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BIG TOBACCO. BIG MARIJUANA? LONGITUDINAL TRENDS AND MULTI-DIRECTIONAL TOBACCO AND MARIJUANA USE AMONG YOUTH AND YOUNG ADULTS IN TEXAS

SHANNON ROGERS

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YOUTH AND YOUNG ADULTS IN TEXAS

BY

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DEDICATION

To Giovina and Wyatt.

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LONGITUDINAL TRENDS AND MULTI-DIRECTIONAL TOBACCO AND MARIJUANA USE AMONG
YOUTH AND YOUNG ADULTS IN TEXAS

by

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of the Requirements

for the Degree of

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PREFACE

"We shall, by and by, want a world of hemp more for our own consumption." – John Adams

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El equipo uruguayo: Lucía Turcatti, Viviana Moreno, Lucía Martinez, María Traversa,
Martina Florines, y Dr. Diego Estol

And my family, which has grown by two members from when I started this process.

BIG TOBACCO. BIG MARIJUANA?

LONGITUDINAL TRENDS AND MULTI-DIRECTIONAL TOBACCO AND MARIJUANA USE AMONG YOUTH AND YOUNG ADULTS IN TEXAS

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ABSTRACT. Due to the pace of legal changes in marijuana policy, shifting trends in marijuana use, and emerging products in the tobacco product marketplace (e.g., e-cigarettes), the cycle of risk between marijuana and tobacco use is not currently well-understood. I used longitudinal data from two parallel rapid response surveillance studies of youth (aged 12-19 years) and young adults (aged 18-25 years) living in the five counties (Bexar, Dallas, Harris, Tarrant, and Travis) that surround the four largest cities in Texas (Austin, Houston, San Antonio, and Dallas/Fort Worth). I used Generalized Linear Mixed Models (GLMMs) and six-panel cross-lagged regression models to analyze temporal precedence in use and dual use of these products over time (2014 to 2017). Overall, I found dual use to be more common among adolescents than young adults and tobacco and marijuana use and dual use to rise during adolescence and gradually fall during young adulthood. I identified reciprocal temporal relationships between both substances for adolescents and young adults, but marijuana use was particularly predictive of subsequent tobacco use among adolescents. Dual marijuana and tobacco use decreased throughout young adulthood, or at least until age 25, but single product use remained common. I advocate for distinct, developmentally-appropriate interventions that focus on *both* the use of marijuana and tobacco for sustainable prevention and cessation.

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BACKGROUND

INTRODUCTION

As of 2019, in the United States (U.S.), 33 states and Washington, D.C. have legalized medical marijuana use, and ten states and Washington, D.C. have legalized recreational marijuana use. In sum, over 70 million Americans, or over 20% of the country's total population, live in a state with legal recreational marijuana use. Further legalization and decriminalization are expected (Carliner et al., 2017), despite controversy regarding the unknown impact of enacting such policies.

One just concern is the impact of marijuana legalization on marijuana and tobacco use prevalence, as research has documented mixed findings (Cerde et al., 2017; Kilmer et al.; 2010; Caulkins et al., 2016; Wall et al., 2011; Cerdá et al., 2012; Greenwald et al., 2009). Concurrently, adult cigarette smoking rates have fallen almost 43% since their peak in 1965 to about 18% today (USDHHS, 2014). Unfortunately, cigarette smoking remains the primary preventable cause of death in the U.S., and 40 million Americans are tobacco-dependent (USDHHS, 2014). An emerging class of tobacco products (e.g., e-cigarettes, hookah) has complicated the public health environment surrounding successful tobacco prevention strategies. Concern over the tandem use of novel products (e.g., e-cigarettes) for both marijuana and tobacco consumption is also developing, as the social acceptability of marijuana use rises coincidentally with the decrease in perceived harm of marijuana (NSDUH, 2016).

As new science is currently racing to assess the harms associated with use patterns of marijuana and these novel tobacco products in real time, the U.S. is attempting to fill the regulatory gaps that currently exist for marijuana use and new tobacco products like electronic

cigarettes. In the U.S., there is no evidence yet regarding which regulations might minimize population harm from marijuana (Richter and Levy, 2014), and controversial marketing of electronic cigarettes as less harmful than conventional cigarettes complicates regulation for these new products.

History has shown that innovations in product development, marketing, and lobbying caused the use of conventional tobacco cigarettes to soar from the 1880s to 1950s, coincident with the rise of lung cancer as the top cause of cancer-related deaths (Milmore and Conover, 1956). Tobacco's addictive potential rose alongside consumers' intake of toxins and industry profits. In 2015, tobacco companies spent \$8.24 billion on cigarette and \$684.9 million on smokeless tobacco advertisements and promotional expenses in the U.S. alone (Federal Trade Commission, 2017). Likewise, the marijuana industry is one of the fastest growing in the U.S., with profits (in the legal market) projected to be \$22 billion by 2020 (Sola, 2016). Further, the unprecedented marketing opportunities on the Internet, with minimal regulation and the ability to market directly to the consumer (Richter and Levy, 2014), could create a lucrative industry and public health disaster.

The tobacco industry has left a not-so-subtle trail of breadcrumbs for the marijuana industry to follow: downplay known adverse health effects and addiction potential, create a large market as quickly as possible, and protect that market through lobbying, political campaign connections and contributions, and other advocacy efforts (Richter and Levy, 2014). The free-market approach to tobacco took 50 years, millions of lives, and billions of dollars to quell, and still one in five Americans smokes conventional cigarettes (USDHHS, 2016). Given some state-specific data that suggest that liberalized marijuana policies do not produce increases in prevalent

marijuana use (Greenwald 2009; European Mon 2011; MacCoun 2011; Vuolo 2013) and ignoring the known health effects of marijuana use, is it conceivable that the marijuana industry could produce advantageous tax revenue, decrease sentencing for minor criminal offenses, and help to eliminate the black market all while having a relatively small impact on public health. The possibility of this psychoactive substance utopia, however, is rendered impossible by economic potential and made unimaginable when the marijuana industry focused on increasing potency and creating new delivery devices. Does this sound familiar?

The marijuana and tobacco industries are changing. Use and dual use of these products are becoming more and more accessible and attractive. Dependence on marijuana and nicotine are real, potential problems that occur with widespread use of these products (USDHHS, 2012; USDHHS, 2014; NIDA, 2017; Hasin, 2017; APA, 2013). Youth, young adults, and adults all face unique vulnerabilities with regard to use of marijuana and tobacco products. Some data are available on the patterns of use and dual use among these age subgroups, but emerging products and changing trends dictate that more specificity of these analyses by product are necessary. Further, since initiation of and transition from one product to another are possible (Timberlake, 2007; Agrawal et al., 2010; Agrawal et al., 2008; Okoli et al., 2008; Cogle et al., 2016), it will be necessary to measure the possibility of product use and dual use from multiple directions. Studying tobacco history will help inform the marijuana marketplace's transformation into Big Marijuana. It is now necessary to anticipate and carry out the research necessary to inform better policy to avoid the hard lessons learned from the slow response to Big Tobacco.

SECTION I.

Methods of marijuana use

In the U.S., marijuana is consumed recreationally and for medical reasons, and new methods of marijuana consumption appear quickly. In a pilot study aimed at assessing the

Figure 1. Common methods of marijuana

administration.



Image taken from:

<https://www.crescolabs.com/consumption-methods/> .

of administration: 1) smoking or inhaling (via joints (cigarette-like papers filled with marijuana), pipes (bowls), water pipes (bongs, hookahs), and blunts (cigars filled with marijuana); 2) eating or drinking marijuana products; or 3) vaporizing the marijuana product (National Academies, 2017). Marijuana products for consumption include the cannabis “bud” or dried flower, resin (hashish or bubble hash), and oil (butane honey oil, shatter, wax, crumble) (National Academies, 2017) (See **Figure 1**).

feasibility of using word-detectors on social media to identify previously unidentified drug terms, 115 terms were determined to relate to marijuana (65 terms for marijuana itself, 50 terms related to paraphernalia, and 30 net terms deemed to be novel to researchers) in July 2016 alone (Simpson et al., 2018). Marijuana is known to be used in a variety of ways, generally

categorized into three major modes

While the marijuana flowers or resin usually contain between 5 and 20 percent THC, marijuana oil can contain up to 75 percent and can be smoked or vaporized by placing the extracted oil on a heated oil rig pipe (i.e. “dabbing”) (National Academies, 2017). Cannabinoids can actually be absorbed by the skin, so topical creams, patches, vaginal sprays, and rectal suppositories are known methods of THC-administration by direct application (National Academies, 2017). Marijuana products are also used to make food, snacks, beverages, clothing, and beauty products (National Academies, 2017). To date, there is no high-quality national survey data available on the prevalence of non-herbal forms of marijuana—that is, edible, topical, or other concentrates of marijuana--, but available evidence suggests that they are most common in states with recreational or more tolerant medical marijuana policies (Pacula et al., 2016). Evidence also suggests that recreational marijuana users more commonly smoke marijuana (93%) than vaporize (3%) or consume edibles (8%) (Pacula et al., 2016).

The Health Impacts of Marijuana Use

There is limited certainty as to the short- and long-term health impacts of marijuana use. Issues with self-reported marijuana use, inaccurate data collection on marijuana strength, limited participant follow-up, small sample sizes, residual confounding, non-prospective study designs, inconsistent adjustment for alcohol or other substance use such as tobacco, and limitations on generalizability by gender, race/ethnicity, and age subgroups are some of the problems that the National Academy of Sciences (NAS) cites in its 2017 summary report on the evidence of the causal health effects of marijuana use (National Academies, 2017). What is

known with some causal certainty (defined as “conclusive”¹ or “substantial” evidence), per this report, is summarized in **Table 1**, organized by age subgroup—e.g. children, adolescents, young adults, and adults. A summary of health impacts for which there is limited or no evidence is found in **Table 2**.

The known health effects of marijuana use—i.e. health impacts measured with some causal certainty—for children (<12 years) include low birth weight. For youth (12-17 years), marijuana use is causally associated with the development of schizophrenia or other psychoses, with the highest risk among the most frequent users, and development of marijuana use disorder (MUD) (National Academies, 2017). The health impacts of marijuana use for adults (≥18 years) include lower birth weight of offspring, problematic respiratory symptoms and more frequent chronic bronchitis episodes, development of MUD, and increased risk of motor vehicle crashes (National Academies, 2017). Of note, there is causal evidence that adult marijuana use does have therapeutic benefits of improving chronic pain, reducing chemotherapy-induced nausea and vomiting, and improving patient-reported multiple sclerosis spasticity symptoms (National Academies, 2017). There is not (yet in some instances) causal evidence of an association of marijuana use and cancer, myocardial infarction, development of asthma, sudden infant death syndrome, impaired academic achievement, and numerous other physical and psychosocial outcomes (see **Table 2**).

Of particular note (as evidenced in Table 1), there have been no studies with conclusive or substantial evidence of the health impacts of marijuana use that are specific to young adults

¹ See **Tables 3 and 4** for summaries of weight of evidence categories from the NAS (2017) and Surgeon General (2012, 2014, 2016) reports.

aged 18 to 25 years, the age subgroup with the highest prevalence of marijuana use. Studies often specify age inclusion criterion that requires participants to, simply, be at least 18 years old; thus, it is difficult to disentangle impacts for “young adults” from “adults,” as the former are often (but not always) included in the latter. Regardless, biological and psychological maturation changes that occur over the course of young adulthood into mature adulthood warrant young adults’ classification as a separate subpopulation (Bonnie et al., 2014). As such, it may be inaccurate to assume that the health risks of marijuana use for adults would be the same for young adults until more research is available to support or refute that assumption. Indeed, young adults’ prevalent use rates of marijuana and tobacco are unique, as compared with adolescents and mature adults (NSDUH, 2016).

Further, there is far less causal evidence available on the health outcomes of marijuana use than is available on health outcomes for tobacco use, including that for cigarettes and e-cigarettes. More research, including longitudinal studies, on children, youth, young adults, and adults will be necessary to help fill in these gaps. Additionally, more research on the health outcomes of marijuana use by delivery device or method is required. Recall that marijuana can be smoked or inhaled (e.g., via joints, pipes (bowls), water pipes (bongs, hookahs), and blunts (cigars filled with marijuana)); ingested (e.g., via edibles, like chocolates); and vaporized (e.g., via e-cigarette-type devices) (see above section, Methods of Marijuana Use).

Problem Marijuana Use or Marijuana Use Disorder (MUD) (See Dictionary, Appendix A)

MUD, the diagnosis given for problematic marijuana use, occurs when clinically significant impairment—including health problems, persistent or increasing use, and failure to meet major obligations at work, school, or home—accompanies the recurrent use of marijuana

(NSDUH, 2016). Using the American Psychiatric Association's 2000 Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) (See Dictionary, Appendix A, for comparison of DSM-IV and DSM-V MUD definitions), criteria, the 2016 National Survey on Drug Use and Health (NSDUH) estimated that 2.3% of youth aged 12 to 17 years, 5.0% of young adults aged 18 to 25 years, and 0.8% of adults aged 26 years or older had a MUD in the past year (NSDUH, 2016). MUD was the most common illicit drug disorder in 2016 among individuals aged 12 or older, prevalent in about 4.0 million people in the U.S. (NSDUH, 2016). By comparison, 15.1 million people had an alcohol use disorder, and 1.8 million had a prescription pain reliever disorder (NSDUH, 2016).

Increasing marijuana use nationwide, particularly among some age groups (Hasin et al., 2015), the increasing strength of marijuana (ElSohly et al., 2016), and different, increasingly popular routes of marijuana administration (Pacula et al., 2016) may reflect an increased vulnerability to the development of problem marijuana use relative to earlier national survey estimates from 2001-2005 when MUD prevalence was around 1.5% across all age groups, nationwide (NAS, 2017; Grucza et al., 2017). The lack of standardized and consistent characterizations of "risky" or "problem" marijuana use patterns that precede MUD make the assessment of risk factors for developing problem marijuana use difficult and may lead to underestimates of MUD nationwide (Casajuana et al., 2016).

Increases in marijuana use frequency are associated with the development of MUD (Cogle et al., 2016). Some primary literature, not included in the health impacts of marijuana

use discussed above, suggests that long-term, heavy use² of marijuana results in memory and attention impairments that worsen with increasing years of regular use (Solowij et al., 2002) and with the initiation of use during adolescence (Schweinsburg et al., 2008). The implications of MUD and MUD onset at an earlier age, then, exacerbate health impacts. There are also data to suggest that being male, smoking cigarettes, and initiating marijuana use at an earlier age are risk factors for development of problem marijuana use, defined as the various levels of hazardous or potentially harmful marijuana use patterns, including those related to MUD (Behrendt et al., 2009; Blanco et al., National Academy of Sciences, 2017).

Hasin et al. (2017) reported that past-year prevalence of marijuana use almost doubled from 2001-2001 to 2012-2013 among 18-29 year olds (10.5% to 21.2%), 30-34 year olds (4.1% to 10.1%), 45-64 year olds (1.6% to 5.9%), and those 65 years and older (0.0% to 1.3%). Likewise, the prevalence of MUD, in the general population, as defined by the DSM-IV, almost doubled among all age subgroups from 2001-2002 to 2012-2013: 18-29 year olds (4.4% to 7.5%), 30-34 year olds (1.2% to 2.9%), 45-64 year olds (0.4% to 1.3%), and those 65 years and older (0.0% to 0.3%) (Hasin et al., 2017). Although Grucza et al. (2017) attributes these apparent doubling in prevalence rates to the artefactual social acceptability of marijuana use and methodological survey changes, Hasin et al. (2017) contrast their findings with the comparisons from a decade before (comparing 1991-1992 with 2001-2002) in which the increase in MUD occurred only among users. Hence, the most recent MUD estimates indicate the increased prevalence of marijuana users occurred in the general population. Hasin et al.

² Heavy marijuana use is defined as smoking marijuana a median of 29 days in the past 30 days (Solowij et al., 2002; Pope, 1996)

(2017), while acknowledging that their study was unable to predict legalization's impact on prevalent use and MUD rates, advised, however, that alcohol and nicotine law and policy history have been related to changes in use with cause for real public health safety concerns.

Other Substance Use

There is also public health concern about the association between marijuana use and the subsequent use of other licit and illicit drugs, although the predictors of the progression from marijuana use to other illicit drugs remain largely unknown (Secades-Villa et al., 2015). In 2016, about 1 in 10 Americans aged 12 or older in 2016 year reported using illicit drugs within the past month (NSDUH, 2016). In the same year, 63.4 million Americans were past-month tobacco users, 11.5 million misused prescription pain relievers in the past year, and 136.7 million were past-month alcohol drinkers (NSDUH, 2016). Given these rates of licit and illicit substance use, it is necessary to understand how and when individuals start using one or multiple substances and if the use of one substance—e.g. marijuana—may enhance susceptibility to using other drugs or vice versa (Panlilio et al., 2012). To date, there have been no good-quality systematic reviews that report on marijuana use and the initiation, rates, or co- or poly-use patterns of tobacco, nicotine, opiates, alcohol, or mixed drug use (National Academies, 2017).

There are a few primary studies that evaluate the association between marijuana use and use of other substances such as alcohol (Buu et al., 2015), tobacco (Timberlake et al., 2007; Mayet et al, 2016), and other illicit drugs (Blanco et al., 2016; Mayet et al., 2016). These studies are described below. While useful, it is important to note they are limited by sex, country, and age sub-group, which makes it difficult to generalize to other subpopulations or synthesize

trends, particularly in environments with different policies that affect the availability of marijuana products to certain age groups and geographic areas.

Tobacco. Using two waves of nationwide surveys on health and behaviors in France, Mayet et al. (2016) found that, for a sample of adults aged 18-34 in 2005 and 2010, the probability of initiating any tobacco product use after marijuana use was significantly greater than the probability of initiating marijuana after tobacco use (Note: researchers did not distinguish among particular methods of tobacco or marijuana use). Timberlake et al. (2007) found that lifetime (lifetime marijuana use ≥ 10) and past-month marijuana use were predictive of an earlier initiation into daily cigarette smoking and a greater likelihood of developing nicotine dependence six years later among 17- to 21-year olds from 1995 to 2001.

Other illicit drugs. Mayet et al. (2016) also found in their sample of adults aged 18-34, that initiating opioid use after marijuana use did not differ significantly from the probability of starting with opioid use. Blanco et al. (2016) observed that for a sample of adults aged 18 and older, marijuana use in 2001-2002 was associated with subsequent substance use disorders in 2004-2005, including MUD, alcohol use disorder, and “any other” drug use disorder.

Alcohol. In a sample of predominantly African-American individuals aged 14-24 years during 1994 to 2002, Buu et al. (2015) discovered that early-onset marijuana users³, late-onset marijuana users⁴, and those using marijuana more frequently⁵ were all at higher risk of heavy

³ Buu et al. (2015) defined the age for early-onset marijuana use as occurring at the median age of the sample’s use or younger.

⁴ Buu et al. (2015) do not clearly define the age for late-onset marijuana use; rather, it seems to be relative to early-onset users—that is, one was an early user, a late user, or a non-user of marijuana.

⁵ Buu et al. (2015) assessed the frequency of marijuana use in the last 30 days with a 0-6 scale in which 0=0 times; 1=1-2 times; 2=3-5 times; 3=6-9 times; 4=10-19 times; 5=20-39 times; and 6=40+ times.

alcohol drinking (see Dictionary, Appendix A) compared to those who did not use marijuana at all.

A more detailed presentation of what is known about marijuana and tobacco co-use is found in

Section V (Trajectories of Marijuana and Tobacco Use)

Summary

Marijuana use can occur in many forms, though smoking remains the most common. Studies of the health impacts of marijuana use are emerging, limited, and often only generalizable to a small subpopulation or to a single method of marijuana use. Nonetheless, causal evidence of an association of marijuana use and low birth weight for children (<12 years), development of MUD for youth (12-17 years) and adults (≥ 18 years), and problematic respiratory symptoms for adults are just some of the reasons for public health concern over marijuana use, particularly for youth and frequent marijuana users. Little research has focused exclusively on young adults, though marijuana use is particularly relevant to this sub-group. More research is necessary to determine the effect size and directionality of the association between marijuana use and other drug use, including tobacco, other illicit drugs, and alcohol. Despite the growing prevalence of MUD and illicit drug use in the U.S., there are many unknowns regarding patterns of use and dual use of marijuana and other drugs, particularly by method of administration and by age sub-groups.

SECTION II.

Methods of Tobacco Use

Just as with marijuana use, tobacco use comes in many forms. Though there are numerous routes of administration (see **Figure 2**), cigarettes, chewing tobacco, cigars, cigars, pipes, and electronic cigarettes are the most popular methods of tobacco use in the U.S. (USDHHS, 2014). Smoked forms of tobacco—referred to as combustible tobacco—include cigarettes, cigars, pipes, kreteks, bidis, and waterpipes/hookah (O'Connor, 2011). Common forms of non-combustible (smokeless) tobacco in the U.S. include chewing tobacco, moist and dry snuff, and dissolvable tobacco. Lastly, there are other forms of nicotine delivery that include e-cigarettes.

Combustible Tobacco Use

Smoked tobacco use is characterized by the burning of tobacco; the smoke can either be inhaled or held in the mouth before exhaled (O'Connor, 2011). Cigarettes are composed of tobacco, chemical additives, a filter, and paper wrapping (USDHHS, 2010). Cigars are traditionally comprised of shredded tobacco wrapped in tobacco leaf (National Cancer Institute, 1991), and sub-varieties of cigar vary by size like little cigars which often contain a filter; to cigarillos, which are medium-sized cigars, often filled with marijuana via a practice called “blunting”; to large cigars (Kozlowski et al., 2008; Delnevo et al., 2007). Waterpipes, or hookahs, employ indirect heating of the tobacco and generate smoke which is passed through a chamber that contains water before reaching the user’s mouth via a hose (Chaouachi, 2006).

Figure 2. Examples of forms of tobacco use in the U.S. (Adapted from O'Connor, 2011)

Combustible (Smoked)

Cigarettes



Cigars



Hookah (Waterpipes)



Non-combustible

Electronic cigarettes (e-cigarettes)



Non-combustible Products

Electronic nicotine delivery systems, or electronic cigarettes (e-cigarettes), are often constructed to resemble cigarettes and work by vaporizing a nicotine-containing solution, that includes flavorings (Etter et al., 2011). Further discussion of e-cigarettes is found in Section III.

The Health Impacts of Tobacco Use

In a review of more than 50 years of studies (prior to 1964-2012), the Advisory Committee to the Surgeon General summarized the evidence regarding the health consequences of smoking (USDHHS, 2014). The Advisory Committee concluded that cigarette smoking is associated with about a 70% increase in the age-specific overall death rate compared to non-smokers; overall mortality risk increases with the amount of cigarettes smoked; overall mortality ratios of cigarettes smokers compared to non-smokers are highest at earlier ages and

decline with increasing age; and that overall mortality ratios are higher for those with an earlier age of cigarette smoking onset compared to those who begin later in life (USDHHS, 2014). Life expectancy among current smokers is shortened by about 11 years for women and by about 12 years for men, compared with never-smokers (Jha et al., 2013). In 2004, the Surgeon General's Report noted that smoking affects nearly every organ in the body; its 2014 Report provides additional support for that finding (USDHHS, 2014). **Table 1** summarizes the primary health outcomes for children, adolescents, young adults, and adults, informed by "conclusive"⁶ evidence, resulting from active smoking of cigarettes and e-cigarettes.

Cigarettes. The list of health consequences and diseases causally linked to cigarette smoking has expanded since the first Surgeon General's report in 1964 and continues to grow, as new causal conclusions are still being added. Children (<12 years of age) are known to experience numerous respiratory symptoms and middle ear disease (USDHHS, 2014). Youth (aged 12-17 years) experience congenital defects and low birth weight from maternal smoking, impaired lung function, and asthma-related symptoms, among other outcomes (USDHHS, 2014). Early abdominal aortic atherosclerosis has been causally linked to cigarette smoking among young adults (aged 18-25 years) (USDHHS, 2014). Adults (aged 18 and older) are known to experience cancer, cardiovascular disease, immune function and related disorders, reproductive health outcomes, cognitive and mental health problems, and other health outcomes (USDHHS, 2014).

⁶ See **Tables 3 and 4** for summaries of the weight of evidence categories from the NAS (2017) and Surgeon General (2012, 2014, 2016) reports.

E-cigarettes. The health consequences from the use of e-cigarettes have been less studied than those from conventional cigarettes, but potential adverse health effects from e-cigarette use come from inhalation of the aerosol; administration of nicotine, flavor additives, chemicals, and other particulates; and other effects such as nicotine addiction, developmental effects on the brain from nicotine exposure, e-cigarette influence on the use of other substances such as illicit drug use, effects on psychosocial health, and accidents like battery explosion or accidental overdose (USDHHS, 2016). Children can experience preterm delivery or stillbirth, negative impacts on brain development, and sudden infant death syndrome (USDHHS, 2016). Respiratory irritation, later adult nicotine addiction, increased drug-seeking behavior, and poisoning are just a few of the health outcomes known to occur among youth who use e-cigarettes (USDHHS, 2016). Young adults are known to experience increases in heart rate and blood pressure, respiratory irritation, neurobiological insult, and eye irritation, among many other outcomes (USDHHS, 2016). Similarly, adults can experience respiratory and eye irritation (USDHHS, 2016). Notably, e-cigarettes may be potentially less addictive than conventional cigarettes (USDHHS, 2016).

Not summarized in **Table 1** are the health effects of tobacco products *other than* cigarettes and e-cigarettes (discussed broadly below): cigars and hookahs.

Cigars and pipes. Cigar smoke contains higher concentrations of toxic and carcinogenic compounds than cigarettes, making it a major source of fine-particle and carbon monoxide indoor air pollution (Baker et al., 2000). Cigar smoking is a known cause of lung cancer, upper aerodigestive tract cancer (Baker et al., 2000), and colon cancer (Mitchell et al., 1999). Cigar use

is associated with cancers of the mouth, nose, and upper airway, while cigar use, also appears to be associated with pancreatic cancer (O'Connor, 2011).

Hookahs. Hookah use, or waterpipe smoking, involves the inhalation of waterpipe smoke, which imposes oxidative stress and inflammatory responses in the lungs, which leads to an increased risk of declined lung function (Javed et al., 2017; Yalcin et al., 2017). Hookah smoking is known to be more dangerous than smoking cigarettes, primarily due to carbon monoxide exposure (Eisenberg and Shihadeh, 2009). Studies of the health impacts of these tobacco products, which are becoming increasingly common among youth and young adults (Cobb et al., 2010; Amrock et al., 2013) are still underway and emerging. Further, some data suggest that hookah smoking may be a precursor to cigarette smoking for some individuals (Kulak et al., 2018; Ward et al., 2006; Ward et al., 2007).

Summary

Within the past several decades, market diversification has expanded the product offering for tobacco and nicotine delivery; tobacco and nicotine can currently be consumed in a variety of forms that can be classified as combustible and non-combustible. Though the literature is quite developed regarding the negative health effects of nicotine and tobacco exposure—especially for conventional cigarettes, e-cigarettes, cigars, use of these products remains high worldwide. While some forms of tobacco or nicotine use may be less harmful (e.g., e-cigarettes), relative to other forms of use (e.g., cigarettes), no form of tobacco or nicotine use is considered “safe” or harmless, despite being marketed as harm-reducing. A developed literature base suggests that use of one product (e.g., e-cigarettes) increases the risk of use of another tobacco or nicotine-containing product (e.g. cigarettes). Further, as

marijuana and tobacco often share modes of administration, co-use of these products is of real concern for efforts aimed at tobacco cessation and MUD prevention.

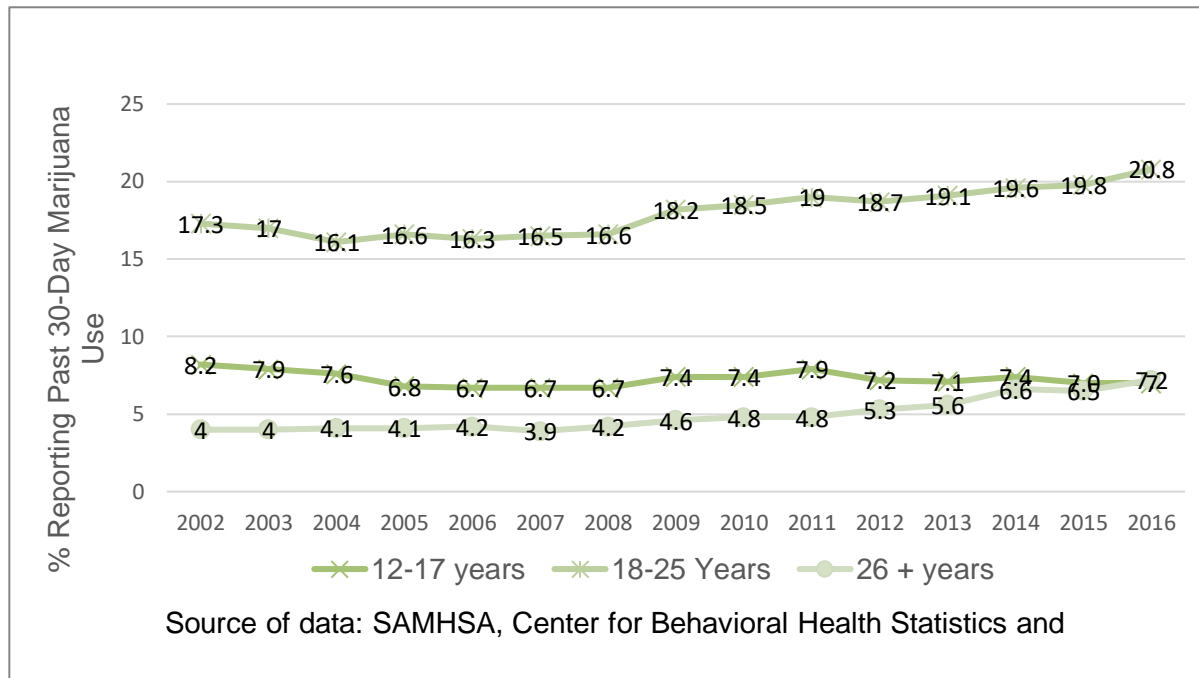
SECTION III.

Trends in Marijuana and Tobacco Use

Marijuana use trends

Prevalent marijuana use peaked in the late 1970s with over a third of high-school seniors (37%) and one in eight Americans over age 12 (12.8%) reporting past 30-day use in 1976 (MTF, 2017). Self-reported past 30-day marijuana use declined in the subsequent decades, and by 1992 was one third of its peak (12.1% of high school seniors, and 4.4% of Americans over age 12) reported past 30-day marijuana use) (MTF, 2017). Thereafter, marijuana use rapidly increased, almost doubling from 1992 to 1997 (11.9% to 23.7%) until use stagnated until around 2007 (MTF, 2017). Post-2007 marijuana use has resulted in steady yearly increases among the general population, (MTF, 2017) and today, marijuana is the most widely used illicit drug in the United States (**Figure 3**). (SAMSHA).

Figure 3. Prevalent past 30-day marijuana use among 12-17 year olds, 18-25 year olds, and those 26 years and older in the U.S. from 2002-2015, %



Marijuana use among youth

Adolescents approaching young adulthood are at the highest risk for initiating marijuana use (SAMSHA 2013, 2016). The 2013 National Survey on Drug Use and Health (NSDUH) estimated that around 70% of past year illicit drug initiates reported marijuana as their first drug, and 40.1% of past year marijuana users initiated before the age of 18 (SAMSHA 2013). Among adolescents aged 12-17 years in 2016, current (or past-30 day) marijuana use was fairly similar among males (6.8%) and females (6.1%) and was highest among American Indian or Alaska Native (9.7%), compared with Whites (6.6%), Blacks (6.5%), Hispanics (6.1%), and Asians (3.5%) (NSDUH, 2016). From 2002 to 2016 among youth 12 to 17 years, past 30-day marijuana

use has been inconsistently teetering between roughly 8.2% (2002) and about 7.0% (2016), with occasional year-to-year increases and decreases (NSDUH, 2016) (see **Figure 3**).

An analysis of NSDUH data from 2014 (N=55,271) showed that the odds of marijuana dependence or abuse among marijuana-using youth aged 14-17 were almost two times the odds of older marijuana-users aged 18-44, even at relatively low levels of marijuana use (Richter et al 2016). The most recent 2016 NSDUH estimates, consistent with these data, showed that 12-17-year-old individuals by far comprised the largest percentage of past year marijuana initiates at 4.8% among the total population and 9.3% among persons at risk for initiation⁷, with the majority of past-year initiates being 16 to 17 years of age (NSDUH, 2016). Thus, most initiation of marijuana use has already occurred in adolescence, by the time individuals reach young adulthood, and as much as 80% of patterns of use established during emerging adulthood continues into adulthood (Bachman, 2002).

Marijuana use among young adults

Although initiation primarily occurs in adolescence, marijuana use is most prevalent among young adults aged 18-25 years (SAMSHA 2013, 2016). Past 30-day marijuana use among young adults aged 18 to 25 years has been gradually rising since 2006 and reached 20.8% in 2016 (**Figure 3**) (SAMSHA, 2016). In a study of young adult marijuana users (N=36,309), the prevalence of past-year marijuana abuse or dependence increased significantly from 4.4% to 7.5% from 2001 to 2013 (Hasin, 2015). Among young adults aged 18-25 years, in 2016,

⁷ The NSDUH defines Persons at Risk for Initiation for a Specific Substance as “those who did not use the substance in their lifetime or who used the substance for the first time in the past year” (NSDUH, 2016)

prevalent marijuana use was higher for males (24.0%) than females (17.5%) (NSDUH, 2016).

With the exception of American Indian or Alaska Natives, Blacks had the highest prevalence of current marijuana smoking, with 23.2% of young adults reporting current marijuana use, compared to Whites (22.1%), and Hispanic (18.7%) young adults (NSDUH, 2016).

Trends in intensity of marijuana use

In general, intensity of marijuana use parallels marijuana use prevalence: that is, groups with high use prevalence tend to also be those with high intensity of use, with some important exceptions (Johnston et al., 2017). Firstly, Americans with less than a high school education report less past 30-day use than Americans with a high school diploma or partial college education, but those with less than a high-school education are most likely to report daily or near-daily use (44.8%) (Johnston et al., 2017). Secondly, 26-34-year-olds report less past-month use than 18-25-year-olds but report substantially more heavy use among current users (7.4%) (Johnston et al., 2017). Lastly, while heavy use among past-month users is lowest among 12-17-year-olds (7.4%), 6 percent of high school seniors who used marijuana in the past month reported *daily* use (Johnston et al., 2017).

One result from the increase in prevalent marijuana abusers is that the majority of marijuana consumption is more and more concentrated in a relatively small percentage of heavy marijuana users (Davenport and Caulkins, 2016). It is estimated that the approximately one-third of daily or almost daily marijuana users account for nearly two-thirds of the reported days of past-month use and three-fourths of marijuana expenditures (Davenport and Caulkins, 2016). As a proportion of past-month marijuana users, the heavy use group has grown from roughly 11% in 1992 to 35% in 2014 (Burns et al. 2013). Furthermore, Burns et al. (2013) found

an increase in the proportion of Hispanic daily/near-daily marijuana users over the same time period, increasing from 8% in 2002 to 14% in 2011; there was a decrease in the proportion of non-Hispanic white daily/near-daily marijuana users (75% in 2002 to 66% in 2011) and little change in the proportion of non-Hispanic black daily/near-daily users (14% in 2002 and 16% in 2011).

Tobacco use trends

Cigarette use is defined as smoking “part or all of a cigarette” (NSDUH, 2016) and remains by far the most commonly used method of tobacco use among young adults in the United States. Among middle school (grades 6-8) and high school (grades 9-12) youths, however, e-cigarettes are now more popular than conventional cigarettes (Kasza et al., 2017; Wang et al., 2018). Among high school (grades 9-12) youths in 2017, e-cigarettes (9.9%) were the most prevalently used tobacco product in the past 30-days, followed by cigarettes (7.5%), cigars (6.3%), hookah, (3.2%), and smokeless tobacco (3.0%) (Wang et al., 2018). Among middle school (grades 6-8) youths in 2017, e-cigarettes (2.9%) were also the most popular tobacco product used within the past 30 days, followed by conventional cigarettes (2.2%), cigars (1.4%), smokeless tobacco (1.2%), and hookah (1.1%) (Wang et al., 2018). For adults (aged 25 and older) in the same study, past 30-day use of cigarettes (17.9%) was most prevalent, followed by use of any cigar product (6.9%), e-cigarettes (5.0%), smokeless tobacco (3.1%), and lastly by hookah (2.1%) (Kasza et al., 2017).

Overall, cigarette use has been declining since its peak in the mid-1960s, but lifetime (62.9%), past year (28.5%), and past 30-day (23.5%) cigarette use among persons aged 12 or older still remained quite high in 2016 (NSDUH, 2016). Cigars were quite common until the

twentieth century, when use shrank dramatically until 1993, when use began to rise rapidly again (USDHHS, 2014). The introduction of small cigars, resembling cigarettes, more targeted marketing, and the introduction of the “filtered cigar” have resulted in annual increases in total cigar use (since little cigar consumption dropped significantly in 2009) (USDHHS, 2014). E-cigarette use has rapidly increased in the U.S. since 2007, and large increases in use among youth and have been observed since 2010 (USDHHS, 2016). Hookah, or waterpipe smoking, is widespread, gaining popularity in the U.S., and is now the second most popular tobacco product among young adults age 18 to 24 years (Salloum et al., 2017; Kasza et al., 2017)

Cigarettes

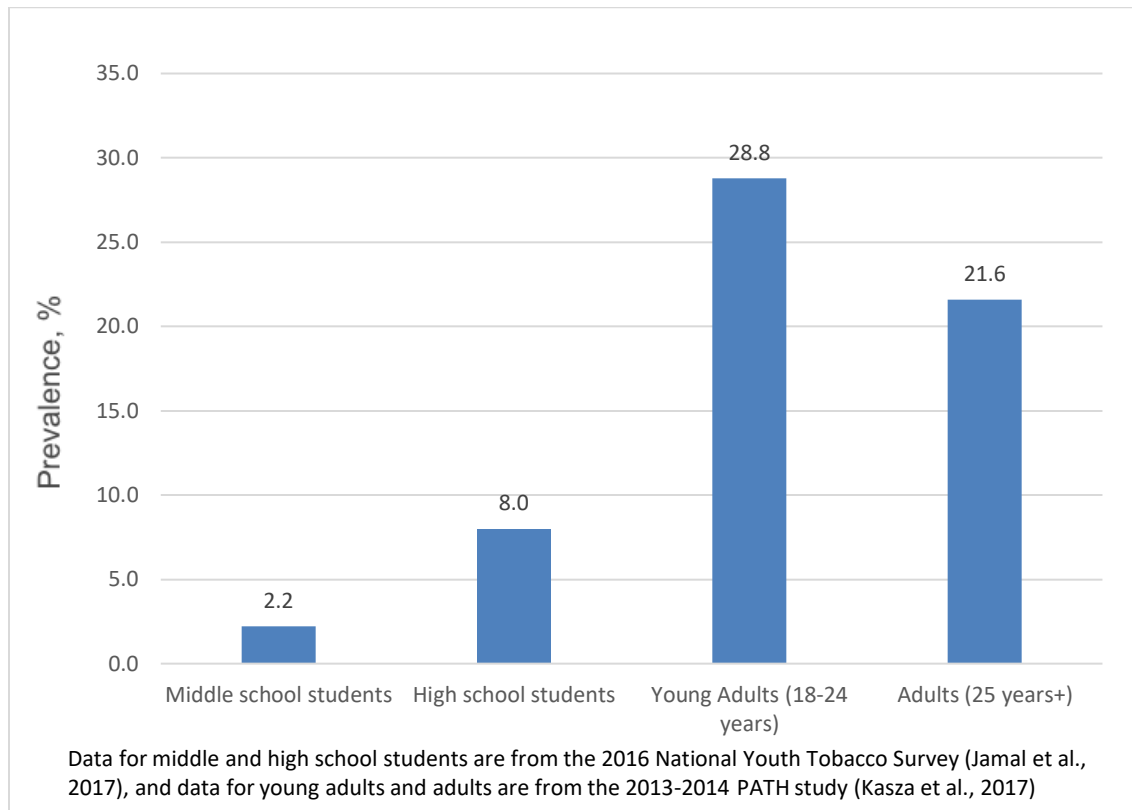
As with marijuana, nearly all cigarette smoking begins before 18 years of age, a point illustrated and confirmed by both NSDUH and Surgeon General analyses (USDHHS, 2012; SAMSHA 2012). In 2012, among adult smokers aged 30-39 asked about their first experience with cigarette smoking, the mean age of smoking initiation was 15.3 years, and the mean age of beginning to smoke daily was 18.2 years (USDHHS, 2014). The most recent 2015 and 2016 NSDUH estimates, however, show a slightly older age at initiation: 18-20-year-olds comprised the largest percentage of past-year tobacco cigarette initiates at 5.7% among the total population and 8.7% among persons at risk for initiation⁸, closely followed by 12-to-17-year-olds at 5.0% and 5.9% among the total and at-risk populations, respectively (NSDUH, 2016). New research (Perry et al., 2018; Thompson et al., 2018) confirms this, showing that young adults now have significantly higher incidence rates than youth to initiate ever and current use of

⁸ NSDUH defines Persons at Risk for Initiation for a Specific Substance as “those who did not use the substance in their lifetime or who used the substance for the first time in the past year” (NSDUH, 2016)

cigarettes, e-cigarettes, cigar products, and hookah. In sum, almost no cigarette smoking initiation (<1.5%) and little transition to daily smoking (<4.3%) occur in adulthood—e.g. after 26 years of age (USDHHS, 2014).

