2020

Characterizing patterns of cannabis use and related health effects among young adults using ecological momentary assessment

Alyssa Rudy
Virginia Commonwealth University

CHARACTERIZING PATTERNS OF CANNABIS USE AND RELATED HEALTH EFFECTS AMONG YOUNG ADULTS USING ECOLOGICAL MOMENTARY ASSESSMENT

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Psychology at Virginia Commonwealth University.

by

Alyssa Rudy

B.S., University of Wisconsin - Whitewater, 2014

M.S., Virginia Commonwealth University, 2018

Director: Dr. Caroline Cobb

Assistant Professor

Department of Psychology

Virginia Commonwealth University

Richmond, Virginia

November, 2020

Acknowledgements

This dissertation is dedicated to all of those who strive for criminal justice and drug policy reform.

To my participants, thank you for your time, and thank you for believing in scientific exploration. To cannabis and tobacco researchers, thank you for carving the path for me.

My sincerest thank you to Dr. Caroline Cobb. Thank you for believing in and funding this project. Thank you for challenging me and pushing me to be a better writer and scientist. You have been my most compassionate guide throughout my time at VCU. You were always supportive of my dreams, and this journey would not have been possible without you. This dissertation is *our* success and triumph. Thank you.

I would like to thank my committee members, Drs. Eric Benotsch, Andrew Barnes, Joseph Porter, and Joe Dzierzewski. Thank you for your time, feedback, and combined expertise.

Thank you to Savannah Cook for your contributions to this project. You were instrumental to the success of this study.

Thank you to my family, Curt and Diane Rudy, Nicole and Brad Staehler, Jeff and Ashley Rudy, and Jackson, Easton, Carson, Griffin, Bennett, and Lawson, for being an incredible support system. Mom and Dad, thank you for always letting me choose my own path. I love you.

Finally, I would like to thank Dr. Remington Rice. Thank you for allowing me to spill out all my thoughts, feelings, and emotions at the end of every day. Thank you for being my best friend. I love you. We did it!!

Abstract

Introduction: Rapid changes in cannabis use policy and prevalence, particularly among young adults, and the lack of information regarding cannabis harms warrant investigation regarding the daily use patterns of cannabis users. Little is known regarding how variability in cannabis use frequency and administration method use patterns may be associated with differential acute cannabis-related health effects (i.e., subjective intoxication and respiratory symptoms). The purpose of the study was to characterize daily and weekly cannabis use patterns and associated cannabis-related intoxication and respiratory symptoms and test the interactions of cannabis use frequency and cannabis administration method use on cannabis-related intoxication and respiratory symptoms among young adult heavy cannabis users

Methods: Participants included 27 young adults who used cannabis at least 5 days per week and were 18 to 25 years old. Participants were asked to complete two weeks of surveys sent to their cell phones three times daily. Assessments included cannabis use frequency (measured in hits), cannabis administration method use (classified into two groups: combusted methods [joint, blunt, bowl/pipe, bong] and combination methods [any of the previously listed methods and vaporizer or dab]), and cannabis-related intoxication (mental and physical high) and respiratory symptoms (coughing/wheezing, throat irritation, and phlegm/chest mucus). Data were analyzed using linear mixed models, a two-way analysis of variance, and a two-way analysis of covariance. All analyses were conducted using SPSS ($p<0.05$).

Results: Cannabis hits frequency, number of cannabis administration methods used, and cannabis-related intoxication were highest or most severe in the evenings. Day of week effects were not observed for any outcomes. High frequency cannabis users reported significantly higher cannabis-related intoxication symptoms compared to low frequency users. Among only those in the high frequency cannabis use group, combination administration method users reported significantly higher intoxication compared to combusted administration method users. No differences in respiratory symptoms among cannabis administration method sub-groups or use frequency sub-groups were observed.

Conclusions: Current study results inform interventionists, cannabis users, public health officials, and policy makers with the goal of reducing the negative health effects associated with cannabis use. Future research should measure cannabis-related intoxication effects in various ways to more fully understand cannabis impairment. The use of biological and behavioral measures in clinical and natural settings would aid this goal. Research on respiratory symptoms and cannabis use would benefit from the development of validated instruments, which measure acute cannabis-related respiratory symptoms. Overall, current study results act as a foundation for future researchers to examine further cannabis-related health effects among heavy cannabis users.

Table of Contents

List of Figures

List of Tables

List of Abbreviations

ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
CCQ	Clinical COPD Questionnaire
COVID-19	SARS-CoV-2
DFAQ-CU	Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory
DSM-IV	Diagnostic and Statistical Manual for Mental Disorders, fourth ed.
DSM-5	Diagnostic and Statistical Manual for Mental Disorders, fifth ed.
EMA	Ecological momentary assessment
EMM	Estimated marginal mean(s)
EVALI	E-cigarette or vaping product use-associated lung injury
FDA	United States Food and Drug Administration
NIDA	National Institute on Drug Abuse
SEM	Standard error of the mean
THC	Tetrahydrocannabinol
US	United States

Introduction

Overview and Motivation for Study

Cannabis, a well-known drug class used for recreational and medicinal purposes, is the most frequently used illegal drug in the United States (US; CBHSQ, 2018). Prevalence trends demonstrate that cannabis use has increased among young adults (CBHSQ, 2018). In 2015, 19.8% of young adults aged 18-25 used cannabis in the past month, which increased to 20.8% in 2016 and increased to 22.1% in 2017 (CBHSQ, 2018). Importantly, as of 2017, young adults aged 21-24 used cannabis daily more than any other age group (9%), the highest rate of daily use since 1982 (Schulenberg et al., 2018). At the same time, cannabis policies for recreational and medicinal use are rapidly evolving in the US (National Conference of State Legislatures, 2018a, 2018b). These changes in cannabis use and policies warrant investigation on the daily use patterns of cannabis users to prevent negative health consequences associated with cannabis use. Cannabis use can be associated with harmful abuse and dependence behaviors; however, cannabis use is also associated with therapeutic effects. It is unclear which cannabis use patterns are the most harmful to users. Areas for exploration on cannabis-related harms include effects associated with varying cannabis use frequency and administration method (i.e., combusted versus non-combusted method) use. Differential levels of cannabis use frequency and use of individual or combination cannabis administration methods may produce markedly different cannabis-related health symptoms including intoxication and negative respiratory effects. Importantly, these latter health symptoms could result in immediate as well as long-term negative health consequences. The proposed study aims to characterize patterns of cannabis use frequency and cannabis administration method use, as well as their effects and interaction on health-related symptoms among young adults in the US.

Cannabis: Cannabinoids, Cannabis Forms, and Cannabis Administration Methods

Cannabis, frequently known as marijuana, is a plant, which can grow as several different species (i.e., strains). The three most common species are *Cannabis sativa, Cannabis indica,* and *Cannabis ruderalis* (Sawler et al., 2015). Many varieties of cannabis are sexually propagated hybrids, which contain genes from different species (Emboden, 1974). Each cannabis plant and/or variety has a unique cannabinoid profile, which can determine its legal status (i.e., an agricultural hemp product vs. an illegal drug; Russo & Marcu, 2017; U.S. Food and Drug Administration, 2019a). Cannabinoids are a class of chemical compounds, which are found endogenously (as anandamide) and exogenously (such as in a cannabis plant). These cannabinoids interact with specific cannabinoid receptors (CB_1 and CB_2) in the brain and other areas of the body (Ameri, 1999; El-Alfy et al., 2010; Mehmedic et al., 2010; Nguyen et al., 2017). Of import, CB_1 receptors are mainly concentrated in the brain, while CB_2 receptors are located primarily in immune cells (Matsuda, Lolait, Brownstein, Young, & Bonner, 1990; Munro, Thomas, & Abu-Shaar, 1993).

Over 100 cannabinoids have been identified in cannabis plants; however, the most common types include Δ9-tetrahydrocannabinol (THC) and cannabidiol (Ameri, 1999; Lafaye, Karila, Blecha, & Benyamina, 2017; Russo & Marcu, 2017). THC is a volatile viscous oil that is highly lipophilic (Sharma, Murthy, & Bharath, 2012) and is the primary psychoactive cannabinoid in cannabis plants, which is associated with a subjective intoxication or “high” (M. J. E. Loflin et al., 2017; Sharma et al., 2012). The pleasurable and rewarding effects of THC have been the primary reasons for the widespread use and abuse of cannabis (Sharma et al., 2012). It is important to note that CBD popularity and use is rising due to recent changes in policies regarding the sale and production of this compound (Corroon & Kight, 2018; Corroon &

Phillips, 2018). Previous to 2018, cannabis with any amount of THC was deemed federally illegal to grow, consume, or possess; however, the Agriculture Improvement Act of 2018 revised federal laws to allow the growth, consumption, and possession of cannabis with less than 0.3% THC content (U.S. Senate Committee on Agriculture Nutrition and Forestry, 2018). This type of cannabis is known as hemp. Hemp is grown and consumed primarily for its high CBD content, but hemp has other purposes including textiles, paper, and construction (Small & Marcus, 2002). For the purposes of this dissertation, hemp is not a focus, and when the term “cannabis” is used, we refer to products with greater than 0.3% THC content.

THC concentration in cannabis has increased over time. In the 1980s, average THC concentration from seized dried cannabis products was 3% and has increased to approximately 17% in 2017 (Chandra et al., 2019; ElSohly et al., 2016). Highly concentrated THC products are becoming more popular in the form of cannabis concentrates (e.g., hash oil, dabs; Cavazos-Rehg et al., 2018; Daniulaityte et al., 2017; M. Loflin & Earleywine, 2014; Zhang, Zheng, Zeng, & Leischow, 2016). Reports of THC content in cannabis concentrates indicate an average THC content of 55.7% in 2017, and other reports indicate THC content up to 80% (Chandra et al., 2019; Stogner & Miller, 2015).

This evolution of increased THC concentrations in cannabis products has occurred in tandem with changes in the means to consume cannabis (i.e., administration methods; Russell, Rueda, Room, Tyndall, & Fischer, 2018). Many forms of cannabis (e.g., dried, concentrate, edible, etc.) are consumed via many various administration methods, which complicates study and scientific terminology in this area. In terms of administration methods, cannabis can be consumed in many ways including joints, blunts, bongs, bowls/pipes, vaporizers, concentrate/“dab” rigs, and edibles, which may be associated with differential patterns of use and health effects (see Figures 1 and 2; Rudy, 2018). Joints consist of dried cannabis wrapped in a cigarette rolling paper, and blunts consist of dried cannabis wrapped in tobacco leaves/hollowed tobacco cigars (Schauer, King, Bunnell, Promoff, & McAfee, 2016). Bongs and bowls/pipes are devices, often made of glass, in which dried or concentrated cannabis is placed in a concave bowl (see Figure 1, Panel A; Kelly, 2005). Joints, blunts, bongs, and bowls/pipes are used by directly igniting cannabis and subsequently inhaling the emitted smoke; therefore, these administration methods are considered combusted administration methods. Vaporizers or electronic cigarettes (e-cigarettes) are devices, which contain a battery, heating element, or atomizer, which when activated, warms cannabis-containing material (dried, concentrated, or liquid form) to a temperature that produces an aerosol to be inhaled (see Figure 1, Panel B; Lee, Crosier, Borodovsky, Sargent, & Budney, 2016). For the purposes of this dissertation, the term "vaporizer" will be used. Concentrate/"dab" rigs (i.e., dabs) are devices that use a blowtorch or electronic heating element to indirectly heat cannabis-containing material (typically concentrated) to be inhaled (see Figure 2; Raber, Elzinga, & Kaplan, 2015). Finally, edibles are food products that are made with cannabis (in many forms). Unlike combusted administration methods, vaporizers, concentrate/"dab" rigs, and edibles are not consumed through directly lighting cannabis on fire; therefore, these methods are considered "other" administration methods.

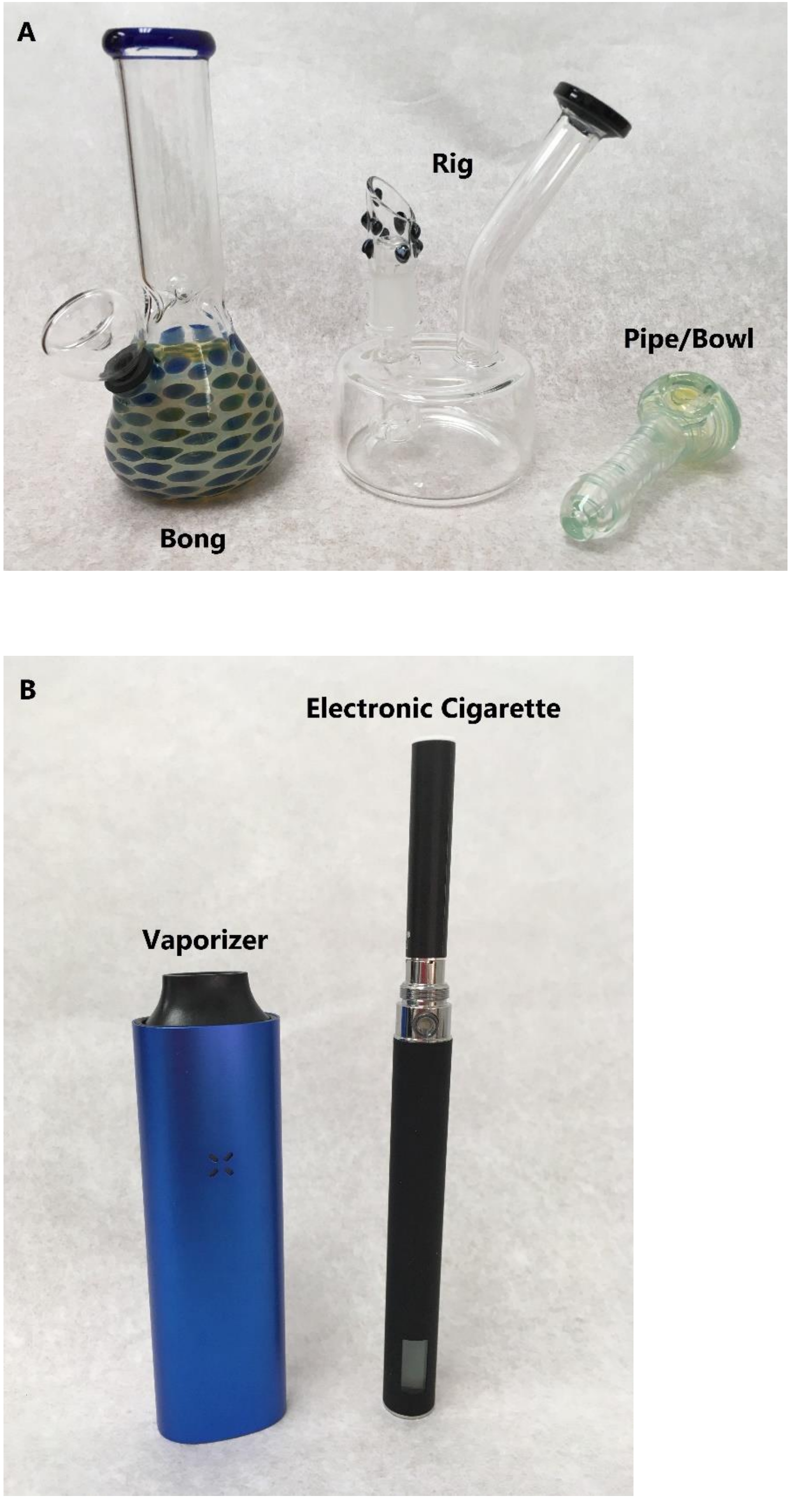

Figure 1. Devices for cannabis consumption. Panel A displays typical glass devices including a bong, concentrate/"dab" rig, and bowl/pipe. Panel B displays electronic devices including a dry material vaporizer and an electronic cigarette where cannabis-containing liquid would be loaded.

Figure 2. A cannabis concentrate/”dab” rig. A cannabis concentrate/”dab” rig typically includes a dome, which helps contain the cannabis emissions, and a nail (where the concentrate preparation is placed).

Clinical Effects of Cannabis Use

Despite the range of cannabis administration methods available to consume cannabis-containing products, a large amount of clinical research to date has focused on the effects of combusted dried cannabis (usually in the form of joints) and the effects of the primary psychoactive cannabinoid, THC (Heishman, Huestis, Henningfield, & Cone, 1990; Russell et al., 2018); although see (Millar, Stone, Yates, & O'Sullivan, 2018 for CBD review). In terms of speed of drug delivery, THC can be detected in blood plasma within seconds after inhalation via combusted administration methods (Grotenhermen, 2003; Sharma et al., 2012). A recent study of vaporized cannabis among infrequent cannabis users indicated that use of Volcano vaporizer device (with dried cannabis) resulted in higher peak blood-level THC concentrations compared to when the same THC doses were consumed using a pipe and lighter (Spindle et al., 2018). Oral cannabis consumption results in a slower delivery of THC and longer time to peak plasma concentration compared to smoked and vaporized cannabis (Grotenhermen, 2003; Newmeyer et al., 2016). Of import, THC is rapidly metabolized to 11-hydroxy-delta-9-THC, which is a pharmacologically active metabolite with a duration of action of 4-6 hours (Advokat, 2014). The speed of delivery and associated administration method, dose of THC and its metabolites as well as other relevant cannabinoids influence the onset and range of clinical effects observed for cannabis. Of those with the highest applicability for the proposed project include subjective (e.g., mood, intoxication) effects, respiratory effects, other adverse effects (e.g., impaired memory/performance), and therapeutic effects.

Subjective effects of cannabis use are generally classified into two categories: positive and negative (Green, Kavanagh, & Young, 2003; Zeiger et al., 2012). Positive subjective effects of cannabis use include increased euphoria, relaxation, creativity, sociability, and energy, and improved mood (Zeiger et al., 2012). Negative subjective effects of cannabis use include increased depression, anxiety, paranoia, hallucinations, feelings of guilt and laziness, drowsiness, and inability to concentrate (Zeiger et al., 2012). There are also other types of subjective effects, which can be classified into either category. These effects include increased appetite, talkativeness, and intoxication (Green et al., 2003; Zeiger et al., 2012). Cannabis intoxication is often indexed via the subjective item "high" or "stoned," which asks participants to rate how they feel at that moment (Bidwell et al., 2018; Wachtel, ElSohly, Ross, Ambre, & de Wit, 2002). Subjective ratings of "high" consistently have been positively associated with THC blood levels delivered via combusted cannabis in controlled settings (Bidwell et al., 2018; Heishman et al., 1990; Schwope, Bosker, Ramaekers, Gorelick, & Huestis, 2012). Cannabis intoxication can also be measured by assessing physical or body intoxication and mental intoxication (e.g., "How mentally stoned do you feel right now?"; Bidwell et al., 2018). Much like these broader intoxication measures, available data suggests that subjective ratings of physical and mental intoxication are strongly correlated with blood THC levels (rs>0.60, ps<0.05; Bidwell et al., 2018). Appropriate measures of acute cannabis intoxication are critical due to the associated health consequences including increased risk of traffic accidents and decreased inhibition leading to risk-taking behavior (Oomen, van Hell, & Bossong, 2018; Rogeberg & Elvik, 2016).

