Only (2%), Hookah Only (10%), Cigarettes Only (19%), Combustibles Only (23%), and Poly, No Smokeless (45%). As expected, the Poly, No Smokeless class was the “riskiest” class in that the proportion of young adults reporting symptoms of nicotine dependence and had ever used marijuana were highest within this class compared to other classes. The Combustibles Only class had similarly high proportions of these individuals.

The prevalence of young adult males was significantly higher within the ENDS, Combustibles Only, and Poly, No Smokeless classes compared to other classes. The proportion of NH whites was also significantly higher in the Poly, No Smokeless class compared to other classes. As such, these population subgroups may be at increased risk for the negative health consequences associated with excessive nicotine exposure,
concurrent marijuana use behaviors, and nicotine dependence. LTA demonstrated that the Combustibles Only class could also be considered a high risk class, as young adults who report lifetime use of cigarettes, hookah, and cigar products at W1 had a 31% chance of transitioning into the Poly, No Smokeless class at W2. In other words, these individuals have a relatively high chance of starting to use ENDS between W1 and W2. Young adults in the Poly, No Hookah class at W1 also had an 11% chance of transitioning to the Poly, No Smokeless class (i.e., adding hookah). However, given subtle but potentially important differences in the measurement and interpretation of latent classes across waves, findings regarding transitions in patterns of young adult tobacco use should be interpreted cautiously. Further attention to measurement differences in use patterns, particularly with a rapidly changing social backdrop, is a necessary next step.

Taken together, findings from chapter three demonstrate that patterns of poly-use are quite common by the time nicotine users reach young adulthood, and further, that sex and racial/ethnic disparities exist in these poly-use classes. This suggests early intervention is key in preventing nicotine dependence, as well as other health consequences associated with increased exposure to nicotine. Future research using more contemporary, national data is warranted in order to understand how comprehensive patterns of nicotine use might differ during adolescence, as well as how these patterns might transition into poly-use over time.

Several latent class and latent transition models of adolescent nicotine use have been examined to date. Most notably, Gilreath et al., (2015) demonstrated that Californian adolescents in 2014 were best represented by four distinct patterns of use nicotine use behaviors: non-users (72%), polytobacco experimenters (13.9%), e-cigarette
and hookah users (8%) and poly tobacco users (5.6%). The authors concluded that e-cigarettes and hookah were being used regularly by Californian adolescents who did not experiment with or use other tobacco products. But these product were also likely to be used in combination with cigarettes, cigars, and smokeless tobacco (Gilreath et al., 2015).

Huh & Leventhal (2016) used LTA to model transitions in patterns of nicotine use from 2013 to 2014 in a similar sample of Californian adolescents. Comparable patterns of use were identified at both waves: non-users, e-cigarette/hookah users, and polytobacco users. Interestingly, adolescents in the e-cigarette/hookah use class at W1 had a 19% chance of transitioning into polytobacco use by W2. This transition was even more likely than a transition from no-use to e-cigarette/hookah use (13%). The authors concluded that the use of increasingly popular alternative nicotine delivery systems such as e-cigarettes and hookah could be an intermediate between non-use and poly-tobacco use (Huh & Leventhal, 2016).

Given that these findings represent adolescents in California from 2013-2014, it is speculated that patterns of nicotine use might look slightly different in more contemporary, national samples. The dramatic spike in adolescent ENDS use following 2014 suggests that a prevalent class of exclusive ENDS users is likely to emerge in more contemporary data (rather than e-cigarette/hookah class). This class is expected to be particularly likely to transition to poly-use over time. Future research is necessary to determine if the prevention of ENDS use among youth could reduce polytobacco use and the overall impact of nicotine on the United States.
3.3 Integrating Findings on Sociodemographic Disparities in Nicotine Use Behaviors

Across both empirical studies presented in this dissertation, important findings emerged regarding differences in patterns and trends in nicotine use by demographic characteristics such as sex and race/ethnicity. Findings from chapter two demonstrate that sex differences in rates of nicotine and marijuana use vary by age. In 2015/2016, rates of past 30-day ENDS, cigarette, and hookah use were similar for males and females during adolescence, however, prevalence was higher for males compared to females after age 18. Interestingly, a crossover effect was observed for the prevalence past 30-day marijuana use. Rates of marijuana use were higher for females compared to males at ages 16 and 17, but prevalence was higher for males after age 19.

Further, evidence from chapter three indicates that the proportion of young adult males was higher within latent classes characterized by the use of multiple nicotine delivery systems, as well as exclusive ENDS use. Taken together, findings from both chapters are generally consistent with prior research. Males seem to be more vulnerable the use of ENDS, as well as polytobacco use (Arrazola et al., 2015; Camenga et al., 2014; Gilreath et al., 2015, Johnston, O’Malley, Miech, Bachman, & Schulenberg, 2016; Rigotti, Lee, & Wechsler, 2000; Singh et al., 2016). Thus, this population may be at increased risk for the development of nicotine dependence and other negative health outcomes.