Based on the 2016 NSDUH estimates of past 30-day cigarette smoking, prevalent cigarette use is highest among young adults aged 18-25 years (23.5%), compared with prevalent use among 12-17-year-olds (3.4%) and 26 or older (20.2%) (NSDUH, 2016). Some age subgroups, however, have higher prevalent cigarette use when considered individually. For example, while just 20.6% of individuals 18 or older reported past-month cigarette use, 27.8% of individuals age 25 and 25.4% of individuals age 40-44 report past-month use (NSDUH, 2016). After adults 18-25 and 26-44 years of age, prevalent smoking declines with age (NSDUH, 2016) **(Figure 4)**.

Figure 4. Past 30-day prevalence of cigarette use among youth (2016), young adults, and adults (2013-2014)



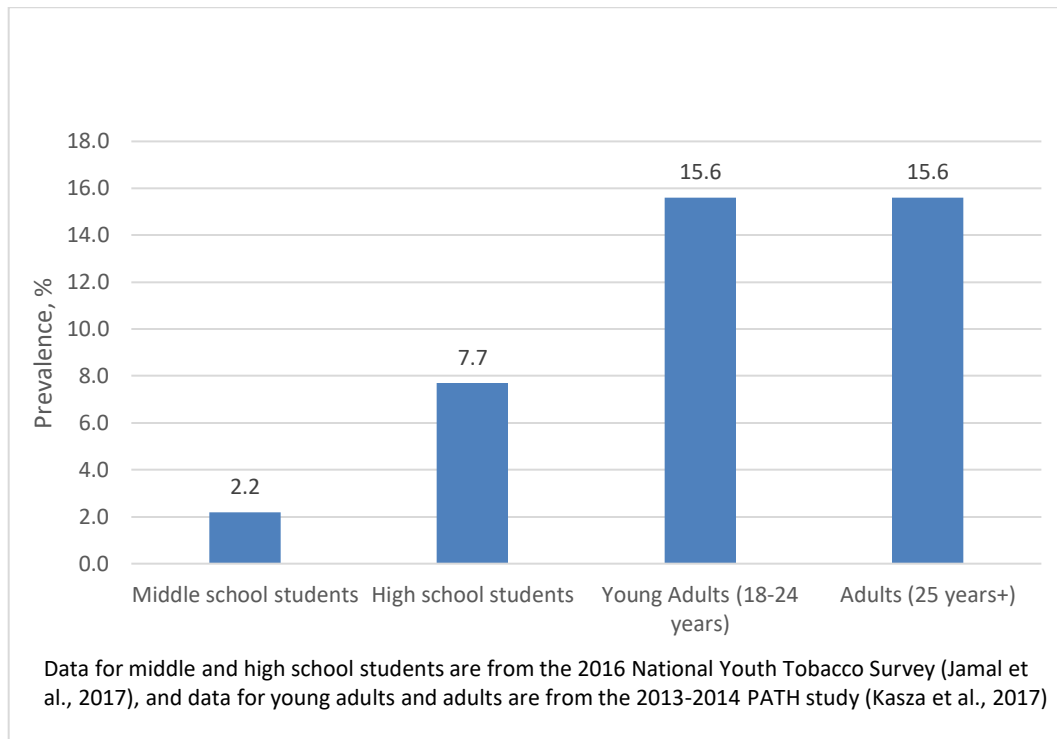
Among adolescents aged 12-17 years, in 2016, prevalent past 30-day cigarette use is similar among males (3.8%) and females (3.1%) and is highest among Whites (4.6%), behind American Indian or Alaska Native (7.2%), compared with Blacks (1.6%), Hispanics (2.1%), and Asians (1.1%) (NSDUH, 2016). Of note, higher prevalent smoking is found among youth living below the poverty level compared to those living at or above this level (NSDUH, 2016). Among young adults aged 18-25 years, in 2016, prevalent past 30-day cigarette smoking was higher for males (23.1%) than females (18.4%), a pattern observed for all racial/ethnic groups (NSDUH, 2016).

Cigars

Although the use of cigars declined in the 1990s, the declines in use stalled in the early 2000s, as cigar smoking appears to be increasing among Black high school females (USDHHS, 2012). Data from the 2013-2014 wave of the PATH study showed that ever use of any cigar product for youths aged 12-17 years was 7.5%, and current use was 2.5%, with the highest prevalence of use among youths aged 15-17 years (Kasza et al., 2017) (**Figure 5**). Young adults aged 18-24 years had the highest past 30-day use of any cigar in the same years (14.1%) of any age subgroup, and adult past 30-day use of any cigar was 6.9% (Kasza et al., 2017). Notably, cigarillo “use in the previous 30 days”⁹ and current cigarillo use³ were by far highest among young adults aged 18-24 years (12.4% and 10.7%, respectively) compared to youth subgroups and adults aged 25 and older, all of whom had use in the previous 30 days and current use <5% (Kasza et al., 2017).

⁹ Kasza et al. (2017) used the PATH definitions for the following measures: (1) *use in the past 30 days* for youth and adults: data are for participants who had smoked or used the product (even one or two times) in the previous 30 days and (2) *current use* for youth and adults: for each tobacco product other than cigarettes and hookah, current use indicates that the participant now smokes or uses the product every day or some days. For cigarettes, the “current regular use” category was used, which indicates that the participant has smoked at least 100 cigarettes in his or her lifetime and now smokes every day or some days. For hookah, current use indicates that the participant now uses the product every day, some days, usually weekly, or usually monthly.

Figure 5. Past 30-day prevalence of cigar use among youth (2016), young adults, and adults (2013-14)

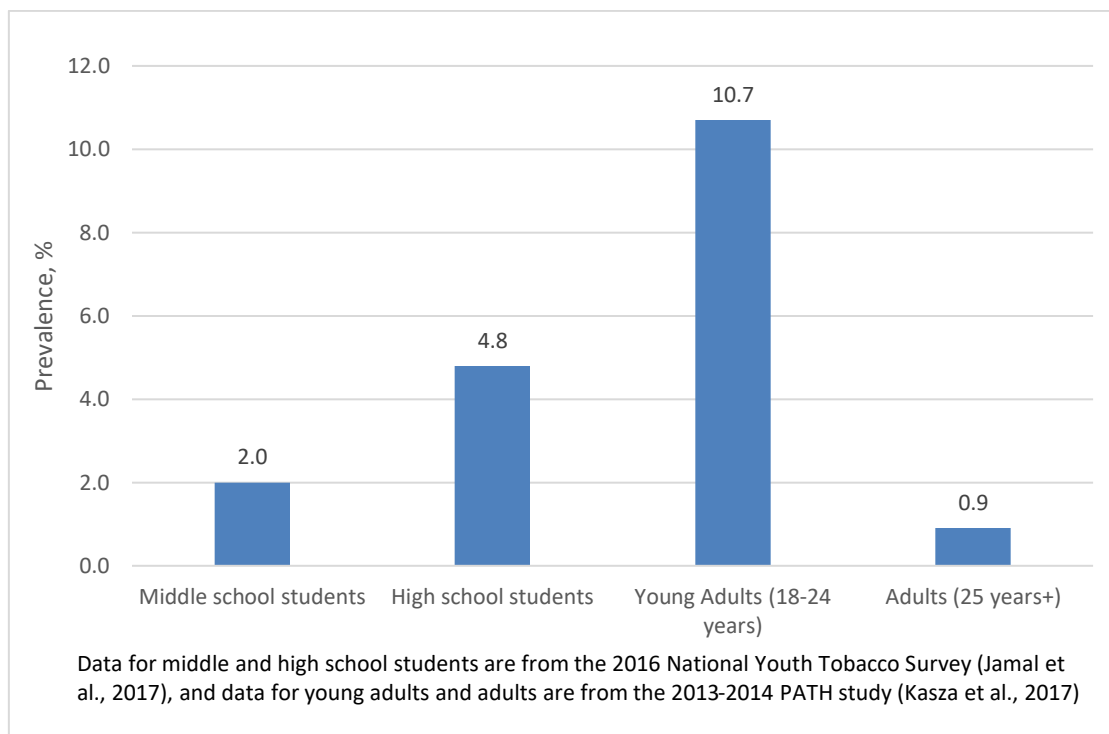


Hookah

From 2011 to 2015, there were significant increases in current hookah use among middle and high school students until 2014-2015, when current hookah use decreased among high school students (Singh et al., 2016). In 2015, 7.2% of high school students (6.9% of girls and 7.4% of boys) and 2.0% of middle school students (2.0% of girls and 1.9% of boys) reported hookah use in the past 30 days (Singh et al., 2016). Among young adults, hookah is the second most popular tobacco product after cigarettes, yet over half of current hookah users are also non-cigarette users (Primack et al., 2013). Hookah use among U.S. college students ranged between 20-40% for ever use and 5-15% for current use (Primack et al., 2013). Also, among young adults, female sex and African-American race are inversely associated with sustained

hookah use—defined as hookah use on at least 6 occasions in the last 12 months (Primack et al., 2015). Hookah use among adults age 25 years and older appears to be far less popular than for young adults. Data from the 2013-2014 wave of the PATH study showed that among adults age 25 years and older, hookah use in the previous 30 days was 0.9%, and current use was slightly higher at 2.1% (**Figure 6**) (Kasza et al., 2017).

Figure 6. Past 30-day prevalence of hookah among youth (2016), young adults, and adults (2013-14)



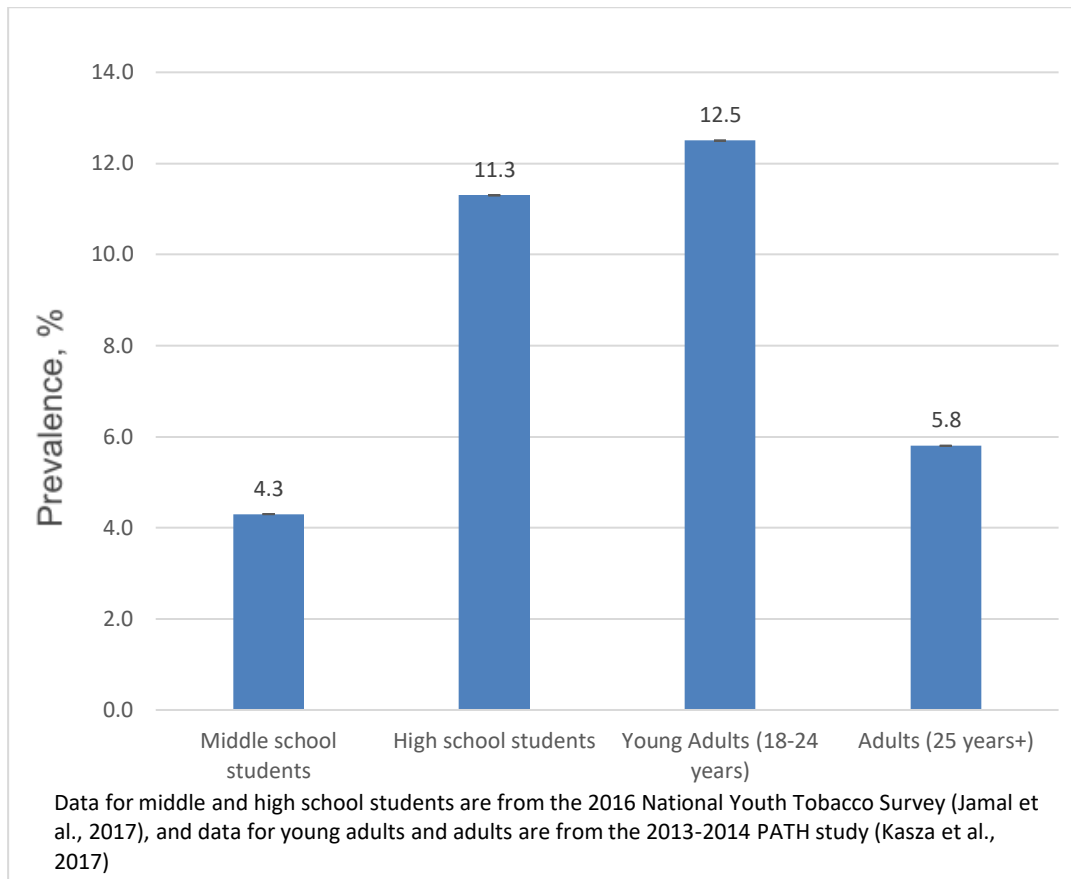
E-cigarettes

E-cigarettes include a group of devices—referred to by consumers as “e-cigarettes,” “e-cigs,” “cigalikes,” “e-hookahs,” “mods,” “vape pens,” “vapes,” and “tank systems—that allow users to inhale an aerosol which typically contains nicotine, flavorings, and additives (USDHHS, 2016). The e-cigarette was available in the U.S. market by the mid-2000s, sales started to rapidly

increase by 2007, and use increased 900% among high school students from 2011 to 2015 (USDHHS, 2016). Data from the 2011 National Youth Tobacco Survey (NYTS) from showed that current e-cigarette use, or use during at least 1 day in the past 30 days, among high school students was 1.5%; by 2015, prevalence was 16%, higher than conventional tobacco cigarette use (Jamal et al., 2017). Product diversity, novelty, product innovations, and disagreement among public health scientists about the devices' harmfulness make the evaluation of the effects of e-cigarettes difficult (USDHHS, 2016). However, the devices deliver nicotine, making nicotine addiction a primary concern, as nicotine exposure is harmful, particularly for youth and young adults (USDHHS, 2016).

According to data from the NYTS, ever use of e-cigarettes among students in grades 6-12 increased from 3.3% in 2011 to 6.8% in 2013 to 19.8% in 2014 to 27% in 2015 before declining slightly between 2015 and 2016 (Jamal et al., 2017). Past 30-day use of e-cigarettes among students in grades 6-12 increased from 1.1% in 2011 to 2.1% in 2012 to 3.1% in 2013 to 9.3% in 2014 to 11.3% in 2015 (Jamal et al., 2017). As was the case for ever use, past 30-day use of e-cigarettes was higher among high school students than middle school students (**Figure 7**) (Jamal et al., 2017).

Figure 7. Past 30-day prevalence of e-cigarette use among youth (2016), young adults, and adults (2013-14)



Single tobacco product use is indicative of susceptibility to other tobacco products (Gilpin and Pierce, 2003; Bobard et al., 2008; Nasim et al., 2012; USDHHS, 2012; Agaku et al., 2013; Schuster et al., 2013). Among a sample of adolescents (n=13,651) from the nationally-representative Population Assessment of Tobacco and Health (PATH) study, adolescent e-cigarette users were particularly susceptible to using other products, with 73% susceptible to cigarettes, 71% to hookah, 56% to cigars, and 26% to smokeless tobacco, and susceptibility to using other tobacco products was higher among e-cigarette users than those who had used other tobacco products (Trinidad et al., 2017).

The 2013-2014 National Adult Tobacco Survey (NATS) showed that among young adults aged 18-24 years, the prevalence of ever use and current use of e-cigarettes was 35.8% and 13.6%, respectively (Hu et al., 2016). Among adults aged 25 and older, the prevalence of ever use and current use of e-cigarettes was slightly lower at 16.4% and 5.7%, respectively (Hu et al., 2016). Among both young adults and adults age 25 and older, ever and current use were higher for males than females and for Whites than any other racial/ethnic group (Hu et al., 2016). The prevalence of ever use of e-cigarettes has followed a slow but not continual increase among young adults since 2011, when prevalence was 6.9%, to 2014 when prevalence reached 14.3% (Schoenborn & Gindi, 2015). Prevalence doubled from 2013 to 2014 (Schoenborn & Gindi, 2015). In 2010, young adults aged 18-24 years were more likely than older adults age 25-44 and 45-64 years to be ever users of e-cigarettes, but by 2014, ever use of e-cigarettes was statistically equivalent between these age groups of young and older adults, varying between 11.9% and 15% (Schoenborn & Gindi, 2015).

E-cigarette use among young adults has been shown to be a specific risk factor for later cigarette initiation, rather than an extension of existing multiple tobacco product use behavior (Loukas et al., 2018). In a study of 2558 cigarette-naïve 18-to-25 year-old Texas college students, a significantly higher proportion of baseline e-cigarette users reported initiating cigarette use by Wave 4 (1.5 years later) (20.1%) compared with baseline non-e-cigarette users (8.4%) ($\chi^2_{[1]}=61.25$, $p<0.001$) (Loukas et al., 2018).

Zhu et al. (2014) identified 466 brands and 7764 unique descriptors of e-cigarette flavors in 17 months of internet searches, resulting in a net increase of 10.5 brands and 242 new flavors per month (Zhu et al., 2014). At this rate of product placement and advertising, there is due

concern about e-cigarette availability, regulation, and dual purposing of e-cigarettes. Data suggest that e-cigarette use is associated with future cigarette use (yet not vice versa) among youth (Bold et al., 2018; USDHHS, 2016) and that e-cigarettes are a popular vehicle for the vaporization of substances other than nicotine, like liquid THC (marijuana) for young adults and adults (Azagba, 2017; Kenne et al., 2017; Morean et al., 2017).

Data from the 2014-2015 cross-sectional Canadian Student Tobacco, Alcohol and Drugs Survey (n=23,429) of students in grades 6 to 12 showed that 15% of respondents reported using marijuana at least once in the past month, and the likelihood of marijuana use was significantly higher for e-cigarette only¹⁰ (OR=9.46, 95%CI 6.60-13.58) and cigarette-only users (OR=15.36, 95%CI 10.09-23.37) (Azagba, 2017). In a study of US high school students (n=1941) in Hawaii, 17% of the sample were e-cigarette only users, 12% used both e-cigarettes and cigarettes, and 3% used cigarettes only (Wills et al., 2015). Notably, e-cigarette only users were of “intermediate risk” status between nonusers and dual users, implying that the e-cigarettes class recruited medium-risk adolescents who would otherwise have been less susceptible to tobacco product use (Wills et al., 2015). In a study of 1542 undergraduate college e-cigarette users from a U.S. university, 6.94% reported using an e-cigarette to vaporize a substance other than nicotine (OSUE), and most of those (77.9%) reported using marijuana in an e-cigarette (Kenne et al., 2017). Current tobacco cigarette smokers were significantly more likely to report OSUE (51.0%) compared with never (33.7%) and former (15.4%) smokers (Kenne et al., 2017). In a study of 522

¹⁰ Adjusted multinomial logistic regression of marijuana use in the past month with non-use as the base outcome; odds ratios (OR) and 95% Confidence (95%CI) shown in parentheses for odds of cigarette only use and dual use compared to odds of e-cigarette only use once or twice (Azagba, 2017).

adult e-cigarette users, 17.8% reported lifetime and 11.5% reported past-month marijuana vaporization (Morean et al., 2017).

The extent to which e-cigarettes are used and the consequences of such use in the vaporization of other substances are not yet known, yet e-cigarettes are now the most commonly used tobacco product among youth (USDHHS, 2016). E-cigarette use is strongly associated with the use of other tobacco products among youth and young adults, so there is concern about increased susceptibility to tobacco product use, especially given targeted marketing strategies aimed to sell the perception of e-cigarettes as healthier alternatives to cigarettes (USDHHS, 2016).

Summary

Marijuana is the most widely used illicit drug in the U.S. Adolescents approaching young adulthood are at the highest risk for initiating marijuana use, and current marijuana use among young adults aged 18 to 25 years is highest for all age groups and has been gradually rising since 2006. So, too, has the prevalence of past-year MUD increased from 2001 to 2013 among the general U.S. adult population (age 18 years and older). Given the widespread use of marijuana, there is concern of the development of MUD arising from frequent marijuana use. In general, groups with high marijuana use prevalence tend to also be those with high intensity of use, with some important exceptions (namely heavy marijuana users and adults over age 50).

While marijuana use has been gradually rising from its drop-off in 1992 when past-month marijuana use was one third of its peak, tobacco cigarette use has been largely declining since its peak in the mid-1960s (**Figures 8-10**). Tobacco product diversification, however, has resulted in tremendous changes to the tobacco cigarette trajectory. Now, among youths aged

15 to 17 years, e-cigarettes are more popular than traditional tobacco cigarettes, and hookah is the second most popular tobacco product among young adults. Most importantly, e-cigarette use is strongly associated with the use of other tobacco products among youth and young adults. Consequently, there is growing concern about increased susceptibility to tobacco product use among e-cigarette users. Further, the ability to use popular tobacco devices such as e-cigarettes or hookahs for both tobacco and marijuana product use elucidates another public health concern: co-, dual, or poly- use of tobacco and marijuana products.

Figure 8. Prevalent past 30-day marijuana and tobacco use among youth (12-17 years), 2002-2016

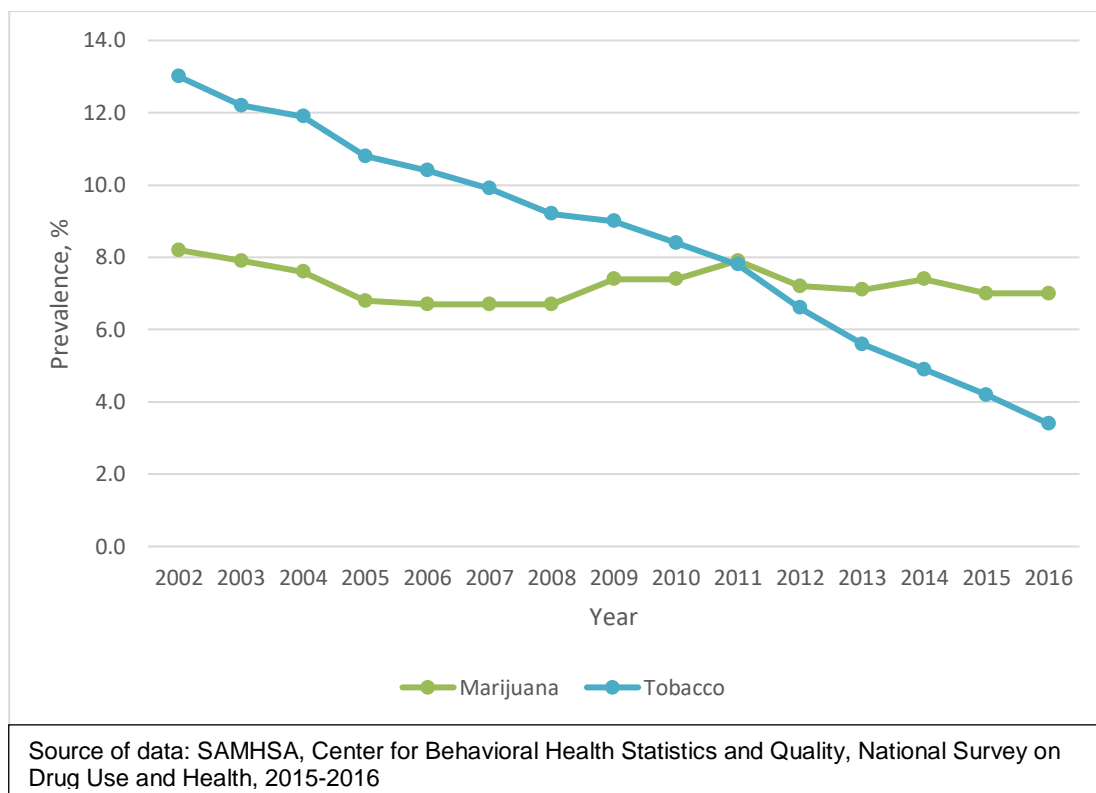


Figure 9. Prevalent past 30-day marijuana and tobacco use among young adults (18-25 years), 2002-2016

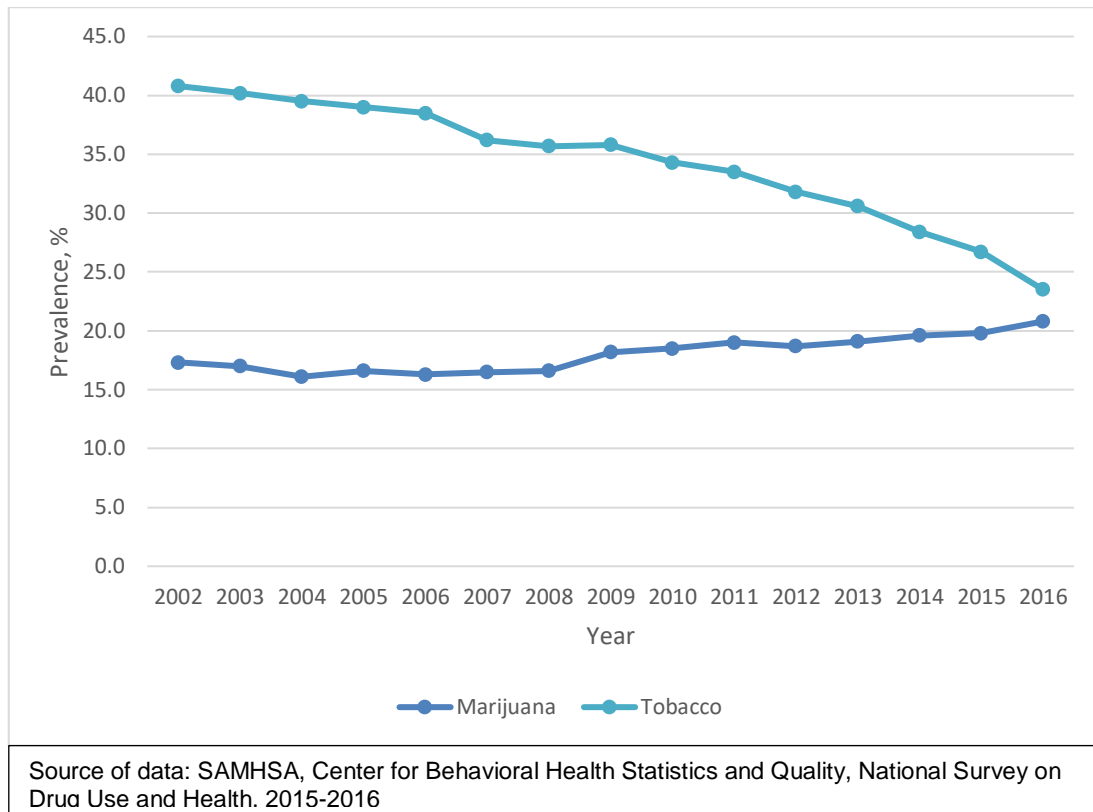
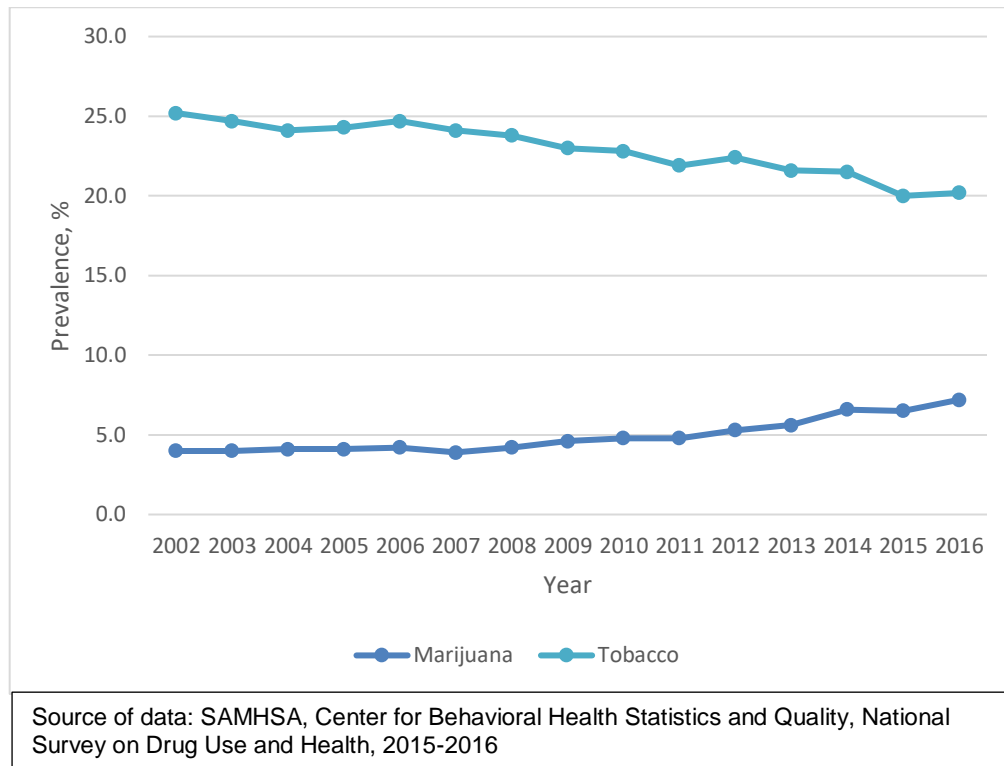


Figure 10. Prevalent past 30-day marijuana and tobacco use among adults (26+ years), 2002-2016



SECTION IV.

A Brief Review of the Marijuana and Tobacco Industries

During the 1970s and 1980s, tobacco use was considered a “gateway” to marijuana use among youth and young adults, but by 2005, marijuana use more often preceded tobacco use, resulting in a “reverse gateway” phenomenon (Ramo et al., 2013). The product diversification of the tobacco market—namely the explosive popularization of e-cigarettes—however, has slowed the two-decade-long declining tobacco use trajectory. The uptick in e-cigarette use, particularly among youth and young adults, has unknown impact on marijuana use. Similarly, the liberalization of marijuana regulation has resulted in increased availability and new products to meet consumer demand. These related, parallel processes are not happening in vacuums; rather, they will affect one another as users of all ages can now ambulate between dual-use and dual-marketed products. What may have been a clearly directional relationship between marijuana preceding tobacco use in 2005 may be quite different now. Particular age subgroups’ choice method(s) of product administration and co-use may shape a new phenomenon of co-marijuana and tobacco use with unforeseen and as yet unknown health consequences.

Marijuana: the “New Tobacco Industry?”

In 1998, tobacco industry litigation resulted in the release of millions of documents now housed in the Legacy Tobacco Documents Library at University of California San Francisco (Barry et al., 2014). These documents, which do not include many industry documents either destroyed or protected under “attorney-client privilege,” reveal that as early as 1970, all three multinational tobacco companies—Philip Morris, British American Tobacco, and RJ Reynolds—considered the manufacture of marijuana-containing cigarettes due to large sales potential and

to eliminate any product rivalry (Ellis, 1970; Philip Morris, 1970; Callahan Research Ass; 1972).

In January of 1971, news media in the U.S. speculated that the tobacco industry would enter the marijuana market, and *Time* magazine reported that “Tobacco men...figure [the marijuana market] could be legalized within five years” (Barry et al., 2014). In 1980, British American Tobacco circulated a memorandum discussing future product development and potential to normalize its use:

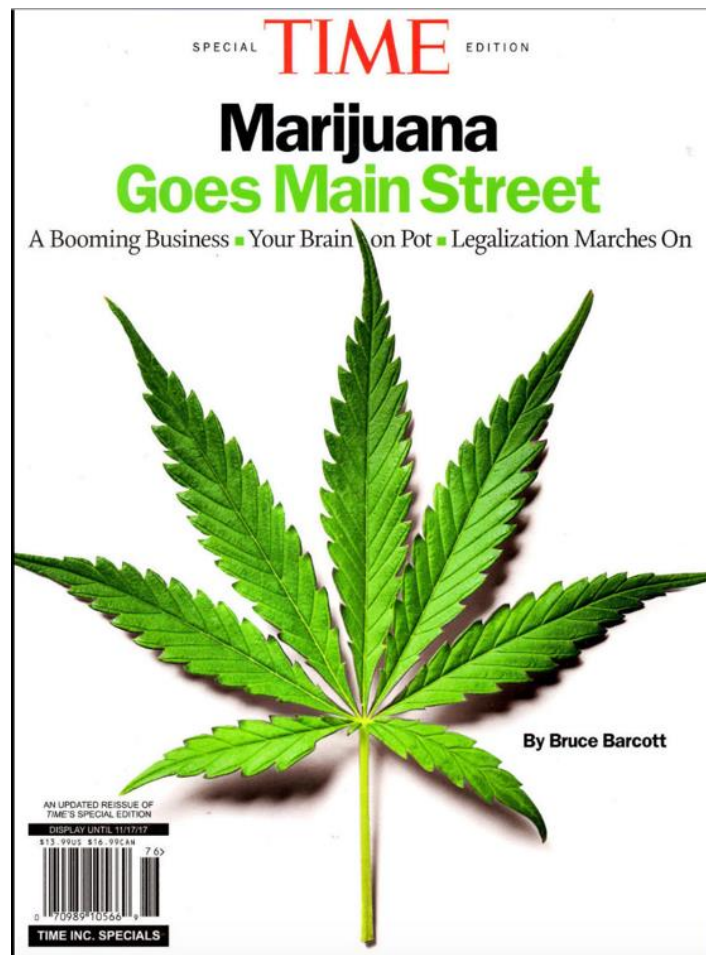
“The mood affecting drug requirements of the population will in the future increase, but the range of requirements will encompass tranquilisers e.g. valium, endorphin/encephalin (brain opiates), marijuana, nicotine analogues, etc. At present the taking of many of these drugs is either medically prescribed or regarded as deviant behavior, but could be “socialized” like alcoholic drinking and tobacco smoking (Vagg and Champman, 2005)”

From 1970 to 1990, the tobacco industry conducted a series of studies on marijuana smokers primarily focused on youth, African Americans, and individuals of lower socioeconomic status (Barry et al., 2014). Cigarette companies purposely aligned their marketing campaigns to target youth and African Americans and noted a strong connection between menthol cigarette smokers and marijuana users (Barry et al., 2014). In the decade that followed, no internal documents from the multinational tobacco companies show interest in marijuana legalization, presumably due to President Richard Nixon’s “war on drugs,” until the early 1990s when use began to rise again among youth and young adults (Golub et al., 2005).

The discussion of industry documents is important because, despite public statements denying their involvement in marijuana research, tobacco companies have been closely monitoring marijuana’s social acceptability and preparing for its market debut for the last 40 years, both in the United States and the United Kingdom (Barry et al., 2014). The marijuana debate is not new; nor is industry’s interest in the marketing of marijuana products novel. What

is new is the recent rate at which U.S. marijuana policy is changing (see the 2017 special issue of *Time* magazine, **Figure 11**, below), albeit several decades after first predicted. These policies appear to either reflect and/or support the normalization, and therefore socialization, of marijuana use, just like the tobacco industry predicted. Multinational tobacco companies have been preparing to enter the marijuana market with incentives to increase use for almost 50 known years, so it would be no surprise for the same companies that turned cigarettes into the world's most widely used vessel for nicotine delivery to want to promote and sell marijuana, the world's most-used illicit drug (Proctor, 2011).

Figure 11. Cover of *Time* magazine's 2017 Special Edition.



Drug policy, and namely marijuana policy, reform advocates cite adverse social consequences like the imprisonment of thousands of primarily young, black men (Levine & Reinerman, 1991; Earlywine, 2007); the “war on drug’s” generation of the black market, crime, violence, corruption, and their associated societal costs (Caulkins, et al., 2012; Earlywine, 2007); and marijuana’s less severe morbidity and mortality profile (Joffe et al., 2004) as reasons to legalize marijuana use. Absent from their list of considerations, however, is the multinational tobacco industry’s potential effect on market entry: market power to manipulate the consumer and regulatory frameworks and capacity to engineer marijuana products to maximize them as drug delivery systems (Sklair, 2002). While some claim that increased marijuana tax from small entrepreneurs will help states fund academic and health efforts, others fear that the tobacco corporation will overtake the marijuana market and create and/or exacerbate yet another public health problem (Sklair, 2002).

As Candi CdeBabca, a Colorado resident and Mexican-American youth worker who voted to legalize retail marijuana in her state, said:

“We have just swapped one kind of drug dealer for another. I believed it would positively impact communities of colour by decriminalizing it. So watching it unfold has been surprising...It’s your typical capitalist who is in our neighborhood now and benefiting from an industry that at one time was our only option.” (McGreal, 2016).

In fact, after recreational marijuana use was legalized in Colorado, the city of Denver’s zoning laws required commercial marijuana growers to move into industry-zoned areas, which happen to be in some of the poorest parts of the city (McGreal, 2016). In Colorado’s Pueblo County, there are 20 licensed retail marijuana stores, outnumbering all of the McDonald’s, Starbucks, and Walmart stores combined; 31% of high school students report “using marijuana” (compared to the national average of 22.5% of 12th graders reporting past 30-day marijuana use

in 2016); and hospitals voice concern over a “rise in newborns testing positive for the drug” (McGreal, 2016). Pueblo County commissioner Sal Pace argues that the marijuana industry has created 1300 jobs, brought in \$4m in tax revenue, and helped to “[regulate] the product.” (McGreal, 2016).

Summary

Tobacco and marijuana are related via shared genetic factors, similar route of administration (i.e. smoking), and co-administration (e.g. blunts, or marijuana wrapped in a cigar shell) (Agrawal et al., 2012). Aware of these shared factors, the tobacco industry has been anticipating and preparing for the arrival of marijuana into mainstream use since 1970. While research has shown evidence for gateway, reverse gateway, and substitution effects (Beenstock and Rahav, 2002; Agrawal et al., 2007; Leatherdale et al., 2007) between marijuana and tobacco, the current social and political environment will require new research to understand the patterns and processes of tobacco and marijuana use and co-use. The marijuana and tobacco industries will be sure to keep pace with consumer demand, so research on use patterns and consequences of use must, too.

SECTION V.

Trajectories of Marijuana and Tobacco Use

There is a large body of work demonstrating the association between tobacco use and marijuana use among young people (Agrawal et al., 2008; Behrendt et al., 2009; Okoli et al.,

2008; Timberlake et al., 2007; Tullis et al., 2003; Ramo & Prochaska, 2012; Ramo et al., 2013; Leatherdale, 2007; Passarotti et al., 2015). However, this body of literature is primarily comprised of cross-sectional studies that cannot elucidate temporal relationships between use of these two products and do not often differentiate between specific forms, frequency, or intensity of marijuana and/or tobacco use. Less is known about how tobacco and marijuana use co-vary over the entire lifespan, from adolescence to young adulthood. Moreover, it is important to consider whether the new climate surrounding marijuana legalization and the popularity and availability of e-cigarette products will affect tobacco and marijuana dual use. Will tobacco use continue to primarily precede marijuana use in time, and further, will these patterns vary across the developmental life course and by product type? Examining these questions, given today's landscape and marketplace, is critical for informing policy and practice in relevant ways, in the future.

Data have thus far suggested that dual product use may be attributable to increases in prevalence of marijuana use among tobacco users, rather than increases in tobacco use among marijuana users (Schauer et al., 2015; SAMHSA, 2016). Further, known mechanisms by which tobacco and marijuana use are related include shared genetic factors, similar methods of administration (e.g. smoking) and co-administration (e.g. "blunts" that contain marijuana and/or tobacco inside of a cigar shell), and substitution or facilitation effects in which marijuana use causes smokers to smoke fewer cigarettes or vice versa in which marijuana use causes smokers to increase their cigarette use intensity (Ramo et al., 2013).