Another important class of clinical effects of cannabis relates to respiratory effects, which have been the subject of much previous work in this area (Howden & Naughton, 2011; Martinasek, McGrogan, & Maysonet, 2016; National Academies of Sciences, 2017; Tetrault et al., 2007) considering the majority of cannabis is consumed via administration methods requiring combustion and/or inhalation (Russell et al., 2018). Like tobacco smoke, cannabis smoke contains particulate matter and carcinogens but the concentrations and constituents of each vary dramatically (Moir et al., 2008). Previous and recent systematic reviews including one performed by the National Academies of Sciences (2017) support the idea that cannabis use has negative respiratory effects. Chronic cannabis use has been associated with increased risk for cough, sputum production, wheezing, and dyspena (shortness of breath; Ghasemiesfe et al., 2018). Effects of chronic cannabis use on development of lung cancer, pulmonary function, and chronic obstructive lung disease are not conclusive, but some positive associations have been observed among studies linking cannabis use to these negative health outcomes (Ghasemiesfe et al., 2018; Martinasek et al., 2016). Importantly controlling for and/or determining the impact of concurrent tobacco use and administration method use involving cannabis/tobacco co-use (i.e., blunts) on the study of cannabis respiratory effects remains challenging for researchers (Tashkin & Roth, 2019). Adding to this body of literature is some support for an association between cannabis use and improved airway dynamics under specific acute use conditions (National Academies of Sciences, 2017), but attempts to harness this effect for clinical purposes have been ineffective, likely due to the negative respiratory effects of other constituents present in cannabis smoke (Tashkin & Roth, 2019). Early evidence from cross-sectional and clinical trial data sources suggests cannabis consumption with vaporizers may reduce negative respiratory symptoms and/or improve pulmonary function (Earleywine & Barnwell, 2007; Sexton, Cuttler, Finnell, & Mischley, 2016; Van Dam & Earleywine, 2010). Contrary to these reports has been a recent surge in e-cigarette or vaping product use-associated lung injury (known as EVALI) cases and deaths in the US (1,299 cases and 26 deaths as of October 8, 2019) from devices containing THC and/or nicotine products (Centers for Disease Control and Prevention, 2019). Specific chemical exposures associated with these negative effects is unknown at this time (Centers for Disease Control and Prevention, 2019). Data regarding respiratory effects associated with use of rigs/dabs (used to heat cannabis concentrates) is limited, but at least two case reports of respiratory failure and one for severe pneumonitis have been reported in the literature (Anderson & Zechar, 2019; McMahon, Bhatt, Stahlmann, & Philip, 2016). These early studies should be interpreted carefully considering the little information known about cannabis vaporizer and concentrate use. As has been shown with tobacco products (U.S. Department of Health and Human Services, 2014), respiratory and other health effects may differ dramatically depending on characteristics of the cannabis administration method and patterns of cannabis use. Future research should aim to understand differences in respiratory effects between these cannabis administration methods acutely and over time.

Other adverse health effects of cannabis use include a range of physiological effects, cognitive process effects, and the development of mental health conditions. For example, cannabis has been linked with suppression of antibody production in the immune system (Rieder, Chauhan, Singh, Nagarkatti, & Nagarkatti, 2010) as well as decrease in several inflammatory cytokines (National Academies of Sciences, 2017). Acutely, cannabis increases heart rate and blood pressure via increased sympathetic nervous system activation, and these effects have been linked to (but not conclusively associated with) greater risk for triggering myocardial infarctions (Franz & Frishman, 2016; National Academies of Sciences, 2017). Cognitive processes impaired by cannabis use acutely and some cases residually or chronically include working memory, inhibition/impulsivity, attention/concentration, and reaction time (Ameri, 1999; Crean, Crane, & Mason, 2011; Sharma et al., 2012; Volkow, Baler, Compton, & Weiss, 2014). Similar to intoxication, many of these cognitive impairments are often associated with adverse behavioral outcomes including poor academic performance, impaired driving, and increased likelihood for hospitalization (Arria, Caldeira, Bugbee, Vincent, & O'Grady, 2015; Gerberich et al., 2003;

Rogeberg & Elvik, 2016; Sewell, Poling, & Sofuoglu, 2009). Importantly, cannabis use among youth and young adults can affect the developing brain resulting in impaired neuronal connectivity as well as reduced volumes in some brain areas such as the hippocampus as demonstrated by neuroimaging studies performed on long-term cannabis users (Filbey & Yezhuvath, 2013; Jacobus & Tapert, 2014; Zalesky et al., 2012). Results highlight the impact of earlier age of onset on neurological and cognitive effects of cannabis use (Volkow et al., 2014). Cannabis use is also associated with development of mental disorders including substance use disorders (other than cannabis use disorder) as well as risk for identifying with a mood disorder such as anxiety or depression and psychotic disorder (National Academies of Sciences, 2017). Critically the directionality of relationships between cannabis use and mood/psychotic disorders remains unclear (National Academies of Sciences, 2017; Volkow et al., 2014). Last but not least, heavy cannabis use frequency and earlier age of cannabis use onset have been associated with the development of problematic cannabis use, which include characteristics used to define cannabis use disorder by the American Psychological Association (see **Trends in Cannabis Use and Dependence**; National Academies of Sciences, 2017).

In addition to these subjective, respiratory, and other adverse effects, cannabis use is also associated with a menagerie of therapeutic health effects (National Academies of Sciences, 2017). In terms of the strongest levels of evidence, cannabis use has been shown to produce analgesic (Rivera-Olmos & Parra-Bernal, 2016; van de Donk et al., 2019) and anticonvulsive effects (Carlini & Cunha, 1981; Schrot & Hubbard, 2016). Cannabis use can alleviate symptoms and complications with Alzheimer's disease, multiple sclerosis, and epilepsy (Karl, Garner, & Cheng, 2016; Leo, Russo, & Elia, 2016; Lippiello et al., 2016; Patti et al., 2016). Many of these effects may underlie the increasing use of cannabis as well as individual cannabinoids as a medical treatment (Dronabinol, synthetic form of THC; Epidiolex, plant-derived purified form of CBD; U.S. Department of Health and Human Services, 2004; U.S. Food and Drug Administration, 2018) or via self-diagnosis in US states with legalized recreational cannabis (Sarvet et al., 2018). Importantly, very few of cannabis/cannabinoid-based products are FDA-approved drugs, but due to the changing regulatory environment in the US and elsewhere, large numbers of cannabis-containing dietary supplements are emerging with little empirical data to support their use (U.S. Food and Drug Administration, 2019b).

Trends in Cannabis Use and Dependence

Trends in national past 30-day cannabis use rates and cannabis dependence have been monitored for nearly 50 years (U.S. Substance Abuse and Mental Health Data Archive, 2019). Current (past 30-day) cannabis use among US adults aged 18 and older was 9.9% in 2017 (CBHSQ, 2018). Using data from the same source, among US adults aged 18-25, current cannabis use was 20.8% in 2016 and increased to 22.1% in 2017 (CBHSQ, 2018). In contrast, 7.9% of US adults aged 26 and older used cannabis in the past month in 2017 (CBHSQ, 2018). Among young adult (aged 18-25) past month cannabis users, 44.3% used cannabis daily or almost daily in 2017, which is higher than any other age group (CBHSQ, 2018). One strength of obtaining cannabis use rates via the aforementioned national US datasets is the ability to monitor yearly changes in lifetime, past year, past month, and daily cannabis use. However, a limitation to this type of data collection is the lack of fine-detail information about cannabis use patterns including the frequency of use per day or week (Asbridge, Duff, Marsh, & Erickson, 2014).

As defined by the American Psychiatric Association Diagnostic and Statistical Manual for Mental Disorders, fifth edition (DSM-5), cannabis substance use disorder is classified by the presence of two or more specified criteria occurring within a 12-month period including 1) tolerance, 2) withdrawal, 3) a great deal of time spent in activities necessary to obtain, use, or recover from the effects of cannabis, 4) persistent desire or unsuccessful efforts to cut down or control cannabis use, 5) often taken in larger amounts over time, 6) continued use despite social or interpersonal problems caused by the effects of cannabis use, 7) important activities reduced due to cannabis use, 8) recurrent substance use in places which are physically dangerous, 9) persistent cannabis use despite knowledge of harms, 10) cannabis use which results in failure to conduct personal obligations, and 11) craving or strong urges to use cannabis (APA, 2013). Many of the nationally representative monitoring systems have not transitioned to this current definition and instead utilize substance use dependence and abuse classification guidelines from the Diagnostic Statistical Manual for Mental Disorders, fourth edition (DSM-IV). The newer cannabis use disorder definition incorporates all of the previous cannabis dependence use criterion and the majority of the abuse criterion with two exceptions: one addition – craving or strong urges to use the substance – and one removal – substance-related legal problems (BehaveNet, 2016).

Due to the recent changes in diagnostic criterion, the available data collapses cannabis use and abuse categories in order to identify the prevalence of cannabis use disorder. Although current cannabis use has increased, the prevalence of cannabis use disorders among those aged 12 and older has decreased from 1.8% in 2002 to 1.5% in 2017 (CBHSQ, 2018). For young adults (aged 18-25), cannabis use disorder decreased from 6.0% in 2002 to 5.2% in 2017 (CBHSQ, 2018). Among US adults, cannabis use disorder slightly decreased from 1.5% in 2002 to 1.4% in 2017 (CBHSQ, 2018). Taken together, national data across multiple groups suggest that overall cannabis use is increasing moderately while the prevalence of cannabis use disorders has experienced little change over the same time period. These discrepancies in cannabis use and disorder incidence may be due to changes in substance disorder criteria, lagged effects in disorder development, and/or poor measurement of cannabis use rates. Continued and more detailed surveillance is essential to better understand these trends.

Influence of Cannabis Policy Changes on Prevalence

Changes in cannabis policies may also be driving changes in cannabis use and disorder prevalence. Although cannabis remains illegal under the US federal government, some state governments have alternative laws regarding cannabis use and cultivation. California was the first state to legalize the use, possession, and production of cannabis for medicinal reasons in 1996 (National Conference of State Legislatures, 2018b), and since then, 34 states, Washington, DC, and 3 US territories have legalized cannabis for medicinal use (National Conference of State Legislatures, 2018b). In 2012, Colorado was the first state to legalize cannabis for recreational use (National Conference of State Legislatures, 2018a), and since then, 10 states and Washington, DC legalized cannabis for recreational use (National Conference of State Legislatures, 2018a). These laws allow for the use, possession, and production of cannabis to any adult over the age of 21 (Marijuana Policy Project, 2019). Specifically in the state of Virginia, the possession, sale, and use of cannabis remains illegal to anyone, regardless of age (The National Organization for the Reform of Marijuana Laws, 2019). However, the use of CBD and hemp products is legal in Virginia, as is consistent with federal laws on hemp-derived CBD (see **Cannabis: Cannabinoids, Cannabis Forms, and Cannabis Administration Methods;** U.S. Senate Committee on Agriculture Nutrition and Forestry, 2018). Changes in cannabis policies inevitably invoke other consequences including changes in cannabis use patterns.

Several studies have evaluated changes in cannabis use prevalence due to cannabis legalization in US states. Previous research in this area focuses mostly on changes in cannabis use due to changes in *medicinal* cannabis policies, and there is limited research on how the legalization of recreational cannabis impacts cannabis use. There are two known published studies on the impact of recreational cannabis policy changes on cannabis use among youth. A secondary data analysis of cannabis use among 8th, 10th, and 12th grade youth in Washington state pre- and post- cannabis legalization was conducted (Dilley et al., 2019). Results indicated that after recreational cannabis legalization, cannabis use did not change among youth in 8th and 10th grades and decreased among youth in 12th grade compared to pre-legalization (legal market opened in 2014; (Dilley et al., 2019). However, according to a secondary data analysis of a national dataset (Monitoring the Future) of 8th, 10th, and 12th graders in Washington state, cannabis use increased among 8th and 10th graders post-legalization, but changes in cannabis use were not found among 12th graders (Cerda et al., 2017). Interestingly, among 8th, 10th, and 12th graders in Colorado, no changes in cannabis use were found between pre-legalization and post-legalization (Cerda et al., 2017). These studies indicate a discrepancy on the impact of recreational cannabis legalization on cannabis use rates among youth, and less is known regarding the impact of changes in cannabis policies among other high risk groups such as young adults.

There are no known published studies that have evaluated the impact of recreational policy changes on cannabis use among adults, and few studies have identified the relationship between medicinal cannabis policy changes and adult cannabis use. Several cross-sectional studies have identified higher rates of adult cannabis use in states with medicinal cannabis legalization compared to states without medicinal cannabis legalization (Cerda, Wall, Keyes, Galea, & Hasin, 2012; Wen, Hockenberry, & Cummings, 2015). A study conducted in 2017 analyzed cannabis use and cannabis use disorder from three nationally representative longitudinal surveys among US adults (D. S. Hasin et al., 2017). The study compared states with and without medicinal cannabis legislation during each of the survey periods. Results indicated that the legalization of medicinal cannabis was associated with a higher prevalence of cannabis use and cannabis use disorder compared to states without medicinal cannabis laws across all survey time periods (D. S. Hasin et al., 2017). Importantly, follow-up analyses using the same dataset indicated that daily/near daily cannabis use also increased following medicinal cannabis legalization compared to states without medicinal cannabis laws (D. Hasin et al., 2017). In sum, although changes in medicinal cannabis laws indicate various findings among adolescent cannabis use, data indicate that, for adults, cannabis use and cannabis use disorder prevalence increase in states with medicinal cannabis laws.

Characterizing Cannabis Administration Method Use

Although most previous research with cannabis has focused on the use of joints or other combustible administration methods, there has been a proliferation in use of other cannabis administration methods in the US. In a study of US adult daily cannabis users in 2012, more than half reported weekly usual use of joints (53%), blunts (51%), pipes (55%), or bongs (32%) with fewer individuals endorsing use of vaporizers (6%; Hughes et al., 2014). In 2014, among US adults who used cannabis in the past 30 days, bowls/pipes were the most popular method of administration (49.5%), followed by joints (49.2%), bongs (21.7%), blunts (20.3%), edibles (16.1%), and vaporizers (7.6%; Schauer et al., 2016). Available data suggest similar trends exist for young adult cannabis users – combustible methods are most popular, followed by edibles and vaporizer use. Among a sample of US young adult past 30-day cannabis users assessed in 2017, blunts and bongs were the most popular cannabis administration methods (54.8%, 54.8%), followed by bowls/pipes (50.0%), joints (40.0%), edibles (27.4%), and vaporizers or concentrate/"dab" rig use (19.2%; Rudy, 2018).

Data regarding the type and frequency of cannabis administration method use is limited, but previous work and my own has indicated that young adult heavy cannabis users regularly report using multiple cannabis administration methods (≥3 methods per month) from data measured prospectively (Hughes et al., 2014) as well as retrospectively (Rudy, 2018). In 2014, among a nationally representative sample of US adults who used cannabis in the past 30 days, 58.8% reported using one cannabis administration method, 22.4% reported using 2 cannabis administration methods, and 18.8% of cannabis users indicated using 3 or more cannabis administration methods in the past 30 days (Schauer et al., 2016). However, a gap remains regarding how the frequency of these methods may fluctuate over time and how these methods may influence health effects in young adult heavy cannabis users.

Many previous studies consider cannabis users as homogenous (i.e., equating joint smokers to those who consume only edibles); however, my own research has indicated that cannabis users are heterogeneous in terms of their frequency of cannabis use and cannabis administration methods used. In a sample of young adult past 30-day cannabis users, four latent classes of cannabis users defined by frequency of cannabis administration use were identified (Rudy, 2018). The two largest classes (over 84% of the sample) were characterized by high probabilities of using either blunts or bongs between 1-10 times per month. The two smallest classes (4-13% of the sample) were characterized by high probabilities of using all methods of cannabis administration and for some, at higher frequencies (10+ times per month). More specifically, the third class was characterized by high probabilities of using edibles and concentrate/”dab” rigs and vaporizers, while the fourth (smallest) class was characterized by a high probability of using edibles but a low probability of using concentrate/”dab” rigs and vaporizers. These data highlight critical subgroups among current cannabis users that may benefit from tailored intervention. The two classes who used multiple cannabis administration methods at higher frequencies are likely at higher risk for dependence and possibly health related consequences compared to other types of cannabis users.

Interactions between Cannabis Use Frequency, Administration Method, and Health Effects

As stated previously, research suggests that higher cannabis use frequency is associated with increased intoxication and respiratory symptoms compared to lower cannabis use frequency (Hall & Degenhardt, 2009; Hughes et al., 2014; Walden & Earleywine, 2008). However, less is known about how cannabis use frequency of specific cannabis administration methods may influence these health effects. Vaporizer and concentrate/”dab” rig use has been associated with greater reports of intoxication, which is likely due to the high-THC potency cannabis often used with these methods (Lee et al., 2016; M. Loflin & Earleywine, 2014). In 2014-2015, an online survey was administered to US adult cannabis users (Lee et al., 2016). Among those who had reported lifetime vaporizer use, over half indicated higher intoxication when using a vaporizer with cannabis compared to smoking cannabis (Lee et al., 2016). Likewise, in an online survey administered in 2014 among US adult concentrate/dab users, over a third of concentrate/dab users reported stronger intoxication from concentrates/dabs compared to other cannabis administration methods (M. Loflin & Earleywine, 2014). Edible use has also been associated with greater intoxication due, in part, to the accidental consumption of more than intended and the metabolism of THC through the gastrointestinal tract (Barrus et al., 2016; Hudak, Severn, & Nordstrom, 2015; Lewis, Fleeger, Judge, Riley, & Jones, 2020). Still unknown, these studies did not reveal how frequency of use interacted with intoxication. The interaction between cannabis administration method, frequency of use, and intoxication symptoms remains unclear. Direct comparison of subjective intoxication by cannabis administration method and frequency has yet to be explored in a controlled or naturalistic setting, limiting knowledge in this area.

As stated previously, evidence regarding respiratory outcomes has typically focused on joints, but less in known regarding how non-combusted and other methods of administration affect respiratory symptoms. Moreover, little data is available that examines how cannabis use frequency affects the relationship between administration method and respiratory symptoms. In a systematic review of the respiratory effects of inhaled cannabis conducted in 2016, many studies indicated that cannabis users have reported wheezing, shortness of breath, cough, and phlegm from their use of inhaled cannabis products (Martinasek et al., 2016). Several previous studies indicate that cannabis use with a vaporizer decreased negative respiratory symptoms while there has been an increase in lung-related injuries related to vaporizer use sometimes but not all the time with THC-containing liquids. In a cross-sectional online survey study of US adult cannabis users conducted in 2007, participants reported their usual symptoms of coughing, wheezing, shortness of breath, phlegm, and tightness of chest, in addition to vaporizer use and cigarette use (Earleywine & Barnwell, 2007). Results indicated that cannabis and cigarette use were associated with increased respiratory symptoms, but this effect was lower among vaporizer users (Earleywine & Barnwell, 2007). In 2014, an online, cross-sectional survey was administered to an international sample of cannabis users (Malouff, Rooke, & Copeland, 2014). Qualitative results indicated that over half the sample used cannabis with a vaporizer for its perceived health benefits including “felt easier on my lungs” (p. 128) and “no more coughing up dust and tar” (Malouff et al., 2014, p.128). Unlike the reported respiratory effects of vaporizer use, two case reports of concentrate/dab use resulted in severe pneumonitis (Anderson & Zechar, 2019; McMahon et al., 2016). In sum, these studies indicate that using cannabis with a vaporizer may decrease respiratory symptoms and using cannabis via concentrates/dabs may exacerbate respiratory symptoms, but further research is needed to understand how use frequency may interact with this relationship.

Given this limited evidence, it is likely that high frequency use of cannabis administration methods involving concentrated cannabis (vaporizer and concentrate/"dab" rigs) may produce the highest intoxication symptoms, and combusted administration method (blunts, joints, bongs, etc.) use at high frequencies may be associated with more negative respiratory symptoms relative to other frequency/administration method sub-groups. To best assess these proposed relationships, a study design/data collection method must be selected carefully to maximize ecological validity (cannabis use under naturalistic conditions), reliability (due to the complex behavior patterns of cannabis use) and participant protection (due to specific legal restrictions regarding cannabis).