Chapter two also demonstrated that racial/ethnic differences in rates of nicotine use also vary by age. Past 30-day cigarette and ENDS use were higher for non-Hispanic (NH) whites compared to NH Blacks and Hispanics across ages 15 to 18. Between ages 17 and 22, rates of ENDS and cigarette use were generally higher among both NH whites
and Hispanics compared to NH Blacks. Lanza, Russell, and Braymiller (2017) reported similar findings among adolescents in the National Youth Tobacco Survey. However, prevalence of cigarette and ENDS use were actually significantly higher among young Hispanic adolescents (ages 13 and 14) versus their white and NH Black age-counterparts. Further, results from chapter three indicate that the proportion of NH white young adults is higher within classes characterized by exclusive ENDS use and the use of multiple delivery systems compared to both classes. Taken together, findings from these studies suggest that NH white and Hispanic young people may be most at risk for the development of nicotine dependence and other health consequences related to cigarette, ENDS and polytobacco use.

3.4 Conclusions

In December, 2018, the US Surgeon General declared vaping among youth an epidemic, calling to action teachers, parents, health professionals and policy makers to protect young people from the harms of ENDS use and nicotine addiction. This declaration came in the wake of a nearly 80% increase in ENDS use among high schoolers in the United Stated from 2017 to 2018 (Cullen et al., 2018). There is a strong body of evidence demonstrating that adolescents are particularly vulnerable to ENDS use, and further, that ENDS use is associated with subsequent initiation of cigarettes and other tobacco products (Arrazola et al., 2015; Barnett, Forrest, Porter, & Curbow, 2014; Cobb, Ward, Maziak, Shihadeh, & Eissenberg, 2010; Cobb, Byron, Abrams, & Shields, 2010; Johnston, O’Malley, Miech, Bachman, & Schulenberg, 2016; Primack, Walsh, Bryce, & Eissenberg, 2009; Singh et al., 2016). However, less is known about precisely when
young people are most at risk for the onset of ENDS use and progression to patterns of polytobacco use in the context of increasingly popular pod mod devices like JUUL.

The landscape of marijuana use in the United States is also changing rapidly alongside the ENDS epidemic. As of May, 2019, 10 states have legalized recreational marijuana use among individuals ages 21 and older. New evidence indicates that changes in marijuana legislation have been linked to marijuana use onset among minors, as well as increased odds of marijuana use and dependence among those over age 21 (Center for Behavioral Health Statistics and Quality, 2015; Wen et al., 2015). As such, it is increasingly important to understand patterns of marijuana use among adolescents and adults today. Given that patterns of nicotine and marijuana co-use have been widely documented among adolescents and young adults (Cohn et al., 2015, Mohler-Kuo, Eun Lee, & Wechsler, 2003; Nichter, Nichter, Carkoglu, & Lloyd-Richardson, 2010; Wechsler, Dowdall, Maenner, Gledhill-Hoyt, & Lee, 1998), it is reasonable to be believe that changes in the legalization of recreational marijuana could also impact the ENDS epidemic. Decreases in the perceived risks associated with both marijuana and ENDS use, as well as the increasing availability of specific delivery systems that can be used to consume both substances (e.g., vaping devices, waterpipes), might result in the perfect storm for increased rates of concurrent nicotine and marijuana use behaviors among young people. As such, it is imperative to understand population subgroups who may be most at risk for using ENDS, other tobacco products, and marijuana and at what ages this risk is greatest.

This dissertation provided detailed information regarding specific age-related trends in nicotine and marijuana use among adolescents and young adults, as well as
patterns and transitions in polytobacco use. Important sociodemographic differences were also examined in order to understand precisely who at risk for engaging in particular combinations of these substance use behaviors, and at what ages. Findings from chapters two and three demonstrate complex new knowledge that can be gained from existing national data such as the PATH Study. First, TVEMs revealed that age 16 might be a critical age for the onset of past-month cigarette, ENDS, and marijuana use, and further, that recent cigarette and ENDS use were associated with increased odds of marijuana use across the majority of adolescence and young adulthood. Future research should continue to investigate this cohort of adolescents and young adults as they age, as current age-trends may be a precursor of what’s to come.

Second, LCA and LTA revealed that patterns of polytobacco use are common by young adulthood (age 18) and that prevalence of lifetime marijuana use is highest within latent classes characterized by poly-use. Among young adults, those who reported the use of cigarettes, cigar products, and hookah in 2013/2014 had a relatively high chance (31%) of starting to use ENDS in the subsequent year. Additional research is necessary in order to understand specific pathways from single-product use to poly-use from adolescence into young adulthood, especially given existing literature on progression from ENDS to combustible cigarette smoking and other tobacco use during adolescence (Barrington-Trimis et al., 2016; Cho et al., 2018; Huh & Leventhal, 2016).