New liberalized marijuana use policies coincide with greater public acceptance of marijuana use, discussed in Section I. Further, new products available for tobacco consumption

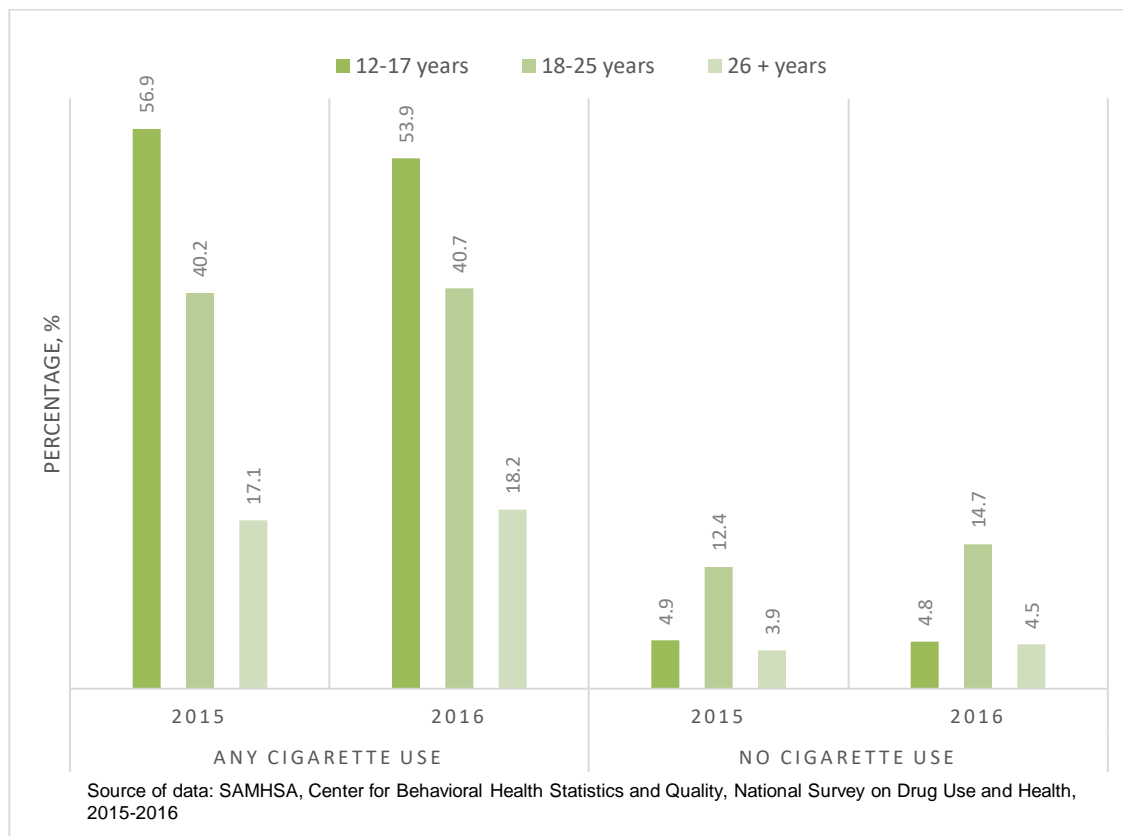
(e.g. e-cigarettes) can be sold and marketed in tandem for marijuana use, promoting dual use (Schauer et al. 2015). It is imperative, therefore, that researchers begin to describe the patterns of use and dual use within and across marijuana and tobacco product types and across the lifespan. Reliable longitudinal data will be necessary to accurately capture these dynamic patterns of use, which will have profound public health implications, particularly given rising rates of use among adolescents and adults and high rates of use among young adults. Although interventions regularly target substance use individually (Prochaska & Prochaska, 2011), it has been shown that interventions targeting tobacco within a broader context of other substance dependence have demonstrated significant post-treatment effects on tobacco use and improved long-term sobriety (Myers and Prochaska, 2008; Prochaska et al., 2004).

Adolescents and young adults

Tobacco and marijuana dual use commonly occur among adolescents—even more so than among young adults and adults. Among past 30-day cigarette smokers aged 12-17 years in 2016, 53.9% used marijuana in the past 30-days, compared with 40.7% of young adult past 30-day cigarette smokers aged 18-25 years and 21.8% of adult past 30-day cigarette smokers aged 18 or older (**Figure 12**) (SAMHSA, 2016). Recent NSDUH estimates of the complementary data—or, the percentage of past 30-day cigarette smoking among past 30-day marijuana smokers—are not available for adolescents or young adults specifically. In fact, this directional relationship—of cigarette smoking among marijuana users—is not commonly assessed in the literature (most likely because it is generally much lower marijuana use among cigarette smokers) and has been reported for adult age sub-groups (Schauer et al., 2015; Richter et al.,

2004) but not for youth or young adults and not with the most recently available nationally-representative data.

Figure 12. Past 30-day marijuana use in among persons aged 12 and older, by past month cigarette use: percentages, 2015 and 2016



Gateway (tobacco use implicated as a gateway to marijuana and/or other illicit drug use) (Beenstock and Rahav, 2002; Bentler et al., 2002; Agrawal et al., 2007; Lai et al., 2000; Leatherdale et al., 2007) and reverse gateway (marijuana use implicated as a gateway to tobacco initiation) effects (Agrawal et al., 2008; Behrendt et al., 2009; Okoli et al., 2008; Timberlake et al., 2007; Tullis et al., 2003) have been commonly explored and cited as the causes of this dual use. Numerous studies have examined the dual use of marijuana and tobacco among adolescents and young adults (Table 5), and most suggest that marijuana users

have higher rates of cigarette use compared to non-users and, vice versa, that tobacco users have higher rates of marijuana use compared to non-smokers. However, because most studies measure the initiation of marijuana use among tobacco users instead of the reverse, it is difficult to say with certainty whether the first use of one is more likely to result in the use of the other.

Unfortunately, most of the studies in Table 5 were conducted with cross-sectional data, qualitatively, outside of the U.S., longitudinally but with older data that cannot account for new tobacco and marijuana delivery devices (e.g. e-cigarettes) or the changes in recreational and medical marijuana policy; or among specific populations—namely African Americans.

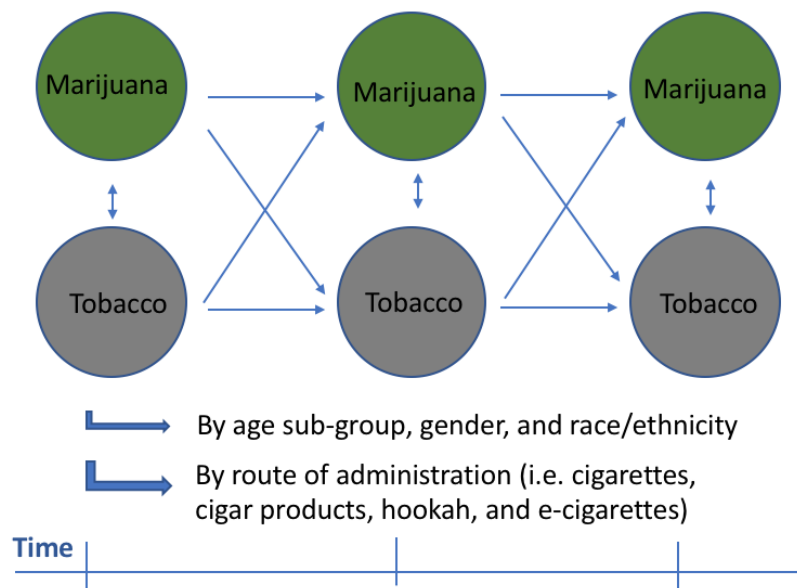
In their now almost 10-year-old quasi-systematic review of English language articles published between 1999 and 2009 examining the dual use of tobacco and marijuana, Ramo et al. (2012) identified three correlates supporting a positive association with dual use of tobacco and marijuana: African-American ethnicity, mental and physical health characteristics, and school characteristics (Ramo et al., 2012). They report inconsistent findings in sex differences in the dual use of both marijuana and tobacco and stress that since dual use is so prevalent among both sexes, tobacco and marijuana dual use should be considered equally important for males and females (Ramo et al., 2012). Lastly, they identified numerous areas of importance (i.e., future directions for research) that were absent in the literature: parenting and peer characteristics related to dual use, patterns of dual use explicitly within youth and young adults, and the impact of prevention interventions measuring tobacco and marijuana dual use (Ramo et al., 2012)

Around the same time that Ramo et al. (2012) attempted to synthesize what was then known about dual use of marijuana and tobacco, Agrawal and Lynskey (2009) summarized the known hypotheses of reasons for dual use (the gateway hypothesis, the reverse gateway hypothesis, the correlated genetic vulnerabilities hypothesis (Neale et al., 2006), and the common environmental risks hypothesis (Conrad et al., 1992; Gifford-Smith et al., 2005; Golub et al., 2005)) and identified another important yet overlooked fifth influencer: route of administration (Agrawal and Lynskey, 2012). They hypothesized that if route of administration contributes to the association between tobacco and marijuana use, then marijuana use and abuse/dependence will be more strongly associated with smoked versus smokeless tobacco use, even after adjusting for nicotine dependence and other known confounders (Agrawal and Lynskey, 2012). From their cross-sectional analysis of 2001-2002 National Epidemiological Study on Alcohol Related Conditions (NESARC) data, they found that those who used smoked forms of tobacco were significantly more likely to be marijuana users ($RRR=3.27$, 95%CI 3.02,3.55)¹¹ and to develop abuse/dependence ($RRR=4.54$, 95%CI =4.03,5.13) after adjusting for other covariates and nicotine dependence (Agrawal and Lynskey, 2012). However, this study did not include routes of administration of marijuana other than smoked marijuana and hashish, did not include e-cigarettes, and was cross-sectional in design, limiting its ability to shed light on patterns of use over the lifespan.

¹¹ RRR, or relative risk ratios, are equivalent to multinomial odds ratios. 95%CI reported is the 95% confidence limits. Those using neither smoked nor smokeless forms are the reference group. Lastly, covariates included sociodemographic, psychiatric, and substance use covariates from NESARC (e.g. sex, age, Caucasian race/ethnicity, poverty, college education, South/Midwest, immigrant, conduct disorder, major depression, generalized anxiety disorder, panic disorder, social anxiety disorder, nicotine dependence, alcohol dependence, other illicit drugs, and family history).

There has not been a more recently conducted meta-analysis or systematic review of correlates of dual use, risk factors for dual use, or consistency in findings other than Ramo et al.'s 2012 synthesis. Ramo et al. (2013) identified that little is understood about the relationship between tobacco and marijuana cognitions in young people who use both marijuana and tobacco. Further, it is unknown how psychosocial factors (such as affect, stress, temperament or novelty-seeking, risk/problem behavior, parental monitoring and authority, and peers) may have different roles in the initiation or continuation of marijuana use over time (Passarotti et al., 2015). Even more fundamental data are missing on the potential multi-directional paths of dual use of marijuana and tobacco (**Figure 13**)—particularly for tobacco use among marijuana users—for age sub-groups of youth and young adults, as mentioned earlier.

Figure 13. Possible multi-directional relationships between marijuana and tobacco cigarette use. Single-headed arrows represent single product use. Double-headed arrows represent co-use.



Thus, there are notable gaps in the tobacco and marijuana dual use literature for adolescents and young adults. More recent descriptions and analyses of longitudinal dual use patterns (e.g. Goodwin et al., 2018) have not considered or reported these patterns by route of administration and do not present their longitudinal results through a lens other than marijuana use among tobacco smokers. Consequently, there is still little known about the transition from initiation of either tobacco or marijuana to established use of one or the other product or dual use during adolescence and into young adulthood. In order to better answer these questions and others mentioned earlier, it is necessary to investigate these patterns of marijuana and tobacco use and dual use in multiple directions, by route of

administration, race/ethnicity, gender, and age subgroups of adolescents and young adults separately over time.

Adults “aged 18 and older”

Despite Ramo et al. (2012)’s claim that most of the studies examining long-term effects of tobacco and marijuana dual use have been conducted in adult samples, it appears that far less is understood about trajectories of and factors associated with dual use among adults. Several studies have examined dual use among adults (Goodwin et al., 2018; Schauer et al., 2015; Richter et al., 2008), though the age criterion for “adults” (>18 years of age) is often inclusive of young adults, whereby reporting results for both age groups together. Hence, young adults’ (aged 18 to 25 years) tobacco and marijuana use can differ substantially from older adults (aged 26 and older), but most research is conducted and reported on adults “aged 18 and older.” As such, it is worthwhile to review the current adult literature with a keen focus on age-specific results, whenever possible.

Richter et al. (2008) used adult data (those >18 years) from the 1997 National Household Survey on Drug Abuse (precursor to the NSDUH survey) and found that compared to nonusers, the adjusted odds of being a smoker were 5.43 for past 30-day marijuana users. More recent NSDUH data show that among past 30-day cigarette smokers aged 26 years and older years in 2016, 17.1% used marijuana in the past 30-days, compared with just 4.5% who did not use cigarettes in the past 30 days (**Figure 12**, above) (SAMHSA, 2016). Among adults, the literature consistently suggests that there is a substitution phenomenon between tobacco and marijuana in which reduction in use of one substance

results in an increase in the use of the other substance (Copersino et al., 2006). Schauer et al. (2015) found that dual use of marijuana and tobacco among adults increased between 2003 and 2012, among males and females, among those ages 26-34 and 50+ years, and across most racial/ethnic groups. Their findings led them to call for more research on dual use for individuals ages 50+ since they observed increases in dual use despite this age group's low marijuana use prevalence (<2%) (Schauer et al. 2015). While we have a general understanding of prevalent use and dual use rates among adults, almost nothing is known about how dual use can vary over the course of adulthood. In 2016, among past 30-day cigarette smokers aged 26 years or older in 2016, 18.2% used marijuana in the past 30 days (SAMHSA, 2016). Since tobacco users represent about 18% of the US adult population, this is troubling for the future of both tobacco and marijuana prevention efforts in this population.

Summary

Numerous studies have examined the dual use of marijuana and tobacco among youth, young adults, and adults, and most suggest that marijuana users have higher rates of cigarette use compared to non-users and, vice versa, that tobacco users have higher rates of marijuana use compared to non-smokers. Less is understood about the risk of initiation of tobacco use among marijuana users since marijuana use among tobacco users is more commonly measured and reported. More research is necessary, considering multiple possible directions of use, methods of use, race/ethnicity, and age subgroups, to begin to understand the transition from initiation of either tobacco or marijuana to established use

of one or the other product or dual use during adolescence, into young adulthood and beyond

TABLES

Table 1. The health effects of tobacco and marijuana use in children, youth, young adults, and adults

Population	Health endpoint	Health Consequence of Exposure		
		Marijuana	Cigarettes	Tobacco E-cigarettes
Children (< 12 years of age)	Cancer			
	Cardiovascular disease			
	Immune function and related disorders, including metabolic disorders			
	Reproductive health outcomes			Preterm delivery and stillbirth
	Lung development and function		Respiratory symptoms; impaired lung function and growth resulting from maternal smoking;^ lower respiratory illness^; coughing, phlegm, wheezing, and dyspnea; asthma-related symptoms	
	Cognitive function & Mental Health			Negative impacts on brain development via prenatal nicotine exposure, associated with dysregulation of catecholaminergic, serotonergic, and other neurotransmitter system; altered development of corpus callosum; deficits in auditory processing; disruptive attention and behavior deficits
	Other	Lower birth weight	Middle ear disease; sudden infant death syndrome^	Negative fetal development; sudden infant death syndrome
	Therapeutic benefit		None	
Youth (12-17 years)	Cancer			
	Cardiovascular disease			
	Immune function and related disorders			
	Reproductive health outcomes		Congenital defects from maternal smoking, including orofacial clefts; low birth weight^	

	<p>Lung development and function</p> <p>Cognitive function & Mental Health</p> <p>Other</p>	<p>Development of schizophrenia or other psychoses, with the highest risk among the most frequent users (note: transition highest among those who started use prior to 15 years of age); development of problem marijuana use</p>	<p>Impaired lung function; early onset of lung function decline; coughing, phlegm, wheezing, and dyspnea; asthma-related symptoms</p>	<p>Respiratory irritation (e.g. upper respiratory irritation) due to exposure to aerosolized solvents</p> <p>Negative impacts on neurobiological brain development and experience-induced plasticity; later adult nicotine addiction; Increase in drug-seeking behaviors; deficits in attention and cognition; mood disorders</p> <p>Eye and irritation from exposure to aerosolized solvents; explosion or fire associated with malfunctioned devices; poisoning through contact exposure or intentional or unintentional ingestion of e-liquid</p>
	Therapeutic benefit	None		
<i>Young adults (18-25 years)</i>	<p>Cancer</p> <p>Cardiovascular disease</p> <p>Immune function and related disorders</p> <p>Reproductive health outcomes</p> <p>Lung development and function</p> <p>Cognitive function & Mental Health</p> <p>Other</p>		<p>Early abdominal aortic atherosclerosis</p>	<p>Measurable increase in plasma nicotine concentrations; increases in heart rate and blood pressure, suggestive of typical cardiovascular effects exerted by nicotine</p> <p>Respiratory irritation (e.g. upper respiratory irritation) due to exposure to aerosolized solvents</p> <p>Neurobiological insult from nicotine; experience-induced plasticity; Risk for nicotine dependence</p> <p>Eye and irritation from exposure to aerosolized solvents; explosion or fire associated with malfunctioned devices; poisoning through contact exposure or intentional or unintentional ingestion of e-liquid</p>

Therapeutic benefit			None	
<i>Adults (26 years +)</i>	Cancer		Oropharynx; larynx; esophagus; trachea, bronchus, and lung; acute myeloid leukemia; stomach; liver; pancreas; kidney and ureter; cervix; bladder; colorectal	Respiratory irritation (e.g. upper respiratory irritation) due to exposure to aerosolized solvents Risk for nicotine dependence Eye and irritation from exposure to aerosolized solvents; explosion or fire associated with malfunctioned devices; poisoning through contact exposure or intentional or unintentional ingestion of e-liquid
	Cardiovascular disease		Stroke; aortic aneurysm; coronary heart disease; atherosclerotic peripheral vascular disease	
	Immune function and related disorders		Diabetes; rheumatoid arthritis; immune function	
	Reproductive health outcomes	Lower birth weight of offspring	Reproductive effects in women, including reduced fertility; male sexual function--erectile dysfunction; ectopic pregnancy; premature rupture of the membranes, placenta previa, and placental abruption; preterm delivery and shortened gestation	
	Lung development and function	Worse respiratory symptoms and more frequent chronic bronchitis episodes	Pneumonia; chronic obstructive pulmonary disease; tuberculosis; asthma; and other respiratory effects	
	Cognitive function & Mental Health	Development of marijuana use disorder (MUD)	Blindness, cataracts, age-related macular degeneration; congenital defects; periodontitis; overall diminished health; nasal irritation^	
	Other	Increased risk of motor vehicle crashes		
Therapeutic benefit			Improving Chronic pain in adults; reduced hemotherapy-induced nausea and vomiting; improving patient-reported multiple sclerosis spasticity symptoms	Potentially less addictive than conventional cigarettes
			None	

Sources:

- 1- National Academy of Sciences (The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research), 2017; US Department of Health and Human Services Surgeon General's 2016 (E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General) and 2014 (The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General)
- 2- U.S. Department of Health and Human Services. The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

Note: Summaries of health endpoints by product are taken from the 2012, 2014, and 2016 Surgeon General Reports (US Department of Health and Human Services) for tobacco and the 2017 report from the National Academy of Sciences for marijuana. For marijuana, Only health endpoints with "substantial," or "conclusive" evidence have been included; endpoints with moderate, limited, or no/insufficient evidence were not included. For tobacco, evidence needed to be sufficient to infer a causal relationship between tobacco exposure and the health outcome of interest. Strong evidence from randomized controlled trials was required to support the conclusion that marijuana or cannabinoids are an effective -treatment (i.e., had some therapeutic benefit) for the health endpoint of interest

[^] Indicates health consequence causally linked to exposure from secondhand tobacco smoke

*See below **Tables 3 and 4** for Weight of Evidence Categories

Table 2. Health impacts of marijuana use¹

Population	Outcome area	Limited or No evidence of...
Adults	<i>Cancers</i>	Cancers
Adults		Cancer-associated anorexia and anorexia nervosa
Adults		Symptoms or irritable bowel syndrome
Adults		Spasticity in patients with paralysis due to spinal cord injury
Adults		Symptoms associated with amyotrophic lateral sclerosis
	<i>Other</i>	Chorea and certain neuropsychiatric symptoms associated with Huntington's disease
Adults		Motor system symptoms associated with Parkinson's disease
Adults		Dystonia
Adults		Achieving abstinence in use of addictive substances
Adults		Mental health outcomes in individuals with schizophrenia or schizophreniform psychosis
Adults	<i>Mental health</i>	Incident esophageal cancer
Adults		Incident prostate cancer, cervical cancer, malignant gliomas, non-Hodgkin lymphoma, penile cancer, anal cancer, Kaposi's sarcoma, or bladder cancer
Adults		Subsequent risk of developing acute myeloid leukemia/acute non-lymphoblastic leukemia, acute lymphoblastic leukemia, rhabdomyosarcoma, astrocytoma, or neuroblastoma in offspring
Adults	<i>Cancer</i>	

Adults	<i>Cardiometabolic Risk</i>	Increased risk of acute myocardia infarction
Adults	<i>Respiratory Disease</i>	Hospital admissions for COPD
Adults		Asthma development or asthma exacerbation
Adults	<i>Immunity</i>	Other adverse immune cell responses in health individuals
Adults		Adverse effects on immune status in individual status in individuals with HIV
Adults		Increased incidence of oral human papilloma virus
Adults	<i>Injury and Death</i>	All-cause mortality
Adults		Occupational accidents or injuries
Adults		Death due to marijuana overdose
Infants, Youth	<i>Prenatal, Perinatal, and Neonatal Exposure</i>	Later outcomes in the offspring (e.g. sudden infant death syndrome, cognition/academic achievement, and later substance use)
Youth	<i>Psychosocial</i>	Impaired academic achievement and education outcomes
Adults		Increased rates of unemployment and/or low income
Adults		Impaired social functioning or engagement in developmentally appropriate social roles
Adults		Sustained abstinence from marijuana use and impairments in cognitive domains of learning, memory, and attention

Adults		Increase in positive symptoms of schizophrenia among those with psychotic disorders
Adults		Likelihood of developing bipolar disorder, among regular or daily users
Adults	<i>Mental Health</i>	Development of any type of anxiety disorder except social anxiety disorder
Adults		Increased symptoms of anxiety
Adults		Increased severity of posttraumatic stress disorder (PTSD) symptoms among those with PTSD
Children	<i>Problem Marijuana Use</i>	Childhood anxiety and childhood depression are risk factors
Youth, Young Adults		Initiation of tobacco use
	<i>Abuse of Other Substances</i>	
Youth, Young Adults		Changes in the rates and use patterns of other licit and illicit substances
<p><i>Source:</i></p> <p>1- National Academy of Sciences (The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research), 2017; US Department of Health and Human Services Surgeon General's 2016 (E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General) and 2014 (The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General)</p>		

Table 3. Weight of evidence marijuana health effects (National Academy of Sciences, 2017)

	Conclusive evidence	Substantial evidence	Moderate evidence	Limited evidence	No or insufficient evidence
Therapeutic effects	There is strong evidence from randomized controlled trials to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.	There is strong evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.	There is some evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.	There is weak evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.	There is no or insufficient evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.
Other health effects	There is strong evidence from randomized controlled trials to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.	There is strong evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.	There is some evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.	There is weak evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.	There is no or insufficient evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.
For this level of evidence	There are many supportive findings from good-quality studies with no credible opposing findings. A firm conclusion can be made, and the limitations to the evidence, including chance, bias, and confounding factors, can be ruled out with reasonable confidence.	There are several supportive findings from good-quality studies with very few or no credible opposing findings. A firm conclusion can be made, but minor limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.	There are several supportive findings from good- to fair-quality studies with very few or no credible opposing findings. A general conclusion can be made, but limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.	There are supportive findings from fair-quality studies or mixed findings with most favoring one conclusion. A conclusion can be made, but there is significant uncertainty due to chance, bias, and confounding factors.	There are mixed findings, a single poor study, or health endpoint has not been studied at all. No conclusion can be made because of substantial uncertainty due to chance, bias, and confounding factors.

Table 4. Weight of evidence categories for tobacco health effects (Surgeon General, USDHHS, 2016)

Level 1	Evidence is sufficient to infer a causal relationship
Level 2	Evidence is suggestive but not sufficient to infer a causal relationship
Level 3	Evidence is inadequate to infer the presence or absence of a causal relationship (which encompasses evidence that is sparse, of poor quality, or conflicting)
Level 4	Evidence is suggestive of no causal relationship

Table 5. Evidence summary of dual use of marijuana and tobacco among particular age groups in the U.S.

Study Authors	Year	Population	Region of Study	Conclusion
Richter et al.	2004	Adults age 18 years and older (1997 NHSDA)	U.S.	Nearly 3/4 of current marijuana users (74%) smoked cigarettes. Compared to nonusers, the adjusted odds of being a smoker were 5.43 for current marijuana users, 3.58 for past year marijuana users, and 2.02 for former marijuana users. Odds for cigarette smoking among current poly-drug users, compared to nonusers, were 2.3 to 1. Level of cigarette smoking was directly associated with frequency of marijuana use.
Timberlake et al.	2007	Young adults (18-27 years) (1994-1995 National Longitudinal Study of Adolescent Health)	U.S.	In the older cohort (17–21-year-olds at wave I), lifetime (>10 times) and past-month marijuana use at wave I were predictive of an earlier initiation into daily cigarette smoking and a greater likelihood of developing nicotine dependence by wave III. Age at first use of cannabis was negatively associated with risk of nicotine dependence in the older, but not younger (18-22-year-olds) cohort.
Tullis et al.	2007	Young adults (median age of 21 years)	Florida, U.S.	Of students currently smoking tobacco and marijuana in the same hour (65% of sample), 73% smoked marijuana before ever smoking cigarettes or began smoking both tobacco and marijuana simultaneously.
Leatherdale	2007	Young adults (2004 Canadian Tobacco Use Monitoring Survey)	Canada	Rates of marijuana use were highest among current smokers and lowest among never smokers. Marijuana use was more prevalent among males, young adults living in rural areas, and increased with age.
Agrawal et al.	2008	Female twins aged 18-29 years (Missouri Adolescent Female Twin Study, 2002-2005)	Missouri, U.S.	Women who used cannabis were at 4.4 and 2.8 increased hazards for transitioning from initiation to regular smoking and from regular smoking to nicotine dependence respectively
Okoli et al.	2008	Youth (mean age 15.4 years) (2004 British Columbia Youth Survey of Smoking and Health II)	British Columbia	Marijuana users were 5.9 times more likely to be current tobacco smokers and reported higher levels of perceived addiction to tobacco as compared with marijuana non-users.

Behrendt et al.	2009	Individuals aged 14-24 years (Early Developmental Stages of Psychopathology Study, 1970-1981)	U.S.	Alcohol, cannabis and other illicit substance use co-occurred with the risk of transition to nicotine dependence in later onset users (e.g. overall difference (age of onset ≤ 11 years): HR 0.69, 95% CI: 0.5–0.9; overall difference (age of onset ≤ 12): HR 0.65, 95% CI: 0.5–0.8; overall difference (age of onset ≤ 13 years): HR 0.67, 95% CI: 0.5–0.8; overall difference (age of onset ≤ 14 years): HR 0.71, 95% CI: 0.6–0.8).
Agrawal et al.	2010	Twins aged 8–17 years (Virginia Twin Study of Adolescent Behavioral Development)	Virginia, U.S.	No empirical evidence to suggest that the predominant sequence of drug use was one where cannabis use preceded onset of cigarette smoking: about 8% of the twins reported a lower age of cannabis versus cigarette initiation, 20% reported the same age at initiation for both, and cigarette smoking followed by cannabis use was the predominant pattern with 31% reporting onset of cannabis use within 1–2 years of starting to smoke cigarettes.
Ramo & Prochaska	2012	Young adults age 18-25 years (2009-2010)	U.S.	Co-use of tobacco and marijuana (53.1%) occurred on nearly half (median = 45.5%; IR = 13.1, 90.3) of the days on which either substance was used and was more frequent among Caucasians, respondents living in the Northeast or in rural areas, in nonstudents versus students, and in daily versus nondaily smokers.
Ramo et al.	2013	Young adults age 18-25 years (2009-2010)	U.S.	Compared with those who smoked only tobacco, co-users were younger and had smoked for fewer years; had higher household income; were more likely to be male, multiethnic, and nondaily smokers; and reported greater alcohol and other drug use. Marijuana in the past 30 days was associated with multiple measures of tobacco use intensity/frequency.
Webster and Chaiton	2014	Youth in grades 7, 9, and 11 from 1981-2011	Ontario, Canada	The prevalence of tobacco-only use, cannabis-only use, and co-use fluctuated considerably. During 1981-1993, there were more tobacco-only users than co-users and cannabis-only users; since 1993 the prevalence of tobacco use has decreased dramatically. Co-use prevalence peaked at 12% (95% confidence interval: 9, 15) in 1999, when prevalence of overall use of both substances was highest. In 2011, 92% of tobacco users also used cannabis, up from 16% in 1991.
Passarotti et al.	2015	Youth in 9th and 10th grades (Social and Emotional Contexts of Adolescent Smoking Patterns Study, 2004-2010)	Chicago, IL, U.S.	At baseline the marijuana Escalators and Non-escalators did not differ on cigarette smoking rates, but at 6 years the Escalators had significantly higher cigarette smoking rates than the Non-escalators

Montgomery	2015	African Americans age 12 years and older (2013 NSDUH)	U.S.	Relative to participants who smoked tobacco only, African Americans who smoked marijuana and tobacco reported less days of cigarette use (17.9 versus 19.8 days), more days of cigar use (11.6 vs 8.8 days), and smoking cigarette (15.9 vs 17.3), cigars (17.6 versus 20.7) and marijuana (15.3 versus 17.1) at a younger age.
Study Authors	Year	Population	Region of Study	Conclusion
Schauer et al.	2015	Adults age 18 years and older (2003-2012 NSDUH)	U.S.	From 2003 to 2012, past 30-day co-use of marijuana followed a significant nonlinear increasing trend (from 4.4% of the sample in 2003–2004 to 5.2% of the sample in 2011–2012). Past 30-day marijuana-only use increased, while adjusted past month tobacco-only use decreased. Tobacco use among marijuana users significantly decreased between 2003 and 2012 (from 74.3% in 2003–2004 to 69.6% in 2011–2012). Marijuana use increased significantly among tobacco users, from 14.2% in 2003–2004 to 17.8% in 2011–2012
Goodwin et al.	2018	Individuals age 12 years and older (2002-2014 NSDUH)	U.S.	Daily cannabis use occurs nearly exclusively among nondaily and daily cigarette smokers compared with former and never smokers (8.03%, 9.01%, 2.79%, 1.05%, respectively). Daily cannabis use increased over the past decade among nondaily (8.03% [2014] vs 2.85% [2002]) and daily smokers (9.01% [2014]; 4.92% [2002]). Daily cannabis use increased most rapidly among former cigarette smokers (2.79% [2014] vs 0.98% [2002]).
Antognoli et al.	2018	Youth age 14-18 (2015-2016)	U.S.	Twenty-five (83%) reported using cigarillos to smoke marijuana blunts. A preference for group smoking and product sharing, and the belief that cigarillos extend the high of marijuana were found to promote the co-use of these products. Cigarillos were also found to be used as a substitute for blunts when marijuana was unavailable or when its use was being restricted or monitored.

PUBLIC HEALTH SIGNIFICANCE

Enormous progress has been made in the reduction of adult tobacco users in the United States in the past five decades: about 43% of adults smoked tobacco in 1965, compared with about 18% in 2014 (CDC, 2014). Despite known negative health consequences, tobacco use still remains the leading preventable cause of death and disease in the U.S. (USDHHS, 2014).

Smoking-attributable healthcare expenditures account for an estimated 5%-14% of annual overall healthcare expenditures in the U.S., as some economic cost studies have shown (Bearman et al., 2011). In an analysis of the non-dental personal healthcare spending of adults aged 19 years and older in the National Health Expenditure Accounts (e.g. Medicare, Medicaid, and private insurance or type of medical services), the total attributable fraction of smoking-attributable healthcare spending amounted to \$170 billion per year (Xu et al., 2015).

Marijuana is the most widely used illicit drug in the world (SAMSHA, 2013), and the percentage of adult Americans who reported using marijuana in the past year has more than doubled in the last ten years (SAMSHA, 2013). Further, marijuana use disorder likewise nearly doubled over the same time frame, rising from 1.5 percent in 2001-2001 to 2.9 percent in 2012-2013 (SAMSHA, 2013). Previous research has demonstrated that tobacco and marijuana use often co-occur, that tobacco use has been implicated as a “gateway drug” to the use of marijuana and other illicit substances among youth and young adults (Beenstock and Rahav, 2002; Bentler et al., 2002; Agrawal et al., 2007; Lai et al., 2000; Leatherdale et al., 2007), or that conversely, marijuana use acts as a “reverse gateway” to the use of tobacco also among youth and young adults (Agrawal et al., 2008; Behrendt et al., 2009; Okoli et al., 2008; Timberlake et al., 2007; Tullis et al., 2003).

While the impact of legalization of marijuana is unclear, the health impacts of marijuana use, conversely, are well established. Marijuana has negative physical, cognitive, neuro-psychological, and psychosocial effects for adolescents, young adults, and mature adults (NCBI, 2017; Volkow et al., 2016, Meier et al., 2012). These effects are typically dose-dependent and worsen for more chronic marijuana users. Tobacco's effects have been well studied, and with each Surgeon General's Report new evidence emerges to expand the list of adverse health effects that result from smoking and exposure to tobacco smoke. As such, almost every organ of the body is impacted by smoking (CDC, 2014), and tobacco and marijuana dual use often leads to worse clinical outcomes, greater nicotine dependence, and the potential to create more barriers to smoking cessation (Baker et al., 2007; Piper et al 2008; Peters et al., 2012).

The cyclical relationship between marijuana and tobacco use is less understood as it relates to specific forms of use and changes in trends over time and the lifespan. Studies that have examined dual use often have little differentiation or specification of form of use, and many studies dichotomize marijuana use to a yes/no variable, limiting the ability to detect a relationship between frequency and intensity of marijuana use and tobacco use outcomes. In their review of the additive health impacts of dual use, Meier and Hatsukami (2016) lamented that numerous studies focus on blunt use as a primary method of dual use despite recent national survey data showing that only 20% of marijuana users smoked marijuana via blunts (compared with 49% using a bowl or pipe and/or joint). They urged for more studies to assess more prevalent forms of co-using tobacco and marijuana and highlighted the need to explore a more dynamic definition of dual use that includes several subtypes (e.g. "heavy tobacco/light marijuana user, light tobacco/heavy marijuana user") that fall along a continuum and vary by

product used (e.g. blunts, pipes, e-cigarettes, etc.) (Meier & Hatsukami, 2016). Lastly, the lack of prospective/longitudinal designs and reliance on cross-sectional data have resulted in an inability to detect changes over transitions through adolescence and into young adulthood.

Given the pace of legal change to marijuana policy, changing trends in individual marijuana use, and emerging products for tobacco use marketed in tandem to marijuana or dual users, researchers must adapt to track new patterns. With this proposal, tobacco use, marijuana use, and marijuana and tobacco dual use patterns will be described and analyzed over time with attention to product type and dual use frequency and intensity, when possible. Further, these patterns will be explored among adolescents and young adults, separately. Consequently, by using longitudinal data, this research will characterize variations in use or dual use of tobacco and marijuana during adolescence and into young adulthood.

RESEARCH QUESTIONS

Given the unknown impact of new legal changes to marijuana policy, changing trends in individual marijuana use, and emerging products for tobacco use marketed in tandem to marijuana or tobacco dual users, the following Research Questions were pursued in the following three Journal Articles:

Research Question 1: In what ways (e.g. product and device type—conventional cigarettes, e-cigarettes, cigar products, and hookah—and use frequency) are tobacco and marijuana consumed by youth and young adults?, Have these methods changed over time (2014-2017)?

RQ_a: Do exclusive and dual tobacco and marijuana use increase, decrease, or remain constant with increasing age for youth and young adults?

RQ_b: Does the prevalence of past 30-day marijuana product use (none vs. any) among past 30-day tobacco product users increase, decrease, or remain constant with increasing age for youth and young adults?

RQ_c: Among past 30-day marijuana product users, how does the prevalence of past 30-day tobacco product use (by specific product—e.g. cigarette, cigar, hookah, and e-cigarette) change with increasing age for youth and young adults

RQ_d: Are these use patterns for tobacco and marijuana significantly different for youth than for young adults?

Research Question 2: How does use of marijuana co-vary with the use of tobacco among youth over time (2014-2017)? Does marijuana use predict the use of tobacco, and/or does tobacco use predict the use of marijuana?

RQ_a: Do these patterns of use and co-use differ across these developmental stages of adolescence (e.g. early (6-8th grade), middle (8th-10th grade), and late (10-12th grade) adolescence)?

RQ_b: Do these patterns of use and co-use differ by tobacco use method (e.g. any tobacco product, any combustible tobacco product, or e-cigarette)

Research Question 3: How does use of marijuana co-vary with the use of tobacco among young adults over time (2014-2017)? Does marijuana use predict the use of tobacco, and/or does tobacco use predict the use of marijuana?

RQ_a: Do these patterns of use and co-use change over young adulthood (18-25 years))?

RQ_b: Do these patterns of marijuana and tobacco use and co-use (above) differ by tobacco product (e.g. any tobacco product, any combustible tobacco product, or e-cigarette)?

JOURNAL ARTICLE (1)

Developmental Trends in Exclusive and Dual Tobacco and Marijuana Use among Youth and Young Adults in Texas

INTRODUCTION

While tobacco use, overall, has declined over the last decade among young people (Substance Abuse and Mental Health Services Administration, 2012; U.S. Department of Health and Human Services, 2012, 2016), the prevalence of marijuana use has held steady among adolescents and increased among young adults. (Substance Abuse and Mental Health Services Administration, 2016). From 2002 to 2016, past 30-day marijuana use among adolescents 12-17 years has inconsistently teetered between roughly 8.2% (2002) and 7.0% (2016), with occasional year-to-year increases and decreases (Substance Abuse and Mental Health Services Administration, 2016). Past 30-day marijuana use among young adults aged 18 to 25 years has been gradually rising since 2006, when the prevalence was 16.3%, and reached 20.8% in 2016 (Substance Abuse and Mental Health Services Administration, 2016). In a study of young adult marijuana users (N=36,309), the prevalence of past-year marijuana abuse or dependence increased significantly from 4.4% to 7.5% from 2001 to 2013 (Hasin et al., 2015a).

An emerging class of tobacco products (e.g., e-cigarettes, hookah) has complicated the public health environment surrounding successful tobacco prevention strategies. Concern over the tandem use of novel products (e.g., e-cigarettes) for both marijuana and tobacco consumption is also developing, as the social acceptability of marijuana use rises coincidentally with the decrease in perceived harm of marijuana (Compton et al., 2016; Substance Abuse and Mental Health Services Administration, 2016). Compared to other types of tobacco use, for example, e-cigarette use rose rapidly among adolescents and young adults, from 2011 through 2015 (USDHHS, 2016). Increasing marijuana use nationwide, particularly among some age groups (Hasin et al., 2015a), the increasing strength of marijuana (ElSohly et al., 2016), and different, increasingly popular routes of marijuana administration (Pacula et al., 2016) may reflect an increased vulnerability to the development of problem marijuana use or marijuana use disorder (MUD) relative to earlier national survey estimates from 2001-2005 when MUD prevalence was around 1.5% across all age groups, nationwide (Grucza et al., 2016; National Academies of Sciences, Engineering, and Medicine (US) et al., 2017).

There is a large body of work demonstrating the association between tobacco use and marijuana use among young people (Agrawal et al., 2008; Behrendt et al., 2009; Leatherdale et al., 2007; Okoli et al., 2008; Passarotti et al., 2015; Ramo et al., 2013; Ramo and Prochaska, 2012; Timberlake et al., 2007; Tullis et al., 2003). Tobacco and marijuana dual use commonly occur among adolescents—even more so than among young adults and adults. Among past 30-day cigarette smokers aged 12-17 years in 2016, 53.9% used marijuana in the past 30-days, compared with 40.7% of young adult past 30-day cigarette smokers aged 18-25 years and 21.8% of adult past 30-day cigarette smokers aged 18 or older (Substance Abuse and Mental Health Services Administration, 2016). Many of the health effects of marijuana are still to be determined

(National Academies of Sciences, Engineering, and Medicine (US) et al., 2017), but the health effects of tobacco are known to be detrimental (U.S. Department of Health and Human Services, 2014). Dual use of marijuana and tobacco can lead to psychosocial problems, greater likelihood of MUDs, and poorer marijuana cessation outcomes (Peters et al., 2012).