Methods to Understand Cannabis Use Patterns and Associated Factors

Ecological momentary assessment (EMA) is a particularly optimal method to understand the interaction of cannabis use frequency, cannabis administration methods, and cannabis-related health symptoms that involves frequent, 'in the moment' naturalistic data collection (Shiffman, 2009). The use of EMA minimizes the likelihood of recall bias, improves ecological validity, and provides data regarding within-person variability (Collins, Kashdan, & Gollnisch, 2003; M. M. Phillips, Phillips, Lalonde, & Dykema, 2014; Shiffman, 2009). EMA can be measured via several mechanisms that can be cell-phone or app-based including automated text messages wherein participants answer daily questions through a web-link using their phone. Text message based-EMA provides privacy for sensitive data due to the automatic recording of data to a secure website compared to other forms of EMA using paper diaries.

Previous EMA studies among cannabis users measured the time course of cannabis quit attempts (Buckner, Zvolensky, & Ecker, 2013), cannabis use patterns and motives (Bonar et al., 2017; Buckner et al., 2015; Hughes et al., 2014), social contexts of cannabis use (K. T. Phillips, Phillips, Lalonde, & Prince, 2018), cannabis use effects (e.g., working memory, anxiety symptoms, craving, and mood; (Buckner, Heimberg, & Schmidt, 2011; Buckner et al., 2015; Buckner, Zvolensky, et al., 2011; Rusby, Westling, Crowley, Mills, & Light, 2019; Schuster, Mermelstein, & Hedeker, 2016; Shrier, Walls, Kendall, & Blood, 2012; Testa, Wang, Derrick, Brown, & Collins, 2019). Among previous studies that have recorded cannabis use patterns, assessment weeks ranged from 2-16 weeks, and assessments spanned 3-5 times per day (Buckner et al., 2015; Hughes et al., 2014; K. T. Phillips et al., 2018). EMA compliance rates for cannabis use range from 70-90% (Buckner et al., 2015; Hughes et al., 2014; Preston et al., 2018; Shrier et al., 2012). These previous studies and design choices indicate that cannabis use pattern and health-related symptom data can be collected successfully via EMA.

Two previous studies have measured cannabis use frequency, administration method use, and intoxication symptoms. In 2012, an EMA study was conducted among US adult daily/almost daily cannabis users (Hughes et al., 2014). The average participant age was 33 years (N = 142). Participants reported data with daily phone calls. Each morning for three months, participants reported their prior day's cannabis use, intoxication symptoms, and other variables. Results indicated that cannabis was used on average 4 times per day, and cannabis use was higher on the weekends compared to weekdays. Most participants (59%) used more than 3 administration methods throughout the study, and 25% of participants used more than 2 administration methods throughout the study. The most commonly reported administration method used was pipe/bong (49% of the total days), followed by blunts (33% of days), and joints (16% of days). The median intoxication on days when cannabis was used was 3.8 (of a 0 “did not get high” to 6 “got very high” scale). Intoxication scores were greater on the days when participants reported using blunts (4.3) compared to days when they reported joint or pipe (3.7) use ($p < 0.001$; Hughes et al., 2014). These data highlight variability in cannabis use patterns as well as a relationship between cannabis administration method used and intoxication scores, but analyses did not examine their potential interaction.

In 2018, a study using EMA was conducted among a younger age group of cannabis users (15-24 years; N = 85) who reported using cannabis at least 2 times/week (Treloar Padovano & Miranda, 2018). Participants reported data using a palm pilot EMA device, and data collection occurred on a self-initiated basis as well as by random prompts for one week. Daily cannabis use frequency, administration method used, subjective intoxication symptom severity, and other related variables were assessed. Results indicated that average cannabis use time was in the afternoon. When tested with logistic multilevel models, cannabis use was significantly less likely to occur in the morning (OR = 0.10, $ps < 0.001$) and afternoon (OR = 0.29, $ps < 0.001$) compared to 12:00am-6:00am (referent group). There was no significant difference between cannabis use frequencies on the weekends compared to the weekdays. The most commonly reported administration method used was blunt (52.6%), followed by bowl (28.1%), bong (8.9%), joint (7.3%), and other (3.2%). As expected, intoxication symptoms significantly increased after cannabis use, compared to before cannabis use (Treloar Padovano & Miranda, 2018). In sum, these studies provide information about daily and weekly cannabis use frequency, daily administration methods used, and changes in intoxication symptoms before and after cannabis use. Missing from this work are measurements of respiratory symptoms. In addition, this foundation of EMA research with cannabis has not addressed the measurement of cannabis use frequency, administration methods use, and related intoxication and respiratory symptoms holistically as well as their interaction to better understand cannabis use patterns and risk for harm.

Statement of the Problem

Cannabis is the most widely used illicit drug among young adults, and this group uses cannabis more than any other age group. Young adults are at a high risk for substance use and dependence including cannabis. Previous literature has revealed the weekly and daily variability of cannabis use frequency, but less is known regarding cannabis administration method use and cannabis-related intoxication and respiratory symptoms among young adult heavy cannabis users. The relationship between cannabis use frequency, administration method use, and cannabis intoxication and respiratory symptoms remains unclear. The current study aims to address these stated problems. The results from the proposed aims will inform cannabis intervention and education efforts and potential policy recommendations.

The Present Study Aims and Hypotheses

This observational two-week clinical study will use EMA to collect real-time data on cannabis use frequency, cannabis administration method use, and cannabis-related intoxication and respiratory symptoms among young adult heavy cannabis users. There are two aims for the current study:

Aim 1. To characterize within week and day patterns of cannabis use frequency, number of administration methods used, and cannabis-related intoxication and respiratory symptoms among young adult heavy cannabis users.

Hypothesis 1a. Consistent with previous data, frequency will vary significantly by day of week and time of day. We predict that cannabis use frequency will be lowest in the mornings and highest in the evenings. We estimate that cannabis use frequency will be higher on the weekends compared to the weekdays.

Hypothesis 1b. Unique to this study, number of cannabis administration methods used will vary significantly by day of week and time of day.

Hypothesis 1c. Unique to this study, self-reported intoxication and respiratory symptoms will vary significantly by day of week and time of day, such that intoxication and respiratory symptoms will be highest in the evenings and weekends and lowest in the mornings and on weekdays.

Aim 2. To test the interaction of cannabis use frequency and cannabis administration method (combusted, other, and combination) use on cannabis-related intoxication and respiratory symptoms over a two-week period among young adult heavy cannabis users.

Hypothesis 2a. Those who use other administration methods at high frequencies will have the highest intoxication symptoms relative to combusted and combination administration method sub-groups.

Hypothesis 2b. Those who use combusted administration methods and at the highest frequencies will report the highest negative respiratory symptoms relative to other and combination administration method sub-groups.

Methods

Participants

A total of 27 young adults who were aged 18-25 and lived in a US metropolitan area where recreational cannabis use was prohibited and CBD was legal were recruited for the current study. The sample size was informed by a power analysis for multi-level structured data (see **Data Analysis**).

For inclusion criteria, participants were between 18-25 years of age (verified by identification card), reported using cannabis at least 5 days per week, had a cell phone that could receive text messages and open web links, and were willing to use their cell phone to receive text messages and complete online surveys for study procedures. Participants also tested positive for cannabis use via urinalysis at screening. Although cannabis can be detected in urine as far as 4 weeks prior, this brief and rapid urinalysis test was the best way to confirm relatively recent cannabis use at screening.

For exclusion criteria, participants must not have been diagnosed with a psychiatric disorder in the past six months (i.e., newly diagnosed or initiated treatment), which was assessed using self-report. This exclusion reduced risk for individuals whose psychiatric conditions may have been well-controlled but was inclusive of the young adult cannabis users who may have been likely to have psychiatric conditions (see Buckner et al., 2015). Previous similarly designed EMA studies of young adult cannabis users had not excluded for psychiatric conditions (unrelated to substance use disorders) with no evidence of adverse consequences (Buckner et al., 2015; Hughes et al., 2014; K. T. Phillips et al., 2018; M. M. Phillips et al., 2014). In addition, participants who reported any medical condition/medication that could affect participant safety or study outcomes were excluded (e.g., chronic obstructive pulmonary disease, asthma). Participants were excluded if they reported past month use of illicit drugs other than cannabis or had a positive urine drug screen (via Accutest MultiDrug Screen-5 Panel, Jant Pharmaceutical Corporation) for cocaine or opiates (unless participant self-reported prescription opioid use). Participants must not have been currently in treatment for illegal substance use (including cannabis or alcohol). Any participant who scored ≥ 27 on the NIDA-Modified ASSIST V2.0 (National Institute on Drug Abuse, 2012) for heavy alcohol use were excluded (scores of 27 or greater indicate a high risk patient). Participants could not be pregnant (tested via urinalysis at screening), intend to become pregnant, or were breastfeeding during the study. Participants who reported being cannabis users but indicated that they used primarily CBD were excluded from the study. Of note is that tobacco use was neither an inclusion or exclusion criteria and was allowed to vary freely among included participants. This choice was more inclusive of the cannabis user population based on preliminary data collected among this same population (>50% were tobacco co-users; see Rudy, 2018) and challenges in defining cannabis-only use when cannabis administration methods often involve tobacco consumption (e.g., blunts). Participants were recruited by IRB-approved advertisements through existing research registries and by word of mouth.

Procedures

Potentially eligible participants underwent a two-part screening process. Recruitment information directed potential participants to complete an online or phone-based screening survey, which evaluated their demographics, health, cannabis and other substance use for initial eligibility screening. Individuals who appeared to meet eligibility criteria from this pre-screening were invited to schedule an in-person appointment at the clinical laboratory. At the in-person screening, informed consent was obtained followed by verification of eligibility status and familiarization with study procedures. During appointment scheduling, participants were reminded to bring their identification card (passport or state license) for age verification and to not arrive under the influence or intoxicated (from cannabis or any other illicit substance) to the appointment. During informed consent, all study procedures and potential risks/benefits were fully described to participants, and they were told they were able to withdraw from the study at any time without any penalty by contacting the study coordinator (via phone, email or text). Participants were not required to sign their informed consent form but indicated agreement verbally to the research assistant (to protect their identity). Once consented, participants completed a set of baseline questionnaires, similar to the phone screening questions. Urinalysis was completed to verify eligibility (pregnancy and drug use status). At this time, participants were measured for their height and weight, and their expired air carbon monoxide was measured (used to assess recent smoke exposure via cannabis and/or tobacco use). To increase participant privacy, participants completed a separate survey, which asked questions about contact information and payment preferences. Following eligibility verification, enrolled participants practiced the data collection procedures (daily text messages). This training involved practice using the text messaging system with the participant's own cell phone and asking questions about any study procedures. At the end of the in-person assessment, eligible participants were given a written list of the daily questions and a study identification card, which had the participant's unique identification number, the research laboratory's phone number, and the date range of the data collection period (two weeks).

On the first Monday after their in-person assessment, eligible participants began the two-week data collection period (see K. T. Phillips et al., 2018; M. M. Phillips et al., 2014) for details regarding the feasibility of a two-week data collection period). In response to three random text messages to their cell phone each day, participants reported daily cannabis use (number of "hits" taken for each administration method since last assessment) and self-reported current cannabis intoxication and respiratory symptoms (see **Daily Measures**). An adaptive random-interval text message schedule was created for each participant based on their individual sleep-wake cycle, which was assessed at the in-person assessment (Mehl & Conner, 2012). Participants were randomly assessed in the morning (reported waking time to 12:00pm), afternoon (12:00pm to 5:59pm), and evening (6:00pm to reported sleep time). For example, if a participant woke up at 9:00am, they were texted at a random time between 9:00am and 12:00pm, and if the participant went to bed at 10:00pm, they were texted randomly between 6:00pm and 10:00pm. Participants were not texted while they were assumed to be sleeping. Text messages containing a web-link to the daily questions were used to collect daily data. Participants were instructed to complete the survey as soon as they received the text message. If participants did not complete the questionnaire, it was counted as a missed assessment. Participants were sent a reminder text 10 minutes after the first text in each time block (i.e., morning, afternoon, and evening) was sent. The first text message within each time block were not sent within one hour of each other. Participants earned $10 for completion of the baseline assessment, $1/completed daily assessment ($3/day), and participants who completed 90% or more of the daily assessments received a $50 bonus following the completion of data collection. Participants could earn up to $102 ($10+$42+$50 bonus). After the final day of data collection, participants were paid via cash in person or emailed Amazon gift card. To increase participant compliance, every Wednesday and Friday throughout the two weeks, participants were notified via text of their response rate percentage and how much payment they had earned (Mehl & Conner, 2012).

Compliance was also maximized by providing participants with letters for employers/professors to help avoid negative consequences associated with participation.

Measures

Baseline measures. The study-applicable measures completed at the in-person screening assessment included demographics, cell phone eligibility questions, daily sleep-wake cycle, psychiatric and health questions, respiratory symptoms, and tobacco/cannabis/other substance use history. Several other measures were completed in the baseline survey that will not be described here because these measures are not considered primary measures of the current study. Other measures included depression symptoms, stress symptoms, pain symptoms, cannabis dependence, marijuana motives, and marijuana effect expectancy.

Demographic measures included gender, age, race/ethnicity, level of school attainment, employment status, income level, and pregnancy/breastfeeding status. Gender was assessed by asking "Which of the following best describes your gender? [Note: cisgender means identifying with the sex assigned to you at birth, while transgender means not identifying with the sex assigned to you at birth]" Answer options included "Cisgender man," "Cisgender woman," "Transgender man," "Transgender woman," "Non-binary/ Gender non-conforming," "Agender," and "Other" which included a text box for participants to write their response. Age was assessed by asking "How old are you?" There was a dropdown answer option to input age in years. Race/ethnicity was assessed by asking "How would you describe your racial or ethnic background?" Answer categories included "White or European-American," "Black, Afro-Caribbean, or African American," "Asian American," "American Indian or Alaska Native," "Native Hawaiian or Other Pacific Islander," "Middle Eastern or Arab American," "Multiracial," or "Other" which included a text box for participants to write their response (*Youth Risk*

Behavior Survey Questionnaire, 2015). Participants were asked “Do you consider yourself Hispanic/Latinx?” with response options “Yes” and “No.” School level was determined by asking “What is the highest level of school you have completed or the highest degree you have received?” Answer options included the following categories: “high school graduate,” “GED or equivalent,” “some college/no degree,” “associate degree,” “bachelor’s degree,” “master’s degree,” and “professional or doctoral degree” (National Institute on Drug Abuse Clincal Trials Network, 2015). Employment status was determined by asking “Which of these best describes your current employment status?” Answer options included “Working now, full-time,” “Working now, part-time,” “Only temporarily laid off, sick leave, or maternity leave,” “Looking for work, unemployed,” “Retired,” “Non-working disabled, permanently or temporarily,” “Keeping house,” “Military,” “Non-working student,” and “Don’t know” (University of Michigan, 2007). Due to few responses in each category, results for employment status were collapsed into three categories: “student,” “working,” and “Non-working.” Household income was assessed by asking “Which of the following income categories best describes your total household income, before taxes, last year?” Answer options included “Less than $10,000,” “$10,000 to $19,999,” “$20,000 to $29,999,” “$30,000 to $39,999,” “$40,000 to $49,999,” “$50,000 to $59,999,” “$60,000 to $69,999,” “$70,000 to $79,999,” “$80,000 to $89,999,” “$90,000 to $99,999,” and “$100,000 or more” (Pew Research Center, 2015). Pregnancy was assessed (in addition to the urine screening) by asking “Are you pregnant, breastfeeding, or intend to become pregnant in the next three weeks?” Answer options included “Yes” and “No.”

Several questions were asked about participants’ willingness to use their personal cell phone for study procedures. Three questions were asked: “Do you have a cell phone with an active texting plan?,” “Do you have a cell phone that has the ability to open web links?,” and

"Are you willing to receive text messages and complete online surveys on your cell phone for study purposes?" Answer options included "Yes" and "No."

Daily sleep-wake cycle was assessed using questions from the Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Participants were asked: "During the past month, what time have you usually gone to bed at night?" "During the past month, what time have you usually gotten up in the morning?" and "During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)" Participants were given a blank box to insert their answer. Results were used to determine when daily text messages would be delivered to participants.

Perceived health was assessed by asking "Would you say that in general your health is… excellent, very good, good, fair, or poor?" (National Center for Chronic Disease Prevention and Health Promotion, 2018). Due to few responses in each category, results for perceived health were collapsed into three categories: "excellent/very good," "good/fair," and "poor." Psychiatric and other health conditions were assessed by asking "Do you have a recent (in the past six months) diagnosis from a doctor, nurse, or other healthcare provider for any psychiatric conditions like depression or anxiety?" and "Do you have a recent or current diagnosis from a doctor, nurse, or other healthcare provider for any health conditions like high/low blood pressure or asthma?" Answer options included "Yes" and "No." Individuals who responded "Yes" were probed for further detail to determine current diagnosis/treatment status to determine eligibility. Medications were assessed by asking "List all medicines that you are currently taking (include medicines as described drugs, over-the-counter drugs, vitamins, and inhalers). Name of drug. Strength. Frequency taken. Date started." Participants were given a blank box to insert their answer.

Respiratory symptoms at baseline were assessed with the Clinical COPD Questionnaire (CCQ, van der Molen et al., 2003). The CCQ includes ten questions total. Six questions assess how often one experiences shortness of breath while at rest and during physical activity, concern about getting a cold, depressive symptoms due to breathing problems, time spent coughing, and time producing sputum (i.e., phlegm or mucus). Answers options for the first six questions included: “never” (0), “hardly ever” (1), “a few times” (2), “several times” (3), “many times” (4), “a great many times” (5), and “almost all the time” (6). The final four questions assessed perceived limitations in strenuous and moderate physical activity and perceived limitations in daily and social activities due to breathing problems. Answer options for the final four questions included: “not limited at all” (0), “very slightly limited” (1), “slightly limited” (2), “moderately limited” (3), “very limited” (4), “extremely limited” (5), and “totally limited, or unable to do” (6). Items were totaled for a composite score ranging from 0-60 with zero indicating low/non-severe respiratory symptoms and 60 indicating high/severe respiratory symptoms.

The NIDA Modified ASSIST V2.0 (NIDA, 2012) was used to identify degree of dependence on cannabis, alcohol, tobacco, and other drugs. The NIDA Modified ASSIST V2.0 was altered for the current study by adding heavy alcohol use as one of the drugs listed in the questions. Lifetime substance use was assessed with the question “In your LIFETIME, which of the following substances have you ever used? * For prescription medications, please report using these substances in any way a doctor did not direct you to use them, including: using it without a prescription of your own, using it in greater amounts, more often, or longer than you were told to take it, or using it in any other way a doctor did not direct you to use it.” Participants responded “Yes” or “No” for each of the following substances: “Cannabis (marijuana, pot, grass, hash, etc.),” “Cocaine (coke, crack, etc.),” “Prescription stimulants (Ritalin, Concerta, Dexedrine, Adderall, diet pills, etc.)," "Methamphetamine (speed, crystal meth, ice, etc.)," "Inhalants (nitrous oxide, glue, gas, paint thinner, etc.)," "Sedatives or sleeping pills (Valium, Serepax, Ativan, Xanax, Librium, Rohypnal, GHB, etc.)," "Hallucinogens (LSD, acid, mushrooms, PCP, Special K, ecstasy, etc.)," "Street opioids (heroin, opium, etc.)," "Prescription opioids (fentanyl, oxycodone [OxyContin, Percocet], Hydrocodone [Vicodin], methadone, buprenorphine, etc.)," "Heavy alcohol use (more than 4 drinks per day)," and "Other – specify: ______." The next four questions assessed use frequency of, strong desires and urges to use, frequency of health, social, legal, or financial problems due to, and failure to complete normal expectations due to the listed substances in the past three months with answer options including "never" (0), "once or twice" (5), "monthly" (6), "weekly" (7), and "daily or almost daily" (8). The next three questions assessed friend or relative concerns about substance use, cessation and reduction attempts, and injection of substances. Answer options for the final three questions included: "no, never" (0), "yes, but not in the past 3 months" (3), and "yes, in the past 3 months" (6). Items were summed to create a composite score. Low risk composite scores are 0-3, moderate risk scores are 4-26, and high risk scores at 27 or greater.