In conclusion, given the rapidly changing context of ENDS and marijuana use in the United States, it is increasingly critical to understand patterns and trends in use among young people today. Innovative statistical techniques provided added insight into who is at risk for using specific nicotine delivery systems at what age, as well as the
factors contributing to polytobacco use and co-use with marijuana. Detailed information of this kind is necessary in order to inform and improve tobacco control efforts, prevent nicotine addiction and the associated health consequences, and to reduce overall burden of nicotine-related illnesses on the United States.
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https://doi.org/10.1136/tobaccocontrol-2014-051670
Appendix A. Model fit statistics for intercept only logistic TVEMs

Table A.1. Cigarettes intercept-only model selection

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Note. N=16,217

Table A.2. ENDS intercept-only model selection

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Note. N=16,197

Table A.3. Hookah intercept-only model selection

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Note. N=16,210

Table A.4. Marijuana intercept-only model selection

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Appendix B. Model fit statistics for Main Effect and Interaction TVEMs

Table B.1. Model selection for main effects

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Appendix C. 5-class solution for the W2 Latent Class Model

Table C.1 Class prevalences and item-response probabilities for the W2 latent class model.

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<th>Class Prevalences</th>
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<th>4</th>
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<td>ENDS Only</td>
<td>2%</td>
<td>10%</td>
<td>16%</td>
<td>20%</td>
<td>51%</td>
</tr>
<tr>
<td>Hookah Only</td>
<td>10%</td>
<td>10%</td>
<td>30%</td>
<td>21%</td>
<td>54%</td>
</tr>
<tr>
<td>Cigarettes + Hookah</td>
<td>16%</td>
<td>30%</td>
<td>25%</td>
<td>79%</td>
<td>19%</td>
</tr>
<tr>
<td>Combustibles Only</td>
<td>20%</td>
<td>30%</td>
<td>25%</td>
<td>79%</td>
<td>19%</td>
</tr>
<tr>
<td>Poly, No Smokeless</td>
<td>51%</td>
<td>54%</td>
<td>79%</td>
<td>19%</td>
<td>63%</td>
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<table>
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<th>Item-response Probabilities</th>
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<td>No</td>
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</tr>
<tr>
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</tr>
<tr>
<td>No</td>
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</tr>
<tr>
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</tr>
<tr>
<td>Cigar Products</td>
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<tr>
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<tr>
<td>Smokeless Tobacco</td>
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<tr>
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Note. Item response probabilities were rounded to the nearest hundredth; those above 0.5 were bolded to indicate a moderate to high probability of endorsing use of each nicotine delivery system.
Appendix D. Individual WISDM and NDSS Items

Table C. Nicotine dependence items as assessed in the PATH Study.

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<tr>
<th>PATH ITEM</th>
<th>Original Instrument</th>
<th>Question Text</th>
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<tr>
<td>R01_AN0055</td>
<td>WISDM</td>
<td>I find myself reaching for [product] without thinking about it</td>
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<tr>
<td>R01_AN0025</td>
<td>WISDM</td>
<td>I frequently crave [product]</td>
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<tr>
<td>R01_AN0030</td>
<td>WISDM</td>
<td>My urges keep getting stronger if I don’t use [product]</td>
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<tr>
<td>R01_AN0035</td>
<td>WISDM</td>
<td>Tobacco products control me</td>
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<tr>
<td>R01_AN0045</td>
<td>WISDM</td>
<td>My tobacco product(s) smoking / use is out of control / My urge to smoke / use tobacco product(s) is out of control</td>
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<tr>
<td>R01_AN0060</td>
<td>WISDM</td>
<td>Usually want to smoke / use tobacco product(s) right after waking up</td>
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<tr>
<td>R01_AN0065</td>
<td>WISDM</td>
<td>I can only go a couple of hours without using [product].</td>
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<tr>
<td>R01_AN0050</td>
<td>WISDM</td>
<td>Frequently smoke / use tobacco product(s) without thinking about it</td>
</tr>
<tr>
<td>R01_AN0095</td>
<td>NDSS</td>
<td>After not smoking / using tobacco product(s) for a while, I need to smoke / use tobacco product(s) in order to feel less restless and irritable</td>
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<tr>
<td>R01_AN0100</td>
<td>NDSS</td>
<td>After not smoking / using tobacco product(s) for a while, I need to smoke / use tobacco product(s) in order to keep self from experiencing any discomfort</td>
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</table>

Note. WISDM = Wisconsin Inventory of Smoking Dependence Motives; NDSS = Nicotine Dependence Syndrome Scale
Curriculum Vitae

JESSICA L. BRAYMILLER, Ph.D.
The Pennsylvania State University
308A Biobehavioral Health Building
(Mail to: 219 Biobehavioral Health Building)
University Park, PA 16802
Email: JLB982@psu.edu

Education

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<td>2019</td>
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<td>The Pennsylvania State University</td>
<td>University Park, PA</td>
<td>Dissertation Chair: Stephanie T. Lanza, Ph.D.</td>
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<tr>
<td>2016</td>
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<td>2014</td>
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<td>Magna Cum Laude; Minors in Biology, Neuroscience</td>
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Selected Honors & Awards

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<td>Ruth W. Ayres-Givens Scholarship for Innovative and Interdisciplinary Research to Benefit the Public, College of Health and Human Development, The Pennsylvania State University</td>
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<td>2016, 2017</td>
<td>Prevention and Methodology Training Program Pre-Doctoral Fellowship (NIH/NIDA T32), The Pennsylvania State University</td>
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Selected Publications