There are notable gaps in the tobacco and marijuana dual use literature for adolescents and young adults. Ramo et al. (2012)'s quasi-systematic review identified three correlates supporting a positive association with dual use of tobacco and marijuana: African-American ethnicity, mental and physical health characteristics, and school characteristics. Agrawal and Lynskey (2009), in their cross-sectional analysis of 2001-2002 National Epidemiological Study on Alcohol Related Conditions data, found that those who used smoked forms of tobacco were significantly more likely to be marijuana users (RRR=3.27, 95%CI 3.02,3.55)¹² and to develop marijuana abuse/dependence (RRR=4.54, 95%CI =4.03,5.13), after adjusting for other covariates and nicotine dependence. However, this study did not include routes of administration of marijuana other than smoked marijuana and hashish, did not include e-cigarettes, and was cross-sectional in design, limiting its ability to shed light on patterns of use over the lifespan and to assess the use of more novel products (e.g., e-cigarettes). More recent descriptions and analyses of longitudinal dual use patterns (e.g., Goodwin et al., 2018) do not present their longitudinal results through a lens other than marijuana use among tobacco smokers, so it is unclear how problematic tobacco use is among marijuana users.

Due to limitations of previous research like these, there is still little known about dual use of marijuana and tobacco throughout adolescence and into young adulthood, particularly now, as the tobacco product market has diversified, and the social acceptability of marijuana has risen, which may have profound impacts on use patterns. Contemporary trend data about the co-variation in these two products is also missing. In order to better understand how youth and young adults are using tobacco and marijuana over the course of adolescent-to-young-adult maturation, we investigate these patterns of exclusive marijuana and tobacco use and dual use of these products by route of administration over age for adolescents and young adults, separately.

Despite the many gaps in the literature on dual use of marijuana and tobacco, the growing body of evidence on tobacco use patterns may provide an important foundation on which to explore marijuana use and dual use of both products. For example, substantial recent evidence has shown that tobacco use onset is changing: initiation of tobacco products among never-using young adults may now be greater than among youth (Bernat et al., 2012; Perry et al., 2018; Thompson et al., 2018). Further, increased ever and current use onset among young adults includes the onset of not only cigarettes (Thompson et al., 2018) but also e-cigarettes, cigar products, and hookah (Perry et al., 2018). Researchers point toward the tobacco control regulations, which include point-of-sale retail, price discounting, samples, digital media, magazines, and adult public entertainment (Bach, 2016), that occurred during the 1990s and

¹² RRR, or relative risk ratios, are equivalent to multinomial odds ratios. 95%CI reported is the 95% confidence limits. Those using neither smoked nor smokeless forms are the reference group. Lastly, covariates included sociodemographic, psychiatric, and substance use covariates from NESARC (e.g. sex, age, Caucasian race/ethnicity, poverty, college education, South/Midwest, immigrant, conduct disorder, major depression, generalized anxiety disorder, panic disorder, social anxiety disorder, nicotine dependence, alcohol dependence, other illicit drugs, and family history).

2000s to explain the decline in adolescent smoking. Additionally, many of the behaviors traditionally associated with adolescence—such as drinking alcohol (Johnston et al., 2017) or getting married (Arnett, 2007) have been shifting to (later) young adulthood, so there may be some trend to delayed behavior initiation.

There is also substantial evidence to show that adolescents approaching young adulthood are at the highest risk for initiating marijuana use (Substance Abuse and Mental Health Services Administration, 2016, 2013). The most recent 2016 NSDUH estimates showed that 12-17-year-old individuals by far comprised the largest percentage of past year marijuana initiates at 4.8% among the total population and 9.3% among persons at risk for initiation¹³, with the majority of past-year initiates being 16 to 17 years of age (Substance Abuse and Mental Health Services Administration, 2016). Data have thus far suggested that dual tobacco and marijuana product use may be attributable to increases in prevalence of marijuana use among tobacco users, rather than increases in tobacco use among marijuana users (Schauer et al., 2015; Substance Abuse and Mental Health Services Administration, 2016). However, recent estimates from longitudinal analyses of tobacco use among marijuana users are not available for youth or young adults, likely because this directional relationship is generally much smaller than cigarette smoking among marijuana users. Consequently, there is still little known about the exclusive use and dual use of tobacco and/or marijuana during adolescence and into young adulthood, but these are important estimates to monitor as marijuana regulation continues to unfold in the U.S. (Hasin, 2017; Schauer et al., 2015).

We therefore ask (i) how do exclusive and dual tobacco and marijuana use change with increasing age for youth and young adults; (ii) how does the prevalence of past 30-day marijuana product use (none vs. any) among past 30-day tobacco product users change with increasing age for youth and young adults; (iii) among past 30-day marijuana product users, how does the prevalence of past 30-day tobacco product use (by specific product) change with increasing age for youth and young adults; and (iv) are these use patterns for tobacco and marijuana different for youth than for young adults? Based on what we can draw from current research on marijuana and tobacco use among these age groups, we hypothesize that (i) any dual use of marijuana and tobacco products will be higher than exclusive use of either product for youth and young adults; (ii) prevalent past 30-day marijuana use will increase among the past 30-day tobacco users and with increasing age for youth and young adults; (iii) prevalent past 30-day tobacco use will increase among past 30-day marijuana users and with increasing age for youth and young adults; and (iv) (though not directly comparable samples) these patterns will be relatively similar for youth as for young adults.

METHODS

Protection of Human Subjects Considerations

Active, informed consent was obtained from both parents and students in TATAMS and from young adults in M-PACT. University of Texas Health Science Center at Houston Institutional Review Board reviewed and approved all study protocols for the TATAMS study

¹³ The NSDUH defines Persons at Risk for Initiation for a Specific Substance as “those who did not use the substance in their lifetime or who used the substance for the first time in the past year” (NSDUH, 2016)

(HSC-SPH-13-0377), and the University of Texas at Austin Institutional Review Board reviewed and approved all protocols for the M-PACT study (2013-06-0034).

Study Design, Setting, and Participants

Longitudinal data were derived from two parallel rapid response surveillance system studies of youth (aged 12-17 years) and young adults (aged 18-29 years) living in the five counties (Bexar, Dallas, Harris, Tarrant, and Travis) that surround the four largest cities in Texas (Austin, Houston, San Antonio, and Dallas/Fort Worth) from 2014 to 2017.

The Texas Adolescent Tobacco and Marketing Surveillance system (TATAMS) collects data from students who were in 6th, 8th, or 10th grade at baseline (n= 3907; weighted N =461,069). Among these, 48.9% were girls and 54.5% Hispanic, 21.4% non-Hispanic white, 17.6% non-Hispanic black students enrolled in 79 participating schools. TATAMS utilized a complex probability sampling design, described elsewhere (Pérez et al., 2017), to pull this population-based sample. Baseline data were collected in the classroom during the 2014-2015 academic year using computerized surveys administered via tablets in English or Spanish (Delk et al., 2017). Subsequent data have been collected outside the classroom every six months since baseline using similarly formatted web-based surveys taken online or with a smartphone in English. At Wave 6, collected in the spring of 2017, the retention rate exceeded 70%.

The Marketing and Promotions Across Colleges in Texas project (M-PACT) collects data from students age 18-29 years in 2-year and 4-year colleges (Loukas et al., 2016). Over 13,000 college students (n=13,714) were eligible to participate, and of these, 5482 (40%) completed the baseline survey in November 2014-February 2015 using computerized online surveys. Among these students, 63.4% were female and 36.3% non-Hispanic white, 31.1% Hispanic, 8.1% non-Hispanic black, and 16.9% Asian. Subsequent data have been collected online every six months since baseline using similarly formatted surveys taken on a computer or smartphone. At Wave 6, the wave of data collected in 2017, the retention rate for this study exceeded 80%. Additional information on sampling methods, eligibility criteria, and study power for the TATAMS and M-PACT studies are detailed elsewhere (Loukas et al., 2016; Perez et al., 2017).

Measures

Survey items were adapted from reliable and valid measures from national and state tobacco surveillance studies that include the Population Assessment of Tobacco and Health (PATH) study (Hyland et al., 2017), National Survey on Drug Use and Health (NSDUH) (Substance Abuse and Mental Health Services Administration, 2014), National Youth Tobacco Survey (NYTS) (Centers for Disease Control and Prevention, 2009), Monitoring the Future (MTF) (Bachman et al., 2005), and Youth Risk Behavioral Survey (YRBSS) (Centers for Disease Control and Prevention, 2013). These items underwent cognitive testing via interviews with 27 youth and 25 young adults, separately, to ensure comprehension (Hinds et al., 2016). The final surveys included over 340 items on tobacco use behaviors, exposure to tobacco media and marketing, and sociodemographic, cognitive, and affective factors (Delk et al., 2017).

Tobacco and Marijuana

At each wave (1-6), items from the TATAMS and M-PACT surveys assessed marijuana and tobacco product use (See Supplemental Table 1, Appendix). Ever and past 30-day use were assessed for tobacco products (conventional cigarettes, e-cigarettes, cigar products, and hookah). Ever use was assessed for the use of marijuana in spliffs, e-cigarettes, cigar products, and hookah. Most items were similar between the surveys, with three notable exceptions. Past 30-day marijuana use for youth was assessed with response options including “I have never used marijuana,” allowing for the derived variable creation of ever marijuana use. The M-PACT survey did not allow for derivation of ever use of marijuana. Secondly, the M-PACT survey asks specifically about marijuana use in a hand-rolled cigarette (“spliff”); the TATAMS survey did not assess marijuana use in this product. Lastly, the M-PACT study did not assess past 30-day use of marijuana in an e-cigarette, marijuana in cigar products, or marijuana in a hookah.

Age

Participants in the TATAMS youth cohort self-reported age and date of birth. The student’s age was calculated by subtracting the student’s reported birthdate from the known survey date (calculated age). If this calculated age matched the age reported by the student (reported age), then the calculated age was assumed to be the student’s true age. In this case, the birthdate reported by the student was unaltered. If the calculated age and reported age for a certain student did not match, the student’s birthyear was changed so that their calculated age would match the age dictated by a strict algorithm. Once everyone’s birthyear was changed, all ages were recalculated by subtracting the subject’s birthdate from the survey date.

The eight-level categorical age variable created for the youth in this analysis was based on the distribution of participants’ ages, which ranged from 10 to 19 years. So as not to lose excessive sample size by excluding ever-users of tobacco or marijuana products at baseline and since so few students ($n=13$) reported being 10 years of age at baseline, students aged 10 to 11 years at baseline were collapsed into a single category, “ ≤ 11 years.” Further, since (first) ever use prior to the age at baseline was not asked, it was impossible to determine the exact age of first ever use if it occurred outside of the survey. Each subsequent age year became a single age category through age 17. Students ages 18 and older were collapsed into a single category of “18+ years” since few students were 19 ($n=71$).

Young adults in the M-PACT cohort self-reported their birth date at Wave 1. Age and subsequent Wave ages were calculated based on the age reported at Wave 1. Young adults were also categorized by age. The nine-level age variable includes participants ranging in age from 18 to 30 years. Since the numbers of participants aged older than 27 to 30 years are substantially smaller than those 18 to 26 years, a single category of “26+ years” was created to collapse those individuals ($n=1246$ total).

Data Analysis

Analyses were conducted using SAS (Cary, NC, version 9.4). Data were analyzed for missingness across waves, which was handled using regression models that employed maximum likelihood estimation methods with robust standard errors (Schafer and Graham, 2002). All TATAMS analyses were weighted to account for the complex survey design, including clustering within schools; to account for non-response; and to generalize back to the population

from which the sample was taken (Pérez et al., 2017). M-PACT analyses were not weighted, as the study design did not necessitate weighting, but did account for clustering within schools (Loukas et al., 2016). All models were adjusted for survey wave in order to assess the independent impact of age on tobacco and marijuana use, accounting for any temporal trends. Sample size was small for certain cells, so we were unable to examine these trends by gender and race/ethnicity. Instead of reporting the stratified or adjusted estimates, the mean overall estimates are reported.

Descriptive statistics

Two-sided chi-square tests were used to detect differences in primary outcome variables between subgroups (e.g., sex and school/age level, marijuana products use, tobacco products use, and alcohol use) at baseline, and differences were deemed statistically significant at the 0.05 alpha level.

Modelling exclusive and dual use at each age

Ever exclusive and dual ever use of marijuana- and tobacco-specific products were examined at each age level for the youth (age ≤ 11 years-18+ years) and young adult (age 18-26+ years) cohorts. To be defined as an exclusive tobacco user, one could not have reported ever use of marijuana; likewise, exclusive marijuana users could not have reported ever use of tobacco. Dual users had to have reported ever use of both tobacco and marijuana. Model selection was used to determine the most appropriate structure for the age variable for both datasets; AIC values (smaller was better) showed age was most flexible and the model best fit with age included as a categorical variable. Weighted logistic regression was applied to the TATAMS data to estimate these rates in order to accommodate population weights.

Modelling past 30-day use trends with increasing age

Past 30-day marijuana use among past 30-day tobacco users and the corollary—past 30-day tobacco use among past 30-day marijuana users—were examined at all Waves 1-6 using Generalized Linear Mixed Models (GLMMs) and by product type (e.g., no tobacco products, any tobacco products, conventional cigarettes, cigar products, hookah, and e-cigarettes (non-combustible tobacco)) when possible (Tables 3a-3b). GLMMs were used to account for repeated measures and clustering of students within schools and to test for changes (e.g., increases or decreases) in the proportions of youth (TATAMS) and young adults (M-PACT) reporting tobacco- and marijuana-specific product use over time (Waves 1-6, 2014-2017). Past-30-day marijuana and tobacco use outcomes were modeled as binary variables with a logit link function. GLMMs allowed for the application of survey weights (TATAMS) and subject as a random effect variable (TATAMS and M-PACT). Significant changes in trends across categories of age were determined in regard to the prevalence of tobacco- and marijuana-specific product use. Past 30-day use was modelled as a dependent variable with age as the independent variable, estimating whether past 30-day use significantly increased or decreased from the youngest age category to oldest age category, i.e. p for linear trend < 0.05 , while adjusting for survey wave (time).

Missing data and analysis samples

Missing data for primary outcomes of ever and past 30-day marijuana and tobacco use were <1% for both youth and young adult cohorts. Missing data on other covariates in Tables 1a-1b were <5% but ranged up to as much as 12% for some variables that were not asked at all survey Waves 1-6 (namely alcohol use and binge drinking). As such, it was appropriate to utilize regression models that employed maximum likelihood estimation methods with robust standard errors, with the assumption that data were missing at random (Schafer and Graham, 2002).

Thus, for the youth cohort, 3907 students (weighted sample size of 461,069) and 5482 young adults provided data on select socio-demographic characteristics and ever use of tobacco and marijuana use and dual use (**Tables 1a and 1b, Figures 1a, 1b**). Of those total samples, 1245 (N=17,464) youth aged ≤ 11 -18+ and 3586 young adults aged 18-26+ were reportedly past 30-day tobacco users (**Figure 2a, 2b**) at any Wave. Similarly, 1395 (N=225,234) youth aged ≤ 11 -18+ and 1107 young adults aged 18-26+ were reportedly past 30-day marijuana users (**Figures 3a, 3b, 4a, 4b**) at any Wave.

RESULTS

Descriptive Analyses

At baseline, youth never tobacco product users (n=3039, N=459,569) differed from ever tobacco product users (n=842, N=459,569) in mean age (years) and by SES, race/ethnicity, alcohol use, environmental factors of family influence on smoking status, and mean sensation-seeking score ($p < 0.05$, **Tables 1a**). At baseline, young adults who reported never having used tobacco products differed from those who had reported ever tobacco use at baseline by sex, mean age, parental education, last month credit card debt, race/ethnicity, alcohol use, and intrapersonal factors ($p < 0.05$, **Table 1b**).

Trends in exclusive and dual use of marijuana and tobacco

Ever exclusive tobacco use, ever exclusive marijuana product use, and ever dual use of both products were examined for both the youth and young adult samples. Although attempts were made to stratify this analysis by product type (i.e. conventional cigarette or marijuana spliff, cigar products, hookah, e-cigarette), exclusive ever use of individual products in the youth sample was too low to report reliable estimates. For young adults, ever exclusive tobacco use was quite high, such that few were exclusive marijuana users. Hence, it became impossible to produce reliable estimates of exclusive marijuana use by product for young adults.

Unsurprisingly, any exclusive use of tobacco products significantly increased with increasing age among youth (p for linear trend < 0.001). Exclusive use of marijuana gradually increased with age among youth, but this increase was not significant (p for linear trend = 0.9169). Dual use of both tobacco and marijuana products in any combination was the most prominent form of use among the youth cohort, and ever use increased with age (p for linear trend = 0.0014), especially beginning around age 14 (**Figure 1a**). By age 18 and older, almost 6% of the cohort reported ever having used both marijuana and tobacco (**Figure 1b**). Among the young adult cohort, any exclusive tobacco use was the most prominent form of ever product use from age 18 to 26 and older, and this use significantly increased with age (p for linear trend < 0.001). The

highest increases in exclusive use of tobacco products occurred by age 21 and age 23. Exclusive marijuana use was so low among the young adult cohort that it registered as 0%. While dual use of tobacco and marijuana ranged from about 5% at age 18 to about 9% at age 26 and older; no significant increase or decrease was observed across these ages (p for linear trend=0.5699).

Trends in prevalent past 30-day marijuana use among past 30-day tobacco users at Waves 1-6

In order to understand past 30-day marijuana use (none vs. any at any Wave 1-6) among past 30-day tobacco users, analyses were subset to include only past 30-day tobacco users at any wave. **Supplemental Table 2** (See Appendix) provides product-specific mean percentage estimates and 95% Confidence Intervals used to produce **Figure 2**. Overall, among youth who reported using tobacco products within the past 30 days at any wave, past 30-day marijuana use almost steadily increased from age 12 when use was around 0% to 18 years and older when use peaked at around 60% (p for linear trend<0.001), with the most pronounced increases seen in the transitions from 12 to 13 years and from 14 to 15 years. Among young adults who reported using tobacco products within the past 30 days at any wave, past 30-day marijuana use almost steadily declined from age 18 to 26 years and older, falling from around 47% to around 24% (p for linear trend<0.001).

Trends in prevalent past 30-day tobacco use among past 30-day marijuana users at Waves 1-6

In order to understand past 30-day tobacco use trends (by product at any Wave 1-6) among past 30-day marijuana users, analyses were subset to include only past 30-day marijuana users at any wave. **Supplemental Table 3** (See Appendix) details the individual mean percentage estimates and 95% Confidence Intervals used to produce **Figure 3a-b** and **Figure 4a-b**. For the youth cohort, among past 30-day marijuana users at any wave, past 30-day tobacco product use rose sharply from 10% at age 12 to around 50% at age 13, when it dropped to around 30% before rising sharply again between age 14 and 15 (30 to 55.94%) and again from age 17 to 18 (53.71% to 77.63%) (p for linear trend<0.001). For the young adult cohort, among those who reported past 30-day marijuana use at any wave, past 30-day tobacco product use remained quite stable at around 20% from age 18 to 23 years, when use fell to around 10% before slowly climbing back to around 15% from age 24 to age 26 years and older (p for linear trend<0.001).

Figure 4 shows past 30-day tobacco use among past 30-day marijuana users by type of tobacco product. Marked differences in use patterns are evident between youth and young adults. For youth, past 30-day cigarette, cigar, hookah, and any combustible tobacco use all rose from around no use to as much as 80% in the transition from age 12 to 13 years before falling off at age 14, until cigarette smoking increased again at age 17 (p for linear trend_{cigarette}=0.0107; p for linear trend_{cigar}=0.0899; p for linear trend_{hookah}=0.2745; p for linear trend_{combustible}=0.0055). Past 30-day use of e-cigarettes, however, started to rise around age 13 and continued to rise steadily until age 18 (p for linear trend_{e-cigarette}=0.5818).

For young adult past 30-day marijuana users, past 30-day non-tobacco-users and combustible tobacco product users showed the most consistent use between age 18 and 26 and older (p for linear trend_{no tobacco}<0.001; p for linear trend_{combustible}=0.6564) (**Figure 4**). Past 30-day cigar use hovered around 10% from age 18 years to 26 and older (p for linear trend_{cigar}=0.0455), while past 30-day hookah use peaked at around 40% at age 20 before slowly falling to around 10% by age 26 (p for linear trend_{hookah}<0.001). Past 30-day cigarette and past

30-day cigarette use follow similar paths from age 18 to 23, teetering between 25% and 40%, when they both increased by as much as 15% while the past 30-day use of other products fell around the same age (p for linear trend_{e-cigarette}=0.3412; p for linear trend_{cigarette}=0.0097).

DISCUSSION

In the current study, we offer contemporary evidence for distinct developmental trajectories of marijuana and tobacco use for youth and young adults, drawn from data that were collected in major metropolitan areas of Texas, from 2014-2017. We originally hypothesized that (i) dual use of any tobacco and marijuana product would be higher than exclusive use of either product, but our findings indicated that dual use was higher than exclusive use of either product among youth only. We also posited that (ii) prevalent past 30-day marijuana use would increase among past 30-day tobacco users and with increasing age for both youth and young adults, but, again, this overall increase was observed among youth only. Among young adults, past 30-day marijuana use gradually decreased with increasing age, with the exception of a small uptick at age 24. We likewise hypothesized that (iii) prevalent past 30-day tobacco use would increase among past 30-day marijuana users with increasing age for both youth and young adults, but sharp increases were observed mostly for youth, not for young adults. Among young adults, the differentiation between tobacco users and non-tobacco users became quite evident. Hence, our last hypothesis—(iv) that these patterns would be relatively similar for youth as for young adults—was incorrect. Though the two populations were not drawn from the same original source but are drawn from the same cities and over the same time period, --and hence are reasonably comparable--, it appears that prevalent dual use of tobacco and marijuana, overall, are more common among youth than exclusive use of either product. Among young adults, exclusive combustible use was more prevalent than exclusive marijuana, e-cigarette or dual use of tobacco and marijuana. Furthermore, there appears to be much more experimentation with tobacco product use among youth marijuana users than young adult ones, which is troubling.

Exclusive and dual use of tobacco and marijuana products among youth from early to late adolescence

The present study mapped use of past 30-day tobacco product use among past 30-day marijuana users and past 30-day marijuana product use among past 30-day tobacco users in order to understand at what age(s) and with which product(s) use was occurring. Most studies to date have not considered marijuana use in conjunction with or exclusive to tobacco use among youth, so characterizations of this sort of youth use profiles may have been previously skewed. Our findings show that ever use and prevalent past 30-day marijuana use are common among youth and increase from early to late adolescence. Dual use of marijuana and tobacco (both ever and prevalent) increase from early to late adolescence more than exclusive tobacco use. Our results echo findings that more ever dual use occurs among youth than among young adults (Substance Abuse and Mental Health Services Administration, 2016). Shared genetic liability to use both tobacco and marijuana products, environmental factors such as peer use, easier access, and reduced perceptions of risk have all been cited as reasons for the increased

likelihood that these novel products (i.e. e-cigarettes and hookah) and subsequent marijuana will be used (Cerdá et al., 2016; Roditis et al., 2016; Roditis and Halpern-Felsher, 2015).

Among past 30-day marijuana users, combustible tobacco products and e-cigarettes were the most commonly used tobacco products, though use of almost all tobacco products (i.e. combustible, conventional cigarette, cigar, hookah, and e-cigarette) increased with age. Our results contrast slightly with recently published research from Audrain-McGovern et al. (2018), which showed that use at age 14 of novel forms of tobacco—i.e. e-cigarette and hookah— increased the odds of initiating to and current use of marijuana almost fourfold at 24 months follow-up, among a sample of public school children in Los Angeles, CA. Likewise, combustible cigarette smoking was found to be associated with an almost four-fold increase in the initiation of marijuana use and an almost two-fold increase in the current use of marijuana (Audrain-McGovern et al., 2018). The slight differences in findings may be attributable to the differences in the composition of the samples and regional or racial/ethnic popularity of particular tobacco products—namely, hookah--, as our sample was drawn from the five urban centers of Texas.

Exclusive and dual use of tobacco and marijuana products among young adults from early to late young adulthood

Exclusive tobacco use is common among young adults, and both ever use and past 30-day tobacco use increase from early to late young adulthood. Recent data show that young adults from 2013 to 2016 began to ever and currently (i.e. within the past 30-days) use all tobacco products more than youth, marking a stark contrast with decades of prior research that showed tobacco use initiation primarily occurred during adolescence (Perry et al., 2018).

We found exclusive marijuana use and dual tobacco and marijuana use to be less common than exclusive tobacco use among young adults. In fact, ever exclusive tobacco use was so high (almost 75%) that the number of exclusive marijuana users was not large enough to produce reliable estimates of exclusive marijuana use among young adults. We, therefore, conclude that while young adults use marijuana at the highest rates of any age sub-group (Substance Abuse and Mental Health Services Administration, 2016), they must most often do so in conjunction with tobacco use. Using data from NSDUH surveys from 2003 to 2012, Schauer et al. (2015) found that the co-use of tobacco and marijuana increased among adults aged 18 years but found disproportionate increases specifically among those ages 26-34 years and 50+ years. Our data show a small increase in dual use of tobacco and marijuana products but gradual decreases in past 30-day use of marijuana among tobacco users and past 30-day tobacco among marijuana users from age 18 to 24 and 25, respectively. Since our findings are not contrary to the findings from Schauer et al. (2015), it is possible, therefore, that dual use of marijuana and tobacco use may continue to increase after late young adulthood (i.e. age 26 and older).

Lastly, while past 30-day use of any combustible tobacco product, among past 30-day marijuana users, far exceeded use of any other product by almost 30%, tobacco e-cigarette use surpassed conventional cigarette use from early to later young adulthood at age 25 when e-cigarette use dipped below conventional cigarette use. This last observation supports previous research that showed smoked tobacco (i.e. conventional cigarette and cigar products) was significantly associated with both marijuana use and marijuana dependence (Agrawal and

Lynskey, 2009). Given the available survey items, we were unable to estimate prevalent past 30-day marijuana use by specific product among past 30-day tobacco users for youth or young adults. We cannot yet therefore assert that combustible marijuana use may be directionally associated with tobacco use.

Exclusive and dual use tobacco and marijuana products among youth and young adults

Our results show that ever dual use of marijuana and tobacco, relative to exclusive use of either product, is more common among youth than among young adults and that dual use increases throughout adolescence. Whether these trends are an indication of use patterns to come in the next few years, given the rapid introduction of novel and less-regulated products into the market, or are likely to taper with maturation into young adulthood has yet to be determined. Our results would suggest that dual marijuana and tobacco use decreases with young adulthood, or at least until age 25. However, troubling evidence suggests that while dual use may decrease overall with age, daily marijuana use occurs almost exclusively among nondaily and daily cigarette smokers, compared with former and never smokers, and daily marijuana use has increased over the past decade, most rapidly among former cigarette smokers (Goodwin et al., 2018). Given that tobacco use is still the primary cause of preventable death and disease in the U.S. (U.S. Department of Health and Human Services, 2014) and legal marijuana policies continue to be implemented (Cerdá et al., 2016), it will be important to continue to monitor dual use among both youth and young adults.

Study strengths and limitations

This study uniquely allows for the comparison of use trends among youth and young adults sampled from parallel rapid-response surveillance systems in the five major metropolitan areas of Texas. Though not directly comparable, the samples represent unique age subgroups that have been shown to be distinct in their uptake and use of tobacco and marijuana products. Further, literature is just emerging on specific tobacco product use trends for these sub-populations, and even less research is available on marijuana product use. As such, the present study provides novel estimates of exclusive and dual use of marijuana and tobacco, past 30-day use of these products, and, when possible, past 30-day product-specific estimates in order to answer questions surrounding at what age(s) and with which product(s) most use is occurring. The samples and study design, therefore, allow for the identification of important ages in the developmental spectrum of adolescence and young adulthood and to do this by specific product (i.e. combustible—conventional cigarette, cigar, or hookah—or non-combustible—e-cigarette) or use population (i.e. past 30-day marijuana or tobacco user).

A few limitations should be considered in the interpretation of this study's findings. The ability to estimate past ever exclusive marijuana use and 30-day use of marijuana by specific product among young adults was limited due to available sample size. The young adult cohort was specifically over-sampled, by original design, for tobacco users, though the use profile for young adults presented here may not be unique only to this sample of young adults but instead more characteristic of the use patterns of young adults as an age sub-group (i.e. there is little indication that the patterns we observed would be unlike those in a more general population of non-tobacco and tobacco users). Secondly, since some questions regarding past 30-day use by specific marijuana product were not asked in the instruments for either the youth or young

adults, it was not possible to produce estimates for all possible combinations of past 30-day use by product. Thirdly, these data may not generalize outside of the five major urban areas of Texas from which the study samples were drawn; though tobacco use data do seem comparable to national estimates (Perry et al., 2018). Lastly, while the demographic compositions of the youth and young adult cohorts were slightly different, the sampling designs for both cohorts were intentionally constructed to create comparable populations from which fair comparisons could be drawn (Loukas et al., 2016; Perez et al., 2017).

Recommendations for future research

As the present study has illustrated, a more dynamic consideration of use (i.e. by product and by use of tobacco or marijuana products among users of the other product) is warranted to characterize use patterns of tobacco and marijuana for youth and young adults. The next step in the characterization of use and dual use of tobacco and marijuana products would, logically, also benefit from the consideration of use frequency. Further, use and dual use could be considered separately by race/ethnicity and gender. Lastly, in order to help understand the behavioral mechanism(s) driving tobacco and marijuana use and dual use, it would be useful to track use of these products directionally (i.e. does use of one product precede or predict the use or dual use of the other or both?), also by product and by use frequency, whenever possible.

TABLES

Table 1a. Baseline characteristics (Wave 1, 2014-15) for total samples of youth aged 11-18 (n=3907; N= 461,069) and young adults aged 18-26 years (N=5482) who provided baseline tobacco and marijuana use data

Youth		Baseline Tobacco Product Use		Baseline Marijuana Product Use	
		Total (n=3893, N=460,506)		Total (n=3864, N=455,357)	
Sex (% , 95%CI)		% or mean	95% CI or SD	%	95% CI
	Male	51.14	(45.93-56.35)	51.40	(46.19-56.60)
	Female	48.86	(43.65-54.07)	48.60	(43.40-53.81)
Age, mean (SD)		14.27	0.19	14.35	0.18
SES, (% , 95%CI)					
	"Very well off"	19.72	(16.33-23.10)	19.74	(16.31-23.17)
	"Living comfortably"	61.9	(59.40-64.40)	61.83	(59.30-64.36)
	Low	18.13	(15.74-20.51)	18.14	(15.67-20.61)
Race/ethnicity, (% , 95%CI)					
	Non-Hispanic White/Other	27.88	(20.52-35.24)	28.00	(20.65-35.36)
	Non-Hispanic Black	17.56	(13.19-21.93)	17.69	(13.32-33.07)
	Hispanic	54.56	(47.42-61.69)	54.30	(47.29-61.31)
Alcohol Use					
	Past 30-day alcohol use (yes)	15.13	(12.08-18.18)	14.09	(11.42-16.76)
	Binge drinking in last 14 days (yes)	32.48	(26.65-38.31)	32.47	(26.65-38.30)
Environmental factors, (% , 95%CI)					
	Family influence (yes)	32.70	(29.84-35.57)	32.90	(29.99-35.81)
	Friend influence (yes)	35.23	(29.82-40.64)	35.27	(29.83-40.72)
Intrapersonal factors, mean (SD)					
	CESD / Emotional Problems	3.72	0.07	3.54	0.12
	Positive Affect - SDQ	2.40	0.17	2.47	0.30
	Sensation Seeking	3.28	0.07	3.21	0.10

Young adults		Baseline Tobacco Product Use		Baseline Marijuana Product Use	
		Total (N=5481)		Total (N=5476)	
Sex, No (%)		% or mean	n or SD	% or mean	n or SD
	Male	36.24	1985	36.22	1982
	Female	63.76	3492	63.78	3490
Age, mean (SD)		20.88	2.53	20.57	2.36
Parental Education					
	Some or no college	34.45	1825	34.44	1823
	College degree or higher	65.55	3472	65.56	3470
College type					
	2-year college	7.44	408	7.43	407
	4-year college	92.56	5073	92.57	5069
Last month credit card debt					
	None^^	57.38	1461	57.38	1458
	\$1-\$4,999	38.02	968	38.02	966
	\$5000-\$9,999	3.46	88	3.46	88
	\$10,000 or more	1.14	29	1.14	29
Race/ethnicity, n (%)					
	Non-Hispanic White	36.34	1992	36.36	1991

	Hispanic	31.13	1706	31.14	1705
	Non-Hispanic Black	8.14	446	8.14	446
	Asian	9.25	16.88	16.87	924
	Other	7.52	412	7.49	410
Alcohol Use					
	Past 30-day alcohol use (yes)	82.65	3010	34.02	1238
	Binge drinking (yes)**	92.31	1500	47.13	765
Intrapersonal factors, mean (SD)					
	CESD	8.06	5.53	7.84	5.40
	Impulsivity	2.05	0.67	2.00	0.66
	Sensation Seeking	2.79	0.68	2.69	0.68

Socioeconomic status (SES) was assessed for youth on the TATAMS survey by asking, “In terms of income, what best describes your family’s standard of living in the home where you live most of the time? Would you say your family is...” (Very well off, living comfortably, just getting by, nearly poor, or poor). The item responses were categorized as by collapsing the lowest three categories into a single category of “everyone else” versus “Living comfortably” versus “Very well off.”

^^Those without a credit card (n=2932, 53.52%) were excluded from the percentages reported above

Race/ethnicity: For TATAMS, Non-Hispanic White/Other category for youth includes race/ethnicity categories of White, Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Other. For M-PACT, the "Other" category was left as undefined in the response options.

Tobacco and marijuana use include those who (1) reported never having ever used any tobacco product at baseline, (2) reported any type of ever combustible (cigarette, cigar product--little filtered cigar, cigarillo, or large cigar) --use at baseline, (3) ever using an e-cigarette at baseline, and (4) ever use of any marijuana product at baseline.

**The binge drinking (sometimes called “heavy episodic drinking”) item is based on the Monitoring the Future item, which is only asked of anyone who reports drinking on 1 or more of the past 30 days. That current (past 30-day) item comes from PATH, which only asks about 5 or more drinks at a time (technically the male standard). Thus, it is possible that female binge drinking (which considers 4 or more drinks or more a binge episode) is being underestimated here.

~**Intrapersonal Factors.** *Positive affect* assessment was based on four items adapted from the Center for Epidemiologic Studies Depression Scale (Radloff, 1977); scores for youth ranged from 1-5, with higher scores indicating higher positive affect (Carey et al., 2018). For young adults, *Depressive symptoms* were assessed with the 10-item short-form Center for Epidemiologic Studies Depression 10 Scale (CES-D 10) (Andresen et al., 1994). Scores ranged from 1-10, with higher scores reflecting higher levels of depressive symptoms. Emotional problems were measured using the five-item emotional problem subscale on Strengths and Difficulties Questionnaire (SDQ; (Muris et al., 2003). SDQ Scores range between 0 and 10, with higher score reflecting more emotional problems (EHCAP, 2014). *Sensation-seeking* was assessed using the Brief Sensation Seeking Scale (Stephenson et al., 2003); scale ranged from 1-5, with higher scores indicating higher sensation seeking.

Impulsivity among young adults was assessed with 3 of the 4 items from the Substance Use Risk Profile Scale (SURPS) (Krank et al., 2011; Woicik et al., 2009); scores range from 1-5, and higher scores reflect higher levels of impulsivity.

Table 1b. Baseline characteristics (Wave 1, 2014-15) for total samples of youth aged 11-18 (n=3907; N= 461,069) and young adults aged 18-26 years (N=5482) by baseline tobacco and marijuana product use status (never vs. ever use)

Youth	Baseline Tobacco Product Use					Baseline Marijuana Product Use				
	Never (n= 3049, N=3447,140)		Ever (n= 844, N=113,366)		p-value	Never (n= 3591, N=415,248)		Ever (n= 273, N=40,109)		p-value
	% or mean	95% CI or SD	%	95% CI		% or mean	95% CI or SD	%	95% CI	
Sex (% , 95%CI)										
Male	75.69	(70.39- 80.99)	24.31	(19.01- 29.61)	0.8008	91.03	(88.15- 93.92)	8.96	(6.08- 11.85)	0.8567
Female	75.06	(70.33- 79.79)	24.94	(20.21- 29.67)		91.36	(88.92- 93.80)	8.64	(6.20- 11.08)	
Age, mean (SD)	13.11	0.17	14.27	0.19	<0.001 *	13.30	0.18	14.35	0.18	<0.001*
SES, (% , 95%CI)										
"Very well off"	79.39	(73.63- 86.14)	20.61	(13.86- 27.37)	0.0037 *	94.87	(92.24- 97.50)	5.14	(2.50- 7.76)	0.1201
"Living comfortably"	76.02	(71.73- 80.32)	23.98	(19.68- 28.27)		91.41	(89.28- 93.54)	8.59	(6.46- 10.72)	
Low	68.55	(61.74- 75.39)	31.45	(24.61- 38.28)		86.30	(80.57- 92.02)	13.70	(7.97- 19.43)	
Race/ethnicity, (% , 95%CI)										
Non-Hispanic White/Other	80.45	(74.72- 86.18)	19.55	(13.82- 25.28)	0.0131 *	94.82	(92.78- 96.85)	5.18	(3.15- 7.22)	<0.001*
Non-Hispanic Black	74.50	(68.66- 80.33)	25.50	(19.67- 31.34)		93.23	(89.88- 96.58)	6.77	(3.42- 10.12)	
Hispanic	73.08	(68.30- 77.85)	26.92	(22.15- 31.70)		88.66	(86.37- 90.95)	11.34	(9.05- 13.63)	
Alcohol Use										
Past 30-day alcohol use (yes)	42.69	(34.73- 50.66)	57.3	(49.34- 65.27)	<0.001 *	66.86	(59.37- 74.34)	33.14	(25.66- 40.63)	<0.001*
Binge drinking in last 14 days (yes)	25.60	(16.71- 34.49)	74.40	(65.51- 83.28)	0.009*	45.22	(34.68- 55.75)	54.78	(44.24- 65.32)	<0.001*
Environmental factors, (% , 95%CI)										
Family influence (yes)	69.58	(73.65- 82.75)	30.42	(25.08- 35.76)	<0.001 *	86.34	(83.14- 89.54)	13.66	(10.46- 16.86)	<0.001*

	Friend influence (yes)	51.64	(46.88-56.39)	48.36	(43.61-53.11)	-	81.69	(78.17-85.21)	18.31	(14.79-21.83)	<0.001*
	Intrapersonal factors, mean (SD)										
	CESD / Positive Affect	3.94	0.05	3.72	0.07	0.0171	3.92	0.04	3.54	0.12	0.0058*
	SDQ / Emotional Problems	2.05	0.08	2.40	0.17	0.051	2.11	0.09	2.47	0.30	0.2431
						<0.001					
	Sensation-seeking	2.76	0.05	3.28	0.07	*	2.86	0.05	3.21	0.10	0.0004*
Young adults	Baseline Tobacco Product Use					Baseline Marijuana Product Use					
		Never (n= 1751)		Ever (n= 3730)		p-value	Never (n= 4129)		Ever (n= 1347)		p-value
		% or mean	n or SD	% or mean	n or SD		% or mean	n or SD	% or mean	n or SD	
	Sex, No (%)										
	Male	29.97	595	70.03	1390	0.0170	73.06	1448	26.94	534	0.0019*
	Female	33.10	1156	66.90	2336	*	76.82	2681	23.18	809	
						<0.001					
	Age, mean (SD)	19.66	1.66	20.88	2.53	*	19.66	1.66	20.88	2.53	<0.001
	Parental Education										
	Some or no college	29.59	540	70.41	1285	0.0126	76.52	1395	23.48	428	0.1048
	College degree or higher	32.95	1141	67.05	2328	*	74.50	2585	25.50	885	
	College type										
	2-year college	31.13	127	68.87	281	0.7122	77.40	315	22.60	92	0.3623
	4-year college	32.01	1624	67.99	3449		75.24	3814	92.57	1255	
	Last month credit card debt										
	None^^	36.55	534	63.45	927		76.34	1113	23.66	345	0.6903
	\$1-\$4,999	16.94	164	83.06	804	<0.001	72.57	701	27.43	265	
	\$5000-\$9,999	10.23	9	89.77	79	*	85.23	75	14.77	13	
	\$10,000 or more	10.34	3	89.66	26		79.31	23	20.69	6	
	Race/ethnicity, n (%)										
	Non-Hispanic White	28.66	571	71.34	1421		71.47	1423	28.53	568	<0.001*

Hispanic	26.38	450	73.62	1256		74.66	1273	25.34	432	
Non-Hispanic Black	34.08	152	65.92	294	<0.001	74.22	331	25.78	115	
Asian	48.32	447	51.68	478	*	84.74	783	15.26	141	
Other	31.80	131	68.20	281		77.80	319	22.20	91	
Alcohol Use										
Past 30-day alcohol use (yes)	17.35	632	82.65	3010	<0.001	65.98	2401	5.93	109	<0.001*
Binge drinking (yes)**	7.69	125	92.31	1500	<0.001	52.87	858	47.13	765	<0.001*
Intrapersonal factors, mean (SD)										
CESD	7.38	5.04	8.06	5.53	<0.001	7.38	5.04	8.06	5.55	<0.001*
Impulsivity	1.89	0.62	2.05	0.67	<0.001	1.89	0.62	2.05	0.67	<0.001*
Sensation Seeking	2.48	0.64	2.79	0.68	<0.001	2.48	0.64	2.79	0.68	<0.001*

Note: Youth sample was restricted to ages 11-18 years and young adult sample restricted to ages of 18-26 years to ensure robust sample sizes, as both youth and young adult cohorts were originally sampled from 6th, 8th, and 10th grades, and 2- and 4-year colleges, respectively, making a wide age range of individuals possible for inclusion.