The next several questions assessed past month illicit drug use and treatment. The first question in this section prompted, "Have you used any illegal drugs excluding cannabis in the past 30 days?" and the second question prompted, "Have you ever received treatment or counseling for your use of alcohol or any drug not counting cigarettes?" Answer options included "Yes" and "No."

Tobacco use history was assessed, and questions included lifetime and current use status of cigarettes, electronic cigarettes, cigars, cigarillos, little cigars, hookah, tobacco pipe, and smokeless tobacco products (dip, snuff, and snus). Instructions clearly stated that these questions refer to tobacco use alone and not in combination with cannabis or THC-containing material/liquid. Lifetime tobacco product use was assessed by asking “Which, if any, of the following tobacco or nicotine products have you ever used or tried? Please select all that apply” (Ganz et al., 2018; Lariscy et al., 2013; Niaura et al., 2019; Rath, Villanti, Abrams, & Vallone, 2012). Past 30-day tobacco product use was determined (for lifetime use products) by asking “During the last 30 days, on how many days have you used any of the following tobacco products? (For cigarettes, cigars, cigarillos, e-cigarettes, and hookah/shisha, "even 1 puff").” Available answer options for lifetime and past 30-day tobacco use included “Cigarettes,” “Traditional cigars (Macanudo, Romeo y Julieta, or Arturo Fuente),” “Pipe (with tobacco),” “Little cigars/cigarillos (like Black & Milds, Swisher Sweets, or Phillies Blunt),” “Electronic cigarettes or E-cigarettes (like Blu, Logic, or NJOY),” “Chewing tobacco (like Levi Garrett, Red Man, or Beech Nut),” “Dip/snuff (like Skoal or Copenhagen),” “Snus (like Camel Snus),” “Dissolvable tobacco products (like Ariva, Stonewall, Camel Orbs, Sticks or Strips),” and “Hookah/shisha (hookah tobacco).”

Cannabis use history and intensity was assessed using the Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use (DFAQ-CU) Inventory (Cuttler & Spradlin, 2017). The DFAQ-CU was developed to accurately assess self-reported cannabis use frequency, amount of cannabis used, and age of cannabis use onset. Unique to the DFAQ-CU, no previous psychometrically tested cannabis use inventory has measured a wide variety of cannabis administration methods, amount of personal cannabis use, and THC levels of the cannabis used (Cuttler & Spradlin, 2017). It was critical to assess these cannabis use characteristics for the current study in order to understand baseline participant attributes. Lifetime cannabis use was assessed by the question “Have you ever used cannabis?” with response options of “No” and

"Yes." To assess last session of cannabis use, the following question was asked, "Which of the following best captures when you last used cannabis?" Response options included "over a year ago," "9-12 months ago," "6-9 months ago," "3-6 months ago," "1-3 months ago," "less than 1 month ago," "last week," "this week," "yesterday," "today." In the original inventory, the answer option "I am currently high" was included for the previous question, and two additional questions appear in the original inventory: "How mentally high are you right now?" and "How physically high are you right now?" This answer option and two following questions were removed for the current study. Participants were told not to come to the laboratory under the influence of any illegal substances and were verbally asked prior to completing consent if they had followed these study directions.

Frequency of cannabis use was characterized by asking 10 items, which are listed below:

(1) "Which of the following best captures the average frequency you currently use cannabis?" Answer options included "I do not use cannabis," "less than once a year," "once a year," "once every 3-6 months (2-4 times/yr)," "once every 2 months (6 times/yr)," "once a month (12 times/yr)," "2-3 times a month," "once a week," "twice a week," "3-4 times a week," "5-6 times a week," "once a day," and "more than once a day.";

(2) "Which of the following best captures how long you have been using cannabis **at this frequency**?" Answer options included "less than 1 month," "1-3 months," "3-6 months," "6-9 months," "9-12 months," "1-2 years," "2-3 years," "3-5 years," "5-10 years," "10-15 years," "15-20 years," and "more than 20 years.";

(3) "Before the period of the time you indicated above, how frequently did you use cannabis?" Answer options included "I did not use cannabis," "less than once a year," "once a

year," "once every 3-6 months (2-4 times/yr)," "once every 2 months (6 times/yr)," "once a month (12 times/yr)," "2-3 times a month," "once a week," "twice a week," "3-4 times a week," "5-6 times a week," "once a day," and "more than once a day.";

(4) "How many days of the past week did you use cannabis?" Answer options included "0 days," "1 day," "2 days," "3 days," "4 days," "5 days," "6 days," and "7 days.";

(5) "Approximately how many days of the past month did you use cannabis?" There was a blank space to indicate how many days.

(6) "Which of the following best captures the number of times you have used cannabis in your entire life?" Answer options included "1-5 times in my life," "6-10 times in my life," "11-50 times in my life," "51-100 times in my life," "101-500 times in my life," "501-1000 times in my life," "1001-2000 times in my life," "2001-5000 times in my life," "5001-10,000 times in my life," and "more than 10,000 times in my life.";

(7) "Which of the following best captures your pattern of cannabis use throughout the week?" Answer options included "I do not use cannabis at all," "I only use cannabis on weekends," "I only use cannabis on weekdays," and "I use cannabis on weekends and weekdays.";

(8) "How many hours after waking up do you typically first use cannabis?" Answer options included "I do not use cannabis at all," "12-18 hours after waking up," "9-12 hours after waking up," "6-9 hours after waking up," "3-6 hours after waking up," "1-3 hours after waking up," "within 1 hour of waking up," "within ½ hour of waking up," and "immediately upon waking up.";

(9) "How many times a day, on a typical weekday, do you use cannabis?" There was a

blank space to indicate how many times; and

(10) “How many times a day, on a typical weekend, do you use cannabis?” There was a blank space to indicate how many times.

Cannabis administration method was assessed by asking 6 items:

(1) “What is the primary method you use to ingest cannabis?” Modified answer options included “I do not use cannabis,” “joint or spliff,” “blunt (cigar sized joints),” “bowl or hand pipe that does not include water,” “bong (water pipe),” “dab,” “vaporizer (e.g., Volcano, vape pen),” and “edibles (brownies, teas, tinctures, sprays).”;

(2) “Which of the following other methods to ingest cannabis do you use regularly (at least 25% of the time you use cannabis)? [Mark all that apply]” Modified answer options included “I do not use cannabis,” “joint or spliff,” “blunt (cigar sized joints),” “bowl or hand pipe that does not include water,” “bong (water pipe),” “dab,” “vaporizer (e.g., Volcano, vape pen),” and “edibles (brownies, teas, tinctures, sprays).”;

(3) “Which of the following methods to ingest cannabis have you used in your lifetime?” Modified answer options included “I do not use cannabis,” “joint or spliff,” “blunt (cigar sized joints),” “bowl or hand pipe that does not include water,” “bong (water pipe),” “dab,” “vaporizer (e.g., Volcano, vape pen),” and “edibles (brownies, teas, tinctures, sprays).”;

(4) “What kinds of cannabis vaporizers do you use regularly (at least 25% of the time that you use cannabis)? [Mark all that apply]” Answer options included “Vaporizer for dried cannabis,” “Vaporizer for cannabis concentrates such as wax or shatter,” and “Vaporizer for oils/liquids containing cannabis.”

(5) “What is the primary form of cannabis you use?” Modified answer options included

"None," "Marijuana (dried, bud, flower)," "Concentrates (e.g., oil, wax, shatter, butane hash oil, dabs)," "Edibles," and "Other." The answer option "Other" will have a blank space.; and

(6) "What other forms of cannabis do you use regularly (at least 25% of the time you use cannabis)? [Mark all that apply]" Answer options included "None," "Marijuana (dried, bud, flower)," "Concentrates (e.g., oil, wax, shatter, butane hash oil, dabs)," "Edibles," and "Other." The answer option "Other" will have a blank space.

To assess the amount of cannabis that participants use, a picture was shown of cannabis (see Figure 3) to assist participants in their estimation. The instructions indicated, "Please use the image below to refer to various quantities of marijuana. The image is not to scale; the dollar bill is included to help provide size perspective… Clearly indicate the number of grams of marijuana you use with a number between 1 – 100. Do NOT include other forms of cannabis you may use (such as concentrates). You may use up to 3 decimals to indicate amounts under 1 gram. Note: 1/8 of a gram = 0.125 grams, ¼ of a gram = 0.25 grams, ½ of a gram = 0.5 grams, ¾ of a gram = 0.75 grams. 1/8 of a ounce = 3.5 grams, ¼ of an ounce = 7 grams, ½ ounce = 14 grams, 1 ounce = 28 grams." Participants used the image to answer the following 3 items that comprise cannabis use amount:

Figure 3. DFAQ-CU inventory image. Image from the DFAQ-CU Inventory for participants to estimate their amount of cannabis use.

(1) “In a typical session, how much marijuana do you personally use?”;

(2) “On a typical day you use marijuana, how much do you personally use?”; and

(3) “In a typical week you use marijuana, how much marijuana do you personally use?”

To further assess amount of cannabis used and estimated strength of cannabis used, participants answered the following 8 items:

(1) “On a typical day you use marijuana, how many sessions do you have?” A blank space was provided to indicate number of sessions.;

(2) “What is the average THC content of the marijuana you typically use? Leave blank if you do not know.” Answer options included “0-4%,” “5-9%,” “10-14%,” “15-19%,” “20-24%,” “25-30%,” and “greater than 30%.”;

(3) “In a typical session you use cannabis concentrates, how many hits do you personally take?” A blank space was provided to indicate number of hits.;

(4) “On a typical day you use cannabis concentrates, how many hits do you personally take?” A blank space was provided to indicate number of hits.;

(5) “How many hits of cannabis concentrates did you personally take yesterday?” A blank space was provided to indicate number of hits.;

(6) “On a typical day you use cannabis concentrates, how many sessions do you have?” A blank space was provided to indicate number of sessions.;

(7) “What is the average THC of the concentrates you typically use? Leave blank if you do not know.” Answer options included “0-9%,” “10-19%,” “20-29%,” “30-39%,” “40-49%,” “50-59%,” “60-69%,” “70-79%,” “80-89%,” and “greater than 90%.”; and

(8) “When you eat edibles, how many milligrams of THC do you personally ingest in a typical session?” A blank space was provided to indicate milligrams of THC.

The following eight questions assessed lifetime cannabis use attributes:

(1) “What is your current age?” A blank space was provided to indicate age.;

(2) “How many years in total have you used cannabis?” A blank space was provided to indicate years.;

(3) “How old were you when you FIRST tried cannabis?” A blank space was provided to indicate age.;

(4) “Has there ever been a time in your life when you used cannabis regularly (2 or more times/months)?” Answer options included “yes” or “no.”;

(5) “How old were you when you FIRST STARTED using cannabis regularly (2 or more times/month)?” A blank space was provided to indicate age.;

(6) “Has there been any time in your life when you used cannabis on a daily or nearly daily basis for 6 months or longer?” Answer options were “yes” and “no.”;

(7) “How old were you when you FIRST STARTED using cannabis on a daily or nearly daily basis?” A blank space was provided to indicate age.; and

(8) “Which of the following best captures the average frequency that you used cannabis before the age of 16?” Answer options included “more than once a day,” “once a day,” “5-6 times a week,” “3-4 times a week,” “twice a week,” “once a week,” “2-3 times a month,” “once a month,” “once every 2 months (6 times/yr.),” “once every 3-6 months (2-4 times/yr.),” “once a year,” “less than once a year,” and “never.”

The final three items of this measure assessed medicinal cannabis use:

(1) “Do you have a physician’s recommendation to use cannabis for medicinal purposes?” Answer options included “no,” “yes,” and “yes, but I use it for both medicinal and recreational purposes.”;

(2) “Which medical conditions do you use cannabis for?” A blank space was provided for completing answer.; and

(3) “What percentage of the time do you use cannabis for recreational (rather than medicinal) purposes?” A blank space was provided for estimating percentage of time.

The DFAQ-CU is scored based on the 6 factors (daily sessions, frequency, age of onset, marijuana quantity, concentrate quantity, and edibles quantity). Each of the items associated with each factor were standardized (z-transformed) to calculate means (Cuttler & Spradlin, 2017).

Finally, one question on the baseline measure assessed CBD use. Instructional text indicated, “THC and CBD are naturally occurring substances found in cannabis plants. Some cannabis plants/products contain only CBD; some cannabis plants/products contain only THC; and other cannabis plants/products contain a combination of both CBD and THC” (World Health Organization, 2018). Participants answered the question “Most of the time that you use a cannabis product, do you use a product that contains...” Answer options included, “all CBD,” “mostly CBD and some THC,” “a combination of CBD and THC,” “mostly THC and some CBD,” “all THC,” and “I don’t know.”

Daily Measures. Daily assessments were collected using online survey links embedded into automated text messages sent to participants’ cell phones. Daily measures included items that assessed cannabis use frequency, cannabis administration methods, and subjective cannabis intoxication and respiratory symptoms. The first question asked for the participant's unique study identification number (assigned at the screening appointment). During each assessment, participants were asked "Since the last assessment, have you used cannabis?" Participants responded "Yes" or "No". The next question asked "How many hours ago did you last use cannabis?" Participants input a number indicating how many hours, and "1" hour indicated one hour ago or less. All measures were developed and/or adapted for this study based on previous work. Psychometric data where available has been included below.

Participants who indicated recent cannabis use were then asked what method(s) of administration they had used since the last assessment with eight questions with the same stem. "Since the last call, have you used…": "a joint," "a blunt," "a bowl/pipe," "a bong, "a vaporizer," "a dab," and "an edible" (Modified from Rudy et al., 2018). Answer options for each administration method were "Yes" and "No." For each administration method that a participant used since the last assessment, participants completed an additional question regarding "hits" of use: "Since the last assessment, how many hits from a... 'joint,' 'blunt,' 'bowl/pipe,' 'bong,' 'vaporizer,' or 'dab/rig'... did you have?" (Shrier et al., 2012). Edibles cannot be quantified in hits; therefore, edibles were assessed differently, "Since the last assessment, how many edibles did you consume?" Participants reported a number in a blank space provided. At each assessment, participants' use of cannabis administration methods were used to categorize them as either combusted-only (joint, blunt, bowl/pipe, bong), other-only (vaporizer, dab, edible), and combination (use of any combusted method and other method since the last assessment). This level of categorization at each assessment (i.e., morning, afternoon evening) was used for Aim 1 analysis. Participants were also categorized in terms of their cannabis administration method use across the two-week data collection period taking into account the total number of assessments available and using the same three levels (combusted, other-only, and combination) for Aim 2 analysis. No specific psychometric data is available for this measure.

To assess intoxication, participants were prompted to indicate their subjective intoxication level on a 5-point scale of 0 (not at all) to 4 (extremely) with two questions “How mentally stoned do you feel right now?” and “How physically stoned do you feel right now?” (Bidwell et al., 2018). Responses to these two intoxication items were summed to create a composite score of intoxication for each assessment (possible scores ranged from 0-8, Aim 1); these sum scores were averaged across the two-week period for Aim 2 analyses. Cronbach’s alpha for the two subjective intoxication items was 0.72, indicating good internal consistency.

Cannabis-related respiratory symptoms were assessed using three questions adapted from EMA studies among individuals with respiratory conditions (Everhart, Smyth, Santuzzi, & Fiese, 2010; Nazarian, Smyth, & Sliwinski, 2006) rated on a seven-point Likert scale (0=not at all, 6=extremely): “Since the last assessment, how bad was your coughing and wheezing?”, “Since the last assessment, how bad was your throat irritation?”, and “Since the last assessment, how bad was your phlegm or chest mucus?” (Everhart et al., 2010; Nazarian et al., 2006). Cronbach’s alpha for the three subjective respiratory symptoms was 0.82, indicating high internal consistency. Responses to these three respiratory items were summed to create a composite respiratory symptom score for each assessment (Aim 1); these sum scores were averaged across the two-week period for Aim 2 analysis.

Finally, there was one additional question at the end of the final text sent to participants. The Marijuana Ladder is a type of visual analog scale with 10 “rungs” on the ladder and 10 corresponding statements that describe states of cannabis use change (Slavet et al., 2006). The statements range from “I enjoy using marijuana and have decided never to change it. I have no interest in changing the way I use marijuana” to “I have changed my marijuana use and will never go back to the way I used marijuana before.” With foundations in the Transtheoretical Model, the statements correspond to the five states of change: pre-contemplation, contemplation, preparation, action, and maintenance (Prochaska & Velicer, 1997). Participants were given instructions that stated “Each rung of this ladder shows where a person might be in thinking about changing their marijuana use. Select the number that best matches where you are now.” Scores ranged from 1 to 10, with 1 indicating no intentions to change and 10 indicating that the person is in the maintenance phase.

In total, participants were asked to complete a maximum of 21 items for each daily assessment and a maximum of 22 items for the final assessment.

Data Analysis

Power Analysis. Power analysis for multilevel models are complex, in that accurate parameter estimates are needed for all estimated model parameters. For this study, the primary outcomes were cannabis use frequency, cannabis administration method use, and cannabis-related intoxication and respiratory symptoms, and there were no previous studies that examined these outcomes in the same manner in which we did. Fortunately, previous studies have provided estimates of the frequency of cannabis use expected per day (Hughes et al., 2014; Walden & Earleywine, 2008). We used these estimates to generate a sample dataset to conduct a power analysis for cannabis use frequency and estimated the sample size needed to detect a difference by day of week and time of day (Aim 1). Using the following equation, $= \boldsymbol{\sigma^2_{tot}}(\mathbf{1} + (\mathbf{n} - \mathbf{1})\boldsymbol{\rho})\frac{(z_{\alpha/2} + z_{\beta})^2}{n\Delta^2}, \mathbf{p} = \frac{\sigma^2_b}{\sigma^2_{tot}}$, where m is the number of participants, $\boldsymbol{\sigma^2_{tot}}$ is the total variance, n is the number of observations per participant, $\boldsymbol{\sigma^2_b}$ is the between subjects’ variance, $\mathbf{z_{\alpha/2}}$ is the alpha level z-score, $\mathbf{z}_\beta$ is the beta level z-score, and Δ is the expected change in frequency. To detect a difference in daily cannabis use frequency with a power ranging from 0.80 to 0.90 and α=.05, the number of subjects needed ranged from 41 to 55. We anticipated 70-90% compliance based on previous studies, which measured cannabis use and alcohol use using EMA (Collins et al., 2003; Hughes et al., 2014; Hughes, Naud, Budney, Fingar, & Callas, 2016). Anticipating conservative retention and enrollment rates, we aimed to recruit 65 participants. We also examined sample sizes used in similarly designed recent studies using EMA to measure cannabis use and alcohol use (assessments 3 times/day for 14 days) and found sample sizes ranging from 50-60 (Cohn, Hagman, Moore, Mitchell, & Ehlke, 2014; K. T. Phillips, Phillips, Lalonde, & Tormohlen, 2015). When data collection ended, we had consented 40 participants, and 27 of those participants were eligible (indicating that we collected 65.9% of the intended sample).