Socioeconomic status (SES) was assessed for youth on the TATAMS survey by asking, "In terms of income, what best describes your family's standard of living in the home where you live most of the time? Would you say your family is..." (Very well off, living comfortably, just getting by, nearly poor, or poor). The item responses were categorized as by collapsing the lowest three categories into a single category of "everyone else" versus "Living comfortably" versus "Very well off."

^^Those without a credit card (n=2932, 53.52%) were excluded from the percentages reported above

Race/ethnicity: For TATAMS, Non-Hispanic White/Other category for youth includes race/ethnicity categories of White, Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Other. For M-PACT, the "Other" category was left as undefined in the response options.

Tobacco and marijuana use include those who (1) reported never having ever used any tobacco product at baseline, (2) reported any type of ever combustible (cigarette, cigar product--little filtered cigar, cigarillo, or large cigar) --use at baseline, (3) ever using an e-cigarette at baseline, and (4) ever use of any marijuana product at baseline.

P-values shown above represent the statistical difference between ever and never tobacco and marijuana users and are considered statistically significantly different* at the 0.05 level.

**The binge drinking (sometimes called "heavy episodic drinking") item is based on the Monitoring the Future item, which is only asked of anyone who reports drinking on 1 or more of the past 30 days. That current (past 30-day) item comes from PATH, which only asks about 5 or more drinks at a time (technically the male standard). Thus, it is possible that female binge drinking (which considers 4 or more drinks or more a binge episode) is being underestimated here.

~**Intrapersonal Factors.** *Positive affect* assessment was based on four items adapted from the Center for Epidemiologic Studies Depression Scale (Radloff, 1977); scores for youth ranged from 1-5, with higher scores indicating higher positive affect (Carey et al., 2018). For young adults, *Depressive symptoms* were assessed with the 10-item short-form Center for Epidemiologic Studies Depression 10 Scale (CES-D 10) (Andresen et al., 1994). Scores ranged from 1-10, with higher scores reflecting higher levels of depressive symptoms. Emotional problems were measured using the five-item emotional problem subscale on Strengths and Difficulties Questionnaire (*SDQ*; (Muris et al., 2003). *SDQ* Scores range between 0 and 10, with higher score reflecting more emotional problems (EHCAP, 2014). *Sensation-seeking* was assessed using the Brief Sensation Seeking Scale (Stephenson et al., 2003); scale ranged from 1-5, with higher scores indicating higher sensation seeking. *Impulsivity* among young adults was assessed with 3 of the 4 items from the Substance Use Risk Profile Scale (SURPS) (Krank et al., 2011; Woicik et al., 2009); scores range from 1-5, and higher scores reflect higher levels of impulsivity.

Supplemental Table 1. Tobacco, marijuana, and alcohol constructs and items used for TATAMS (youth) and MPACT (young adults) surveys

Construct		TATAMS (youth survey)^	MPACT (young adult survey)*
Tobacco Measures cigarette	ever use	Have you EVER tried cigarette smoking, even one or two puffs? (No/Yes)	How old were you the first time you smoked part or all of a cigarette? (Under 10, 11....29, I don't remember how old I was, I have never smoked a cigarette, even 1 or 2 puffs)
	past 30-day use	During the past 30 days, did you smoke a cigarette (No/Yes) During the past 30 days, on how many did you smoke cigarettes? Please enter the number of days (from 0 to 30 days) (_ days)	- On how many of the past 30 days did you smoke cigarettes? (_ days)
e-cigarettes	ever use	Have you EVER used an electronic cigarette, vape pen, or e-hookah, even one or two puffs? (No/Yes)	Have you ever used an ENDS product (i.e., e-cigarette, vape pen, or e-hookah) as intended (i.e., with nicotine cartridges and/or e-liquid/e-juice), even one or two puffs? (No/Yes)
	past 30-day use	During the past 30 days, did you use an electronic cigarette, vape pen, or e-hookah? Remember, marijuana DOES NOT count. (No/Yes) During the past 30 days, did you use an electronic cigarette, vape pen, or e-hookah? (No/Yes) Please enter the number of days (from 0 to 30 days) (_ days)	During the past 30 days, have you used any ENDS product (i.e., an e-cigarette, vape pen, or e-hookah), even one or two puffs, as intended (i.e., with nicotine cartridges and/or e-liquid/e-juice)? (No/Yes) On how many of the past 30 days have you used such a product? (_ days)
cigar products	ever use	Have you EVER tried smoking a little filtered cigar/ large cigar or cigarillo, even one or two puffs? (No/Yes)	Have you ever used a little cigar/cigarillo/large cigar, as intended (i.e. with tobacco), even one or two puffs? (No/Yes)
	past 30-day use	During the past 30 days, did you smoke a little filtered cigar / large cigar or cigarillo? Remember, marijuana-filled DOES NOT count. (No/Yes) During the past 30 days, on how many days did you smoke a little filtered cigar / large cigar or cigarillo? Please enter the number of days (from 0 to 30 days) (_ days)	- During the past 30 days, on how many days did you smoke a cigar product (little cigar/ cigarillo/ large cigar) as intended (i.e. with tobacco)? (_ days, range of 0-30)
hookah	ever use	Have you EVER smoked a hookah, even one or two puffs? (No/Yes)	How old were you when you first tried smoking hookah as intended (i.e. with tobacco), even one or two puffs? (Under 10, 11....29, I don't remember how old I was, I have never smoked a hookah, even 1 or 2 puffs)

Marijuana Measures		past 30-day use	During the past 30 days, did you smoke hookah? Remember, marijuana DOES NOT count. (No/Yes) During the past 30 days, on how many did you smoke hookah? Please enter the number of days (from 0 to 30 days) (___ days)	- During the past 30 days, on how many days have you smoked a hookah as intended? (___ days, range of 0-30)
		past 30-day use	During the past 30 days, how many occasions, or times, if any, have you used marijuana (other names for marijuana are pot and weed)? (I have never used marijuana, 0 times, 1-2 times, 3-5 times, 6-9 times, 10-19 times, 20-39 times, 40 or more times)	During the past 30 days, how many occasions, or times, if any, have you used marijuana (other names for marijuana are pot and weed)? (0 times, 1-2 times, 3-5 times, 6-9 times, 10-19 times, 20-39 times, 40 or more times)
	cigarette	ever use	-	Have you ever smoked marijuana in a hand-rolled cigarette with tobacco/"spliff"? (No/Yes)
	e-cigarette	ever use	Have you EVER smoked marijuana (liquid THC) from an electronic cigarette, vape pen, or e-hookah, even one or two puffs? (No/Yes)	Have you ever smoked marijuana in a ENDS product (i.e. e- cigarette, vape pen, or e-hookah)? (No/Yes)
		past 30-day use	During the past 30 days, on how many days did you smoke marijuana (liquid THC) from an electronic cigarette, vape pen, or e-hookah? Please enter the number of days (from 0 to 30 days) (___ days)	-
	cigar products	ever use	Sometimes people take tobacco out of a little filtered cigar / large cigar or cigarillo and replace it with marijuana. Have you EVER smoked a little filtered cigar / large cigar or cigarillo with marijuana in it, even one or two puffs? (No/Yes)	Have you ever smoked marijuana in large cigar, cigarillo, or "blunt"? (No/Yes)
		past 30-day use	During the past 30 days, on how many days did you some a little filtered cigar /large cigar or cigarillo where the tobacco was taken out and replaced with marijuana? Please enter the number of days (from 0 to 30 days) (___ days)	In the past 30 days, have you smoked marijuana in a large cigar, cigarillo, or "blunt"? (Waves 3- 6 only)
	hookah	ever use	Sometimes people smoke marijuana from a hookah. Have you EVER smoked marijuana in a hookah with a hose such as the one pictured above, even one or two puffs? (No/Yes)	Have you ever smoked marijuana in a hookah? (No/Yes)
		past 30-day use	During the past 30 days, on how many days did you smoke marijuana from a hookah? Please enter the number of days (from 0 to 30 days) (___ days)	-
	Alcohol Measures			

alcohol	past 30-day use	During the past 30 days, on how many days did you have at least one alcohol drink? A drink of alcohol is 1 can or bottle of beer, 1 glass of wine, 1 can or bottle of wine cooler, 1 cocktail or shot of liquor. Do not count taking communion at church. (0 days, 1 or 2 days, 3 to 5 days, 6 to 9 days, 10 to 19 days, 20 to 29 days, all 30 days)	During the past 30 days, on how many days did you have at least one drink of alcohol? (0 days, 1 or 2 days, 3 to 5 days, 6 to 9 days, 10 to 19 days, 20 to 29 days, all 30 days)
	binge drinking	During the past 14 days, on how many days did you have 5 or more drinks of alcohol in a row? (0 days, 1 or 2 days, 3 to 5 days, 6 to 9 days, 10 to 14 days)	During the past 14 days, on how many days did you have 5 or more drinks of alcohol in a row? (0 days, 1 or 2 days, 3 to 5 days, 6 to 9 days, 10 to 14 days)
^In Waves 2-6, respondents were explicitly told to exclude the use of marijuana in these devices/products from these measures.			
*In Waves 2-6, respondents were asked if they used these devices/products as intended (i.e. with tobacco).			

Supplemental Table 2. Prevalence of past 30-Day Marijuana Product Use among Past 30-Day Tobacco youth (n=1245, N=17,464) and young adult (n=3586) users, by Marijuana Product, among youth and young Texas cohorts (2015-2017)

Characteristic		No marijuana products n= 2662 N=2235,835^			Yes marijuana products (n=1395, N=225,234)^		
		Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean
Youth Sample							
Age <=11	(n=698, N=111,620)	100.00%	0.00%	100.00%	0.00%	0.00%	99.79%
Age 12	(n=827, N=106,662)	100.00%	0.00%	100.00%	3.99%	0.52%	24.95%
Age 13	(n=1792, N=341,285)	49.00%	13.89%	85.12%	37.98%	16.79%	24.95%
Age 14	(n=2599, N=432,865)	75.11%	51.22%	89.66%	10.63%	4.92%	21.46%
Age 15	(n=3168, N=517,716)	59.35%	30.88%	82.68%	32.35%	19.64%	48.34%
Age 16	(n=3619, N=534,572)	60.93%	26.45%	87.12%	31.79%	16.63%	52.13%
Age 17	(n=3148, N=471,603)	14.24%	1.99%	57.57%	42.73%	22.08%	66.27%
Age 18+	(n=1770, N=260,092)	35.16%	4.66%	85.76%	61.48%	10.87%	64.90%
Young Adult Sample			n= 4104			n= 1107	
Age 18	(n=1568)	52.56%	45.01%	60.00%	47.44%	40.00%	54.99%
Age 19	(n=1696)	53.98%	46.49%	61.29%	46.02%	38.71%	53.51%
Age 20	(n=1497)	54.72%	46.68%	62.52%	45.28%	37.48%	53.32%
Age 21	(n=1423)	61.04%	52.84%	68.66%	38.96%	31.34%	47.16%
Age 22	(n=810)	68.09%	58.54%	76.33%	31.91%	23.67%	41.46%
Age 23	(n=479)	72.20%	60.19%	81.68%	27.80%	18.32%	39.81%
Age 24	(n=369)	65.48%	51.45%	77.25%	34.52%	22.75%	48.55%
Age 25	(n=294)	78.49%	64.12%	88.17%	21.51%	11.83%	35.88%
Age 26+	(n=576)	76.62%	65.83%	84.79%	23.88%	15.21%	34.17%
<p>*All proc glimmix models above adjusted for survey wave.</p> <p>Past 30-day marijuana product use includes joints, pipes, hookah, blunt, and e-cigarettes (i.e. vape pens, e-hookah, personal vaporizers).</p> <p>Ingested marijuana (such as food, drink, or other edibles) and smokeless tobacco (such as snus, moist snuff, dip, spit, pouches, and chewing tobacco) are not included in this analysis.</p> <p>Combustible tobacco device types include cigars or cigarillos, large cigars, and hookah. Non-combustible marijuana device types include e-cigarettes (i.e. vape pens, e-hookah, personal vaporizers).</p> <p>Cigar products include large cigars, cigarillos, and little (filtered) cigar products.</p> <p>^All youth sample sizes reported are weighted, scaled, and rounded up to the nearest 'whole person.' The scaled weights take into account school type (public, private, charter), POS (was the school close to a tobacco Point-of-Sale), grade (6th, 8th, 10th), and survey wave (Wave 1-6).</p> <p>All missing values are <5% of the sample and are hence not reported for individual strata.</p> <p>^Models have been adjusted for survey wave to take into account any temporal effect survey wave may have on pooled age sample estimates.</p>							

Supplemental Table 3. Prevalence of past 30-Day Tobacco Product Use among Past 30-Day Marijuana youth (n=1395, N=225,234) and young adult (n=1107) users, by Tobacco Product, among youth and young adult Texas cohorts (2015-2017)

Product [^]		No tobacco products			Yes tobacco products			Conventional cigarettes			Combustible Tobacco Products Cigar Products			Hookah			All Combustible Tobacco Products			Non-Combustible E-cigarette		
		(n= 2537, N= 270,383)			(n= 1245, N= 190,686)			(n= 410, N=66,736)			(n=240, N=42,064)			(n= 206, N=37,024)			(n= 671, N= 113,580)			(n= 914, N= 126,042)		
		Mea n %	Lower Mean	Upper Mean	Mea n %	Lower Mean	Upper Mean	Mea n %	Lower Mean	Upper Mean	Mea n %	Lower Mean	Upper Mean	Mea n %	Lower Mean	Upper Mean	Mea n %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean
Youth Sample [^]																						
Age <=11	(n= 10, N=13)	100.0 0%		100.00 %	0.00 %			0.00 %		100.00 %	0.00 %		100.00 %	0.00 %		100.00 %	0.00 %		100.00 %	0.00 %	0.00 %	100.00%
Age 12	(n=53, N=83)	100.0 0%	100.00 %	100.00 %	12.1 6%	1.98% %	48.65% %	0.00 %	0.00% %	100.00 %	0.00 %	0.00% %	0.00 %	0.00% %	100.00 %	0.00 %	0.00 %	0.00% %	0.00 %	0.00 %	0.00 %	100.00%
Age 13	(n=84, N=130)	28.00 %	1.84% %	88.95% %	54.1 5%	29.70% %	76.76% %	53.2 0%	10.39% %	91.77% %	21.1 3%	0.96% %	88.07% %	29.3 4%	1.85% %	90.16% %	81.4 7%	18.73% %	98.82% %	0.00 %	0.00 %	100.00%
Age 14	(n=164, N=215)	87.92 %	51.29% %	98.05% %	29.8 8%	16.43% %	48.03% %	9.05 %	1.35% %	42.01% %	5.94 %	0.86% %	31.52% %	3.79 %	0.48% %	90.16% %	13.1 4%	3.96% %	35.66% %	12.31 %	1.54% %	55.78%
Age 15	(n=364, N=347)	65.15 %	36.80% %	85.72% %	55.9 4%	41.50% %	69.45% %	12.6 2%	2.91% %	41.02% %	4.42 %	0.57% %	27.20% %	10.1 1%	1.29% %	49.12% %	23.5 7%	8.25% %	51.39% %	22.94 %	66.80% %	55.31%
Age 16	(n=400, N=380)	53.54 %	23.24% %	81.43% %	58.0 5%	43.30% %	71.49% %	18.7 9%	4.90% %	50.95% %	12.5 6%	1.54% %	56.93% %	4.28 %	0.54% %	26.77% %	30.9 0%	9.36% %	65.96% %	29.05 %	11.04% %	57.47%
Age 17	(n=279, N=247)	42.67 %	12.82% %	79.02% %	53.7 1%	35.11% %	71.34% %	26.6 3%	5.77% %	68.29% %	26.0 4%	2.37% %	83.61% %	25.7 2%	4.14% %	73.53% %	56.1 5%	19.01% %	87.48% %	38.19 %	9.81% %	77.83%
Age 18+	(n=144, N=135)	20.01 %	2.53% %	70.67% %	77.6 3%	56.14% %	90.39% %	75.3 8%	27.19% %	96.17% %	54.9 8%	4.04% %	97.25% %	9.08 %	0.20% %	82.94% %	86.7 4%	41.99% %	98.34% %	50.06 %	8.01% %	92.03%
Young Adult Sample [^]			n= 1700		n=3586			n=2585			n= 971			n= 1633			n= 3564			n= 1756		
Age 18	(n=1434)	79.57 %	73.69% %	84.42% %	20.4 3%	15.58% %	26.31% %	23.7 8%	17.12% %	32.02% %	12.4 2%	8.99% %	16.92% %	37.8 9%	31.46% %	44.78% %	70.8 3%	63.63% %	77.11% %	37.87 %	31.62% %	44.54%
Age 19	(n=1481)	80.75 %	74.96% %	85.47% %	19.2 5%	14.53% %	25.04% %	28.4 1%	21.11% %	37.04% %	10.1 2%	7.29% %	13.88% %	33.2 2%	27.16% %	39.88% %	72.6 4%	65.52% %	78.76% %	34.53 %	28.67% %	40.90%
Age 20	(n=1251)	82.66 %	77.01% %	87.16% %	17.3 4%	12.84% %	22.99% %	32.8 6%	24.35% %	42.66% %	12.6 0%	9.20% %	17.01% %	41.0 4%	34.08% %	48.38% %	75.3 5%	68.37% %	81.21% %	31.45 %	25.65% %	37.89%
Age 21	(n=1118)	80.80 %	74.49% %	85.85% %	19.2 0%	14.15% %	25.51% %	32.8 4%	23.96% %	43.14% %	12.6 7%	9.08% %	17.40% %	26.8 1%	20.74% %	33.90% %	72.1 7%	64.25% %	78.91% %	30.87 %	24.90% %	37.55%
Age 22	(n=599)	79.22 %	70.69% %	85.77% %	20.7 8%	14.23% %	29.31% %	24.6 0%	15.64% %	36.49% %	12.6 7%	9.08% %	17.40% %	28.3 4%	20.46% %	37.82% %	70.0 1%	59.71% %	78.61% %	36.45 %	28.33% %	45.42%
Age 23	(n=314)	81.27 %	70.48% %	88.75% %	18.7 3%	11.25% %	29.52% %	28.1 6%	15.76% %	45.10% %	12.9 4%	8.41% %	19.40% %	24.5 3%	15.44% %	36.65% %	70.8 5%	56.99% %	81.69% %	29.50 %	20.20% %	40.89%
Age 24	(n=238)	89.18 %	80.29% %	94.35% %	10.8 2%	5.65% %	19.71% %	56.8 0%	36.36% %	75.15% %	10.7 1%	5.91% %	18.61% %	19.0 9%	10.29% %	32.67% %	83.5 2%	71.22% %	91.21% %	43.95 %	30.62% %	58.21%
Age 25	(n=161)	86.81 %	73.38% %	94.02% %	13.1 9%	5.98% %	26.62% %	40.5 5%	19.70% %	65.48% %	19.8 2%	11.37% %	32.27% %	21.9 9%	10.80% %	39.62% %	79.0 7%	60.60% %	90.27% %	39.05 %	25.17% %	54.97%
Age 26+	(n=361)	84.41 %	73.90% %	91.19% %	15.5 9%	8.81% %	26.10% %	54.6 0%	36.20% %	71.82% %	9.65 %	4.45% %	19.68% %	10.2 9%	5.77% %	17.66% %	76.8 3%	62.95% %	86.61% %	28.82 %	20.31% %	39.16%
*All proc glimmix models above adjusted for survey wave.																						
Past 30-day marijuana product use includes joints, pipes, hookah, blunt, and e-cigarettes (i.e. vape pens, e-hookah, personal vaporizers).																						
Ingested marijuana (such as food, drink, or other edibles) and smokeless tobacco (such as snus, moist snuff, dip, spit, pouches, and chewing tobacco) are not included in this analysis.																						
Combustible tobacco device types include cigars or cigarillos, large cigars, and hookah. Non-combustible marijuana device types include e-cigarettes (i.e. vape pens, e-hookah, personal vaporizers).																						
Cigar products include large cigars, cigarillos, and little (filtered) cigar products.																						
[^] All youth sample sizes reported are weighted, scaled, and rounded up to the nearest 'whole person.' The scaled weights take into account school type (public, private, charter), POS (was the school close to a tobacco Point-of-Sale), grade (6th, 8th, 10th), and survey wave (Wave 1-6).																						
All missing values are <5% of the sample and are hence not reported for individual strata.																						
[^] Sample sizes reported are pooled across all ages. Models have been adjusted for survey wave to take into account any temporal effect survey wave may have on pooled age.																						

FIGURES

Figure 1a. Ever exclusive and dual tobacco and marijuana product use, among a cohort of Texas youth (2014-2017) (n=3907; N= 461,069) by age (years)

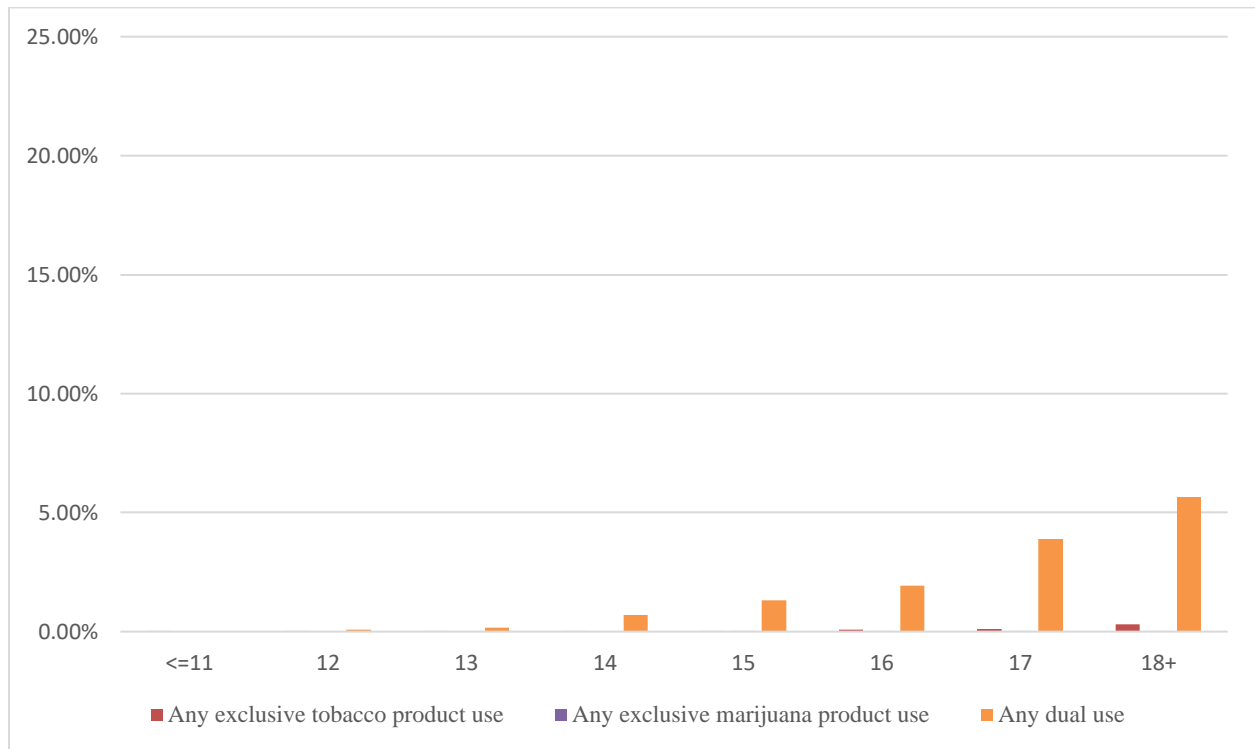


Figure 1b. Ever exclusive and dual tobacco and marijuana product use, among a cohort of Texas young adults (2014-2017) (N=5482) by age (years)

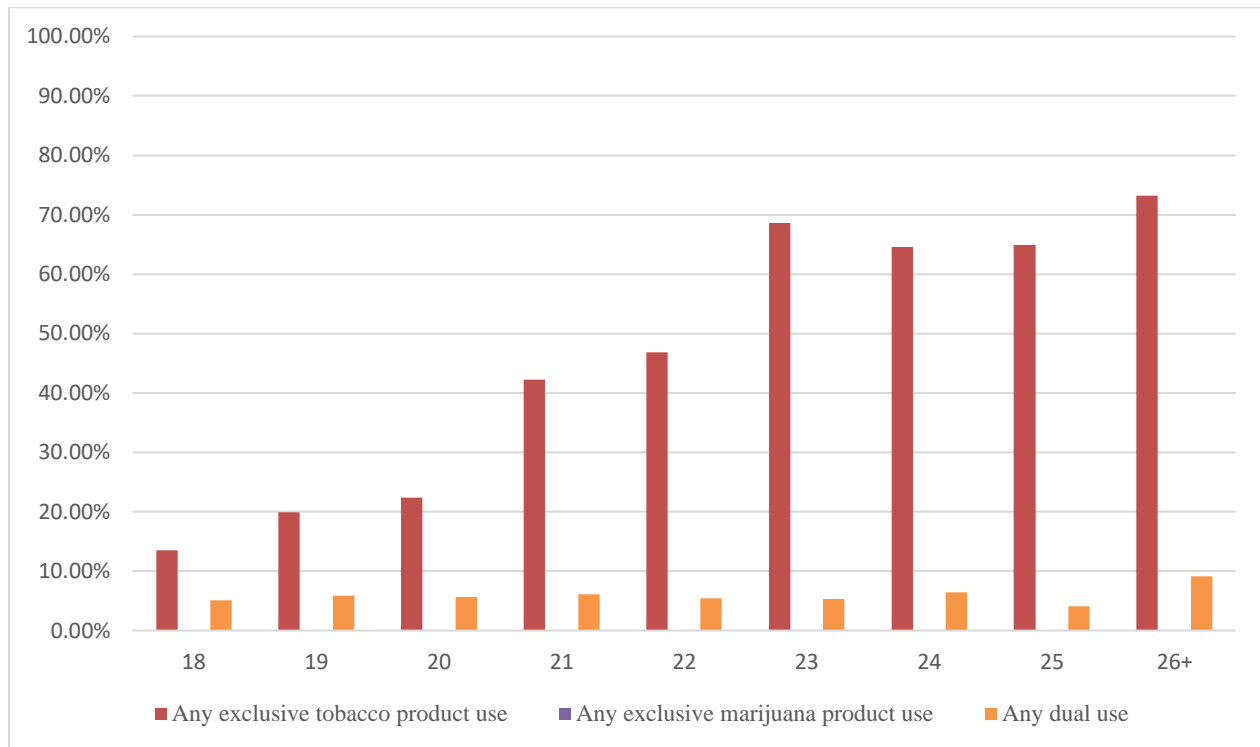


Figure 2a. Prevalent past 30-day marijuana product among past 30-day tobacco users

(n=1245, N=17,464), Texas youth cohort (2014-2017) by age (years)

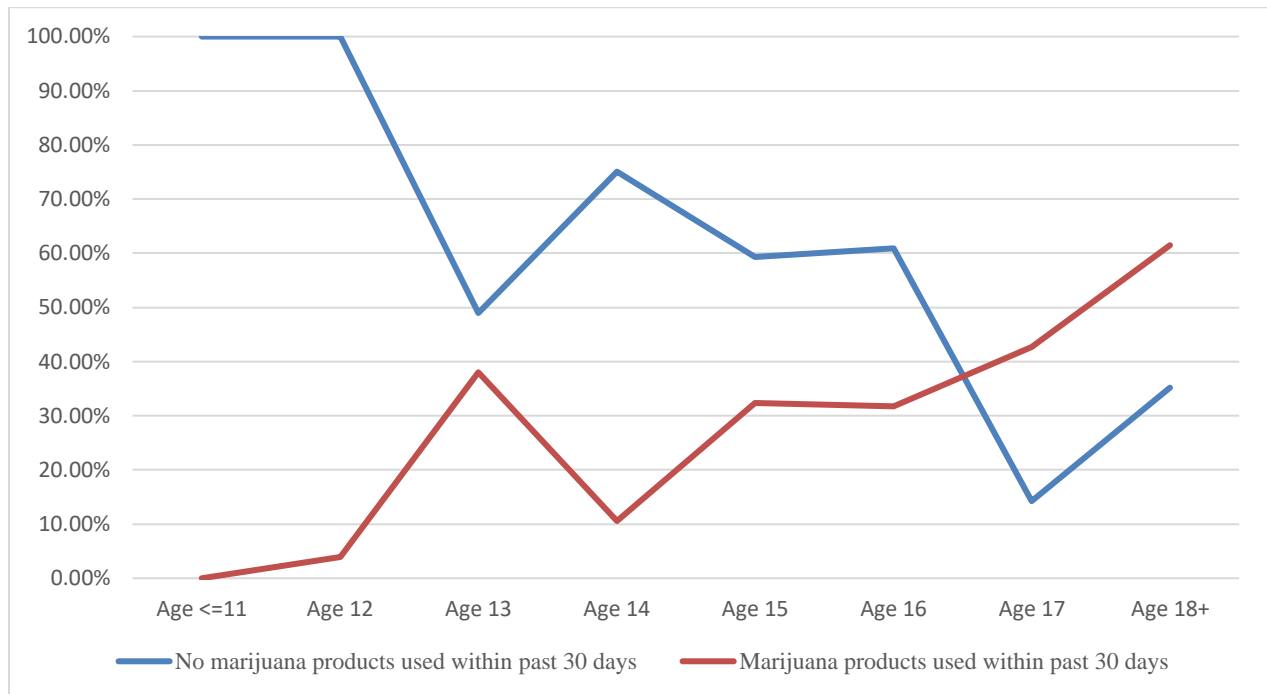


Figure 2b. Prevalent past 30-day marijuana product use among past 30-day tobacco users (n=3586), Texas young adult cohort (2014-2017) by age (years)

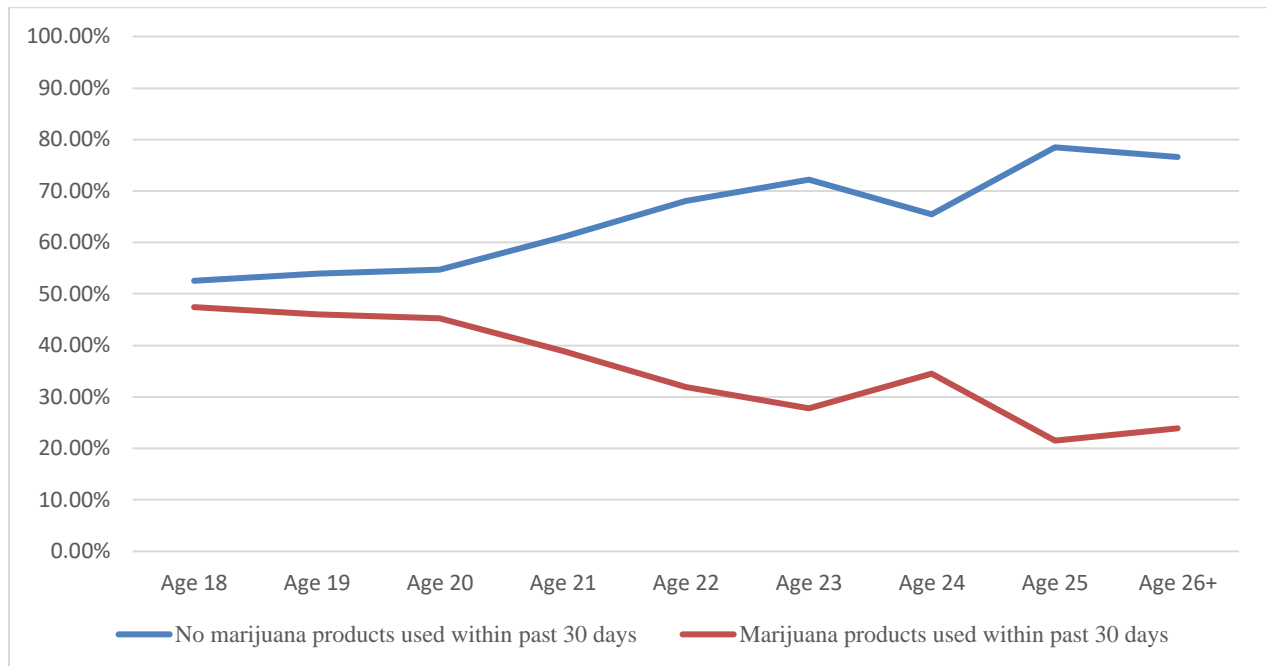


Figure 3a. Prevalent past 30-day tobacco product use among past 30-day marijuana users (n=1395, N=225,234), Texas youth cohort (2014-2017) by age (years)

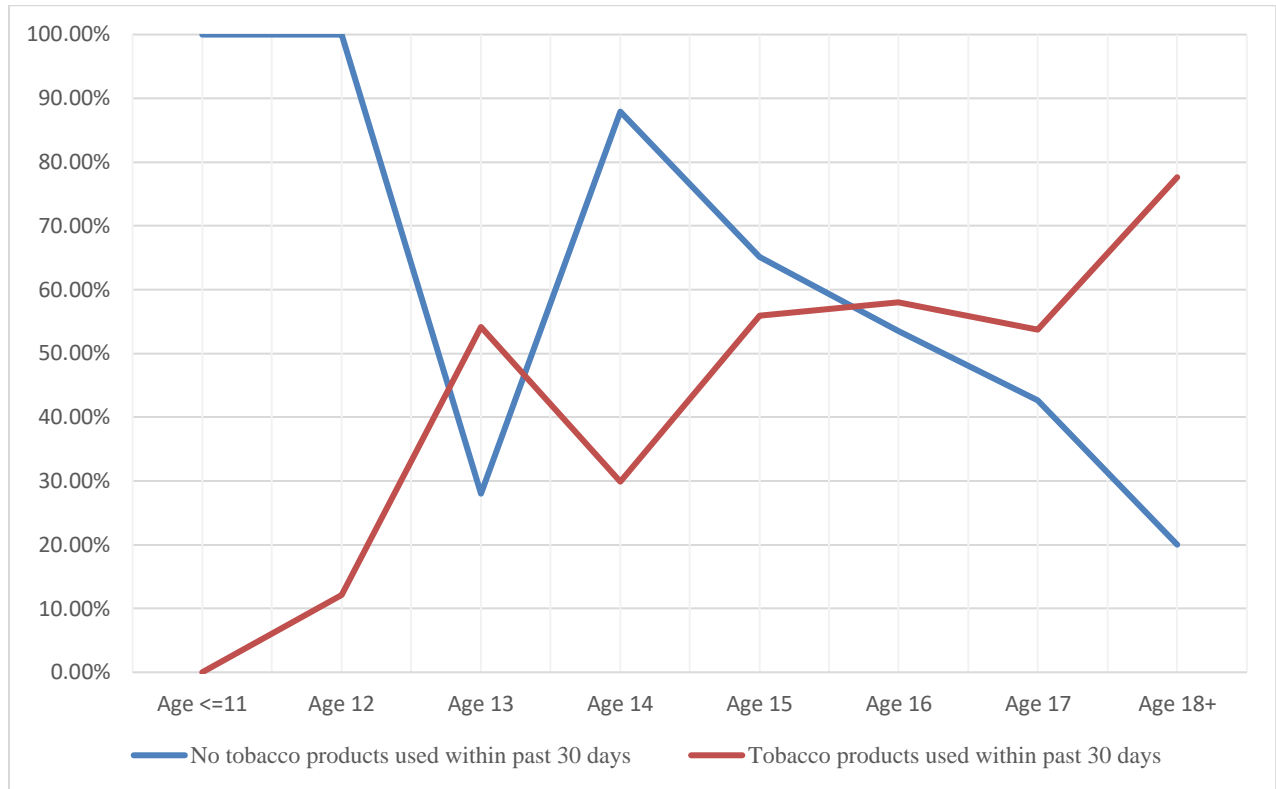


Figure 3b. Prevalent past 30-day tobacco product use among past 30-day marijuana users (n=1107), Texas young adult cohort (2014-2017) by age (years)

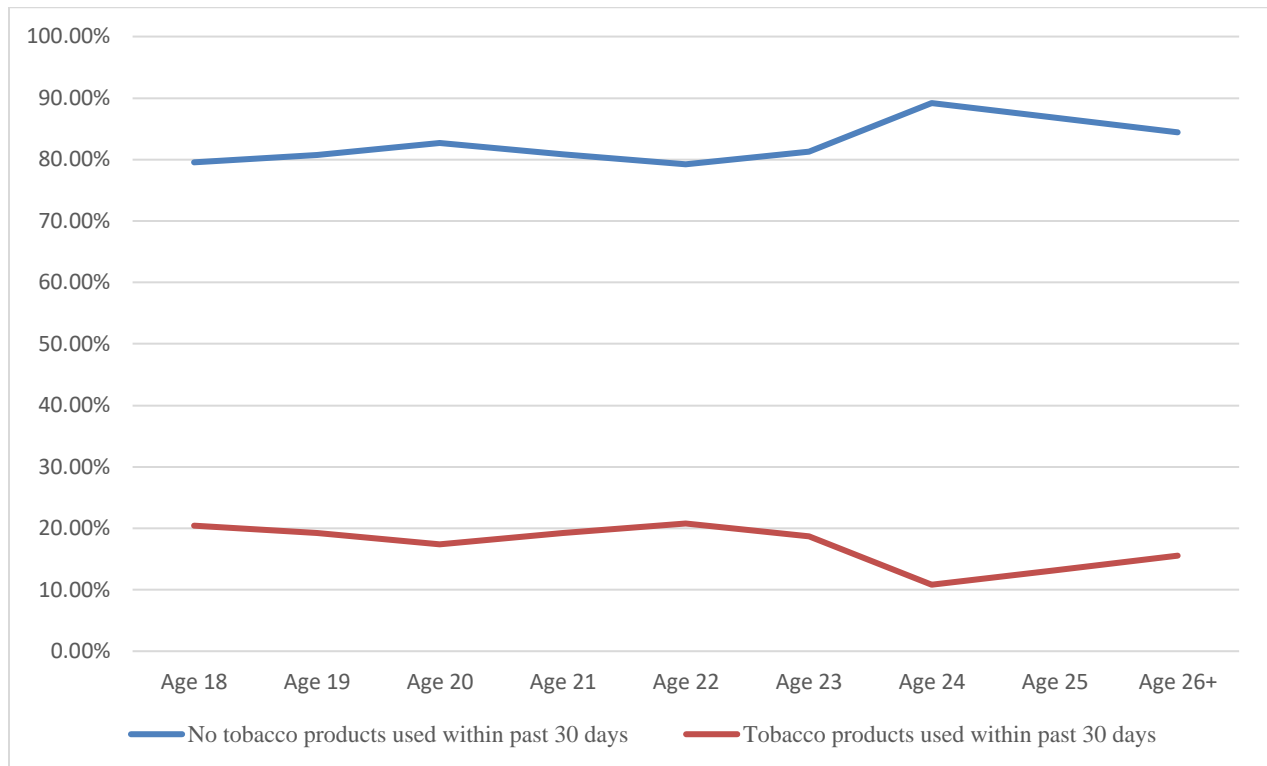


Figure 4a. Prevalence of past 30-Day Tobacco Product Use among Past 30-Day Marijuana users (n=1395, N=225,234), by Tobacco Product, among youth in Texas, US (2015-2017) by age (years)

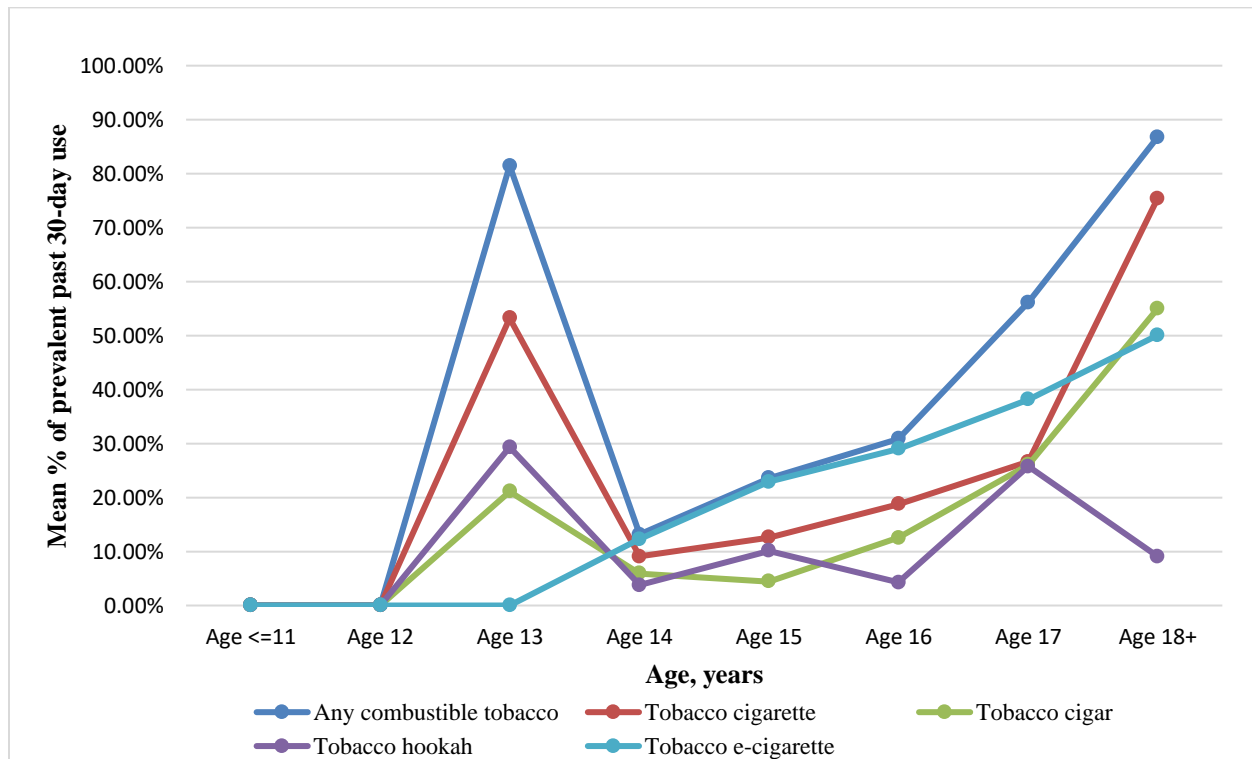
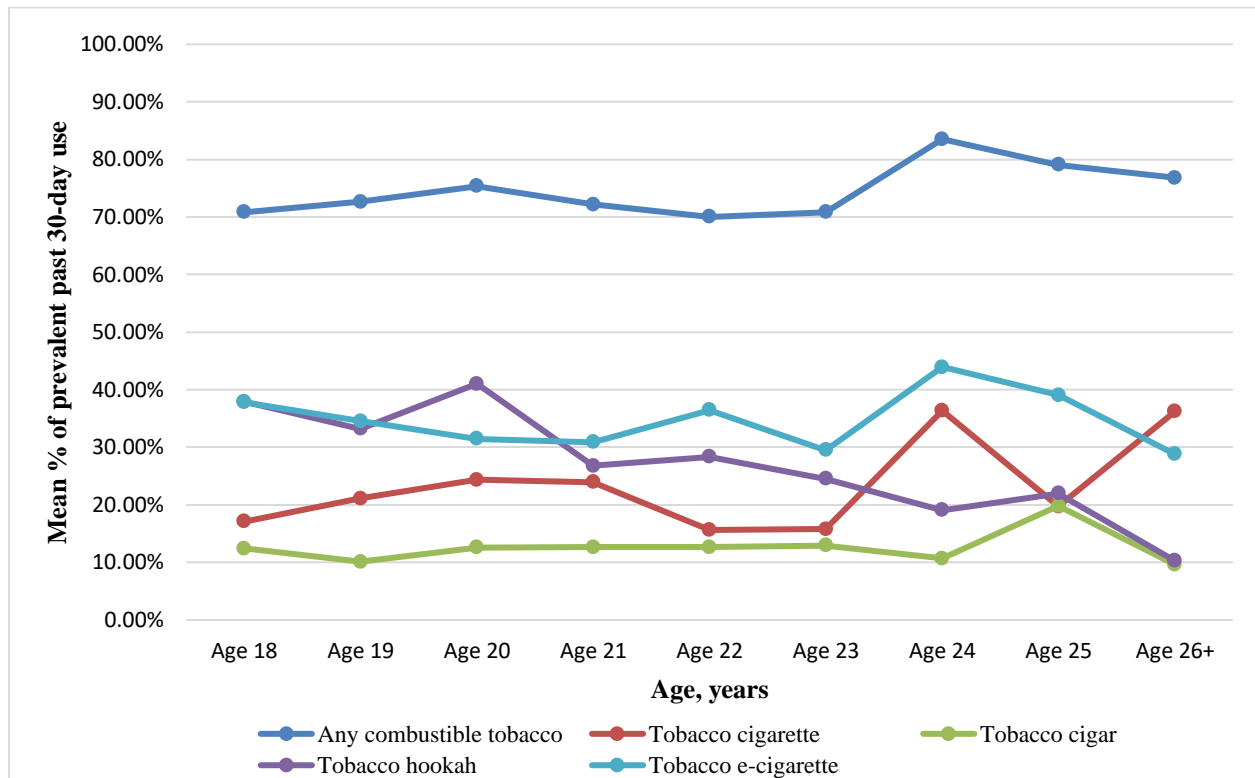


Figure 4b. Prevalence of past 30-Day Tobacco Product Use among Past 30-Day Marijuana users (n=1107), by Tobacco Product, among young adults in Texas, US (2015-2017) by age (years)



JOURNAL ARTICLE (2)

Multi-Directional Paths of Tobacco and Marijuana Use among Adolescents (aged 12-17 years) in Texas: A Six-Wave Cross-lagged Model

INTRODUCTION

Dual use of tobacco and marijuana among young people in past decades has been well documented (Agrawal et al., 2008; Behrendt et al., 2009; Leatherdale et al., 2007; Okoli et al., 2008; Passarotti et al., 2015; Ramo et al., 2013; Ramo and Prochaska, 2012; Timberlake et al., 2007; Tullis et al., 2003). Tobacco and marijuana dual use commonly occurs among adolescents, even more so than among young adults and adults (Substance Abuse and Mental Health Services Administration, 2016). Nationwide, among past 30-day cigarette smokers aged 12-17 years in 2016, 53.9% used marijuana in the past 30-days, compared with 40.7% of young adult past 30-day cigarette smokers aged 18-25 years and 21.8% of adult past 30-day cigarette smokers aged 18 or older (Substance Abuse and Mental Health Services Administration, 2016). Other studies show that marijuana users have higher rates of cigarette use compared to non-marijuana users (Agrawal et al., 2008; Okoli et al., 2008; Richter et al., 2005; Timberlake et al., 2007); and that tobacco users have higher rates of marijuana use compared to non-smokers (Dierker et al., 2018; Goodwin et al., 2018; Leatherdale et al., 2007; Pacek et al., 2018; Passarotti et al., 2015; Ramo et al., 2013; Schauer et al., 2015). However, because most studies measured marijuana use among tobacco users instead of the reverse, it is difficult to say with certainty whether the first use of one product is more likely to result in the use of the other.

Previous research supports gateway (Beenstock and Rahav, 2002; Bentler et al., 2002), reverse gateway (Agrawal et al., 2008; Behrendt et al., 2009; Okoli et al., 2008; Timberlake et al., 2007; Tullis et al., 2003), and substitution effects (Peters et al., 2012; Tullis et al., 2003) hypotheses between marijuana and tobacco use among adolescents. Agrawal and Lynskey (2009) summarized the known hypotheses of reasons for dual use (gateway hypothesis, reverse gateway hypothesis, correlated genetic vulnerabilities hypothesis, and common environmental risks hypothesis) and identified another important yet overlooked fifth influencer: route of administration (Agrawal et al., 2012a). From their cross-sectional analysis of 2001-2002 National Epidemiological Study on Alcohol Related Conditions (NESARC) data, they found that those who used smoked forms of tobacco were significantly more likely to be marijuana users (RRR=3.27, 95%CI 3.02,3.55)¹⁴ and to develop marijuana

¹⁴ RRR, or relative risk ratios, are equivalent to multinomial odds ratios. 95%CI reported is the 95% confidence limits. Those using neither smoked nor smokeless forms are the reference group. Lastly, covariates included sociodemographic, psychiatric, and substance use covariates from NESARC (e.g. sex, age, Caucasian race/ethnicity, poverty, college education,

abuse/dependence (RRR=4.54, 95%CI =4.03,5.13) after adjusting for other covariates and nicotine dependence and compared to those using neither smoked nor smokeless tobacco (Agrawal et al., 2012a). However, this study and others, noted above, did not include other alternative products, such as e-cigarettes, hookah, and cigars, limiting their ability to illuminate contemporary patterns in use of these products. New National Youth Tobacco Survey data show past 30-day use of e-cigarettes increased 48 percent among middle school students between 2017 and 2018 (NIDA, 2018). Similarly, data from the Monitoring the Future Survey showed that past 30-day use of e-cigarettes almost doubled among high school seniors, rising from 11 percent in 2017 to 20.9 percent in 2018 (U.S. Food and Drug Administration, 2018).

As such, the explosive popularization of e-cigarettes and hookah has slowed the two-decade-long declining tobacco use trajectory (Jamal et al., 2017; U.S. Department of Health and Human Services, 2016). Likewise, the liberalization of marijuana regulation has resulted in increased availability and new products to meet consumer demand (Hasin, 2017). Therefore, it is important to consider how the new climate surrounding marijuana legalization and the popularity and availability of alternative products, which can be used to deliver nicotine or marijuana, may have affected tobacco and marijuana use and dual use, as this may have implications in modelling the net population effects of alternative tobacco products (Kalkhoran and Glantz, 2016).

After review of the contemporary tobacco and marijuana dual use literature for adolescents, notable gaps remain. Recent data have demonstrated a prospective relationship between adolescent e-cigarette and hookah use and the risk of both initiating and currently using marijuana (Audrain-McGovern et al., 2018), but no recent study has reported on the relationship in the opposite direction—marijuana use leading to e-cigarette use. Other more recent descriptions and analyses of longitudinal dual use patterns (e.g. (Dierker et al., 2018; Goodwin et al., 2018; Pacek et al., 2018) have not reported these patterns by product type other than cigarettes. Consequently, while there is mounting evidence for unidirectional relationships between cigarettes and marijuana use and the reverse, there is still relatively little known about the transition from other combustible (e.g. hookah, cigars) or non-combustible (e.g. e-cigarettes) tobacco products to established use of marijuana or dual use during adolescence.

In order to address current gaps in the evidence base, the present study investigated bi-directional patterns of past 30-day marijuana and tobacco use, for all combustible and e-cigarette products, from early to middle and late adolescence (ages 11-18 years). We hypothesized that past 30-day use of combustible tobacco products such as cigarettes, cigars, and hookah will lead to marijuana use and dual use and, likewise, that e-cigarette use will predict marijuana use and dual use at subsequent 6-month follow-ups. We also posited that the opposite directional pathways will be meaningful—that is, that marijuana use will lead to combustible and non-combustible tobacco use, but we expect the strength of this relationship to be slightly less in magnitude than those from tobacco to marijuana

South/Midwest, immigrant, conduct disorder, major depression, generalized anxiety disorder, panic disorder, social anxiety disorder, nicotine dependence, alcohol dependence, other illicit drugs, and family history).

product use given previous research on this association (Agrawal et al., 2011, 2012a, 2013; Audrain-McGovern et al., 2018; Peters et al., 2012). The estimates from these analyses will contribute to a better understanding of tobacco and marijuana use and dual use among adolescents, which can aid in projecting how engagement in one risk behavior can predict the future use of either or both behaviors. Further, as Texas boasts a diverse demographic composition that is projected to be representative of the rest of the country over the next decades, the results from this study sample could be nationally prognostic (Vespa et al., 2018).

METHODS

Study Design, Setting, and Participants

Longitudinal data are derived from a rapid response surveillance system study of adolescents (aged 11-18+ years) living in the five counties (Bexar, Dallas, Harris, Tarrant, and Travis) that surround the four largest cities in Texas (Austin, Houston, San Antonio, and Dallas/Fort Worth). The Texas Adolescent Tobacco and Marketing Surveillance system (TATAMS) collected data from students who were in the 6th, 8th, and 10th grade at baseline, in Fall 2014 (n= 3907; weighted N =461,069). Among these, 48.9% were girls and 54.5% Hispanic, 21.4% non-Hispanic white, 17.6% non-Hispanic black enrolled in 79 participating schools. TATAMS utilized a complex probability sampling design, described elsewhere (Perez et al., 2017), to pull this population-based sample. Baseline data were collected in the classroom during the 2014-2015 academic year using computerized surveys administered via tablets in English or Spanish (Delk et al., 2017). Subsequent data have been collected outside the classroom approximately every 6 months since baseline using similarly formatted web-based surveys taken online or with a computer, tablet, or smartphone in English. At Wave 6, collected in the spring of 2017, the retention rate exceeded 70%. This analysis uses data from Waves 1 through 6.

Measures

Survey items were adapted from reliable and valid measures from the following national and state tobacco surveillance studies: the Population Assessment of Tobacco and Health (PATH) study (Hyland et al., 2017), (National Survey on Drug Use and Health (NSDUH) (Substance Abuse and Mental Health Services Administration, 2014), National Youth Tobacco Survey (NYTS (Centers for Disease Control and Prevention, 2009), and Monitoring the Future (MTF) (Bachman et al., 2005), and Youth Risk Behavioral Survey (YRBSS) (Centers for Disease Control and Prevention, 2013). Items underwent cognitive testing via interviews with 27 adolescents and 25 young adults, separately, to ensure comprehension (Hinds et al., 2016). The final surveys had over 340 items on tobacco use behaviors, exposure to tobacco media and marketing, and sociodemographic, cognitive, and affective factors (Delk et al., 2017). Sampling methods, eligibility criteria, and study power for TATAMS is detailed elsewhere (Perez et al., 2017).

Tobacco and Marijuana Measures

At each Wave (1-6), items from the TATAMS survey assessed marijuana and tobacco product use. Past 30-day tobacco use was assessed at Waves 1-6 by product (conventional cigarettes, e-cigarettes, cigar products, and hookah) and by frequency (0-30 days). Tobacco products were also categorized by combustible (conventional cigarettes, cigar products, and hookah) and non-combustible (e-cigarettes) use. Past 30-day marijuana use for adolescents was assessed only by frequency (0-30 days) at Waves 1-6, and both past 30-day tobacco and marijuana use were dichotomized (0 days vs. any) to allow for the comparisons of any tobacco use (0 vs. any), any combustible tobacco use (0 vs. any), and any non-combustible tobacco use (0 vs. any) with any marijuana use (0 vs. any) in the cross-lagged analyses.

Cohort

Participants in the TATAMS adolescent cohort were originally enrolled in grades 6, 8, and 10 at baseline in Fall 2014. These 6th, 8th, and 10th grade cohorts were intentionally chosen to reflect three distinct phases of development—early, middle, and late adolescence—that correspond to ages 11-13 years, 13-15 years, and 15-17 years, respectively (Perez et al., 2017). Cross-lagged analyses are presented separately for these cohorts in order to reflect findings specific to each phase of adolescence and to preserve the ability to interpret results from a theoretical perspective on adolescent development (American Academy of Child and Adolescent Psychiatry, 2003; Perez et al., 2017).

Human Subjects Considerations

Active, informed consent was obtained from both parents and students in TATAMS. University of Texas Health Science Center at Houston Institutional Review Board reviewed and approved all study protocols for the TATAMS study (HSC-SPH-13-0377).

Data Analysis

Analyses were conducted using SAS (Cary, NC, version 9.4) and M-Plus (Los Angeles, CA, version 7.3). All analyses were weighted to account for the complex survey design, including clustering within schools; to account for non-response; and to generalize back to the population from which the sample was taken (Pérez et al., 2017).

Missing data and analysis samples

Missing data for primary outcomes of past 30-day marijuana and tobacco use were <1%. As such, it was appropriate to utilize regression models that employed maximum likelihood estimation methods with robust standard errors, with the assumption that data were missing at random (Schafer and Graham, 2002). Thus, all 3907 students (weighted sample size of 461,069) provided data on select socio-demographic characteristics and past 30-day use of tobacco and marijuana use and dual use.

Descriptive statistics

Descriptive statistics for each adolescent cohort, by grade level, were produced. Two-sided chi-square tests were used to detect differences in primary outcome variables between subgroups (e.g., sex and school/age level, marijuana products use, and tobacco products use), and differences were deemed statistically significant at the 0.05 alpha level.

Modelling multi-directional pathways of use and dual use using cross-lagged models

Six-panel cross-lagged path models were used to simultaneously estimate the following across six survey Waves (1, 2, 3, 4, 5, and 6), with six months between each wave: 1) stability paths, or the autoregressive direct effect within marijuana and tobacco product use across waves (e.g., association between past 30-day tobacco use, from one Wave to the next); 2) bi-directional predictive paths between marijuana and tobacco use at each Wave to use of the other product at the next wave (that is, marijuana use at Wave 1, for example, predicting tobacco use at Wave 2 and vice versa); and 3) correlation coefficients, or the dual use of marijuana and tobacco at each Wave (that is, covariation between tobacco and marijuana use at each age, separately). Past 30-day marijuana- and tobacco-specific product use outcomes were modeled as binary variables (0 days vs. any days), allowing for the calculation of odds ratios.

Nine sets of models—three per cohort, using 0 days vs. any days of product use as the outcome of interest—were created to estimate relationships between (a) past 30-day tobacco use (any product) with past 30-day marijuana use; (b) any past 30-day combustible tobacco use (convention cigarettes, cigar products, hookah) with past 30-day marijuana use; and (c) past 30-day e-cigarette use with past 30-day marijuana use. Analyses were conducted using Mplus (Los Angeles, CA, version 7.3) using the Weighted Least Squares with Mean and Variance adjustment estimation procedure in order to best model categorical data and accommodate missing data (Asparaouhov, 2005). TATAMS data were weighted. Models present the adjusted (for SES, race/ethnicity, and sex) β estimates and associated p-values for multiple pathways of tobacco use, marijuana use, and dual use among the adolescent cohort across Waves 1-6. β estimates and standard errors were converted to odds ratios and 95% confidence intervals, respectively, in the text.

RESULTS

Descriptive analyses

Differences in baseline demographic and socio-demographic characteristics and tobacco and marijuana product use are presented in **Table 1** by cohort (students in 6th, 8th, and 10th grades at baseline in Fall 2014).

Stability paths for all cohorts

Significant stability paths were observed across almost all Waves for almost all past 30-day use of these products and almost all cohorts, with the most notable exceptions seen among the 6th grade cohort (exceptions have been noted with dashed versus solid lines in **Figure 3**). Since the data were collected every 6 months, these small variations in

significant stability paths were not unexpected and represent some of the volatility in use between Waves, particularly among the youngest cohort.

Directionality of use and dual use among the 6th grade cohort

Few statistically significant paths were noted in early adolescence for the 6th grade cohort; when significant, past 30-day tobacco use generally preceded an increase in past 30-day marijuana use (**Figure 1**). For use of any tobacco product, the only significant associations observed were quite small in magnitude. Any past 30-day tobacco product use preceded an increase in past 30-day marijuana use from Wave 2 to 3 and later from Wave 4 to 5. Dual use of any tobacco and marijuana at Waves 5 and 6 was statistically significant but small in magnitude. No statistically significant paths were observed from past 30-day marijuana use to any tobacco use in the past 30-days. Past 30-day combustible tobacco use preceded an increase in past 30-day marijuana use from Wave 2 to 3 ($OR_{\text{combustible tobacco to marijuana from Wave 2 to 3}} = 1.146$; 95% CI 0.948, 1.344), but a decrease in past 30-day marijuana use from Wave 4 to 5. Dual use of combustible tobacco and marijuana was statistically significant at Waves 1, 4, 5, and 6, but was again small in magnitude. No statistically significant paths were observed from past 30-day marijuana use to past 30-day combustible tobacco use. Past 30-day e-cigarette use at Wave 2 preceded past 30-day use of marijuana at Wave 3, but past 30-day marijuana use preceded past 30-day e-cigarette use from Wave 5 to 6. Importantly, the magnitude of the relationship between marijuana to subsequent e-cigarette use was much stronger than the reverse relationship and was the first of this unidirectional relationship to appear among the 6th grade cohort. Dual use of both e-cigarettes and marijuana occurred at almost all Waves, except Waves 2 and 6.

Directionality of use and dual use among the 8th grade cohort

A greater number of statistically significant paths were noted in middle adolescence (8th grade students) compared to early adolescence (6th grade students). Though bi-directional relationships between past 30-day tobacco and past 30-day marijuana use were observed, the magnitude of the relationship for marijuana use preceding an increase in tobacco use was much larger than that for tobacco use preceding an increase in marijuana use; this finding was especially strong for marijuana use preceding an increase in combustible tobacco product use (**Figure 2**). Past 30-day use of any tobacco product preceded past 30-day marijuana use from Wave 1 to 2, Wave 3 to 4, and Wave 5 to 6. Similarly, past 30-day marijuana use preceded past 30-day use of any tobacco product between *all* Waves. Importantly, the magnitude of these relationships was much larger ($OR_{\text{any tobacco to marijuana from Wave 5 to 6}} = 1.038$; 95%CI=1.008, 1.067 vs $OR_{\text{marijuana to any tobacco from Wave 5 to 6}} = 2.006$; 95% CI=1.482, 2.529) for past 30-day marijuana use preceding past 30-day tobacco use. Dual use of any tobacco product and marijuana use was statistically significant at Waves 1, 2, 3, 5, and 6. Notably, past 30-day marijuana use preceded subsequent past 30-day combustible tobacco use at all Waves, too. Past 30-day combustible tobacco use preceded past 30-day marijuana use from Waves 3 to 4, Wave 4 to 5, and Wave 5 to 6, but these relationships were substantially smaller—by almost an order of magnitude—than the

relationships moving in the opposite direction ($OR_{\text{marijuana to combustible tobacco from Wave 3 to 4}} = 1.545$; 95%CI=1.329, 1.761 vs. $OR_{\text{combustible tobacco to marijuana from Wave 3 to 4}} = 1.113$; 95%CI= 1.054, 1.172, for example). Dual use of combustible tobacco and marijuana was significant at all Waves, except at Wave 4. Past 30-day e-cigarette use preceded past 30-day marijuana use from Wave 3 to 4, 4 to 5, and 5 to 6. Past 30-day marijuana use preceded past 30-day e-cigarette use from Wave 1 to 2 and Wave 3 to 4 only. Dual use of both e-cigarettes and marijuana occurred at all Waves 1-6.

Directionality of use and dual use among the 10th grade cohort

A large number of statistically significant paths were noted in late adolescence, similar to middle adolescence. While marijuana use preceded an increase in combustible tobacco product use more strongly than the reverse, e-cigarette use preceded an increase in marijuana use more consistently than its reverse. Among the 10th grade cohort, past 30-day any tobacco product use preceded past 30-day marijuana use only from Wave 4 to 5 and Wave 5 to 6 (**Figure 3**). Past 30-day marijuana use preceded past 30-day any tobacco product use from Wave 3 to 4, Wave 4 to 5, and Wave 5 to 6, and the magnitude of these associations were substantially greater than any tobacco use preceding subsequent marijuana use ($OR_{\text{marijuana to any tobacco from Wave 4 to 5}} = 2.175$; 95%CI=1.708, 2.641 vs. $OR_{\text{any tobacco to marijuana from Wave 4 to 5}} = 1.045$; 95%CI=1.027, 1.063). Dual use of any tobacco product and marijuana was statistically significant at Waves 1, 4, and 5. Past 30-day combustible tobacco use preceded past 30-day marijuana use from Wave 4 to 5 and Wave 5 to 6. Past 30-day marijuana use preceded past 30-day combustible tobacco use from Wave 3 to Wave 4, Wave 4 to 5, and from Wave 5 to 6 but again at a much higher order of magnitude than the opposite direction ($OR_{\text{marijuana to combustible tobacco from Wave 4 to 5}} = 1.367$; 95%CI= 1.150, 1.585 vs. $OR_{\text{combustible tobacco to marijuana from Wave 4 to 5}} = 1.018$; 95%CI= 1.000, 1.099). Dual use was statistically significant at Waves 1, 4, and 5. At almost all Waves 1-6, past 30-day e-cigarette use preceded past 30-day marijuana use, and at all Waves 1-6 dual use of both occurred. Past 30-day marijuana use preceded past 30-day e-cigarette use from Waves 2 to 3 and 5 to 6. Again, the relationships from past 30-day marijuana to subsequent past 30-day e-cigarette use were larger in magnitude than those observed in the opposite direction. For example, $OR_{\text{marijuana to e-cigarette from Wave 5 to 6}} = 1.430$; 95%CI=1.260, 1.601 vs. $OR_{\text{e-cigarette to marijuana from Wave 5 to 6}} = 1.052$; 95%CI=1.005, 1.099.

DISCUSSION

In the current study, we offer new evidence for a prospective and consequential relationship between past 30-day tobacco and subsequent marijuana use, past 30-day marijuana and subsequent tobacco use, and dual use of both products among adolescents. In early adolescence (6th grade cohort), past 30-day tobacco use generally preceded an increase in past 30-day marijuana use, though there were few statistically significant pathways. Though bi-directional relationships between use of these products were observed in middle adolescence (8th grade cohort), past 30-day marijuana use predicted an

increase in past 30-day tobacco use more consistently and more strongly than the reverse – particularly for combustible tobacco product use. Similar findings were observed in late adolescence (10th grade cohort), though past 30-day e-cigarette use preceded an increase in past 30-day marijuana use more consistently than the reverse. Considered together, these most compelling results provide evidence that prevention needs to be sustained across all developmental phases of adolescence and should focus on both marijuana and tobacco use, though the relevance of each product may differ in early, middle, and late adolescence.

Profoundly evident in the results was the magnitude of the consistent and strong directional relationships observed from past 30-day marijuana use to an increase in any tobacco, combustible tobacco, and e-cigarette use (among older aged youth (8th and 10th grade). This evidence supports the well-documented “gateway hypothesis” (Beenstock and Rahav, 2002; Bentler et al., 2002) in the traditional view and perhaps in a new light: that, in addition to leading to combustible tobacco use, marijuana use could also facilitate a transition to other vaped or inhaled substances, as the “vaping culture” (i.e. vape shops, vaping websites, social media, etc.) supports both vaping nicotine and marijuana (Budney et al., 2015; Gostin and Glasner, 2014). Hence, as researchers begin to posit the importance of studying the comorbidities—including subsequent other or dual substance use—associated with rising e-cigarette use among adolescents, it will be equally important to do the same with marijuana use. With recent reports of adolescent e-cigarette use doubling and marijuana use remaining steady from 2017 to 2018 (NIDA, 2018; U.S. Food and Drug Administration, 2018), the importance of these novel findings cannot be overstated. Our results underscore the stability in past 30-day use of these products over time, so prevention needs to be strengthened to ensure transitions to more “regular” use from initiation or experimentation does not occur.

Any tobacco product use and marijuana use

Past 30-day use of marijuana predicted subsequent past 30-day use of any tobacco product more consistently than past 30-day use of any tobacco product predicted subsequent marijuana use. These results are troubling since marijuana users are growing in number and are a population that is vulnerable to developing dependence or problem use (Compton et al., 2016), with particularly deleterious health effects on adolescent users (Hasin, 2017; Meier et al., 2012). The reverse relationship of tobacco use predicting subsequent marijuana use also warrants concern since research has shown adolescents who start using marijuana with prior nicotine exposure may experience more pleasure from their initial marijuana use experience and may consequently escalate to more regular marijuana use (Agrawal et al., 2013; Levine et al., 2011).

It is well-documented that tobacco and marijuana use most commonly co-occur among adolescents aged 12-17 years (Substance Abuse and Mental Health Services Administration, 2016), but this is the first study to longitudinally situate dual use between tobacco and marijuana use (and simultaneously model longitudinal use of these products, too). Results show that dual use was common and occurred even without preceding past 30-day use of tobacco or marijuana, suggesting that there may be an important population

of dual users who do not singularly use marijuana or tobacco. Further, environmental factors such as peer use, easier access to tobacco and marijuana products, and similar methods for use of both products have been shown to increase the likelihood of tobacco and marijuana use (Cerdá et al., 2016; Roditis et al., 2016; Roditis and Halpern-Felsher, 2015). Our results on dual use support the common liability hypothesis, which Vanyukov et al. (2012) reasoned is more able to readily explain the underpinning risks for use of different substances than other theories that specify specific staging (i.e. gateway and reverse gateway hypotheses). Similarly, Mayet et al. (2016) concluded that the common liability theory better explained their observed alternative sequences to the gateway route, reasoning that route of administration may be key to explain the reciprocal interactions they observed between tobacco and marijuana use.

Combustible tobacco use and marijuana use

While much attention has recently been given to bidirectional cigarette and marijuana use, this is the first study to each direction of combustible tobacco (cigarette, hookah, and cigar) and marijuana use in a single model. Important patterns emerged: namely, combustible tobacco use led to subsequent marijuana use among the youngest cohort (6th grade), both 8th and 10th grade cohorts showed past 30-day combustible tobacco use leading to subsequent marijuana use, and stronger sequences of past 30-day marijuana use predicted combustible tobacco use among both 8th and 10th grade cohorts. Marijuana use predicting subsequent combustible tobacco use was strongest among eighth graders, and to our knowledge, this relationship has not been recently documented among this (or any other) adolescent age group. Marijuana use preceding an increase in combustible tobacco use is troubling, given the overwhelming evidence for associations between marijuana use and escalation of “tobacco involvement” (Agrawal et al., 2012b; Pacek et al., 2018; Patton et al., 2005). Pacek et al. (2018) identified the highest prevalent past 30-day cigarette smoking to occur among daily (54.57%), followed by non-daily (40.17%) and non-marijuana (15.06%) users in 2015, contrasting sharply with the declines in cigarette smoking observed among non-marijuana users.

Moreover, dual use of both marijuana and combustible tobacco products were quite common for all cohorts, especially 8th graders. Dual use and bi-directional relationships between both combustible tobacco and marijuana occurred in the 10th grade cohort, and these associations were more concentrated toward later adolescence in Waves 4, 5, and 6 as the adolescents prepared for transition out of high school. Given recent data showing that non-daily cigarette smoking is increasing among marijuana users (Pacek et al., 2018) and that marijuana use disorder is more common among non-daily and daily cigarette smokers compared with former or never smokers (Weinberger et al., 2018), these results are concerning for adolescents who exit high school and continue to use both products with the same frequencies or progress to more regular or problem use of either. Sustained intervention efforts throughout adolescence with particular emphasis on students’ transitional periods into and out of high school are therefore crucial to reduce rates of use and dual use of tobacco and marijuana among adolescents.

E-cigarette use and marijuana use

Although both e-cigarettes (U.S. Department of Health and Human Services, 2016) and marijuana (Hasin, 2017) have been promoted as safer alternatives to combustible tobacco use, they nonetheless can adversely affect public health if they lead to increased likelihood of nonsmokers beginning to use combustible tobacco or initiate marijuana use early (Dierker et al., 2018). Our results were mixed for the 6th and 8th grade cohorts on whether use of marijuana or e-cigarettes more often led to use of the other substance, but dual use was common among all cohorts (occurring at least four out of six Waves, for each). Experimentation and curiosity are possible explanations for the changing directional use, particularly among the 6th grade cohort, but the magnitude of the bi-directional pathways observed among the 8th grade cohort suggests that transitions from use of one product to use of the other product or both products are likely. The fact that these bi-directional relationships to and from e-cigarette and marijuana use are reinforced in the final Waves for the 8th and 10th grade cohorts reveal the need for intensified efforts at reducing e-cigarette and marijuana use in tandem during these transitional times for adolescents.

Among 10th graders, e-cigarette use more often led to subsequent marijuana use, and, again, dual use was common and likely attributable to similar reductions in risk perceptions of both e-cigarettes and marijuana as less harmful than conventional cigarette use (U.S. Department of Health and Human Services, 2016; U.S. Food and Drug Administration, 2018). 8th graders in particular have been shown to be at the highest risk, when compared to 6th and 10th graders, for transitioning from non-susceptible to susceptible to e-cigarette use 12 months later (Carey et al., 2018). Our results are in line with the well-documented exponential increase in e-cigarette use that occurs at the onset of high school (Jamal et al., 2017; U.S. Department of Health and Human Services, 2016) but importantly suggest that prevention efforts should consider marijuana comorbidity when addressing the rising proportion of adolescents using e-cigarettes in the U.S.

Strengths and limitations

This is the first study to employ a six-panel cross-lagged regression model applied to data collected every 6 months to simultaneously estimate autoregressive stability paths within past 30-day marijuana and tobacco product use; bi-directional predictive paths between marijuana and tobacco use; and correlation coefficients, or the dual use of marijuana and tobacco. Notably, these models were applied to three different cohorts, representing early, middle, and late adolescence. These models allowed for temporal clarity and for the visualization of multi-directional pathways of use. Significant additional strengths of this study include its demographically diverse sample measured during distinct developmentally important stages of adolescence, its complex, longitudinal design, and its use of weights to generate a representative population-based sample. Further, the six-month spacing between survey Waves allowed for a more complete picture of volatile past 30-day use of tobacco and marijuana products using a frequency measure of use (0-30 days,

dichotomized). To date, the large majority of studies have focused on ever use of these substances only, which limits inferences about more consistent use of these products.

A limitation of this study, due to available survey items and sample sizes among the cohorts, is that we were unable to further stratify the cross-lagged models by specific products (e.g., cigarettes only, or marijuana consumed in varied forms). Further, in order to produce the most stable estimates, we dichotomized the frequency measures of past 30-day use (0 days vs. any days of use per month) and, as such, cannot provide more specific estimates of risk as it corresponds to number of days of use frequency. The stability paths provided in the models, however, show high consistency in the measures that were available and used. Lastly, as the sample was drawn from five major metropolitan areas of Texas, its generalizability may lessen, but the demographic composition of the sample is representative of the 20-year projected national composition of the U.S.

TABLES

Table 1. Baseline characteristics (Wave 1, 2014-15) for the adolescents aged 11-18 (n=3907; N= 461,069), by cohort (6th, 8th, and 10th grades)

		6th grade (n=1122, N=148,465)		8th grade (n=1322, N=160,080)		10th grade (n=1463, N=152,524)		p-value
		% or mean	95% CI or SD	% or mean	95% CI or SD	% or mean	95% CI or SD	
Sex (% , 95%CI)								0.9996
	Male	51.19	(39.10-63.28)	51.14	(42.63-59.65)	51.02	(45.03-57.00)	
	Female	48.81	(36.72-60.90)	48.86	(40.35-57.27)	48.98	(43.00-54.96)	
Age, mean (SD)		11.52	0.05	13.49	0.04	15.12	0.08	<0.0001*
SES, (% , 95%CI)								0.0244*
	"Very well off"	22.58	(18.68-26.47)	21.43	(13.41-29.45)	15.1	(12.26-17.94)	
	"Living comfortably"	61.96	(58.76-65.17)	60.06	(54.53-65.59)	63.64	(59.64-67.63)	
	Low	14.74	(11.45-18.02)	18.48	(12.90-24.06)	21.03	(17.84-24.21)	
Race/ethnicity, (% , 95%CI)								0.9993
	Non-Hispanic White/Other	27.09	(17.50-36.68)	27.18	(10.97-43.40)	29.47	(22.46-36.48)	
	Non-Hispanic Black	16.88	(10.90-22.85)	17.86	(9.20-26.52)	17.95	(11.51-24.39)	
	Hispanic	56.03	(47.85-65.22)	54.96	(41.33-68.58)	52.58	(43.73-61.43)	
Tobacco use								
Ever use (yes)								
	Any product	8.74	(4.55-12.93)	24.01	(17.99-30.04)	40.71	(36.25-45.16)	<0.0001*
	Combustible	5.34	(2.27-8.42)	15.07	(10.85-19.28)	26.38	(22.37-30.39)	<0.0001*
	Non-combustible (e-cigarette)	7.72	(4.40-11.04)	22.65	(19.44-25.86)	39.99	(35.06-44.93)	<0.001*
Past 30-day use (yes)								
	Any product	3.29	(1.13-5.45)	9.33	(5.60-13.06)	18.26	(14.87-21.65)	<0.0001*
	Combustible	2.18	(0.60-3.76)	5.37	(2.83-7.90)	10.73	(7.78-13.67)	<0.0001*
	Non-combustible (e-cigarette)	1.98	(0.72-3.24)	6.69	(3.85-9.54)	13.48	(11.10-15.86)	<0.0001*
Marijuana use								
Past 30-day use (yes)								
	Any product	2.65	(1.17-4.13)	10.32	(5.73-14.91)	15.86	(12.83-18.89)	<0.0001*
Socioeconomic status (SES) was assessed for adolescents on the TATAMS survey by asking, "In terms of income, what best describes your family's standard of living in the home where you live most of the time? Would you say your family is..." (Very well off, living comfortably, just getting by, nearly poor, or poor). The item responses were categorized as by collapsing the lowest three categories into a single category of "everyone else" versus "Living comfortably" versus "Very well off."								

Race/ethnicity: For TATAMS, Non-Hispanic White/Other category for adolescents includes race/ethnicity categories of White, Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and Other.

Tobacco and marijuana use variables include the reporting of ever use of (1) any tobacco or marijuana product, including cigarette, cigar product --little filtered cigar, cigarillo, and large cigars--, hookah, and e-cigarettes; (2) combustible use, including cigarette, cigar product--little filtered cigar, cigarillo, or large cigar--, and hookah; and non-combustible (e-cigarette) use. Past 30-day use of tobacco products is reported for any tobacco product, combustible tobacco products, and non-combustible tobacco products. Past 30-day marijuana use is reported only for any product, due to survey items. All product usage is reported by cohort at baseline.

FIGURES

Figure 1. Cross-lagged models showing multi-directional pathways of use and dual use among 6th grade cohort in Texas across Waves 1-6 (2014-2016).

β estimates and standard errors are shown in the following format: β estimate (Standard Error). Beta estimates can be exponentiated to obtain odds ratios. Statistically significant pathways are shown with solid arrows, and non-statistically significant pathways are shown with dashed arrows. All pathways are shown, and all models have been adjusted for race/ethnicity, gender, and socioeconomic status. Separate cross-lagged models are shown for past 30-day use of any tobacco and any past 30-day marijuana, past 30-day combustible tobacco and any past 30-day marijuana, and past 30-day e-cigarettes and any past 30-day marijuana. All tobacco and marijuana use outcomes have been dichotomized to show no days of use versus any days of use.