Dataset Preparation. After data collection was completed, the data was checked for missing data and other data irregularities. Regarding missing data, of the 27 eligible participants, 18 (69.0%) completed 90% (38/42 surveys) or more of the total daily surveys. All 27 (100%) participants completed 69% (29/42 surveys) of the total daily surveys. Of the total number of daily surveys administered to all participants (N=1134), 92 surveys were missing (8.1%). The number of missing surveys during week 1 was 41 (of the total 567 week 1 surveys; 7.2%), and the number of missing surveys during week 2 was 51 (of the total 567 week 2 surveys; 9.0%). The number of missing morning daily surveys was 49 (of 378 total morning surveys; 13.0%). The number of missing afternoon daily surveys was 18 (of 378 total afternoon surveys; 4.8%), and the number of missing evening daily surveys was 25 (of 378 total evening surveys; 6.6%). The number of missing daily surveys by day of the week was fairly even across days ranging from 5.6% missing on Wednesdays to 12.3% missing on Thursdays. There were 14 daily surveys (of 1134 total daily surveys; 0.01%) that had at least one missing answer for either of the daily intoxication symptom questions. A conservative approach was taken with the summed intoxication symptom scores, such that if there was a missing answer for one or both of the intoxication symptom questions at each time point, that time point counted as missing. Finally, there were 23 daily surveys (of 1134 total daily surveys; 0.02%) that had at least one missing answer for any of the daily respiratory symptom questions. A conservative approach was taken with summed respiratory symptom scores, such that if there was a missing answer for one or more of the respiratory symptom questions at each time point, that time point counted as missing. In sum, the missingness observed in the study was relatively low compared to other studies with similar designs. Of note, several other similarly designed EMA studies did not utilize any imputation techniques (Bonar et al., 2017; Buckner et al., 2015; Hughes et al., 2014; Shrier et al., 2012). Finally, the planned statistical techniques for which missing data is relevant (i.e., linear mixed models) can handle missing data in the models. Thus, given the distribution of missing data for the current study, the use of previous literature to guide decision-making, and the ability for our planned statistical techniques to handle missing data, no imputation techniques were used for any analyses in this study. There were no other data irregularities to report among the dataset as a whole.

Following data cleaning/preparation, the sample was characterized by demographics, cannabis use behaviors and history using the DFAQ-CU (Cuttler & Spradlin, 2017), and tobacco use behaviors (Ganz et al., 2018; Lariscy et al., 2013; Niaura et al., 2019; Rath et al., 2012). A summed score was created and reported for baseline respiratory symptoms using the CCQ (van der Molen et al., 2003). Enrolled and excluded participants were compared on baseline characteristics using bivariate tests.

Aim 1 Data Preparation and Analysis.

Assumptions for the linear mixed models utilized here included the use of continuous dependent variables, a within-subjects factor with at least two groups (i.e., time points), a between-subjects factors with at least two independent groups, a linear relationship between variables, homogeneity of variance, and the residuals with a normal distribution. All assumptions were met for the linear mixed models except for residual normality. All of the main outcome variables for Aim 1 (cannabis use frequency, number of cannabis administration methods used, intoxication symptoms, and respiratory symptoms) were positively skewed; therefore, we opted to use a square root transformation for each dependent variable. Square root transformed dependent variables were the best model fit compared to log transformations or untransformed variables. The final analytical sample for Aim 1 was 27.

Following data cleaning, linear mixed models were conducted to characterize within week and day patterns of cannabis use frequency, number of administration methods used, and cannabis-related intoxication and respiratory symptoms. Dependent measures for this analysis were 1) cannabis use frequency (i.e., sum of cannabis hits across methods at each assessment ~ 3 time points per day; model 1), 2) number of cannabis administration methods used (i.e., sum of methods with >0 hits endorsed at each assessment ~ 3 time points per day; model 2), cannabis-related intoxication symptoms (i.e., sum score of intoxication items at each assessment ~ 3 time points per day; model 3), and cannabis-related respiratory symptoms (i.e., sum score of respiratory items at each assessment ~ 3 time points per day; model 4). Repeated measures were treated as fixed factors to examine the time course of these dependent measures: 1) assessment time of day [morning, afternoon, evening], 2) day of week [1-7], and 3) week [1, 2]). A subject-level random factor (i.e., participant) was included to maximize model fit for each of our dependent outcomes (assessed using information criteria provided; e.g., -2 Log likelihood values). Interactions were examined including week by day of week, week by time of day, day of week by time of day, and week by day of week by time of day. The interaction of week by day of week was the only interaction term that contributed to the models and was subsequently included in all four models. After choosing the best fitting model, we explored mean differences among measures with significant effects of fixed factors (main effects and/or interactions) using t-tests with an adjustment for false discovery rate (e.g., Bonferroni). Estimated marginal means (EMM) were used for reporting t-tests instead of unadjusted means. EMM are means that adjust for the various factors added to the linear mixed models. Untransformed means, transformed means, and EMM for all linear mixed model outcomes are reported in Appendix A.

All analyses were conducted using SPSS V.25. We opted to use linear mixed models over repeated measures analyses of variance because linear mixed models can handle missing data (as noted in **Data Preparation**). Other advantages of linear mixed models include the ability to account for unequal spacing between time intervals and the ability to specify the variance-covariance structure (Kwok et al., 2008). Thus, linear mixed models provide a more accurate estimate of associations between variables.

Aim 2 Data Preparation and Analysis.

Assumptions for the two-way analysis of variance (ANOVA) utilized here included the use of a continuous dependent variable, two independent variables with two or more independent groups, independence of observations (achieved by using means), a normally distributed dependent variable, and homogeneity of variance. All assumptions were met except the presence of an outlier. Based on the residual distribution of the dependent variable, one outlier was revealed and was subsequently excluded from this analysis.

To determine the interaction of cannabis use frequency and administration method on cannabis-related intoxication symptoms (model 1), we conducted a two-way ANOVA with two independent variables: overall cannabis frequency across the two weeks (summed cannabis use frequency, split into two groups [high frequency and low frequency] based on the response distribution) and cannabis administration method(s) used across the two weeks (combusted-only use, other-only use, combination of methods used). The other-only cannabis administration method sub-group had too few respondents ($n = 1$); therefore, this cannabis administration method sub-group was excluded from analyses. Therefore, due to the excluded case from data cleaning and the excluded case from the other-only cannabis method sub-group, the sample size for model 1 was 25. The dependent variable for model 1 was cannabis-related intoxication symptoms across two weeks. This variable was created by summing the scores of each intoxication symptom question for each time point to create a composite intoxication symptom score for each time point and then the sum scores were averaged across the two-week data collection period. Post-hoc tests were conducted with an appropriate adjustment for false discovery rate (i.e., Bonferroni adjustment). We expected that those who used other administration methods at the highest cannabis use frequencies across two weeks would report the highest intoxication symptoms relative to other method sub-groups.

The two-way analysis of covariance (ANCOVA) shares many of the same assumptions as the two-way ANOVA. Additional two-way ANCOVA assumptions include the use of continuous covariates, a linear relationship between the covariate and dependent variable, homogeneity of regression slopes, and homogeneity of variances. All assumptions were met with three exceptions. There was one outlier, which was excluded from this analysis. Normality of the dependent variable was violated. As such, a square root transformation was conducted on the dependent variable. Finally, the covariate was not linearly associated with the dependent variable; therefore, we proceeded with the analysis with caution.

To determine the interaction of cannabis use frequency and cannabis administration method on cannabis-related respiratory symptoms (model 2), we conducted a two-way ANCOVA with two independent variables: overall cannabis frequency across the two weeks (summed cannabis use frequency, split into two groups [high frequency and low frequency] based on distribution) and cannabis administration method(s) used across the two weeks (combusted-only use, other-only use, combination of methods used). The other-only cannabis administration method sub-group had too few respondents (n = 1); therefore, this sub-group was excluded from analyses. Therefore, due to the excluded case from data cleaning and the excluded case from the other-only cannabis administration method sub-group, the sample size for model 2 was 25. The dependent variable for model 2 was square root adjusted cannabis-related respiratory symptoms across two weeks. This variable was created by summing the scores of each respiratory symptom question for each time point to create a composite respiratory symptom score for each time point. Then the sum scores were averaged across the two-week assessment period. The covariate was baseline respiratory symptoms (reported from the CCQ). Post-hoc tests were conducted with an appropriate adjustment for false discovery rate (i.e., Bonferroni adjustment).

Results

Total Sample Descriptives

In total, 40 participants were consented for the current study, and 27 were eligible for the study. Reasons for study exclusion included: past 30-day illicit substance use other than cannabis (n = 8), low cannabis use frequency (less than 5 days per week, n = 4), and high NIDA Modified-ASSIST score (greater than 27, n = 1). Of note, eligible and ineligible participants did not differ significantly in terms of baseline characteristics with the exception of age and total years of cannabis use (see Table 1).

Eligible participants were mostly female (74.1%), and the average age was 19.8 years (SD = 1.2; see Table 1). The sample was racially diverse with 14 (51.9%) participants identifying as White or European-American, 5 (18.5%) participants identifying as Black, Afro-Caribbean, or African American, 3 (11.1%) participants identifying as Multiracial, 3 (11.1%) participants identifying as Asian American, and 2 (7.4%) identifying as Other. Of the entire sample, 2 (7.4%) identified as Hispanic/Latinx. Most participants (66.7%) indicated that they were a student, while 25.9% were working and 7.4% were non-working or looking for work. Income level was widely distributed with 12 (44.4%) indicating that their income was $10,000 or less, 8 (29.6%) indicating their income was $10,000 to $59,000, and 7 (25.9%) indicating their income was over $60,000. Most participants (57.5%) self-reported that their health was “Excellent” or “Very good” and 42.5% indicated that their health was “Good” or “Fair”. The average baseline respiratory score was 9.67 (SD = 5.48), which indicates relatively low baseline negative respiratory symptom scores across the sample. Of the eligible participants, 21 (77.8%) had used any tobacco product in the past 30 days. Lifetime number of cannabis uses varied widely across participants with most (66.6%) having used cannabis between 101 to 2000 times in their lifetime.

Table 1. Demographic and substance history and use characteristics of the total consented participants, eligible participants, and ineligible participants.

M (SD) or N (%)	Total (N=40)	Eligible (N=27)	Ineligible (N=13)	*p*
Demographics				
Age in years (M, SD)	20.18 (1.68)	19.81 (1.21)	20.92 (2.25)	**<0.05**
Gender				0.19
Male	12 (30.0%)	7 (25.9%)	5 (38.5%)	
Female	27 (67.5%)	20 (74.1%)	7 (53.8%)	
Non-binary/Gender non-conforming	1 (2.5%)	0 (0.0%)	1 (7.7%)	
Race				0.42
White or European-American	21 (52.5%)	14 (51.9%)	7 (53.8%)	
Black, Afro-Caribbean, or African American	7 (17.5%)	5 (18.5%)	2 (15.4%)	
Multiracial	4 (10.0%)	3 (11.1%)	1 (7.7%)	
Asian American	3 (7.5%)	3 (11.1%)	0 (0.0%)	
Other	3 (7.5%)	2 (7.4%)	1 (7.7%)	
American Indian or Alaska Native	2 (5.0%)	0 (0.0%)	2 (15.4%)	
Hispanic/Latinx	4 (10.0%)	2 (7.4%)	2 (16.7%)	0.58
Employment status				0.75
Student	25 (62.5%)	18 (66.7%)	7 (53.8%)	
Working now	12 (30.0%)	7 (25.9%)	5 (38.5%)	
Non-working	3 (7.5%)	2 (7.4%)	1 (7.7%)	
Income				0.63
Less than $10,000	17 (42.5%)	12 (44.4%)	5 (38.5%)	
$10,000-$59,000	14 (35.0%)	8 (29.6%)	6 (46.2%)	
$60,000 or more	9 (22.5%)	7 (25.9%)	2 (15.4%)	
General health				0.75
Excellent/Very good	23 (57.5%)	15 (55.6%)	8 (61.5%)	
Good/Fair	17 (42.5%)	12 (44.4%)	5 (38.5%)	
Poor	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Baseline respiratory score (M, SD)	9.00 (5.35)	9.67 (5.48)	7.50 (4.91)	0.25
Past 30-day tobacco product use				
Any tobacco	31 (77.5%)	21 (77.8%)	10 (76.9%)	0.62
Cigarette	9 (22.5%)	6 (22.2%)	3 (23.1%)	0.62
Traditional cigar	6 (15.0%)	4 (14.8%)	2 (15.4%)	0.65
Little cigar or cigarillo	13 (32.5%)	9 (33.3%)	4 (30.8%)	0.58
Electronic cigarette	21 (52.5%)	14 (51.9%)	7 (53.8%)	0.59
Hookah	7 (17.5%)	5 (18.5%)	2 (15.4%)	0.59
Nicotine replacement therapy	2 (5.0%)	1 (3.7%)	1 (7.7%)	0.55
Cannabis use and history				
Lifetime number of cannabis uses				0.47
51-100 times	2 (5.0%)	0 (0.0%)	2 (15.4%)	
101-500 times	7 (17.5%)	5 (18.5%)	2 (15.4%)	
501-1000 times	8 (20.0%)	7 (25.9%)	1 (7.7%)	

1001-2000 times	9 (22.5%)	6 (22.2%)	3 (23.1%)	
2001-5000 times	4 (10.0%)	3 (11.1%)	1 (7.7%)	
5001-10,000 times	7 (17.5%)	4 (14.8%)	3 (23.1%)	
More than 10,000 times	3 (7.5%)	2 (7.4%)	1 (7.7%)	
Lifetime joint use	37 (92.5%)	26 (96.3%)	11 (84.6%)	0.24
Lifetime blunt use	39 (97.5%)	27 (100.0%)	12 (92.3%)	0.33
Lifetime bowl/pipe use	35 (87.5%)	24 (88.9%)	11 (84.6%)	0.53
Lifetime bong use	38 (95.0%)	26 (96.3%)	12 (92.3%)	0.55
Lifetime vaporizer use	31 (77.5%)	21 (77.8%)	10 (76.9%)	0.62
Lifetime dab use	29 (72.5%)	18 (66.7%)	11 (84.6%)	0.29
Lifetime edible use	35 (87.5%)	25 (92.6%)	10 (76.9%)	0.31
Total years of cannabis use (M, SD)	4.15 (2.16)	3.44 (1.28)	5.62 (2.84)	**<0.05**
Age of cannabis initiation in years (M, SD)	15.77 (1.83)	16.04 (1.58)	15.23 (2.24)	0.20
State of change (contemplation ladder) score (M, SD)	N/A	4.81 (2.10)	N/A	N/A

Note: **Bold** text indicates an alpha level of 0.05 or less. N/A indicates not applicable for this group. Zero participants indicated past 30-day use of pipe, chew, dip/snuff, snus or dissolvable tobacco products. Fisher's Exact Test was used for all bivariate analyses due low cell counts except age, baseline respiratory score, total years of cannabis use, and age of cannabis initiation, which were analyzed with independent samples t-tests and perceived health, which was analyzed with Pearson chi-square.

Lifetime cannabis administration method use ranged between 66.7% (for dabs) and 100% (for blunts). All participants had used a blunt in their lifetime. Participants had been using cannabis on average for 3.44 years (SD = 1.28), and the average age of cannabis use initiation was 16.04 years (SD = 1.58). Finally, the average state of cannabis change at the end of data collection was 4.81 (SD = 2.10), indicating that participants were thinking about the way they use cannabis, but had no intentions to change their cannabis use patterns. In the cannabis ladder, the fourth rung stated "I sometimes think about the way that I use marijuana, but I have no plans to change it," and the fifth rung stated "I often think about the way that I use marijuana, but I have no plans to change it."

Aim 1 Results

All 27 eligible participants in the study were included in the analytical sample for Aim 1. A summary of linear mixed model results for Aim 1 (Models 1-4) is displayed in Table 2.

Model 1: Cannabis hits frequency. The hypothesis that cannabis hits frequency would vary significantly by time of day was supported. There was a significant main effect of time of day (see Figure 4; $F(2{,}988.16) = 16.17$, $p < 0.001$). The hypothesis that cannabis hits frequency would be highest in the evenings and lowest in the mornings was partially supported. Most cannabis hits were consumed in the evenings and the fewest cannabis hits were consumed in the afternoons. Post hoc analyses indicated that there were significantly more cannabis hits consumed in the mornings (EMM = 1.26, SE = 0.14) compared to the afternoons (EMM = 0.95, SE = 0.14, $p < 0.001$, Bonferroni adjusted). Further, there were significantly more cannabis hits consumed in the evenings (EMM = 1.42, SE = 0.14) compared to the afternoons (EMM = 0.95, SE = 0.14, $p < 0.001$; Bonferroni adjusted).

Table 2. Statistical results summary for all linear mixed models in Aim 1.

	Time of day			Day of week			Week			Day of week X Week		
	df	*F*	*p*	df	*F*	*p*	df	*F*	*p*	df	*F*	*p*
Model 1												
Cannabis hits	**2, 988.16**	**16.17**	**<0.001**	6, 988.08	1.38	0.22	1, 987.80	2.07	0.15	**6, 987.86**	**2.43**	**<0.05**
Model 2												
Number of cannabis administration methods used	**2, 1004.56**	**15.61**	**<0.001**	6, 1004.45	0.80	0.57	**1, 1004.18**	**4.32**	**<0.05**	**6, 1004.21**	**3.12**	**0.05**
Model 3												
Intoxication scores	**2, 988.56**	**43.05**	**<0.001**	6, 988.47	0.93	0.47	1, 988.24	0.34	0.56	**6, 988.27**	**2.17**	**<0.05**
Model 4												
Respiratory scores	2, 978.24	2.19	0.11	6, 978.20	1.55	0.16	**1, 978.16**	**11.52**	**<0.001**	6, 978.14	1.72	0.11

Note: **Bold** indicates a significant main effect or interaction with an alpha level of 0.05 or less. df are numerator and denominator degrees of freedom.

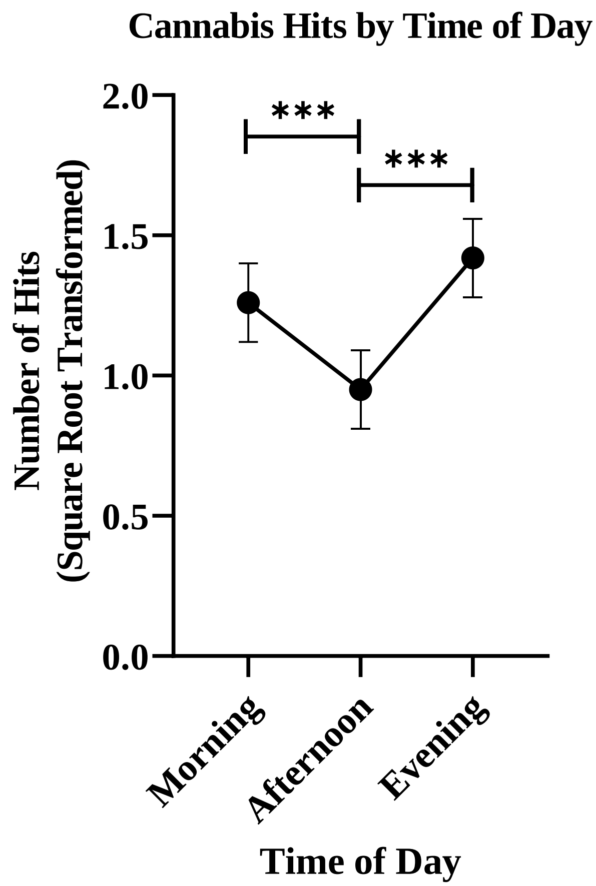

Figure 4. Estimated marginal means (+/- standard error of the mean; SEM) for number of cannabis hits (square root transformed) by time of day. Asterisks (***) indicate a significant difference between morning, afternoon, or evening (p < 0.001, Bonferroni adjusted).