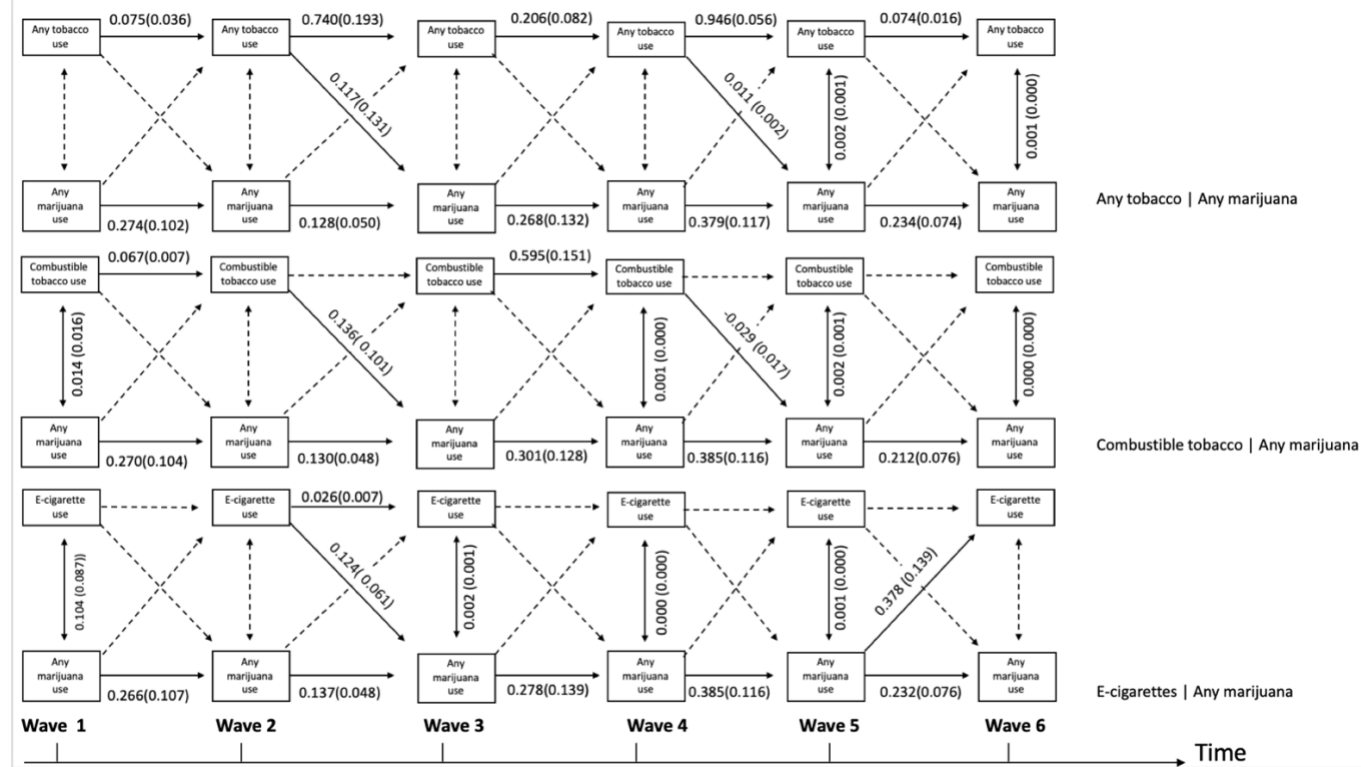


Figure 2. Cross-lagged models showing multi-directional pathways of use and dual use among the 8th grade cohort in Texas across Waves 1-6 (2014-2016).

β estimates and standard errors are shown in the following format: β estimate (Standard Error). Beta estimates can be exponentiated to obtain odds ratios. Statistically significant pathways are shown with solid arrows, and non-statistically significant pathways are shown with dashed arrows. All pathways are shown, and all models have been adjusted for race/ethnicity, gender, and socioeconomic status. Separate cross-lagged models are shown for past 30-day use of any tobacco and any past 30-day marijuana, past 30-day combustible tobacco and any past 30-day marijuana, and past 30-day e-cigarettes and any past 30-day marijuana. All tobacco and marijuana use outcomes have been dichotomized to show no days of use versus any days of use. All tobacco and marijuana use outcomes have been dichotomized to show no days of use versus any days of use.

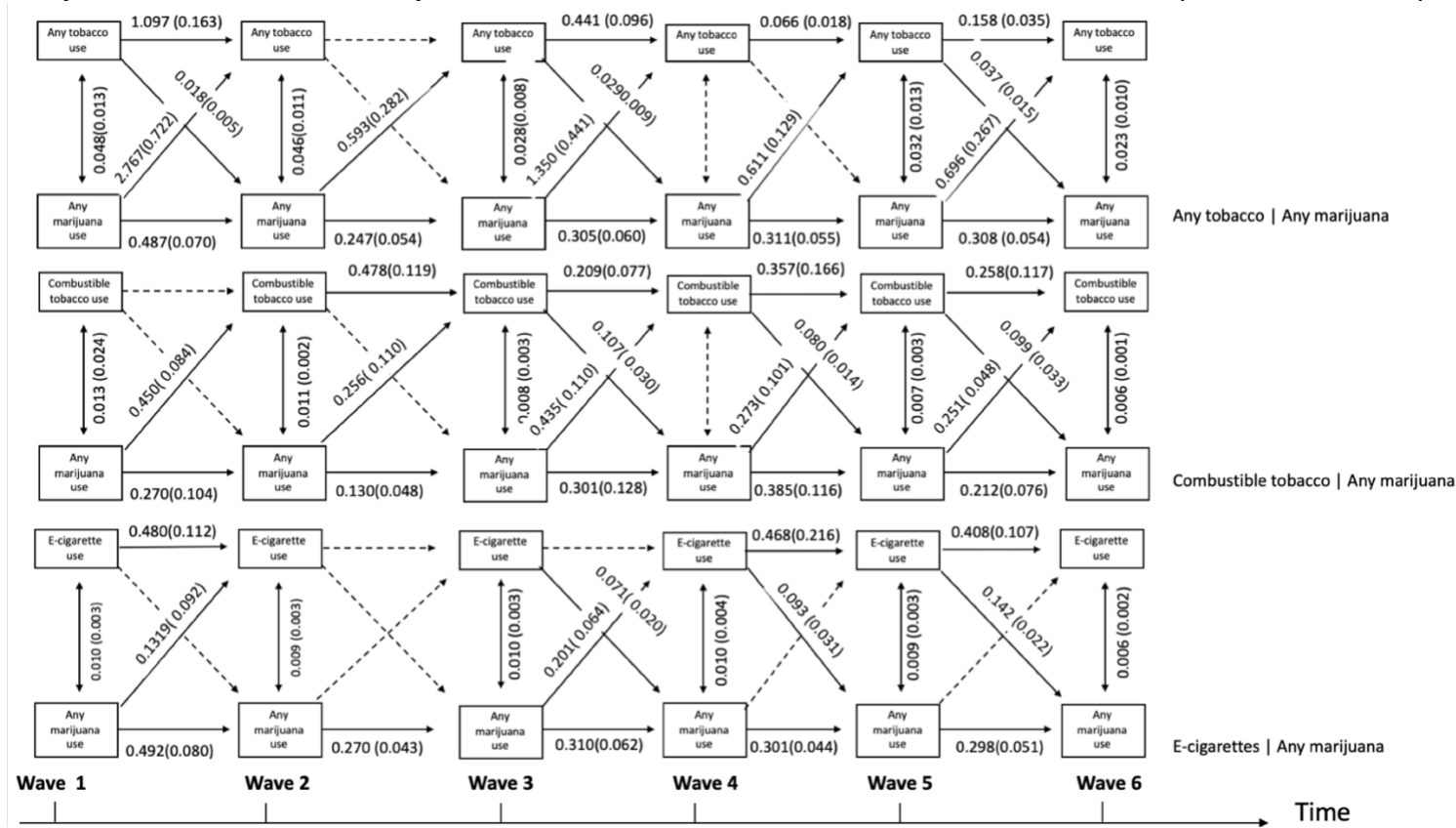
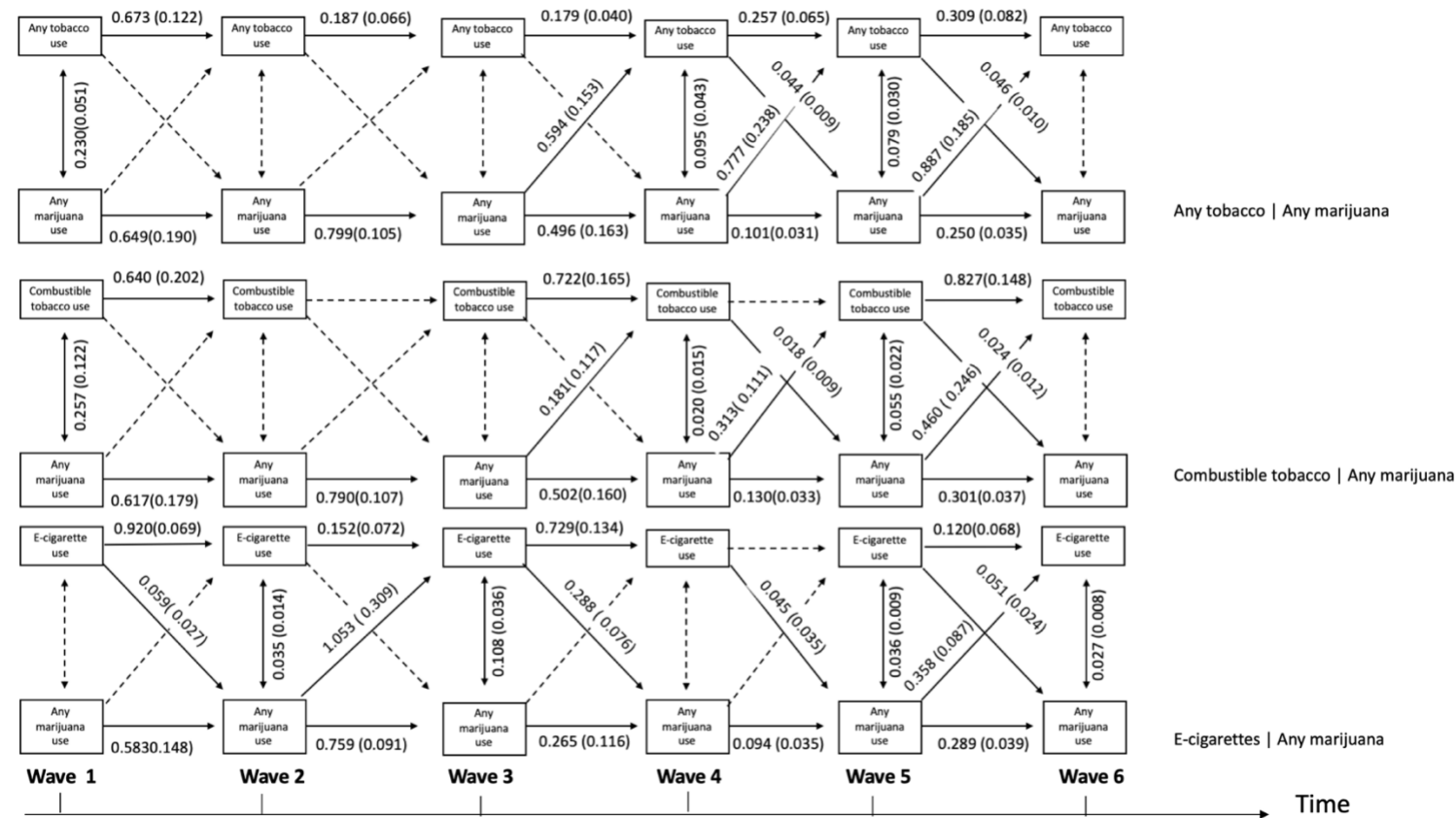


Figure 3. Cross-lagged models showing multi-directional pathways of use and dual use among the 10th grade cohort in Texas across Waves 1-6 (2014-2016).

β estimates and standard errors are shown in the following format: β estimate (Standard Error). Beta estimates can be exponentiated to obtain odds ratios. Statistically significant pathways are shown with solid arrows, and non-statistically significant pathways are shown with dashed arrows. All pathways are shown, and all models have been adjusted for race/ethnicity, gender, and socioeconomic status. Separate cross-lagged models are shown for past 30-day use of any tobacco and any past 30-day marijuana, past 30-day combustible tobacco and any past 30-day marijuana, and past 30-day e-cigarettes and any past 30-day marijuana. All tobacco and marijuana use outcomes have been dichotomized to show no days of use versus any days of use.



SUPPLEMENTAL TABLES

Supplemental Table 1a. Prevalence of past 30-Day Tobacco Product Use by Tobacco Use Frequency, among the adolescent cohort in Texas (n=3907; N= 461,069) (2014-2017)

		No combustible tobacco use			1-5 days of use			Combustible Tobacco Use Frequency			20+ days		
		(n=3741, N=441,460)			(n=1508, N=177,953)			6-19 days of use			(n=349, N=41,173)		
		Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean
<i>early</i>	Age <=11	99.98%	99.89%	100.00%	29.60%	4.06%	80.68%	0.03%	0.01%	0.10%	0.01%	0.00%	0.04%
	Age 12	99.97%	99.89%	99.99%	4.35%	1.31%	13.52%	0.52%	0.08%	3.31%	0.13%	0.01%	1.85%
<i>middle</i>	Age 13	99.66%	99.28%	99.84%	15.48%	6.69%	31.88%	0.68%	0.18%	2.47%	0.40%	0.08%	0.50%
	Age 14	99.69%	99.42%	99.84%	5.63%	2.89%	10.71%	0.50%	0.17%	1.50%	0.21%	0.04%	1.08%
<i>late</i>	Age 15	98.77%	97.83%	99.30%	16.11%	9.72%	25.52%	1.11%	0.43%	2.80%	0.15%	0.02%	1.01%
	Age 16	98.44%	97.24%	99.13%	12.53%	6.40%	23.07%	0.93%	0.34%	2.52%	0.15%	0.02%	1.01%
	Age 17	97.11%	94.01%	98.63%	13.93%	6.53%	27.28%	1.73%	0.48%	6.09%	0.12%	0.01%	1.07%
	Age 18+	87.57%	94.61%	43.86%	8.80%	2.34%	27.98%	1.13%	0.22%	5.55%	0.16%	0.01%	1.80%
	p-value	<0.001*			0.0158*			<0.001*			0.005		
		No e-cigarette use			1-5 days of use			E-cigarette Use Frequency			20+ days		
		(n=3276, N=386,628)			(n=1463, N=172,636)			6-19 days of use			(n=341, N=40,283)		
		Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean
<i>early</i>	Age <=11	No estimate	No estimate	No estimate	21.18%	5.43%	55.68%	0.05%	0.02%	0.12%	2.58%	0.14%	34.11%
	Age 12	91.60%	56.02%	98.94%	2.63%	0.72%	9.11%	0.45%	0.38%	5.17%	0.68%	0.04%	9.68%
<i>middle</i>	Age 13	95.55%	79.77%	99.15%	14.76%	7.56%	26.82%	1.17%	0.34%	3.89%	0.80%	0.16%	3.91%
	Age 14	92.15%	81.59%	96.88%	9.19%	5.60%	14.72%	1.23%	0.57%	2.63%	0.62%	0.23%	1.65%
<i>late</i>	Age 15	92.63%	85.65%	96.36%	11.27%	7.48%	16.62%	1.91%	0.96%	3.76%	0.95%	0.33%	2.73%
	Age 16	89.82%	80.47%	94.97%	9.35%	5.67%	15.04%	1.15%	0.51%	2.54%	0.83%	0.26%	2.63%
	Age 17	93.35%	85.34%	97.13%	9.62%	4.32%	20.08%	2.26%	0.85%	5.90%	0.99%	0.17%	5.58%

Age 18+	92.46%	81.56%	97.14%	3.49%	1.02%	11.20%	1.91%	0.56%	6.33%	1.90%	0.32%	10.37%
p-value		0.4352			0.0454*			<0.001*			0.8381	
<p>*All proc glimmix models above adjusted for survey Wave to account for any temporal effect survey Wave may have on pooled age.</p> <p>Combustible past 30-day marijuana product use includes joints, pipes, hookah, blunt. Marijuana in an e-cigarette includes use of marijuana in a vape pens, e-hookah, or personal vaporizers. Ingested marijuana (such as food, drink, or other edibles) and smokeless tobacco (such as snus, moist snuff, dip, spit, pouches, and chewing tobacco) are not included in this analysis. Combustible tobacco device types include cigars or cigarillos, large cigars, and hookah. Tobacco in an e-cigarette includes tobacco use in a vape pen, e-hookah, or personal vaporizers. Non-combustible marijuana device types include e-cigarettes (i.e. vape pens, e-hookah, personal vaporizers).</p> <p>Cigar products include large cigars, cigarillos, and little (filtered) cigar products.</p> <p>^All adolescent sample sizes reported are weighted, scaled, and rounded up to the nearest 'whole person.' The scaled weights take into account complex survey design, including clustering within schools; to account for non-response; and to generalize back to the population from which the sample was taken (Pérez et al., 2017)</p>												

Supplemental Table 1b. Prevalence of past 30-day marijuana product use by marijuana use frequency, among the adolescent cohort in Texas (n=3907; N= 461,069) (2014-2017)

		No marijuana use			Past 30-day Marijuana Use Frequency								
		(n=3591, N=423,737)			1-5 days of use (n=216, N=25,518)			6-19 days of use (n=57, N=6719)			20+ days (n=55, N=6469)		
		Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean	Mean %	Lower Mean	Upper Mean
Adolescence													
early	Age <=11	99.94%	99.51%	99.99%	0.04%	0.01%	0.22%	0.01%	0.00%	0.12%	0.04%	0.01%	0.33%
	Age 12	99.78%	99.49%	99.90%	0.26%	0.10%	0.66%	0.06%	0.01%	0.23%	0.05%	0.02%	0.16%
middle	Age 13	99.57%	99.23%	99.76%	0.47%	0.26%	0.85%	0.13%	0.05%	0.34%	0.05%	0.01%	0.21%
	Age 14	99.27%	98.77%	99.56%	0.85%	0.54%	1.34%	0.15%	0.05%	0.42%	0.04%	0.01%	0.12%
late	Age 15	97.70%	96.55%	98.47%	2.23%	1.53%	3.24%	0.33%	0.17%	0.65%	0.13%	0.05%	0.34%
	Age 16	96.17%	94.20%	97.48%	3.04%	2.06%	4.45%	0.46%	0.22%	0.99%	0.37%	0.13%	1.06%
	Age 17	93.22%	89.04%	95.88%	5.31%	3.30%	8.42%	0.30%	0.29%	1.63%	0.42%	0.12%	1.43%
	Age 18+	87.62%	77.44%	93.59%	8.46%	4.48%	15.40%	1.43%	0.51%	4.00%	0.49%	0.08%	2.84%
p-value		<0.001*			<0.001*			<0.001*			<0.001*		
*All proc glimmix models above adjusted for survey Wave.													
Combustible past 30-day marijuana product use includes joints, pipes, hookah, blunt. Marijuana in an e-cigarette includes use of marijuana in a vape pens, e-hookah, or personal vaporizers. Ingested marijuana (such as food, drink, or other edibles) and smokeless tobacco (such as snus, moist snuff, dip, spit, pouches, and chewing tobacco) are not included in this analysis.													
Combustible tobacco device types include cigars or cigarillos, large cigars, and hookah. Tobacco in an e-cigarette includes tobacco use in a vape pen, e-hookah, or personal vaporizers. Non-combustible marijuana device types include e-cigarettes (i.e. vape pens, e-hookah, personal vaporizers).													
Cigar products include large cigars, cigarillos, and little (filtered) cigar products.													

JOURNAL ARTICLE (3)

Multi-Directional Pathways of Tobacco and Marijuana Use, including Dual- Use, among Young Adults (18-25 years) in Texas: A Six Wave Cross-lagged Model

INTRODUCTION

The product diversification of the tobacco market—namely the explosive popularization of e-cigarettes—has slowed the two-decade-long declining tobacco use trajectory among young adults aged 18-25 years (Jamal et al., 2017; U.S. Department of Health and Human Services, 2016). In this age group, for past 30-day use, exclusive conventional cigarette use (9.6%) still surpassed exclusive use of e-cigarettes (6.1%) and use of both products (7.5%) in 2013-2014, though ever e-cigarette use more than doubled from 2013 to 2014 (U.S. Department of Health and Human Services, 2016). Marijuana use is most prevalent among young adults aged 18-25, and in just one year, past 30-day use among this age group rose from 20.8% in 2016 to 22.1% in 2017 (Substance Abuse and Mental Health Services Administration, 2017). The uptick in e-cigarette use has had an unknown impact on marijuana use. Co-use of these substances may have unforeseen and as yet unknown health consequences.

Historically, adolescence was regarded as the period during which almost all tobacco use initiation occurred, but new research (Perry et al., 2018; Thompson et al., 2018) has shown that young adults may now have significantly higher rates of tobacco use onset than youth across a variety of tobacco products. The 1998 Master Settlement Agreement and the Family Smoking Prevention (Public Health Law Center, 1998) and Tobacco Control Act (TCA) (U.S. Food and Drug Administration, 2016) greatly impacted the tobacco companies' ability to market and appeal to youth, but young adults remain a significant high-risk group for tobacco use onset, as they are the youngest legal target of tobacco marketing now. Simultaneously, over 70 million Americans (over 20% of the country's total population) now live in a state with legal recreational marijuana use (Carliner et al., 2017). Past 30-day marijuana use was highest among young adults compared to any other age group in 2017, most likely attributable to the inverse relationship observed between perceived harmfulness of marijuana and likelihood of use (Johnston et al., 2017). More troubling, the prevalence of past-year marijuana abuse or dependence (MUD, or Marijuana Use Disorder) among adults aged 18 and older also increased from 4.4% in 2001 to 7.5% in 2013 (Hasin et al., 2015b).

Given young adults' prevalent use of both tobacco and marijuana products, some research has examined the co-variation between use of these products in this age group. Dual use among young people has been well documented (Agrawal et al., 2012a; Leatherdale et al., 2007; Ramo et al., 2013; Ramo and Prochaska, 2012; Tullis et al., 2003). Tobacco and marijuana dual use also commonly occurs among young adults (Substance Abuse and Mental Health Services Administration, 2016) (Schauer et al., 2015). In 2016, among past 30-day cigarette smokers, 40.7% of young adults aged 18-25 years used marijuana in the past 30 days, compared with 53.9% of adolescents aged 12-17 years and 21.8% of all adults aged 18 or older (Substance

Abuse and Mental Health Services Administration, 2016). In parallel, despite declines in prevalent daily cigarette smoking from 2002 to 2015, the prevalence of past 30-day cigarette smoking among those aged 12 and older remained 40.17% among non-daily and 54.57% among daily marijuana users, respectively, compared to non-marijuana users (15.06%), and prevalent daily smoking remained four times higher among daily marijuana users than non-users (36.95% vs. 9.70%) (Pacek et al., 2018).

Co-use of tobacco and marijuana products has been associated with greater health risks than the well-documented risks associated with single use of cigarettes (U.S. Department of Health and Human Services, 2014), e-cigarettes (U.S. Department of Health and Human Services, 2016), and marijuana (National Academies of Sciences, Engineering, and Medicine (US) et al., 2017). A review of clinical correlates of co-use found that, compared to marijuana-only users, those who used both tobacco (e.g. conventional cigarettes, cigars, or smokeless tobacco) and marijuana had significantly more psychosocial problems, a greater likelihood of marijuana use disorder (MUD), and poorer marijuana cessation outcomes (Peters et al., 2012). Further, co-use of cigarettes and smoked marijuana may have an additive effect, leading to potentially more severe health consequences (Barsky et al., 1998; National Academies of Sciences, Engineering, and Medicine (US) et al., 2017). As marijuana and tobacco often share modes of administration, co-use of these products is of real concern for efforts aimed at tobacco cessation and MUD prevention.

Concern of co-use goes beyond health effects, as some literature among young adults suggests that use of one tobacco or nicotine product (e.g., e-cigarettes) increases the risk of use of another tobacco or nicotine-containing product (e.g., cigarettes) (Loukas et al., 2016, 2018). One study of Hispanic young adults (mean age of 22.7 years) showed that, among those who were not past-month marijuana users, past-month e-cigarette users in 2014 had had 1.97 the odds of being past-month marijuana users in 2015 (95% CI 1.01,3.86) (Unger et al., 2016). The same study did not find e-cigarette use to be associated with either cigarette or marijuana smoking cessation (Unger et al., 2016). A second study of young adults aged 18 to 25 years found 30.9% reported past-month tobacco-only use and 21.3% reported past-month co-use of marijuana and at least one tobacco product, but causal relationships between the two product types could not be determined since the study was cross-sectional (Cohn et al., 2019). Other recent descriptions and analyses of longitudinal dual use patterns (e.g. (Dierker et al., 2018; Goodwin et al., 2018; Pacek et al., 2018) have not reported these reciprocal patterns by product type other than cigarettes. Consequently, while there is evidence that shows e-cigarettes predict marijuana use, there is still relatively little known about the transition from combustible (e.g. cigarettes, hookah, cigars) tobacco products to use of marijuana during young adulthood. Almost all research to date has focused on the onset of these use behaviors, while very little has examined current, past 30-day use of these products, instead.

In order to better answer these questions and others mentioned earlier, the present study investigated associations of past 30-day marijuana and tobacco use (e.g., e-cigarettes and combustible tobacco products) in multiple directions, including dual use, for all combustible and e-cigarette products among a cohort of young adults (age 18-25 years) in major metropolitan areas of Texas who were surveyed from 2014 to 2017 every six months. We hypothesized that past 30-day use of combustible tobacco products such as cigarettes, cigars,

and hookah would lead to past 30-day marijuana use and, likewise, that past 30-day e-cigarette use will also lead to past 30-day marijuana use. We also posited that the opposite pathways would be meaningful—that is, that past 30-day marijuana use would lead to past 30-day combustible tobacco and e-cigarette use—, but we expected the strength of these relationships to be slightly less in magnitude than those from tobacco to marijuana product use, since tobacco use is more prevalent than marijuana use and legally consumable for this sample. The estimates from these analyses should be useful in projecting future use of both tobacco and marijuana among young adults in the U.S., as Texas boasts a diverse demographic composition that is projected to be representative of the rest of the country over the next decades (Vespa et al., 2018).

METHODS

Protection of Human Subjects Considerations

Active, informed consent was obtained from young adults in M-PACT. University of Texas at Austin Institutional Review Board reviewed and approved all protocols for the M-PACT study (2013-06-0034).

Study Design, Setting, and Participants

Longitudinal data were derived from a rapid response surveillance system study of young adults (aged 18-29 years) living in the five counties (Bexar, Dallas, Harris, Tarrant, and Travis) that surround the four largest cities in Texas (Austin, Houston, San Antonio, and Dallas/Fort Worth). The Marketing and Promotions Across Colleges in Texas project (M-PACT) collects data from students age 18-29 years in 2-year and 4-year colleges (Loukas et al., 2016). Over 13,000 college students (n=13,714) were eligible to participate, and of these, 5482 (40%) completed the baseline survey in November 2014-February 2015 using computerized online surveys (63.4% female and 36.3% non-Hispanic white, 31.1% Hispanic, 8.1% non-Hispanic black, 16.9% Asian). Subsequent data have been collected online every six months since baseline until spring 2017 using similarly formatted surveys taken on a computer or smartphone. At Wave 6, the retention rate for this study exceeded 80%. This analysis uses data from Waves 1 through 6.

Measures

Survey items were adapted from reliable and valid measures from national and state tobacco surveillance studies like the Population Assessment of Tobacco and Health (PATH) study (Hyland et al., 2017), (National Survey on Drug Use and Health (NSDUH) (Substance Abuse and Mental Health Services Administration, 2014), National Youth Tobacco Survey (NYTS) (Centers for Disease Control and Prevention, 2009), and Monitoring the Future (MTF) (Bachman et al., 2005), and Youth Risk Behavioral Survey (YRBSS) (Centers for Disease Control and Prevention, 2013). These items underwent cognitive testing via interviews with 25 young adults to ensure comprehension (Hinds et al., 2016). The final surveys had over 340 items on tobacco use behaviors, exposure to tobacco media and marketing, and sociodemographic,

cognitive, and affective factors (Delk et al., 2017). Sampling methods and eligibility criteria for the M-PACT study are detailed elsewhere (Loukas et al., 2016).

Tobacco and Marijuana Measures

At each wave (1-6), items from the M-PACT survey assessed marijuana and tobacco product use (see Table 1). Past 30-day use was assessed at Waves 1-6 for tobacco products (conventional cigarettes, e-cigarettes, cigar products, and hookah). Participants were asked if they had used the following products in the past 30-days, as intended (that is, with tobacco or with nicotine cartridges and/or e-liquid/e-juice), even one or two puffs: conventional cigarettes (yes/no), any cigar products- (i.e. large cigars, small, filtered cigars, and/or cigarillos) (yes/no), hookah (yes/no), and any electronic nicotine delivery system (e-cigarette) (i.e. an e-cigarette, vape pen, or e-hookah), even one or two puffs, as intended (i.e. with nicotine cartridges and/or e-liquid/e-juice)?, (i.e. an e-cigarette, vape pen, or e-hookah). Response options were yes or no. Tobacco products were also categorized by combustible (conventional cigarettes, cigar products, and hookah) and non-combustible (e-cigarettes) use. Past 30-day marijuana use for young adults was assessed with a single question, “During the past 30 days, how many occasions, or times, if any, have you used marijuana? (Other names for marijuana are pot and weed.)” Responses were dichotomized into 0 days vs. any days of past 30-day marijuana use to parallel the yes/no binary response options of the tobacco products.

Age

Participants in the M-PACT young adult cohort were aged 18-29 years at baseline in Fall 2014/Spring 2015. Young adults aged 26 years and older were intentionally over-sampled on their use of tobacco products. As such, and due to their small sample size (n=261) compared to young adults age 18-25 years (n=5221), young adults aged 26 and older were excluded from this analysis.

Data Analysis

Analyses were conducted using SAS (version 9.4) and MPlus (version 7). Data were analyzed for missingness across waves, which was handled using regression models that employ maximum likelihood estimation methods with robust standard errors (Schafer and Graham, 2002).

Missing data and analysis sample

Missing data for primary outcomes of past 30-day marijuana and tobacco use were <1%. As such, it was appropriate to utilize regression models that employed maximum likelihood estimation methods with robust standard errors, with the assumption that data were missing at random (Schafer and Graham, 2002). Thus, for the young adult cohort, 5221 young adults provided data on select socio-demographic characteristics and ever and past 30-day use of tobacco and marijuana product use (**Table 1**).

Descriptive statistics

Descriptive statistics for the young adult cohort are presented in **Table 1**. Two-sided chi-square tests were used to detect differences in primary outcome variables between subgroups (e.g., sex, race/ethnicity, school type, and socioeconomic status proxy measures, marijuana products use, and tobacco products use), and differences were deemed statistically significant at the 0.05 alpha level.

Modelling multi-directional pathways of use and dual use using cross-lagged models

Six-panel cross-lagged path models were used to simultaneously estimate the following across six study waves (Waves 1-6), each approximately 6 months apart: 1) stability paths, or the autoregressive direct effect within marijuana and tobacco product use across waves (e.g., association between past 30-day tobacco use, from one Wave to the next); 2) bi-directional predictive paths between marijuana and tobacco use at each Wave to use of the other product at the next wave (that is, marijuana use at Wave 1, for example, predicting tobacco use at Wave 2 and vice versa); and 3) correlation coefficients, or the dual use of marijuana and tobacco at each Wave (that is, covariation between tobacco and marijuana use at each age, separately). Past 30-day marijuana- and tobacco-specific product use outcomes were modeled as binary variables (0 days vs. any days), allowing for the calculation of odds ratios.

Three models—using 0 days vs. any days of product use as the outcome of interest—were created to estimate relationships between (a) past 30-day tobacco use (any product) with past 30-day marijuana use; (b) any past 30-day combustible tobacco use (conventional cigarettes, cigar products, hookah) with past 30-day marijuana use; and (c) past 30-day e-cigarette use with past 30-day marijuana use. Analyses were conducted using Mplus (Los Angeles, CA, version 7.3) using the Weighted Least Squares with Mean and Variance adjustment estimation procedure in order to best model categorical data and accommodate missing data. Theta parameterization was applied to the residual variances for the observed categorical dependent variables (Muthén et al., 2016). The school variable was used to account for clustering within universities. Models present the adjusted (for age, race/ethnicity, and sex) β estimates and associated p-values for multiple pathways of tobacco use, marijuana use, and dual use among the young adult cohort across Waves 1-6. Standardized β estimates (Std β) and standard errors were converted to odds ratios and 95% confidence intervals, respectively, in the text.

RESULTS

Descriptive analyses

Differences in baseline socio-demographic characteristics and tobacco and marijuana product use are presented in **Table 1** (at baseline in Fall 2014). Past 30-day combustible tobacco use was almost twice as prevalent as past 30-day e-cigarette use among these young adults aged 18-25 in 2014 (31.8% vs. 16.9%), and past 30-day marijuana use was about 25% at baseline in 2014.

Stability paths between all products for all cohorts

Significant stability paths were observed across all Waves for all past 30-day use of all tobacco, combustible tobacco, e-cigarette, and marijuana products (**Figures 1-3**). For example, past 30-day use of any tobacco product and past 30-day use of marijuana at Wave 1 predicted greater odds of past 30-day use of that same product at Wave 2 ($OR_{\text{any tobacco use at Wave 2 given use at W1}} = 2.641$; 95% CI=2.554,2.730; $OR_{\text{any marijuana use at W2 given use at W1}} = 2.335$; 95% CI=2.250,2.424). Since the data were collected every 6 months, these significant stability paths underline the stability in past 30-day use, over time, controlling for age, race/ethnicity, and gender.

Directionality of use and dual use of any tobacco product use and marijuana use

Dual use of these products occurred at each Wave, and both past 30-day use of any tobacco and past 30-day use of marijuana dimly predicted greater odds of use of the other substance at Waves 3-6 (**Figure 1**).

Over and above stability paths and dual use associations, any past 30-day tobacco product use predicted subsequent marijuana use from Waves 3-6, with fairly consistent magnitudes, with the odds of using marijuana in the past 30 days at Wave 6 for those who used any tobacco products in the past 30 days at Wave 5 being 1.156 (95% CI=1.105,1.209), compared to those who did not use any tobacco in the past 30-days at Wave 5. Past 30-day marijuana use predicted any tobacco use at almost all Waves, and the strongest association occurred from Wave 4 to 5, with the odds of using any tobacco in the past 30 days at Wave 5 being 1.150 (95% CI=1.100,1.203) for those who had used marijuana in the past 30 days at Wave 4, compared to those who had not. Statistically significant dual use of both any tobacco product and marijuana occurred at Waves 1, 2, 4 and 5, but the odds of dual use were opposite in direction at Waves 4 and 5, compared with Waves 1 and 2 ($OR_{\text{dual use at Wave 1}} = 1.921$, 95%CI =1.862,1.983 vs. $OR_{\text{dual use at Wave 4}} = 0.869$, 95%CI =0.761,0.993). Overall, the strength of the associations for the cross-lagged paths linking past 30-day tobacco use and past 30-day marijuana use were much smaller than the stability paths for or dual use of tobacco and marijuana use.

Directionality of use and dual use of combustible tobacco products and marijuana use

Dual use of these products occurred at Waves 1, 2, 4, and 5, and past 30-day use of combustible tobacco and marijuana weakly predicted use of the other substance from Waves 3-6 (**Figure 2**). Past 30-day marijuana use predicted an increase in combustible tobacco use at all Waves, except from Wave 1 to 2, when marijuana use predicted a reduction in the odds of subsequent combustible tobacco use ($OR_{\text{combustible tobacco use at W2 given marijuana use at W1}} = 0.941$; 95% CI=0.905,0.978). Past 30-day combustible tobacco use predicted subsequent marijuana use only from Wave 5 to 6, and the magnitude of these reciprocal paths were comparable to those from marijuana to combustible tobacco use. The odds of dual use of both combustible tobacco and marijuana products increased from Waves 1 to 2 before decreasing from Waves 4 to 5.

Directionality of use and dual use of e-cigarettes and marijuana use

Dual use of these products occurred at all Waves except Wave 6, and the significant reciprocal pathways between past 30-day use of e-cigarettes and marijuana predicting the use of the other substance at subsequent Waves were primarily observed from Waves 3 to 6 (**Figure 3**).

Past 30-day e-cigarette use predicted subsequent marijuana use from Waves 3 to 6, and e-cigarette use at Wave 2 actually predicted a reduction in the odds of past 30-day marijuana use at Wave 3 ($OR_{\text{marijuana use at W3 given e-cigarette use at W2}} = 0.906$; 95%CI=0.852,0.962). Conversely, the odds of using marijuana in the past 30 days at Wave 6 for those who used e-cigarettes in the past 30 days at Wave 5 were 1.203 (95% CI= 1.159,1.249), compared to those who had not used e-cigarettes at Wave 5. The reciprocal paths observed between past 30-day marijuana use and subsequent e-cigarette use were comparable in magnitude to those observed between past 30-day e-cigarette use and subsequent marijuana use. Dual past 30-day use of both e-cigarettes and marijuana occurred at each Wave, except Wave 6, but the odds of dual use decreased from Waves 3 to 6 ($OR_{\text{dual use at W1}} = 1.697$, 95%CI = 1.648, 1.748; $OR_{\text{dual use at W2}} = 1.257$, 95%CI =1.136,1.392; $OR_{\text{dual use at W3}} = 0.694$, 95%CI =0.623,0.773). $OR_{\text{dual use at W4}} = 0.738$, 95%CI =0.645, 0.845; $OR_{\text{dual use at W5}} = 0.574$, 95%CI = 0.517,0.637).

DISCUSSION

This study is the first study to simultaneously examine prospective relationships between past 30-day tobacco and subsequent (i.e. after 6 months) past 30-day marijuana use, past 30-day marijuana and subsequent (i.e. after 6 months) past 30-day tobacco use, and dual use of both products among young adults. Overall, we found that combustible tobacco use and e-cigarette use are prospectively associated with greater risk of future marijuana use, while controlling for stability of use over time, age, race/ethnicity, and gender. Similarly, we found that marijuana use is prospectively associated with greater risk of future combustible tobacco and e-cigarette use. Dual use of these substances was common, but the odds of dual use decreased with increasing age.

Reciprocal pathways: bi-directional paths and the substitution phenomenon

The autoregressive cross-lagged models “stratified” by combustible and e-cigarette products revealed that the moderately strong, positive, reciprocal associations between combustible tobacco, e-cigarettes, and marijuana use were not unidirectional. That is, our results for young adults neither solely support previous theories of gateway (tobacco use implicated as a gateway to marijuana and/or other illicit drug use) (Agrawal et al., 2007; Beenstock and Rahav, 2002; Bentler et al., 2002; Lai et al., 2000; Leatherdale et al., 2007) nor reverse gateway (marijuana use implicated as a gateway to tobacco initiation) effects (Agrawal et al., 2008; Behrendt et al., 2009; Okoli et al., 2008; Timberlake et al., 2007; Tullis et al., 2003) among young adults. Similar route of administration (Agrawal et al., 2012a) or common liability theory (Vanyukov et al., 2012), may better explain our results; however, due to the structure of the marijuana survey item (i.e. the inability to distinguish method of marijuana use as combustible or e-cigarette at Waves 1-6), we are unable to extrapolate our results to this degree.

Additionally, we observed negative coefficients for two pathways—one for marijuana use predicting lesser odds of past 30-day combustible tobacco use and a second for e-cigarette use predicting lesser odds of past 30-day marijuana use. Though not abundant, these inverse pathways provide some support for the substitution phenomenon (Copersino et al., 2006), in

which reduction or increase in use of one substance results in a corresponding increase or decrease, respectively, in the use of the other substance. E-cigarettes have gained controversial attention as potential cessation devices or as “safer” alternatives to conventional cigarettes (Abrams, 2014; Henningfield, 2003), and, likewise, perceptions surrounding the harm associated with marijuana use have been declining among young adults since 2002 (Azofeifa et al., 2016; Cohn et al., 2017). It is, therefore, not surprising to see results that suggest young adults’ preference for a “safer” product (e.g. marijuana over combustible tobacco). Cautionary evidence, however, has shown that use of e-cigarettes may lead to greater tobacco product use (U.S. Department of Health and Human Services, 2014) or marijuana use (Audrain-McGovern et al., 2018; Unger et al., 2016). Our model, however, does not account for the possibility that e-cigarette or marijuana users may instead be switching *completely* to combustible tobacco use. Future research should consider autoregressive cross-lagged models that simultaneously examine combustible, e-cigarette, and marijuana use in a single model in order to tease apart the trajectories of use in this regard.