It was hypothesized that cannabis use frequency would be higher on the weekends compared to the weekdays; this hypothesis was not supported. However, there was a significant week by day of week interaction (See Figure 5; $F(6,987.86) = 2.43$, $p < 0.05$). Post hoc analyses indicated that on Mondays during week 1, cannabis hits consumed were significantly higher (EMM = 1.56, SE = 0.18) compared to week 2 (EMM = 1.14, SE = 0.18; $p = 0.025$; Bonferroni adjusted). On Thursdays during week 1, cannabis hits consumed were significantly higher (EMM = 1.35, SE = 0.18) compared to week 2 (EMM = 0.95, SE = 0.19; $p = 0.035$; Bonferroni adjusted). On Sundays during week 1, cannabis hits consumed were significantly lower (EMM = 0.91, SE = 0.18) compared to week 2 (EMM = 1.32, SE = 0.18; final day of data collection; $p = 0.026$; Bonferroni adjusted). Within weeks, during week 1, cannabis hits consumed were significantly higher on Monday (EMM = 1.56, SE = 0.18) compared to Sunday (EMM = 0.91, SE = 0.18; $p = 0.01$; Bonferroni adjusted).

Model 2: Number of cannabis administration methods used. It was hypothesized that the number of cannabis administration methods used would vary significantly by time of day and day of the week, and this hypothesis was partially supported. There was a significant main effect of time of day (see Figure 6; $F(2,1004.56) = 15.61$, $p < 0.001$), but there was insufficient evidence to indicate a main effect of day of the week. Post hoc analyses indicated, in the mornings, the number of cannabis administration methods was significantly higher (EMM = 0.56, SE = 0.05) compared to the afternoons (EMM = 0.46, SE = 0.05; $p < 0.001$; Bonferroni adjusted). In the evenings, the number of cannabis administration methods used was significantly higher (EMM = 0.66, SE = 0.05) compared to afternoons (EMM = 0.46, SE = 0.05; $p < 0.001$; Bonferroni adjusted) and compared to the mornings (EMM = 0.56, SE = 0.05; $p < 0.001$; Bonferroni adjusted).

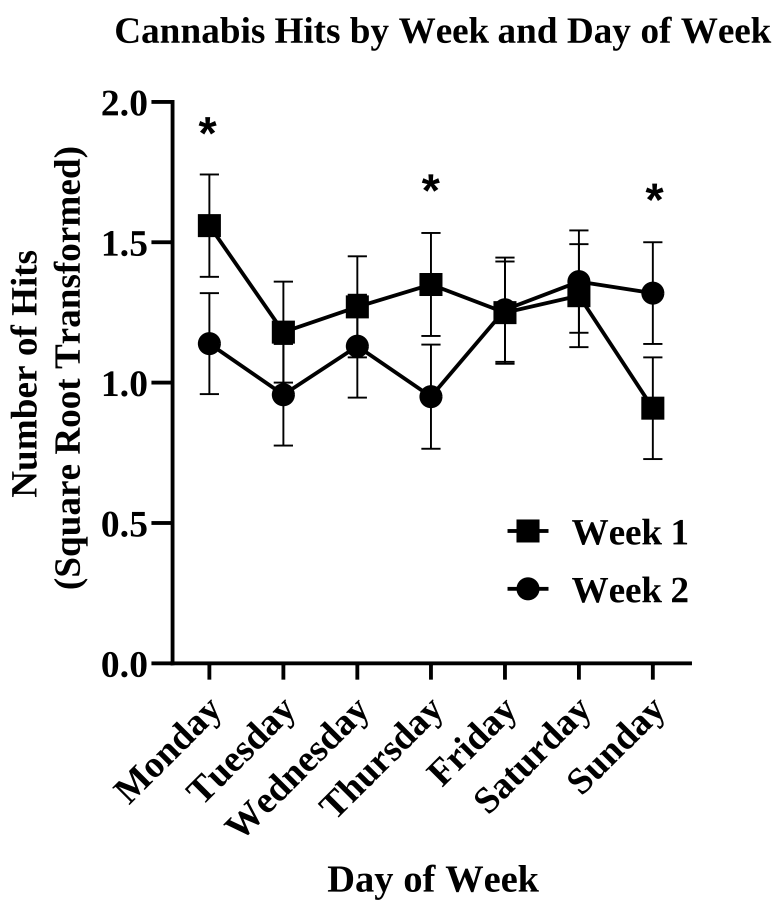

Figure 5. Estimated marginal means (+/-SEM) for number of cannabis hits (square root transformed) by week and day of week. Asterisks (*) indicate a significant difference between week 1 and week 2 ($p < 0.05$, Bonferroni adjusted).

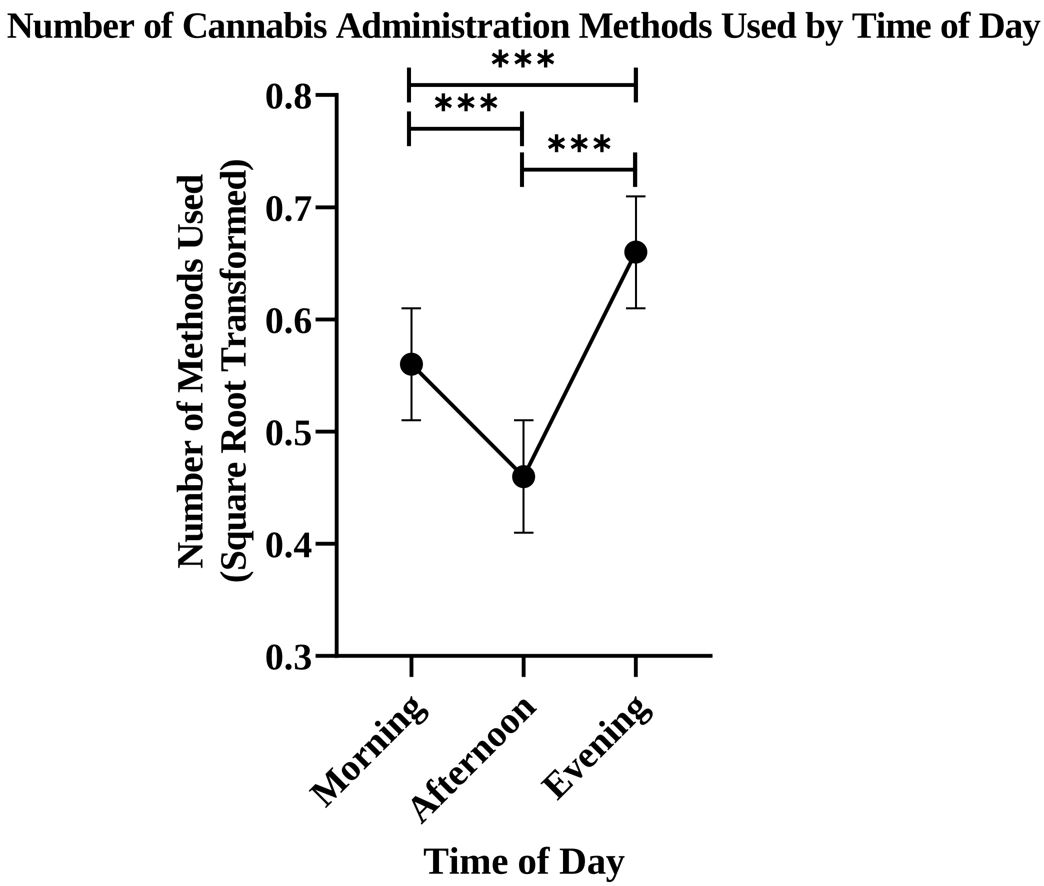

Figure 6. Estimated marginal means (+/-SEM) for number of cannabis administration methods used (square root transformed) by time of day. Asterisks (***) indicate a significant difference between morning, afternoon, or evening (p < 0.001, Bonferroni adjusted).

Exploratory analyses indicated that there was a significant main effect of week on the number of cannabis administration methods used (see Figure 7; $F(1,1004.18) = 4.32$, $p < 0.05$). Post hoc analyses indicated that, during week 1, the number of cannabis administration methods used were significantly higher (EMM = 0.59, SE = 0.05) compared to week 2 (EMM = 0.53, SE = 0.05; $p = 0.038$; Bonferroni adjusted). Exploratory analyses also indicated that there was a significant week by day of week interaction on the number of cannabis administration methods used (see Figure 8; $F(6,1004.21) = 3.12$, $p < 0.05$). Post hoc analyses indicated that on Tuesdays of week 1, the number of cannabis administration methods used was significantly higher (EMM = 0.65, SE = 0.07) compared to week 2 (EMM = 0.43, SE = 0.07; $p = 0.012$; Bonferroni adjusted). On Thursdays during week 1, the number of cannabis administration methods was significantly higher (EMM = 0.65, SE = 0.07) compared to week 2 (EMM = 0.46, SE = 0.07; $p = 0.015$; Bonferroni adjusted). On Sundays during week 1, the number of cannabis administration methods used was significantly lower (EMM = 0.41, SE = 0.07) compared to week 2 (EMM = 0.60, SE = 0.07; $p = 0.017$; Bonferroni adjusted). Within weeks, during week 1, the number of cannabis administration methods used was significantly higher on Monday (EMM = 0.68, SE = 0.07) and Thursday (EMM = 0.65, SE = 0.07) compared to Sunday (EMM = 0.41, SE = 0.07; $p = 0.018$; Bonferroni adjusted).

Model 3: Intoxication scores. It was hypothesized that cannabis-related intoxication symptoms would vary significantly by time of day, such that intoxication symptoms would be highest in the evenings and lowest in the mornings. This hypothesis was supported; there was a significant main effect of time of day (see Figure 9; $F(2,988.56) = 43.05$, $p < 0.001$).

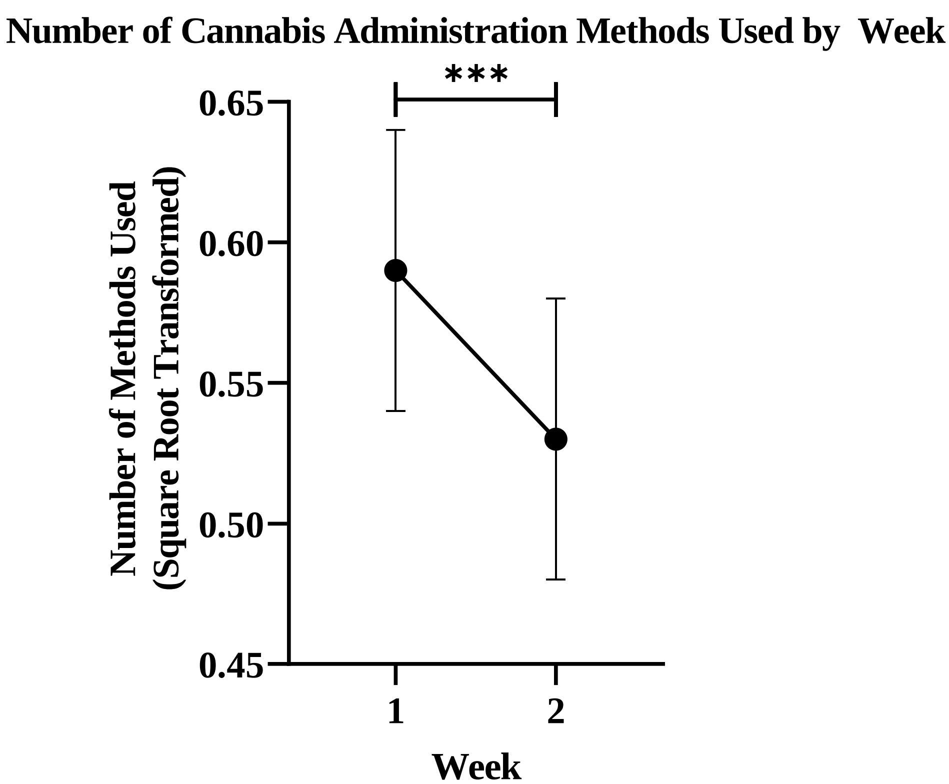

Figure 7. Estimated marginal means (+/-SEM) for number of cannabis administration methods used (square root transformed) by week. Asterisks (***) indicate a significant difference between week 1 and week 2 (p < 0.001, Bonferroni adjusted).

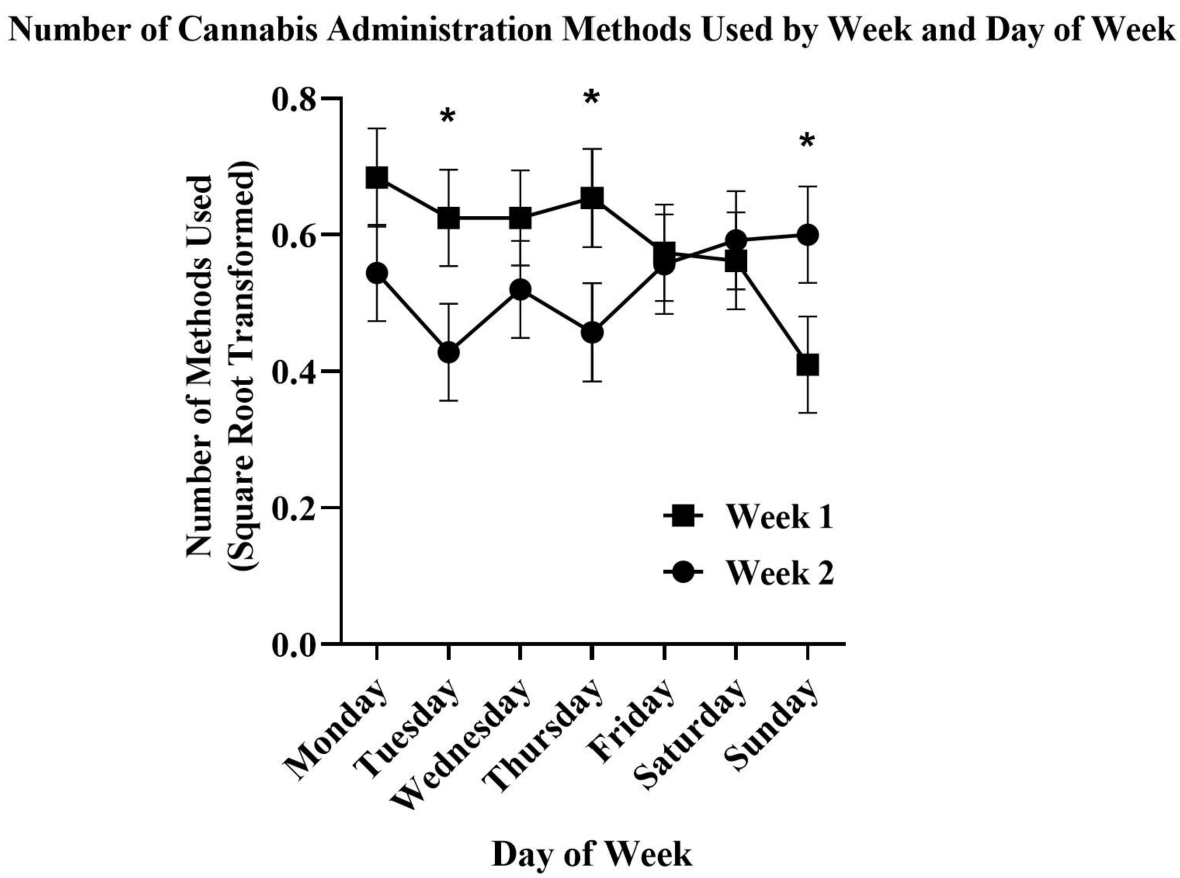

Figure 8. Estimated marginal means (+/-SEM) for number of cannabis administration methods used (square root transformed) by week and day of week. Asterisks (*) indicate a significant difference between week 1 and week 2 ($p < 0.05$, Bonferroni adjusted).

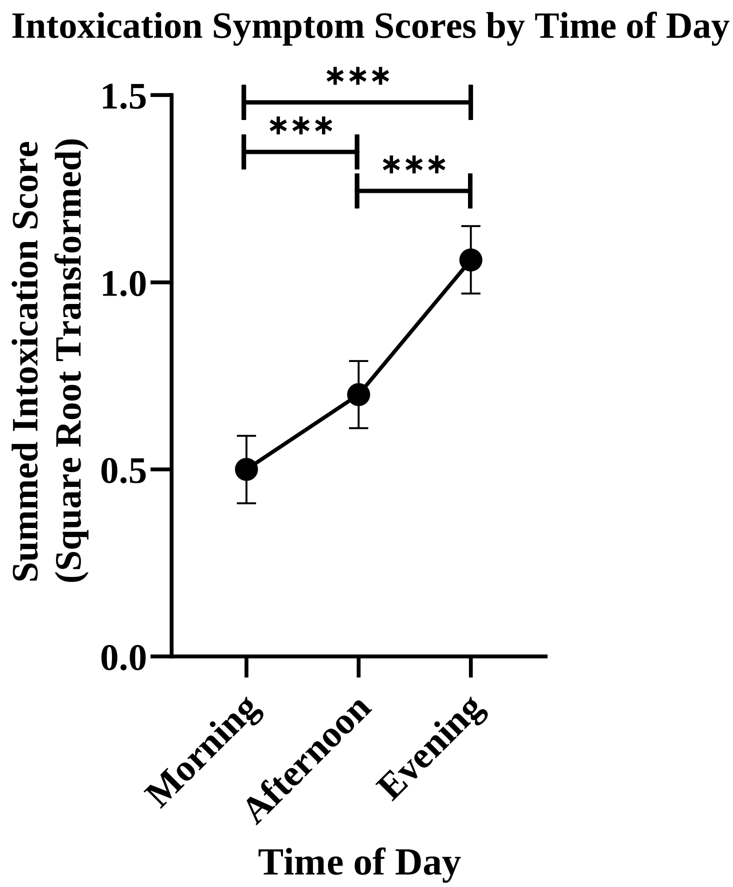

Figure 9. Estimated marginal means (+/-SEM) for summed intoxication scores (square root transformed) by time of day. Asterisks (***) indicate a significant difference between morning, afternoon, or evening ($p < 0.001$, Bonferroni adjusted).

Post hoc analyses indicated that in the afternoons, intoxication symptom scores were significantly higher (EMM = 0.70, SE = 0.09) compared to mornings (EMM = 0.50, SE = 0.09; $p < 0.001$; Bonferroni adjusted). In the evenings, intoxication symptom scores were significantly higher (EMM = 1.06, SE = 0.09) compared to mornings (EMM = 0.50, SE = 0.09; $p < 0.001$; Bonferroni adjusted) and compared to afternoons (EMM = 0.70, SE = 0.09; $p < 0.001$; Bonferroni adjusted).

It was hypothesized that cannabis-related intoxication symptoms would vary significantly by day of week, such that intoxication symptoms would be highest on the weekends compared to weekdays. There was insufficient evidence to suggest that this hypothesis was supported. However, there was a significant week by day of week interaction (see Figure 10; $F(6,988.27) = 2.17$, $p = 0.05$). Post hoc analyses indicated that on Thursdays of week 1, intoxication symptom scores were significantly higher (EMM = 0.88, SE = 0.13) compared to week 2 (EMM = 0.56, SE = 0.13; $p = 0.016$; Bonferroni adjusted). On Sundays of week 1, intoxication symptom scores were significantly lower (EMM = 0.54, SE = 0.13) compared to week 2 (EMM = 0.84, SE = 0.12; $p = 0.025$; Bonferroni adjusted).

Model 4: Respiratory scores. It was hypothesized that cannabis-related respiratory symptoms would vary significantly by day of week and time of day, such that respiratory symptoms would be highest in the evenings and on the weekends compared to mornings and on the weekdays. Results did not support this hypothesis. Instead, results indicated that there was a significant main effect of week (see Figure 11; $F(1,978.16) = 11.52$, $p < 0.001$), but not day of week or time of day. Post hoc analyses indicated that during week 1, respiratory symptom scores were significantly higher (EMM = 1.07, SE = 0.15) compared to week 2 (EMM = 0.91, SE = 0.15; $p = 0.001$; Bonferroni adjusted).

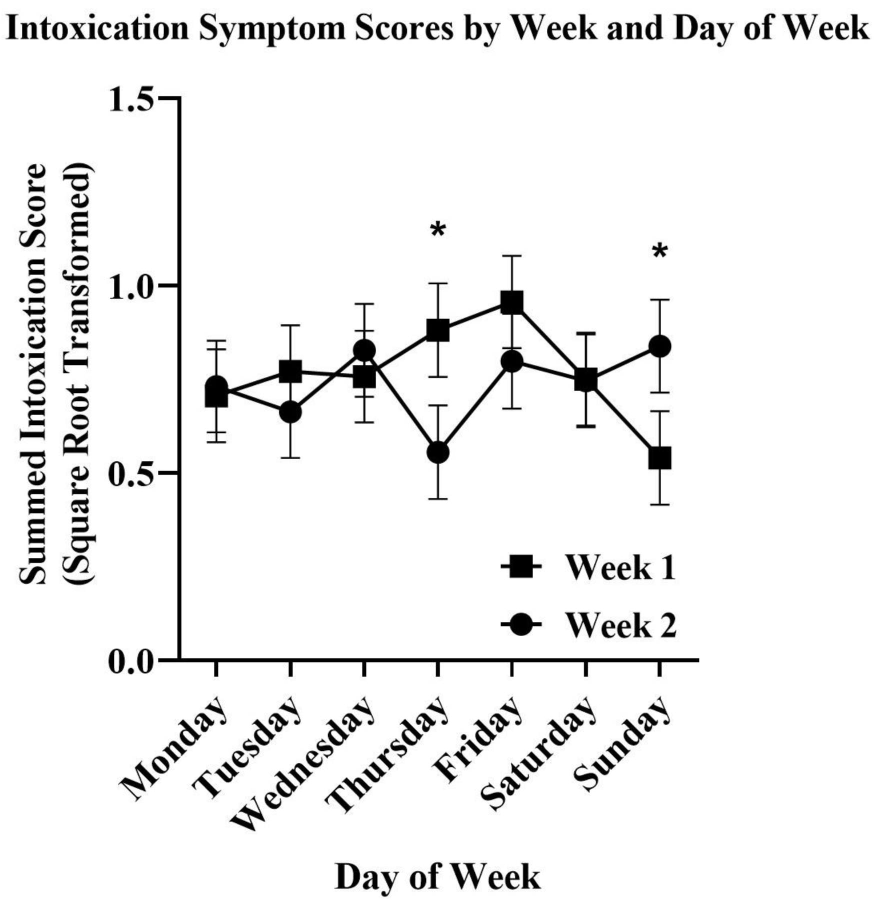

Figure 10. Estimated marginal means (+/-SEM) for summed intoxication scores (square root transformed) by week and day of week. Asterisks (*) indicate a significant difference between week 1 and week 2 ($p < 0.05$, Bonferroni adjusted).

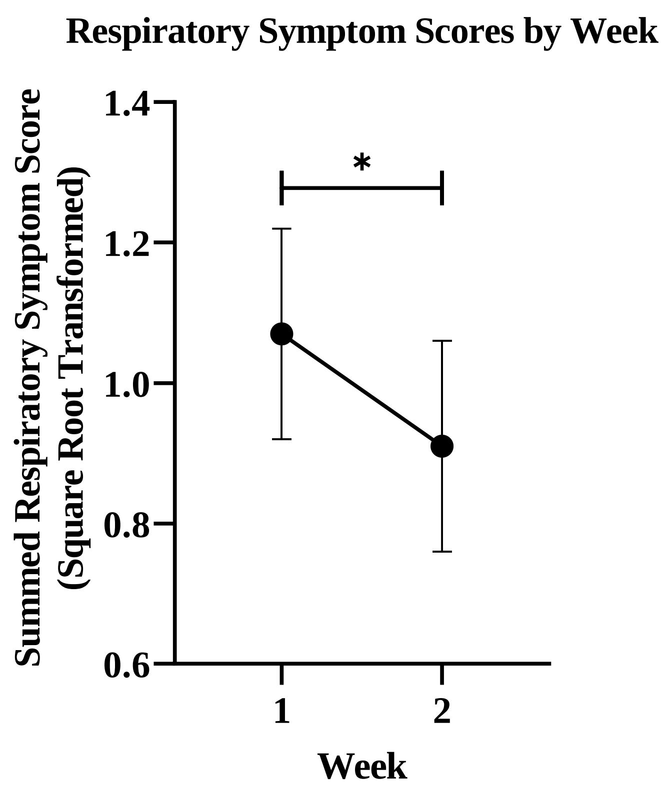

Figure 11. Estimated marginal means (+/-SEM) for summed respiratory symptom scores (square root transformed) by week. Asterisks (*) indicate a significant difference between week 1 and week 2 ($p < 0.05$, Bonferroni adjusted).

Aim 2, Hypothesis 2a Results

Characteristics of the overall analytical sample (n = 25), cannabis administration method sub-group (i.e., combusted-only and combination), and hits frequency sub-group (i.e., low hits frequency and high hits frequency) samples for Hypothesis 2a are displayed in Table 3. Over half of participants (n = 14, 56.0%) were classified into the combusted-only cannabis administration method sub-group and 11 (44.0%) were classified into the combination cannabis administration method sub-group. Among those in the combusted-only cannabis administration method sub-group, bowl/pipe and bong were the most prevalent methods used during the study (endorsed by > 71.4%), and blunt (35.7%) and joint (57.1%) were the least common methods used during the study. Among those in the combination cannabis administration method sub-group, during the study, bong and vaporizer use were the most common methods reported (endorsed by > 72.7%), and blunt (45.5%) was the least prevalent method endorsed during the study. Approximately half of participants (n = 12, 48.0%) were classified into the low hits frequency sub-group and 13 (52.0%) participants were classified into the high hits frequency sub-group. The average number of total summed hits consumed during the study among the low hits frequency sub-group was 54.9 (SD = 26.1), and among the high hits frequency sub-group, the average number of total summed hits consumed was 185.1 (94.1). See additional descriptives in Table 3.

A 2x2 between-groups ANOVA was conducted to test the main effects and potential interaction between sub-groups of cannabis administration method and sub-groups of cannabis use frequency (high vs. low sub-groups) on mean cannabis-related intoxication symptom scores facross two weeks. The independent variables were sub-group of cannabis administration method (combustion vs. combination) and frequency of cannabis use measured in hits (high vs. low sub-groups).

Table 3. Aim 2, Characteristics of the overall, cannabis administration method sub-group, and hits frequency sub-group samples used for Hypothesis 2a.

M (SD) or N (%)	Overall (n = 25)	Combusted -only (n = 14)	Combination (n = 11)	Low hits frequency (n = 12)	High hits frequency (n = 13)
Demographics					
Age in years (M, SD)	19.8 (1.3)	19.8 (1.1)	19.8 (1.5)	20.1 (1.4)	19.5 (1.1)
Gender					
Male	6 (24.0%)	2 (14.3%)	4 (36.4%)	3 (25.0%)	3 (23.1%)
Female	19 (76.0%)	12 (85.7%)	7 (63.6%)	9 (75.0%)	10 (76.9%)
Race					
White or European-American	12 (48.0%)	5 (35.7%)	7 (63.6%)	4 (33.3%)	8 (61.5%)
Black, Afro-Caribbean, or African American	5 (20.0%)	4 (28.6%)	1 (9.1%)	4 (33.3%)	1 (7.7%)
Multiracial	3 (12.0%)	1 (7.1%)	2 (18.2%)	2 (16.7%)	1 (7.7%)
Asian American	3 (12.0%)	2 (14.3%)	1 (9.1%)	1 (8.3%)	2 (15.4%)
Other	2 (8.0%)	2 (14.3%)	0 (0.0%)	1 (8.3%)	1 (7.7%)
Hispanic/Latinx	2 (8.0%)	1 (7.1%)	1 (9.1%)	2 (16.7%)	0 (0.0%)
Employment status					
Student	16 (64.0%)	8 (57.1%)	8 (72.7%)	6 (50.0%)	10 (76.9%)
Working	7 (28.0%)	5 (35.7%)	2 (18.2%)	4 (33.3%)	3 (23.1%)
Non-working	2 (8.0%)	1 (7.1%)	1 (9.1%)	2 (16.7%)	0 (0.0%)
Income					
Less than $10,000	11 (44.0%)	8 (57.1%)	3 (27.3%)	5 (41.7%)	6 (46.2%)
$10,000-$59,000	7 (28.0%)	3 (21.4%)	4 (36.4%)	5 (41.7%)	2 (15.4%)
$60,000 or more	7 (28.0%)	3 (21.4%)	4 (36.4%)	2 (16.7%)	5 (38.5%)
General health					
Excellent/Very good	14 (56.0%)	8 (57.1%)	6 (54.5%)	8 (66.7%)	6 (46.2%)
Good/Fair	11 (44.0%)	6 (42.9%)	5 (45.5%)	4 (33.3%)	7 (53.8%)
Poor	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Past 30-day tobacco product use					
Any tobacco	20 (80.0%)	11 (78.6%)	9 (81.8%)	10 (83.3%)	10 (76.9%)
Cigarette	6 (24.0%)	4 (28.6%)	2 (18.2%)	4 (33.3%)	2 (15.4%)
Traditional cigar	4 (16.0%)	2 (14.3%)	2 (18.2%)	2 (16.7%)	2 (15.4%)
Little cigar or cigarillo	9 (36.0%)	5 (35.7%)	4 (36.4%)	4 (33.3%)	5 (38.5%)
Electronic cigarette	13 (52.0%)	7 (50.0%)	6 (54.5%)	5 (41.7%)	8 (61.5%)
Hookah	5 (20.0%)	3 (21.4%)	2 (18.2%)	2 (16.7%)	3 (23.1%)
Nicotine replacement therapy	1 (4.0%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	1 (7.7%)
Cannabis use history and study cannabis use					
Total years of cannabis use (M, SD)	3.4 (1.2)	2.9 (0.9)	3.9 (1.4)	6.4 (1.6)	3.7 (1.2)
Age of cannabis initiation (M, SD)	16.1 (1.6)	16.4 (1.2)	15.7 (2.0)	16.5 (1.4)	15.7 (1.7)

Total summed hits during study (M, SD)	122.6 (95.6)	85.8 (57.3)	169.5 (115.6)	54.9 (26.1)	185.1 (94.1)
Study joint use	14 (56.0%)	8 (57.1%)	6 (54.5%)	6 (50.0%)	8 (61.5%)
Study blunt use	10 (40.0%)	5 (35.7%)	5 (45.5%)	3 (25.0%)	7 (53.8%)
Study bowl/pipe use	16 (64.0%)	10 (71.4%)	6 (54.5%)	7 (58.3%)	9 (69.2%)
Study bong use	20 (80.0%)	11 (78.6%)	9 (81.8%)	9 (75.0%)	11 (84.6%)
Study vaporizer use	8 (32.0%)	0 (0.0%)	8 (72.7%)	4 (33.3%)	4 (30.8%)
Study dab use	6 (24.0%)	0 (0.0%)	6 (54.5%)	0 (0.0%)	6 (46.2%)
Study edible use	6 (24.0%)	3 (21.4%)	3 (27.3%)	2 (16.7%)	4 (30.8%)

Note: Results are based upon individuals who met assumptions based on their summed intoxication scores and who were included in the combusted-only or combination cannabis administration method sub-groups (n = 25).

The dependent variable was mean cannabis-related intoxication symptom scores across the two weeks. It was hypothesized originally that those who use other administration methods at high frequencies will have the highest intoxication symptoms relative to combusted and combination administration method sub-groups. However, the proposed hypothesis could not be conducted due to few participants in the other administration method sub-group. As such, the results to test for differences between the combusted-only and combination administration method sub-groups on cannabis-related intoxication symptoms are described.

There was a significant main effect of cannabis use frequency on mean cannabis-related intoxication symptom scores ($F(1,21) = 31.38$, $p < 0.001$), such that for high frequency cannabis users, intoxication symptom scores were significantly higher (EMM = 2.03, SE = 0.16) compared to low frequency cannabis users (EMM = 0.69, SE = 0.18). There was insufficient evidence to suggest that there was a main effect of cannabis administration method sub-group on average cannabis-related intoxication symptom scores, ($F(1,21) = 2.19$, $p = 0.15$). Further, there was insufficient evidence to suggest that there was an interaction between cannabis use frequency and cannabis administration method sub-group on average cannabis-related intoxication symptom scores, ($F(1,21) = 2.91$, $p = 0.10$). Despite this finding, due to the low sample size, exploratory nature of the study, and EMM among the variables of interest (see Figure 12), pairwise comparisons among the interaction model were probed. Post-hoc comparisons indicated that among only high frequency cannabis users, mean intoxication symptom scores were significantly lower in the combusted-only cannabis administration method group (EMM = 1.65, SE = 0.24) compared to the combination cannabis administration method group (EMM = 2.41, SE = 0.22; $p < 0.05$; Bonferroni-adjusted).

Intoxication Symptom Scores by Cannabis Hits Frequency Sub-group and Administration Method Sub-group

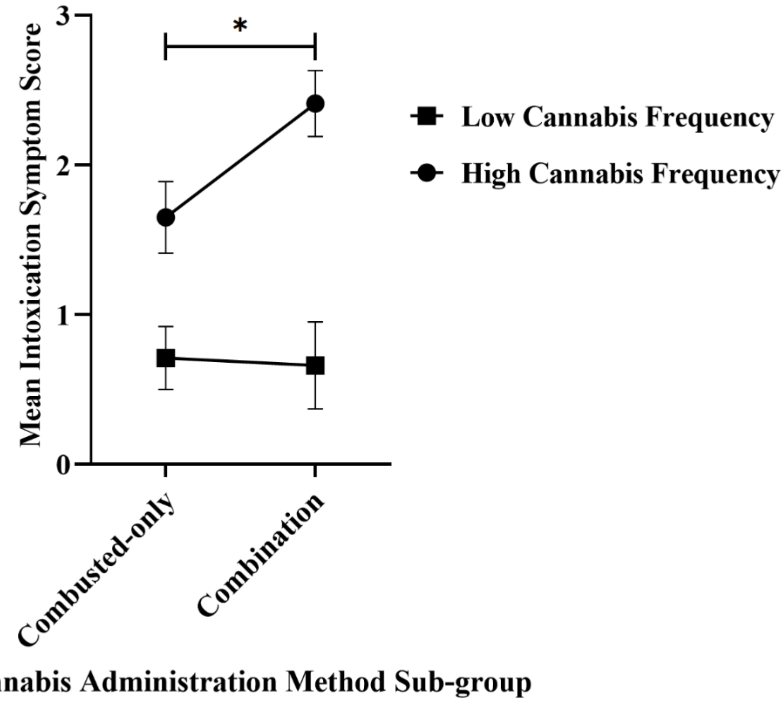

Figure 12. Estimated marginal means (+/-SEM) for intoxication symptom scores across cannabis hits frequency sub-group and administration method sub-group. Asterisks (*) indicate a significant difference in intoxication symptoms between combusted-only and combination administration method sub-groups among only the high frequency cannabis use group ($p < 0.05$, Bonferroni adjusted).

Aim 2, Hypothesis 2b Results

Characteristics of the overall analytical sample (n = 25), cannabis administration method sub-groups (i.e., combusted-only and combination), and hits frequency sub-groups (i.e., low hits frequency and high hits frequency) for Hypothesis 2b are displayed in Table 4. The combusted-only and combination cannabis administration method sub-groups, as well as the high and low cannabis hits frequency sub-groups for Aim 2, Hypothesis 2b were very similar to the groups in Aim 2, Hypothesis 2a (with the exception of 2 participants). As such, to read more detailed descriptions of these groups, see **Aim 2, Hypothesis 2a Results**. To see specific descriptives for Aim 2, Hypothesis 2b, see Table 4.

For Aim 2, Hypothesis 2b, a 2x2 between-groups ANCOVA was conducted to test the main effects and potential interaction between sub-groups of cannabis administration method and frequency of cannabis use (measured in hits) on mean cannabis-related respiratory symptom scores across two weeks. The independent variables were sub-group of cannabis administration method (i.e., combustion vs combination sub-groups) and frequency of cannabis use measured in hits (i.e., high vs. low sub-groups). The dependent variable was mean cannabis-related respiratory symptom scores across the two weeks. The covariate was baseline respiratory score from the CCQ. It was hypothesized that those who use combusted administration methods and at the highest frequencies would report the highest negative respiratory symptoms relative to other and combination cannabis administration method sub-groups. Similar to Aim 2, Hypothesis 2a, the other cannabis administration method sub-group was not included in this analysis due to low sample size. Therefore, the results to test for differences between the combusted and combination cannabis administration method sub-groups on cannabis-related respiratory symptom scores are described

Table 4. Aim 2, Characteristics of the overall, cannabis administration method sub-group, and hits frequency sub-group samples used for Hypothesis 2b.

M (SD) or N (%)	Overall (n = 25)	Combusted -only (n = 13)	Combination (n = 12)	Low hits frequency (n = 12)	High hits frequency (n = 13)
Demographics					
Age in years (M, SD)	19.8 (1.2)	19.8 (1.2)	19.8 (1.4)	20.1 (1.4)	19.5 (1.1)
Gender					
Male	7 (28.0%)	2 (15.4%)	5 (41.7%)	4 (33.3%)	3 (23.1%)
Female	18 (72.0%)	11 (84.6%)	7 (58.3%)	8 (66.7%)	10 (76.9%)
Race					
White or European-American	12 (48.0%)	4 (30.8%)	8 (66.7%)	4 (33.3%)	8 (61.5%)
Black, Afro-Caribbean, or African American	5 (20.0%)	4 (30.8%)	1 (8.3%)	4 (33.3%)	1 (7.7%)
Multiracial	3 (12.0%)	1 (7.7%)	2 (16.7%)	2 (16.7%)	1 (7.7%)
Asian American	3 (12.0%)	2 (15.4%)	1 (8.3%)	1 (8.3%)	2 (15.4%)
Other	2 (8.0%)	2 (15.4%)	0 (0.0%)	1 (8.3%)	1 (7.7%)
Hispanic/Latinx	2 (8.0%)	1 (7.7%)	1 (8.3%)	2 (16.7%)	0 (0.0%)
Employment status					
Student	17 (68.0%)	8 (61.5%)	9 (75.0%)	7 (58.3%)	10 (76.9%)
Working now	6 (24.0%)	4 (30.8%)	2 (16.7%)	3 (25.0%)	3 (23.1%)
Non-working	2 (8.0%)	1 (7.7%)	1 (8.3%)	2 (16.7%)	0 (0.0%)
Income					
Less than $10,000	10 (40.0%)	7 (53.8%)	3 (25.0%)	4 (33.3%)	6 (46.2%)
$10,000-$59,000	8 (32.0%)	3 (23.1%)	5 (41.7%)	6 (50.0%)	2 (15.4%)
$60,000 or more	7 (28.0%)	3 (23.1%)	4 (33.3%)	2 (16.7%)	5 (38.5%)
General health					
Excellent/Very good	14 (56.0%)	8 (61.5%)	6 (50.0%)	8 (66.7%)	6 (46.2%)
Good/Fair	11 (44.0%)	5 (38.5%)	6 (50.0%)	4 (33.3%)	7 (53.8%)
Poor	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Baseline respiratory score (M, SD)	9.5 (5.6)	8.8 (3.5)	10.3 (7.4)	10.0 (5.3)	9.1 (6.1)
Past 30-day tobacco product use					
Any tobacco	20 (80.0%)	10 (76.9%)	10 (83.3%)	10 (83.3%)	10 (76.9%)
Cigarette	6 (24.0%)	4 (30.8%)	2 (16.7%)	4 (33.3%)	2 (15.4%)
Traditional cigar	4 (16.0%)	2 (15.4%)	2 (16.7%)	2 (16.7%)	2 (15.4%)
Little cigar or cigarillo	9 (36.0%)	5 (38.5%)	4 (33.3%)	4 (33.3%)	5 (38.5%)
Electronic cigarette	13 (52.0%)	6 (46.2%)	7 (58.3%)	5 (41.7%)	8 (61.5%)
Hookah	5 (20.0%)	3 (23.1%)	2 (16.7%)	2 (16.7%)	3 (23.1%)
Nicotine replacement therapy	1 (4.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)	1 (7.7%)
Cannabis use history and study cannabis use					
Total years of cannabis use (M, SD)	3.3 (1.2)	2.9 (0.9)	3.8 (1.3)	2.9 (1.2)	3.7 (1.2)

Age of cannabis initiation (M, SD)	16.2 (1.6)	16.5 (1.2)	15.8 (1.9)	16.7 (1.4)	15.7 (1.7)
Total summed hits in study (M, SD)	123.6 (95.0)	88.1 (59.0)	162.2 (113.1)	57.0 (27.1)	185.2 (94.1)
Study joint use	13 (52.0%)	7 (53.8%)	6 (50.0%)	5 (41.7%)	8 (61.5%)
Study blunt use	9 (36.0%)	4 (30.8%)	5 (41.7%)	2 (16.7%)	7 (53.8%)
Study bowl/pipe use	17 (68.0%)	10 (76.9%)	7 (58.3%)	8 (66.7%)	9 (69.2%)
Study bong use	20 (80.0%)	10 (76.9%)	10 (83.3%)	9 (75.0%)	11 (84.6%)
Study vaporizer use	9 (36.0%)	0 (0.0%)	9 (75.0%)	5 (41.7%)	2 (30.8%)
Study dab use	6 (24.0%)	0 (0.0%)	6 (50.0%)	0 (0.0%)	6 (46.2%)
Study edible use	6 (24.0%)	3 (23.1%)	3 (25.0%)	2 (16.7%)	4 (30.8%)

Note: Results are based upon individuals who met assumptions based on their summed respiratory symptom scores and who were included in the combusted-only or combination cannabis administration method sub-groups (n = 25).