Dual use: reductions in dual use over time could mean consolidation, not cessation

Cohn et al. (2019) found that 21% of young adults reported past 30-day marijuana and tobacco dual use in 2014-2015, an estimate four times higher than the estimate of 5.2% reported from a sample of the general population of US adults aged 18 or older in 2011-2012 (Schauer et al., 2015), though regrettably not specific to combustible tobacco or e-cigarettes. We found dual use of combustible tobacco with marijuana and dual use of e-cigarettes with marijuana to both be quite strong at early Waves but to decrease from Waves 4-6 and 3-6, respectively. Despite these later decreases in dual use that we observed, considerable research has shown that young adults tend to use a variety of substances (Cohn et al., 2016; Vanyukov et al., 2003), particularly in combination with or subsequent to alcohol use (Barry et al., 2016). Young adults could also, therefore, be co-using other substances along with marijuana and tobacco use, too, like alcohol. Future research should consider the covariation in and sequence of tobacco and marijuana use with regard to alcohol and other substance use, too.

It is also possible that these findings reflect that more young adults may be consolidating their use (i.e., transitioning to single use of one product instead of dual use of two products) than are successfully ceasing their tobacco or marijuana use as they mature through young adulthood. Although we observed decreases in dual use of combustible tobacco with marijuana and e-cigarettes with marijuana, we simultaneously observed strong stability in single use of these products from Waves 1 to 6. Hence, while young adults may not continue to co-use these products into later young adulthood, the odds of continued single use of combustible tobacco products, e-cigarettes, and marijuana are higher for those that used than for those that did not use these products at previous Waves. Further, the decreases observed in dual use did not occur at the same time as the negative reciprocal path coefficients; that is, the decreased odds of dual use did not occur at the same Waves as the reductions in odds of past 30-day combustible tobacco use or past 30-day marijuana use. This observation is consistent with Unger et al. (2016), who did not find e-cigarette use to be associated with either cigarette or marijuana smoking cessation, though they are often marketed to be so (U.S. Department of Health and Human Services, 2016). Lastly, troubling research from Schauer et al. (2015) showed that dual use of marijuana and tobacco among adults increased among those

26-34 years from 2003 to 2012, so it is possible that dual use may increase again for certain individuals in later adulthood. Taken together, these results should help structure interventions specific to young adults that target use and dual use in early young adulthood in order to curb dual use, consolidation, or subsequent escalation of use of one or more products in later young adulthood.

Strengths and limitations

This is the first study to employ a six-panel cross-lagged regression model applied to data collected every 6 months to simultaneously estimate autoregressive stability paths within past 30-day marijuana and tobacco product use; bi-directional predictive paths between marijuana and tobacco use; and correlation coefficients, or the dual use of marijuana and tobacco. Notably, this study presented results for any tobacco, combustible tobacco, and e-cigarette products separately in relation to marijuana use. The autoregressive cross-lagged models allowed for temporal clarity and for the visualization of multi-directional pathways of use. Significant additional strengths of this study include its demographically diverse sample of young adult college students. Further, the six-month spacing between survey Waves allowed for a more complete picture of tobacco and marijuana product use.

A limitation of this study, due to available survey items and sample sizes among the cohorts, is that we were unable to further stratify the cross-lagged models by specific products (e.g., cigarettes only, or marijuana consumed in varied forms). Further, in order to produce the most stable estimates, we dichotomized the frequency measures of past 30-day use (0 days vs. any days of use per month) and, as such, cannot provide more specific estimates of risk as it corresponds to number of days of use frequency. The stability paths provided in the models, however, show high consistency in the measures that were available and used. Lastly, as the sample was drawn from five major metropolitan areas of Texas, its generalizability may lessen, but the demographic composition of the sample is quite representative of the 20-year projected national composition of the U.S. (Vespa et al., 2018). Further, our estimates of past 30-day combustible tobacco, e-cigarette, and marijuana use at baseline were comparable with other national estimates such as National Adult Tobacco Survey (Wang et al., 2018), The Population Assessment of Tobacco and Health (PATH) (Perry et al., 2018), and the National Survey on Drug Use and Health (Substance Abuse and Mental Health Services Administration, 2017).

Table 1. Baseline characteristics (Wave 1, 2014-15) for young adults aged 18-25 in M-PACT Texas cohort (N=5221)

		n or mean	% or SD	p-value
Sex				
	Male	1892	36.26	<0.0001*
	Female	3326	60.72	
Age, mean (SD)		20.15	1.84	N/A
Race/ethnicity				
	Non-Hispanic White	1850	35.43	<0.0001*
	Hispanic	1637	31.35	
	African Ancestry	423	8.1	
	Asian Ancestry	915	17.53	
	Other	396	7.58	
Parental Education				
	Some or no college	1716	34.02	<0.0001*
	College degree or higher	3228	65.98	
College type				
	2-year college	351	6.72	<0.0001*
	4-year college	4870	93.28	
Tobacco use				
Past 30-day use (yes)				
	Any product	1854	35.52	<0.0001*
	Combustible	1661	31.82	
	Non-combustible (e-cigarette)	882	16.9	
Marijuana use				
Past 30-day use (yes)				
	Any product	1277	24.49	N/A
Race/ethnicity: the "Other" category was left as undefined in the response options.				
Tobacco and marijuana use include those who reported having ever used the following products within the past 30 days of the baseline survey: any tobacco product; any type of combustible (cigarette, cigar product--little filtered cigar, cigarillo, or large cigar); any ENDS product , (i.e. an e-cigarette, vape pen, or e-hookah), even one or two puffs, as intended (i.e. with nicotine cartridges and/or e-liquid/e-juice); and any marijuana product.				

Figure 1. Autoregressive cross-lagged models showing multi-directional pathways of use and dual use of any past 30-day tobacco product (i.e. conventional cigarettes, any cigars, hookah, and e-cigarettes) and any past 30-day marijuana use among young adults aged 18-25 in Texas across Waves 1-6 (2014-2016).

Standardized (StdYx) β estimates and standard errors are shown in the following format: β estimate (Standard Error). Beta estimates can be exponentiated to obtain odds ratios. Statistically significant pathways are shown with solid arrows, and non-statistically significant pathways are shown with dashed arrows. All pathways are shown, and all models have been adjusted for race/ethnicity, gender, and age. Separate cross-lagged models are shown for past 30-day use of any tobacco and any past 30-day marijuana, past 30-day combustible tobacco and any past 30-day marijuana, and past 30-day e-cigarettes and any past 30-day marijuana. All tobacco and marijuana use outcomes have been dichotomized to show no days of use versus any days of use.

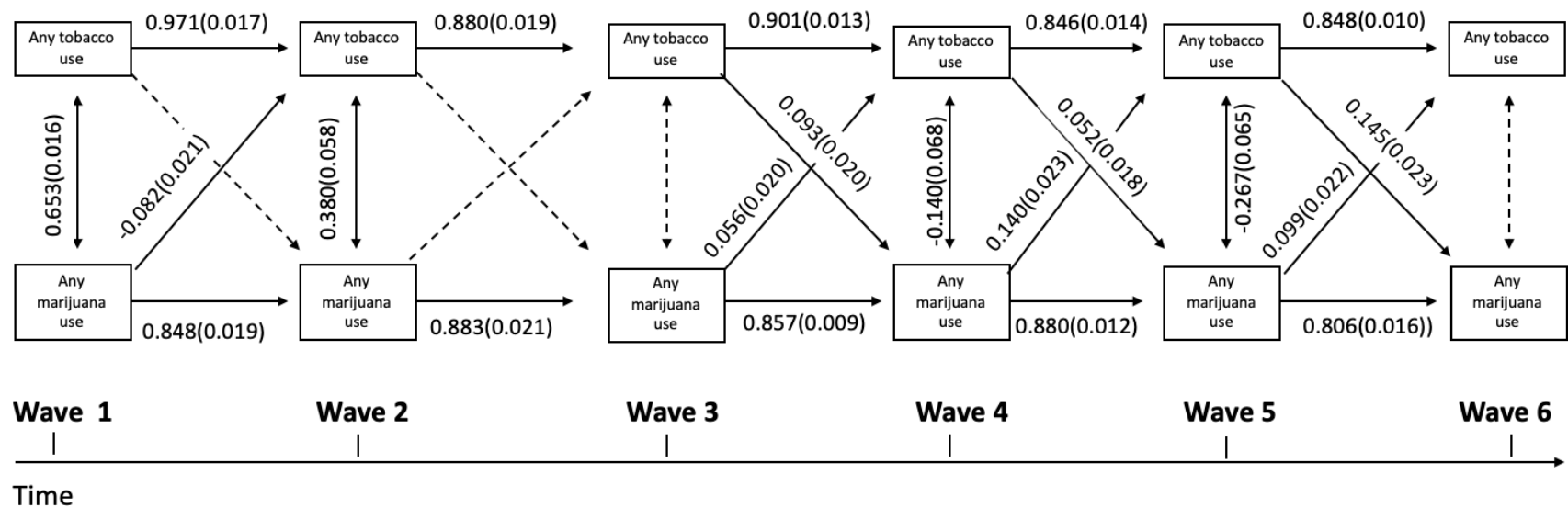


Figure 2. Autoregressive cross-lagged models showing multi-directional pathways of use and dual use of past 30-day combustible tobacco products (i.e. conventional cigarettes, cigars, and hookah) and any past 30-day marijuana use among young adults aged 18-25 in Texas across Waves 1-6 (2014-2016).

Standardized (StdYx) β estimates and standard errors are shown in the following format: β estimate (Standard Error). Beta estimates can be exponentiated to obtain odds ratios. Statistically significant pathways are shown with solid arrows, and non-statistically significant pathways are shown with dashed arrows. All pathways are shown, and all models have been adjusted for race/ethnicity, gender, and age. Separate cross-lagged models are shown for past 30-day use of any tobacco and any past 30-day marijuana, past 30-day combustible tobacco and any past 30-day marijuana, and past 30-day e-cigarettes and any past 30-day marijuana. All tobacco and marijuana use outcomes have been dichotomized to show no days of use versus any days of use.

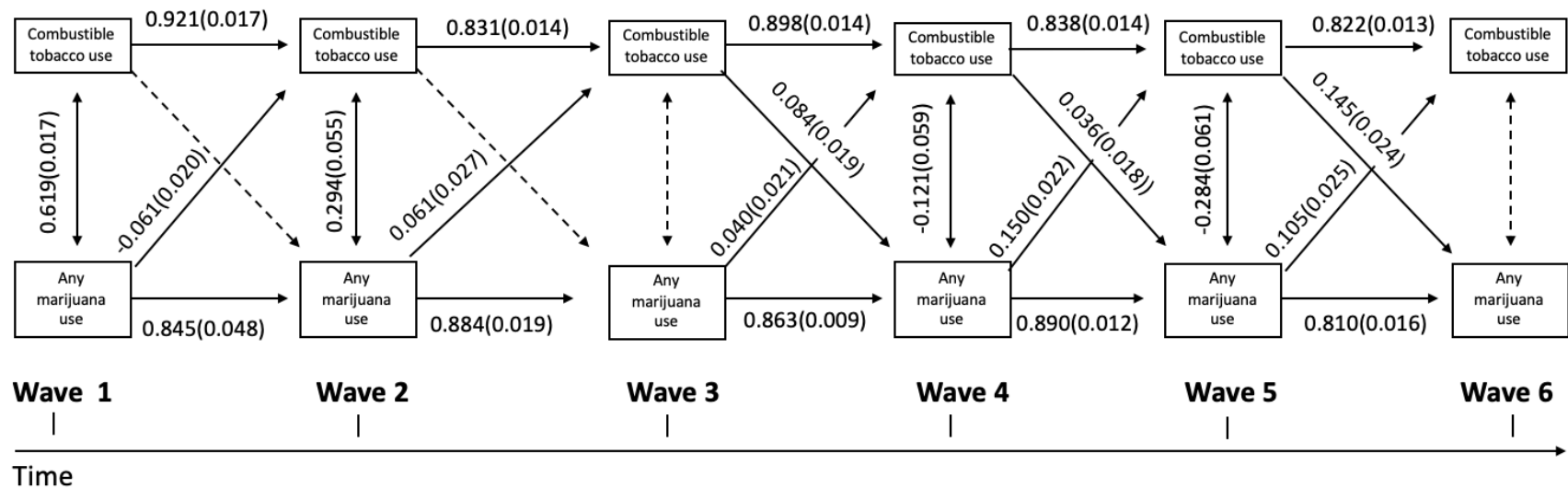
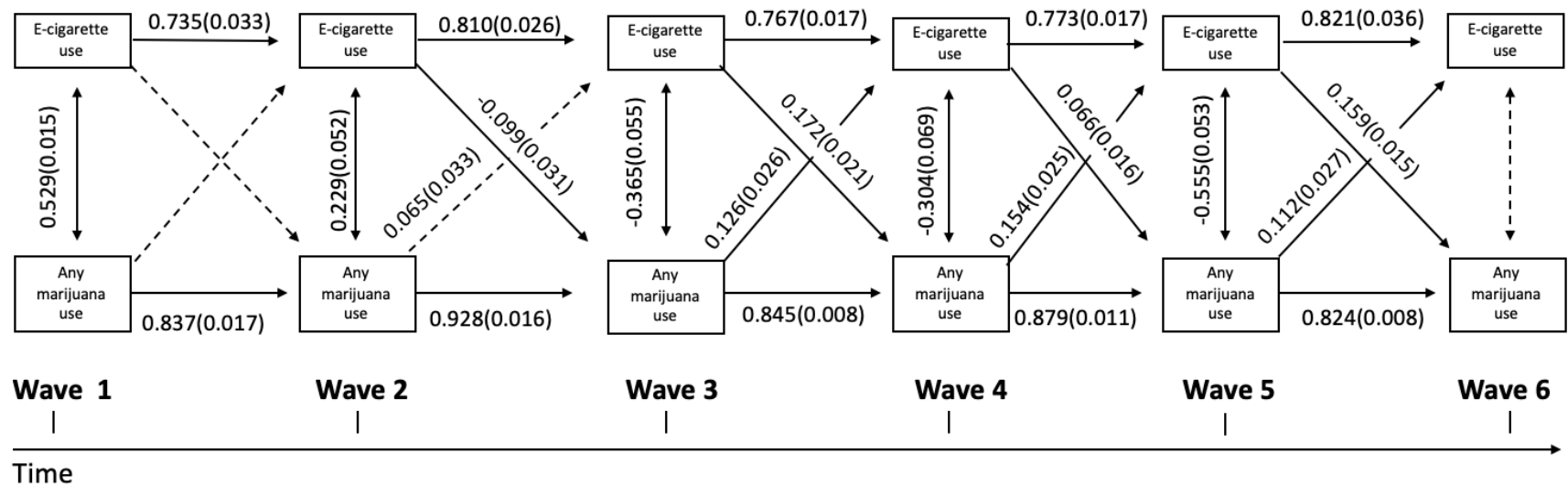


Figure 3. Autoregressive cross-lagged models showing multi-directional pathways of use and dual use of any past 30-day e-cigarettes and any past 30-day marijuana use among young adults aged 18-25 in Texas across Waves 1-6 (2014-2016).

Standardized (StdYx) β estimates and standard errors are shown in the following format: β estimate (Standard Error). Beta estimates can be exponentiated to obtain odds ratios. Statistically significant pathways are shown with solid arrows, and non-statistically significant pathways are shown with dashed arrows. All pathways are shown, and all models have been adjusted for race/ethnicity, gender, and age. Separate cross-lagged models are shown for past 30-day use of any tobacco and any past 30-day marijuana, past 30-day combustible tobacco and any past 30-day marijuana, and past 30-day e-cigarettes and any past 30-day marijuana. All tobacco and marijuana use outcomes have been dichotomized to show no days of use versus any days of use.



DISCUSSION

Past 30-day marijuana use among high school seniors is almost twice that of past 30-day cigarette use (Johnston et al., 2017), and although initiation of marijuana use primarily occurs in adolescence, marijuana use is most prevalent among young adults aged 18-25 years (SAMSHA 2013, 2016). E-cigarette use has surpassed conventional cigarette use among adolescents (Jamal et al., 2017), but past 30-day conventional cigarette use remains highest among young adults aged 18-25 years (23.5%), compared with prevalent use among 12-17 year olds (3.4%) and those 26 years or older (20.2%) (NSDUH, 2016). New research (Perry et al., 2018; Thompson et al., 2018) has shown that young adults have significantly higher incidence rates than youth specific to ever and current use of cigarettes, e-cigarettes, cigar products, and hookah, suggesting initiation of these products may be occurring later in the life course. Almost no cigarette smoking initiation (<1.5%) and little transition to daily smoking (<4.3%) occur in adulthood—e.g. after 26 years of age (USDHHS, 2014). Thus, these developmental periods are, therefore, crucial to the health and substance use behaviors of future adults.

While the pace of legal changes to marijuana policy races onward, marijuana use trends are changing, and emerging products for tobacco use (e.g., e-cigarettes) could be marketed in tandem to marijuana and dual users. The present body of work described and analyzed relationships between marijuana and tobacco dual use and exclusive use over time with attention to product type, when possible, among adolescents and young adults, separately. By using three years of longitudinal data measured every six months (2014-

2017), this research characterized temporal patterns in use of these substances, over time. Recommendations for future interventions and research directions are explored, specific to findings from this research.

Developmental trends in exclusive and dual tobacco and marijuana use among youth and young adults in Texas

Developmental trends in youth

Data from a rapid response surveillance study of youth (age 11-19 years) was used to examine ever and past 30-day use of tobacco and marijuana products (Waves 1-6, 2014-2017). Most studies to date have not analyzed marijuana use in conjunction with or exclusive to tobacco use, so previous characterizations of use patterns may have been over- or under-estimated, or not estimate at all. We used Generalized Linear Mixed Models to examine ever exclusive, ever dual, and exclusive and dual past 30-day use of marijuana- and tobacco- (e.g., conventional cigarettes, cigar products, hookah, and e-cigarettes, when possible) at each age level. We later compared trends in use among adolescents with trends in use among young adults using data from a parallel surveillance study over the same time period (2014-2017).

Exclusive ever tobacco use was almost undetectably low among adolescents, across all ages, but dual ever use of marijuana and tobacco (both ever and prevalent) increased from early to late adolescence from around 0% at age 11 to about 6% by age 18+. Shared

genetic liability to use both tobacco and marijuana products, personality factors like sensation seeking, and social-environmental factors such as peer use, easier access, and reduced perceptions of risk are all plausible reasons for the increased likelihood that these novel products (i.e. e-cigarettes and hookah) and subsequent marijuana are used (Cerdá et al., 2016; Roditis et al., 2016; Roditis and Halpern-Felsher, 2015). Among past 30-day marijuana users, combustible tobacco products and e-cigarettes were the most commonly used tobacco products, though use of almost all tobacco products (i.e. combustible, conventional cigarette, cigar, hookah, and e-cigarette) increased with age among this group, from around 4% at age 14 to 86% at age 18+ for combustible tobacco products.

The erratic prevalent mean percentages of past 30-day tobacco use by product, among past 30-day marijuana users, illustrated the product experimentation that many adolescents likely undertook from the ages of 12 to 18 years. Overall, mapping the patterns of use by substance and product revealed distinct patterns specific to age groups within the adolescent cohort, consistent with adolescent development theory (American Academy of Child and Adolescent Psychiatry, 2003; Perez et al., 2017). The age sub-groups paralleled the developmental phases of early, middle, and late adolescence that were employed to later stratify the auto-regressive cross-lagged panel analysis of adolescent tobacco and marijuana use and dual use.

Developmental trends in young adults

Data from a second parallel rapid response surveillance study of young adults (aged 18-26+ years) was used to examine ever and past 30-day use of tobacco and marijuana

products from Waves 1-6, 2014-2017, including exclusive and dual use. Generalized Linear Mixed Models were again used to examine ever exclusive, ever dual, and exclusive and dual past 30-day use of marijuana- and tobacco-specific products (e.g., conventional cigarettes, cigar products, hookah, and e-cigarettes, when possible) at each age level among young adults. Overall, we found exclusive tobacco use to be common among young adults; both ever use and past 30-day tobacco use to increase from early to late young adulthood; and exclusive marijuana use and dual tobacco and marijuana use to be less common than exclusive tobacco use among young adults, especially when compared to the adolescent sample.

We noted that while young adults used marijuana at the highest rates of any age sub-group (Substance Abuse and Mental Health Services Administration, 2016), they most often did so in conjunction with tobacco use. Unlike for youth, past 30-day use of any combustible tobacco product, among past 30-day marijuana users, far exceeded use of any other product by almost 30% for young adults. E-cigarette use dipped below conventional cigarette use for young adults at age 25. Our results would suggest that dual marijuana and tobacco use decreases with young adulthood, or at least until age 25. (We duplicate the same finding of decreasing dual use among young adults later using auto-regressive cross-lagged models.)

However, while dual use decreased overall with age among young adults, it will still be important to continue to monitor use and dual use among both youth and young adults. New evidence has shown that daily marijuana use has increased over the past decade, most

rapidly among former cigarette smokers (Goodwin et al., 2018), and that dual use of marijuana and tobacco increased among slightly older adults (aged 26-34 years) from 2003 to 2012 (Schauer et al., 2015). Whether the trends we observed for adolescents and young adults are an indication of use patterns to come in the next few years, given the rapid introduction of novel and less-regulated products into the market, or are likely to taper with maturation into young adulthood has yet to be determined.

Multi-directional paths of tobacco and marijuana use among adolescents in Texas

While there is mounting evidence for unidirectional and some bi-directional relationships between cigarette smoking and marijuana use and the reverse, there is still relatively little known about the transition from other combustible (e.g. hookah, cigars) or non-combustible (e.g. e-cigarettes) tobacco products to established use of marijuana or dual use during adolescence. We therefore investigated multi-directional patterns (i.e. stability of single use of tobacco or marijuana, reciprocal paths between tobacco and marijuana, and dual use of both) of past 30-day marijuana and tobacco use, for all combustible and e-cigarette products, from early to middle and late adolescence (ages 11-18 years). In this way, we were able to expand on the first longitudinal trends analysis by situating marijuana, tobacco, and dual use in time and age.

Six-panel cross-lagged regression models, with six months between each study wave, were used to model bi-directional past 30-day use and dual use of marijuana- and tobacco-specific products (e.g., conventional cigarettes, cigar products, hookah, and e-

cigarettes) from 2014-2017 among three population-based cohorts of adolescents in Texas: those who were in the 6th, 8th, and 10th grades in 2014-15 at baseline. We found that in early adolescence (6th grade cohort), past 30-day tobacco use generally preceded an increase in past 30-day marijuana use. In middle adolescence (8th grade cohort), past 30-day marijuana use predicted an increase in past 30-day tobacco use more consistently and more strongly than the reverse – particularly for combustible tobacco product use. Similar findings were observed in late adolescence (10th grade cohort), though past 30-day e-cigarette use preceded an increase in past 30-day marijuana use more consistently than the reverse. For all adolescent age groups, the magnitude of the relationship for marijuana use preceding an increase in tobacco use was greater than that for the reverse.

Considered together, these compelling results provide evidence that prevention needs to be sustained across all developmental phases of adolescence and should focus on both marijuana and tobacco use, though we saw that the relevance of each differed in early, middle, and late adolescence. The magnitude of the consistent, strong directional relationships observed from past 30-day marijuana use to an increase in any tobacco, combustible tobacco, and e-cigarette use provide evidence to support the well-documented “gateway hypothesis” (Beenstock and Rahav, 2002; Bentler et al., 2002), though perhaps in a direction not generally hypothesized in contemporary research.

Our finding that marijuana use so strongly predicted subsequent use of both combustible tobacco and e-cigarettes among adolescents is novel. Thus, as interventions arise to combat the emerging “vape culture” (i.e. vape shops, vaping websites, social media,

etc.) and e-cigarette use in which vaping nicotine and marijuana is supported (Budney et al., 2015; Gostin and Glasner, 2014), it will be equally important to consider the subsequent use of combustible tobacco products, especially among adolescent marijuana users. Lastly, though past 30-day use of marijuana predicted subsequent past 30-day use of any tobacco product more consistently than past 30-day use of any tobacco product predicted subsequent marijuana use, the reverse relationship still existed and warrants concern. Adolescents who start using marijuana with prior nicotine exposure may experience more pleasure from their initial marijuana use experience and may subsequently escalate to more regular marijuana use (Agrawal et al., 2013; Levine et al., 2011).

As the panel analysis demonstrated, the use of these substances among adolescents creates a cycle of risk in which use of one substance increases the odds of use of the other substance, which itself has increased odds of use of the other substance or both. Taking into consideration the results from the prior longitudinal trends analysis for adolescents in which use of tobacco and marijuana increased from age 11 to 18 years, adolescence continues to remain a high-risk developmental period for substance use, despite the fact that tobacco product initiation may be pushing later into young adulthood (Perry et al., 2018; Thompson et al., 2018).

Multi-directional paths of tobacco and marijuana use among young adults in Texas

We performed a second, separate six-panel auto-regressive cross-lagged analysis to model bi-directional past 30-day exclusive use and dual use of marijuana- and tobacco-

specific products (e.g., conventional cigarettes, cigar products, hookah, and e-cigarettes) from 2014-2017 among the M-PACT cohort of young adult college students in Texas. As we observed in the comparative trend analysis, adolescents and young adults have very distinct patterns of tobacco and marijuana use and dual use. Overall, we found combustible tobacco use and e-cigarette use to be prospectively associated with greater risk of future marijuana use, while controlling for the stability of use over time, as well as age, race/ethnicity, and gender. Similarly, we found that marijuana use was prospectively associated with greater risk of future combustible tobacco and e-cigarette use. Dual use of these substances was common, but the odds of dual use decreased with increasing age.

While our panel analysis among adolescents showed evidence for the gateway hypothesis (though perhaps in a reverse direction than may be hypothesized), our results for young adults neither solely support previous theories of gateway (tobacco use implicated as a gateway to marijuana and/or other illicit drug use) (Agrawal et al., 2007; Beenstock and Rahav, 2002; Bentler et al., 2002; Lai et al., 2000; Leatherdale et al., 2007) nor reverse gateway (marijuana use implicated as a gateway to tobacco initiation) effects (Agrawal et al., 2008; Behrendt et al., 2009; Okoli et al., 2008; Timberlake et al., 2007; Tullis et al., 2003) among young adults. We did not observe unidirectional reciprocal relationships among young adults nor one product with a stronger path coefficient in magnitude, but we did note decreases in dual use later in young adulthood. Research has shown that young adults tend to use a variety of substances (Cohn et al., 2016; Vanyukov et al., 2003), particularly in combination with or subsequent to alcohol use (Barry et al., 2016).

We reasoned that, therefore, young adults could be co-using other substances or may be consolidating their use as they mature through young adulthood.

These results for young adults offer evidence to contradict the widely-marketed notion of e-cigarettes and marijuana as less harmful substances to use (U.S. Department of Health and Human Services, 2016). The use of these substances instead resulted in the increased odds of continued use of these substances alone or, in some cases, use of the other substance. Cessation of either product will be difficult to achieve among young adults with interventions that target individual products, as others have suggested (Myers and Prochaska, 2008; Prochaska et al., 2004).

Most troubling is the implication of these results when considered with those from the adolescent panel analysis. Among all adolescent age groups, the magnitude of the relationship for marijuana use preceding an increase in tobacco use was greater than that for combustible tobacco or e-cigarettes predicting an increase in marijuana use. Young adults use marijuana at the highest prevalence of any age group in the U.S. and, in our sample, used combustible tobacco (31.82%) at rates almost one and a half times that of marijuana (24.49%) and twice that of e-cigarettes (16.90%). If marijuana and e-cigarette use trajectories for adolescents continue into young adulthood in the future, this will be devastating to not only the adolescents who use the substances but to the achievements in adolescent and young adult tobacco cessation efforts. The data for these analysis were taken at what has become the relative beginning of the popularization of the marijuana (Carliner et al., 2017; Johnston et al., 2017) and e-cigarette markets (U.S. Department of

Health and Human Services, 2016). Time will tell whether use escalates into young adulthood and whether it declines with adult maturation.

Strengths and Limitations

The collection of analyses presented here uniquely allows for the comparison of use trends among youth and young adults sampled from parallel rapid-response surveillance studies in the five major metropolitan areas of Texas from 2014 to 2017. Though not directly comparable, the samples represent unique age subgroups that have been shown to be distinct in their uptake and use of tobacco and marijuana products. Further, as literature is just emerging on specific tobacco product use trends for these sub-populations, and even less research is available on marijuana product use, we present novel estimates of exclusive and dual use of marijuana and tobacco, past 30-day use of these products, and, when possible, past 30-day product-specific estimates in order to answer questions surrounding at what age(s) and with which product(s) most use is occurring.

We also produced the first study to employ two separate six-panel cross-lagged regression models applied to data collected every 6 months to simultaneously estimate autoregressive stability paths within past 30-day marijuana and tobacco product use; bi-directional predictive paths between marijuana and tobacco use; and correlation coefficients, or the dual use of marijuana and tobacco among adolescents and young adults, separately. These models allowed for temporal clarity and for the visualization of multi-directional pathways of use. To date, the large majority of studies have focused on ever use

of these substances only and include only two or three panels at most, which limits inferences about more consistent use of these products.

The ability to estimate past ever exclusive marijuana use and 30-day use of marijuana by specific product among young adults was limited due to available survey items. The young adult cohort was specifically over-sampled, by original design, for tobacco users, though the use profile for young adults presented here may not be unique only to this sample of young adults but instead more characteristic of the use patterns of young adults as an age sub-group (i.e. there is little indication that the patterns we observed would be unlike those in a more general population of non-tobacco and tobacco users). Secondly, our auto-regressive cross-lagged models did not account for the possibility that e-cigarette or marijuana users may instead be switching to combustible tobacco and/or alcohol use. Future research should consider autoregressive cross-lagged models that include combustible tobacco, e-cigarette, marijuana, and alcohol use in order to test tease apart the trajectories of use in this regard.

Thirdly, these data may not generalize outside of the five major urban areas of Texas from which the study samples were drawn; though tobacco use data do seem comparable to national estimates (Perry et al., 2018). However, while the demographic compositions of the youth and young adult cohorts were slightly different, the sampling designs for both cohorts were intentionally constructed to create comparable populations from which fair comparisons could be drawn (Loukas et al., 2016; Perez et al., 2017). Our estimates of past 30-day combustible tobacco, e-cigarette, and marijuana use at baseline were comparable

with other national estimates such as National Adult Tobacco Survey (Wang et al., 2018) and the National Survey on Drug Use and Health (Substance Abuse and Mental Health Services Administration, 2017).

APPENDICES

Appendix A: Dictionary

General

1. Drug addiction¹⁵: a chronically relapsing disorder and is characterized by the compulsive desire “to seek and use drugs with impaired control over substance use, despite negative consequences”

Marijuana

1. Marijuana abuse or dependence, Cannabis Use Disorder (CUD), Marijuana Use Disorder (MUD), Problem marijuana use¹⁶:

The DSM-IV criteria for marijuana dependence (as used by NSDUH) includes:

1. spent a lot of time engaging in activities related to use of the drug,
2. used the drug in greater quantities or for a longer time than intended,
3. developed tolerance to the drug,
4. made unsuccessful attempts to cut down on use of the drug,
5. continued to use the drug despite physical health or emotional problems associated with use,
6. reduced or eliminated participation in other activities because of use of the drug,
- and 7. experienced withdrawal symptoms when respondents cut back or stopped using the drug.

For marijuana, dependence is defined as meeting three or more of these seven criteria. However, experiencing withdrawal symptoms is not included as a criterion for some illicit drugs based on DSM-IV criteria. For these substances, dependence is defined as meeting three or more of the first six criteria.

Respondents who used (or misused) a specific illicit drug in the past 12 months and did not meet the dependence criteria for that drug were defined as having abuse were defined as meeting the abuse criteria for that drug if they reported one or more of the following:

¹⁵ Source: Prud’homme, Mélissa, et al. “Cannabidiol as an Intervention for Addictive Behaviors: A Systematic Review of the Evidence.” *Substance Abuse: Research and Treatment*, vol. 9, Jan. 2015, p. SART.S25081. *CrossRef*, doi:10.4137/SART.S25081.

¹⁶ Source: American Psychiatric Association, and American Psychiatric Association, editors. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*. 5th ed, American Psychiatric Association, 2013.

1. problems at work, home, and school because of use of the drug;
2. regularly using the drug and then doing something physically dangerous;
3. repeated trouble with the law because of use of the drug; and
4. continued use of the drug despite problems with family or friends.

The DSM-V defines marijuana dependence, synonymous with Marijuana Use Disorder (MUD) as: A problematic pattern of cannabis use leading to clinically significant impairment or distress as manifested by at least two of the following occurring in a 12 month period:

1. Cannabis is often taken in larger amounts over a longer period than was intended.
2. There is a persistent desire or insignificant effort to cut down or control cannabis use.
3. A great deal of time is spent in activities necessary to obtain cannabis, use cannabis or recover from its effects.
4. Craving or a strong desire or urge to use cannabis.
5. Recurrent cannabis use resulting in failure to fulfill major role obligations at work, school or home.
6. Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.
7. Important social, occupational or recreational activities are given up or reduced because of cannabis use.
8. Recurrent cannabis use in situations which is physically hazardous.
9. Cannabis use is continued despite knowledge of having persistent or recurrent physical or psychological problems that are unlikely to have been caused or exacerbated by cannabis.
10. Tolerance, as defined by either:
 - 1) A need for markedly increased amounts of cannabis to achieve intoxication and desired effect, or
 - 2) A markedly diminished effect with continued use of the same amount of cannabis.
11. Withdrawal, as manifested by either:
 - 1) The characteristic withdrawal symptoms for cannabis, or
 - 2) A closer related substance is taken to relieve or avoid withdrawal symptoms

The severity of the disorder is also noted, depending on the number of symptoms noted:

- Mild – Two or Three Symptoms
- Moderate- Four or five symptoms
- Severe- Six or more symptoms

(Source: American Psychiatric Association, 2013)

2. Problem marijuana use
See entry for marijuana abuse or dependence

Tobacco

1. Past month smoking:
The prevalence of cigarette smoking is most commonly described by using the term “current cigarette smoking,” and many surveillance mechanisms define *current cigarette smoking* differently. The NSDUH definition of current smoking, similar to the Youth Risk Behavior Surveillance System’s (YRBSS), is “having smoked part or all of a cigarette during the past 30 days” and does not include 100 cigarettes smoked in one’s lifetime as a threshold for adolescents or young adults but does for adults (USDHHS, 2014).

Alcohol¹⁷

1. Binge drinking: National Institute on Alcohol Abuse and Alcoholism defines binge drinking as a pattern of drinking that brings blood alcohol concentration (BAC) levels to 0.08 g/dL. This typically occurs after 4 drinks for women and 5 drinks for men—in about 2 hours.

The Substance Abuse and Mental Health Services Administration (SAMHSA), which conducts the annual National Survey on Drug Use and Health (NSDUH), defines binge drinking as 5 or more alcoholic drinks for males or 4 or more alcoholic drinks for females on the same occasion (i.e., at the same time or within a couple of hours of each other) on at least 1 day in the past month.

2. Heavy alcohol use: SAMHSA defines heavy alcohol use as binge drinking on 5 or more days in the past month.

¹⁷ Source: National Institute on Alcohol Abuse and Alcoholism. *Drinking Levels Defined*. <https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking>.

Appendix B: Executed Institutional Review Board Approval Letters for Conduct of Research



Committee for the Protection of Human Subjects

6410 Fannin Street, Suite 1100
Houston, Texas 77030

NOTICE OF APPROVAL TO IMPLEMENT REQUESTED CHANGES

June 26, 2018

HSC-SPH-17-0704 - Big Tobacco. Big Marijuana? Longitudinal Trends and Multi-directional Dual Tobacco and Marijuana Use among Youth, Young Adults, and Adults in the U.S.
PI: Dr. Shannon Rogers

Reference Number: 172567

PROVISIONS: Unless otherwise noted, this approval relates to the research to be conducted under the above referenced title and/or to any associated materials considered at this meeting, e.g. study documents, informed consent, etc.

APPROVED: By Expedited Review and Approval

CHANGE APPROVED: Revised protocol to utilize different de-identified datasets

REVIEW DATE: June 26, 2018

APPROVAL DATE: June 26, 2018

CHAIRPERSON: L. Maximilian Buja, MD

A handwritten signature in dark ink that reads "L. Maximilian Buja".

Upon receipt of this letter, and subject to any provisions noted above, you may now implement the changes approved.

CHANGES: The principal investigator (PI) must receive approval from the CPHS before initiating any changes, including those required by the sponsor, which would affect human subjects, e.g. changes in methods or procedures, numbers or kinds of human subjects, or revisions to the informed consent document or procedures. The addition of co-investigators must also receive approval from the CPHS. ALL PROTOCOL REVISIONS MUST BE SUBMITTED TO THE SPONSOR OF THE RESEARCH.

UNANTICIPATED RISK OR HARM, OR ADVERSE DRUG REACTIONS: The PI will immediately inform the CPHS of any unanticipated problems involving risks to subjects or others, of any serious harm to subjects, and of any adverse drug reactions.

RECORDS: The PI will maintain adequate records, including signed consent documents if required, in a manner that ensures subject confidentiality.

NOTICE OF APPROVAL TO IMPLEMENT REQUESTED CHANGES

March 06, 2019

HSC-SPH-17-0704 - Big Tobacco. Big Marijuana? Longitudinal Trends and Multi-directional Dual Tobacco and Marijuana Use among Youth and Young Adults in the U.S.
PI: Dr. Shannon Rogers

Reference Number: 184820

PROVISIONS: Unless otherwise noted, this approval relates to the research to be conducted under the above referenced title and/or to any associated materials considered at this meeting, e.g. study documents, informed consent, etc.

APPROVED: By Expedited Review and Approval

CHANGE APPROVED: Revised title; revised protocol with reduction in scope

REVIEW DATE: March 6, 2019

APPROVAL DATE: March 6, 2019

CHAIRPERSON: L. Maximilian Buja, MD

L. Maximilian Buja

Upon receipt of this letter, and subject to any provisions noted above, you may now implement the changes approved.

CHANGES: The principal investigator (PI) must receive approval from the CPHS before initiating any changes, including those required by the sponsor, which would affect human subjects, e.g. changes in methods or procedures, numbers or kinds of human subjects, or revisions to the informed consent document or procedures. The addition of co-investigators must also receive approval from the CPHS. **ALL PROTOCOL REVISIONS MUST BE SUBMITTED TO THE SPONSOR OF THE RESEARCH.**

INFORMED CONSENT: Informed consent must be obtained by the PI or designee(s), using the format and procedures approved by the CPHS. The PI is responsible to instruct the designee in the methods approved by the CPHS for the consent process. The individual obtaining informed consent must also sign the consent document. Please note that if revisions to the informed consent form were made and approved, then old blank copies of the ICF MUST be destroyed. Only copies of the appropriately dated, stamped approved informed consent form can be used when obtaining consent.

UNANTICIPATED RISK OR HARM, OR ADVERSE DRUG REACTIONS: The PI will immediately inform the CPHS of any unanticipated problems involving risks to subjects or others, of any serious



Committee for the Protection of Human Subjects

6410 Fannin Street, Suite 1100
Houston, Texas 77030

Dr. Shannon Rogers
UT-H - SPH - Epidemiology & Disease Control

August 07, 2017

HSC-SPH-17-0704 - *The Impact of Recreational Marijuana Legalization on Patterns and Predictors of Use among Youth and Young Adults in the United States and Uruguay*

The above named project is determined to qualify for exempt status according to 45 CFR 46.101(b)

CATEGORY #4 : *Research, involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects.*

CHANGES: Should you choose to make any changes to the protocol that would involve the inclusion of human subjects or identified data from humans, please submit the change via iRIS to the Committee for the Protection of Human Subjects for review.

INFORMED CONSENT DETERMINATION:

Waiver of Consent Granted

HEALTH INSURANCE PORTABILITY and ACCOUNTABILITY ACT (HIPAA):

Exempt from HIPAA

STUDY CLOSURES: Upon completion of your project, submission of a study closure report is required. The study closure report should be submitted once all data has been collected and analyzed.

Should you have any questions, please contact the Office of Research Support Committees at 713-500-7943.

harm to subjects, and of any adverse drug reactions.

RECORDS: The PI will maintain adequate records, including signed consent documents if required, in a manner that ensures subject confidentiality.

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