After adjusting for baseline respiratory symptoms, there was insufficient evidence to suggest a main effect of high frequency cannabis use (EMM = 1.38, SE = 0.16) and low frequency cannabis use (EMM = 1.01, SE = 0.17) on respiratory symptom scores ($F(1,20) = 2.40$, $p = 0.14$). There was insufficient evidence to suggest that there was a main effect of combusted cannabis administration method use (EMM = 1.24, SE = 0.16) and combination cannabis administration method use (EMM = 1.15, SE = 0.17) on average cannabis-related respiratory symptom scores after controlling for baseline respiratory symptoms, ($F(1,20) = 0.148$, $p = 0.704$). There was insufficient evidence to suggest that there was an interaction between cannabis use frequency and cannabis administration method sub-group on average respiratory symptoms after controlling for baseline respiratory symptoms, ($F(1,20) = 0.74$, $p = 0.40$). Despite this finding, due to the low sample size, exploratory nature of the study, and EMMs among the variables of interest (see Figure 13), post-hoc comparisons among the interaction model were probed using a Bonferroni adjustment; however, no significant mean differences were revealed.

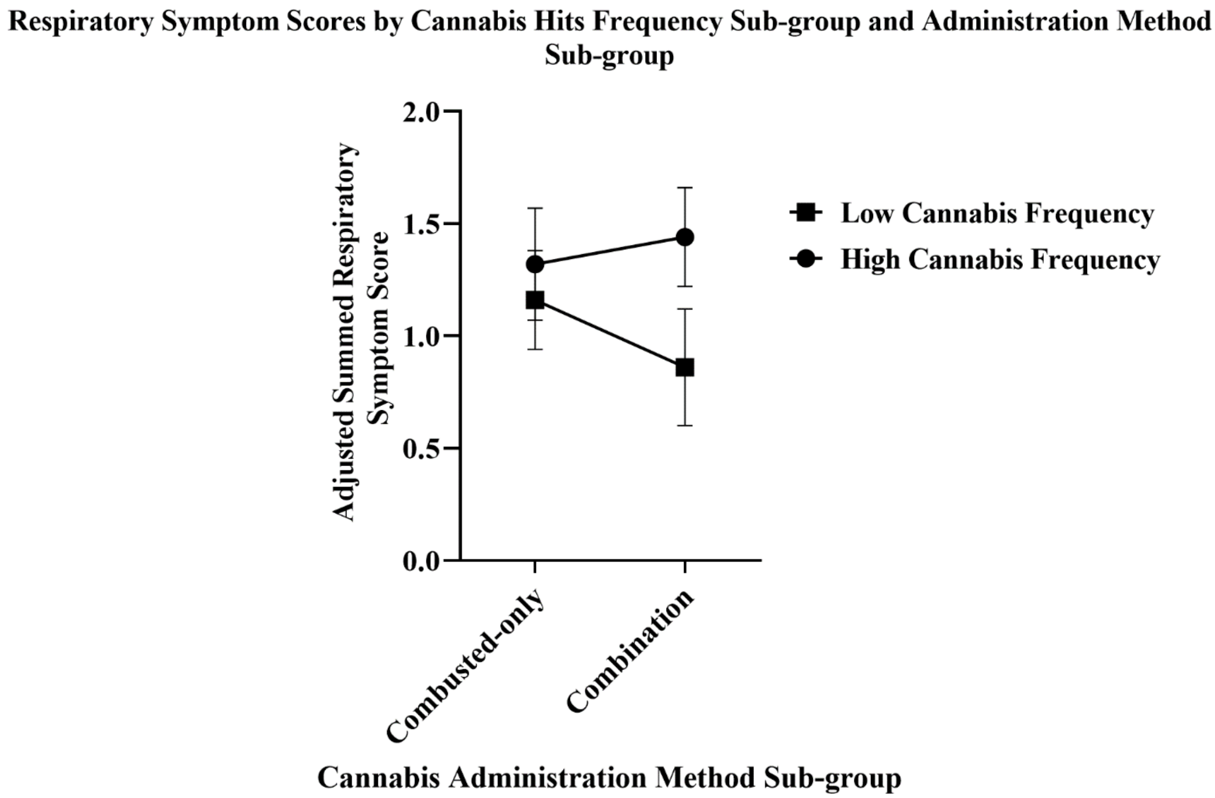

Figure 13. Estimated marginal means (+/-SEM) for respiratory symptoms across cannabis hit frequency sub-group and administration method sub-group.

Discussion

The purpose of this two-week EMA study among young adult heavy cannabis users was to characterize within week and day patterns of cannabis use frequency, number of cannabis administration methods used, and cannabis-related intoxication and respiratory symptoms and to test the interaction of cannabis use frequency and cannabis administration method use on cannabis-related intoxication and respiratory symptoms.

For Aim 1, it was hypothesized that cannabis use frequency would be lowest in the mornings and highest in the evenings. Results indicated that cannabis use frequency was highest in the evenings and lowest in the afternoons. It was hypothesized that cannabis use frequency would be higher on the weekends compared to the weekdays. Results did not support this hypothesis, but there were some differences in cannabis use frequency between weeks 1 and 2 of data collection, and during week 1, more hits were consumed on Monday compared to Sunday. It was hypothesized that the number of cannabis administration methods would vary by day of week and time of day. Results indicated that the number of cannabis administration methods was highest in the evenings, followed by mornings and afternoons. There was no indication that number of cannabis administration methods varied significantly by day of week. However, some evidence suggested that the number of cannabis administration methods used on some days of the week differed by week. Finally, it was hypothesized that cannabis-related intoxication and respiratory symptoms would vary significantly by day of week and time of day. Results indicated that intoxication symptoms were highest in the evenings, followed by afternoons and mornings. Results also indicated that intoxication symptoms significantly differed on some days of the week by week. There was no indication that intoxication symptoms significantly differed by day of week. Respiratory scores did not significantly differ by day of week or time of day, as hypothesized; however, there was evidence that respiratory scores differed by week, such that week 1 had higher respiratory symptom reports compared to week 2.

For Aim 2, results indicated that high cannabis hits frequency users reported significantly higher average intoxication symptoms compared to low hits frequency users. Exploratory analyses indicated that among only those in the high cannabis hits frequency use group, combination cannabis administration method sub-group users reported higher intoxication compared to the combusted-only cannabis administration method sub-group. Finally, it was hypothesized that those who used combusted cannabis administration methods at the highest frequencies would report the highest respiratory symptoms relative to the combination cannabis administration method sub-group. There was no evidence to suggest a difference in respiratory symptoms among cannabis administration method sub-groups or cannabis hits frequency sub-groups.

Based on the results of the current study, cannabis use frequency by time of day and day of week was consistent with some previous literature on cannabis use among heavy cannabis users. Cannabis use was highest in the evenings in the current study, which was similar to results from a previous EMA study among young adults in the US who reported cannabis use for one week using palm pilots (Treloar Padovano & Miranda, 2018). Results from the same study and from the current study failed to find evidence that cannabis use frequency differed by day of the week (Treloar Padovano & Miranda, 2018). These results are inconsistent with another EMA study among US adult heavy cannabis users who reported daily cannabis use for three months by using an Interactive Voice Response (i.e., phone call) system (Hughes et al., 2014). Results from this study indicated that weekend cannabis use was higher compared to weekdays (Hughes et al., 2014). Findings may have differed across these three studies due to differences in participant age or employment/student status. In Treolar Padovano and Miranda (2018), participant ages ranged from 15 – 24 years, and employment/student status was not reported; however, due to the inclusion of participants under 18 years in the US, it is presumed that many participants were in high school. In the current study, age ranged from 18-25 years, and most participants were college students (66.7%); whereas, in Hughes et al. (2014), the average participant age was 33 years, and 48% of participants were employed. These data may be an indication that those who are older in age (i.e., older than average US high school or college age) or who are employed may use cannabis more on the weekends compared to weekdays due to weekday obligations for which cannabis use may interfere negatively, such as employment (Macdonald et al., 2010). For those who are younger or are in high school or college, these data may be an indication that these groups have more flexibility or have fewer obligations for which cannabis use may interfere negatively. These findings highlight the importance of interventionists to consider the time that cannabis use occurs (i.e., days of week and times of day), targeted cannabis user age, and contexts of cannabis use (e.g., during work or school obligations).

Results from the current study indicated that the number of cannabis administration methods used was highest in the evenings, followed by mornings and afternoons. These results are novel; no previous studies have identified number of cannabis administration methods used across time of day. The pattern of more cannabis administration methods used during the evenings, followed by mornings and afternoons was consistent with the cannabis use frequency data from the current study. Although this specific finding is novel, results from the current study and previous research are consistent with previous literature in that use of multiple cannabis administration methods is common among young adult heavy cannabis users (Hughes et al., 2014; Rudy, 2018; Schauer et al., 2016). Further, previous studies have relied on cannabis use reports from the past 30 days wherein use of multiple cannabis administration methods were reported (Rudy, 2018; Schauer et al., 2016). However, the current study relied on past two-week reports, indicating that young adult heavy cannabis users may be performing more risky behaviors by using more cannabis administration methods in more concentrated time spans (i.e., use of multiple cannabis administration methods over two weeks compared to four weeks) than previously known. These findings showcase an immediate need to understand the safety of using numerous cannabis administration methods and the health implications of using multiple cannabis administration methods within shorter timeframes than previously identified.

Data from the current study suggest that cannabis use is highest in the morning, decreases in the afternoon, and increases again in the evening. Users reported more cannabis use in the mornings and evenings possibly due to acute withdrawal effects, including irritability and anxiety, experienced overnight and during the afternoons. The psychological effects of cannabis can last anywhere from 2-12 hours depending on the route of administration (i.e., oral vs. inhaled; Grotenhermen, 2003). After the psychological effects diminish, withdrawal symptoms begin. Over the course of the night, while cannabis users are sleeping, they likely begin experiencing acute withdrawal effects. Overnight withdrawal effects may explain the frequency of morning cannabis use observed in the current study. Cannabis users may continue to experience the psychological effects of their cannabis use throughout the morning into the afternoon. However, when evening time arrives, cannabis users may begin to experience withdrawal symptoms once more and use cannabis to avoid those symptoms.

Other novel results from the current study indicated that cannabis-related intoxication symptoms were highest in the evenings, followed by afternoons and mornings. These findings suggest that intoxication symptoms increased throughout the day; a pattern not studied previously in the literature. Interestingly, intoxication symptoms did not follow the same patterns associated with cannabis use frequency or number of cannabis administration methods used, which indicated the greatest intensity of use in the evenings, followed by mornings, and afternoons. Although all three outcomes were highest in the evenings, intoxication may have been lowest in the mornings due to intoxication effects diminishing while participants slept. The effect of sleep on intoxication is plausible because the average time for subjective cannabis drug effects to extinguish after inhaled cannabis administration is 8 hours (e.g., Spindle et al., 2018). In the current study, the baseline average number of hours spent sleeping was 7 hours (SD = 0.82), which explains the low reports of cannabis-related intoxication symptoms in the mornings. An increase in self-reported intoxication symptoms throughout the day has important implications. High intoxication in the evenings among heavy cannabis users could indicate that other risky behaviors, such as the use of other illicit substances or intoxicated driving, may also occur during the evenings in conjunction with cannabis use. The current study excluded those who reported past 30-day use of other illicit substances; however, future studies should seek to include groups who engage in high risk behaviors in order to understand how cannabis-related intoxication symptoms interact with the use of other illicit substances or other risky behaviors.

Results from the current study indicated that high frequency cannabis users reported significantly higher average intoxication symptoms compared to low frequency users; another finding that has not been reported in previous literature. Although these specific results have not been observed before, other forms of evidence indicate that self-reported cannabis intoxication symptoms are highest shortly after cannabis use (Spindle et al., 2018; Treloar Padovano & Miranda, 2018). Results from an EMA study of US young adult cannabis users who self-reported cannabis intoxication symptoms on a daily basis for one week indicated that intoxication was highest after cannabis use, but more fine-detailed assessments of intoxication by time of day or use frequency were not assessed or reported (Treloar Padovano & Miranda, 2018). Similarly, results from a clinical laboratory study in which US adult cannabis users were administered vaporized and smoked cannabis indicated that self-reported cannabis intoxication was highest immediately following cannabis administration (i.e., 10 minutes after drug administration) in both vaporized and smoked cannabis conditions compared to 0.5, 1, 1.5, 2, 3, 4, 5, 6, and 8 hours following drug administration (Spindle et al., 2018). In sum, previous literature indicates that cannabis intoxication is highest immediately following cannabis administration. Findings from previous studies contextualize the current results because high frequency cannabis users likely remain more intoxicated throughout the day due to less time between drug administrations compared to low frequency cannabis users who allow more time to pass between cannabis uses, resulting in lower average intoxication symptoms among this group.

Another novel finding from the current study was that among only those in the high frequency use group, combination cannabis administration method sub-group users (i.e., those who use any combination of cannabis administration methods excluding edibles) reported higher cannabis-related intoxication symptoms compared to the combusted-only cannabis administration method sub-group users (i.e., those who use only joints, blunts, pipes/bowls, and/or bongs). Although this result is exploratory and should be tested further, these findings are consistent with previous literature. Results from an online survey from 2014-2015 indicated that US adult cannabis users reported higher intoxication symptoms when using a vaporizer with cannabis compared to smoking cannabis (Lee et al., 2016). Similarly, US adult dab users from an online survey in 2014 reported higher intoxication symptoms from dabs compared to other cannabis administration methods (M. Loflin & Earleywine, 2014). These results should be further studied by measuring the intoxication effects from individual cannabis administration methods using behavioral measures, field sobriety tests, and biological measurements in controlled clinical laboratory settings. Another important component of understanding the relationship between cannabis use behavior and cannabis intoxication is measuring the THC content of used cannabis. As such, the accurate measurement of THC content of cannabis used by participants in their natural environment is essential to understand more fully patterns of cannabis use behavior and associated intoxication/impairment.

Respiratory scores did not significantly differ by day of week or time of day, as hypothesized. Although these results are surprising when compared to previous literature, the current findings are consistent with other results from the current study, given the lack of main effects by day of week on cannabis use frequency, number of cannabis administration methods used, or cannabis-related intoxication symptoms observed. However, due to the main effects of time of day observed in other results from the current study, an absence of a main effect of time of day on respiratory symptoms was unexpected. These findings were also surprising because previous literature indicates that cannabis users experience a higher incidence of negative respiratory symptoms as a result of their cannabis use (Aldington et al., 2007; Ribeiro & Ind, 2016). One potential reason for this disparity could be the chosen measures used to assess respiratory symptoms. The three questions used to measure respiratory symptoms were not specifically developed to understand cannabis-related respiratory symptoms, and the questions used in the current study evaluated symptom severity, instead of symptom frequency. At the time of study development and data collection, there were no available instruments that met our two most important needs: an instrument that 1) measured specifically acute cannabis-related respiratory symptoms and 2) contained few questions, which would be less burdensome for participants. The three respiratory symptom questions used here (i.e., severity of coughing/wheezing, throat irritation, and phlegm/chest mucus) originated from EMA studies related to understanding asthma symptoms (Everhart et al., 2010; Nazarian et al., 2006). These items were chosen based on their successful use in previous EMA studies (Everhart et al., 2010; Nazarian et al., 2006), their brevity, and the finding that these same symptoms (i.e., cough, phlegm production, and wheeze) had been reported previously among cannabis users over time (Ribeiro & Ind, 2016). However, a more comprehensive instrument with questions regarding severity and frequency of commonly reported negative respiratory symptoms from cannabis use (including cough, phlegm production, shortness of breath, throat irritation, and wheeze) may be needed for future studies. Further, these results highlight a need for the development of valid and reliable instruments, which measure specifically acute cannabis-related negative respiratory symptom severity and frequency in order to understand more fully the health effects of cannabis use.

It was hypothesized that those who used combusted cannabis administration methods at the highest frequencies would report the highest respiratory symptoms relative to the combination cannabis administration method sub-group. Results indicated that cannabis-related respiratory symptoms did not differ across cannabis administration method sub-group nor cannabis hits frequency sub-group. Although this finding is surprising, results from the current study indicated that cannabis-related respiratory symptoms were reported among our sample, albeit respiratory symptom severity was low (untransformed median = 1.00, actual range = 0 – 16, possible range = 0 – 18). As such, these data indicate that there was similar respiratory symptom severity among heavy cannabis users, regardless of use frequency and administration method (with the exception of edibles, which were not included in analyses for this study). To contextualize these results with other populations, an EMA study was conducted in 2006 in which people with asthma reported how bad their coughing and wheezing was during a 1-week period (Nazarian et al., 2006). Similar to the current study, the respiratory question scale ranged from 0 (not at all) to 6 (extremely). Results indicated that among adult asthma patients, the average respiratory score was 3.60 (SD = 3.59; Nazarian et al., 2006). In sum, results from the current study and from previous literature indicate that respiratory symptoms among cannabis users are relatively low. More research is needed to further contextualize the results from the current study. For example, future research should identify subjective respiratory symptoms of electronic cigarettes with and without nicotine and other inhaled substances, relative to cannabis-related respiratory symptoms.

There are several implications for the finding that heavy cannabis users reported some negative respiratory effects from using cannabis, regardless of the inhaled administration method and use frequency among this group. These results can be useful for cannabis interventionists, public health officials, and policymakers. For interventionists, these results indicate that heavy cannabis users (those who use greater than 5 days per week) exhibit some acute negative respiratory symptoms as a result of their cannabis use. Therefore, heavy cannabis users in particular may be a target group for cannabis cessation treatment, with the goal of diminishing the risk of negative respiratory effects from their cannabis use. Although future studies should examine whether light cannabis users (those who use cannabis less frequently than 5 days per week) report any respiratory symptoms as a result of their cannabis use. Interventionists would benefit from understanding which groups of cannabis users are most in need of their services. Current study results may serve as an impetus for public health officials to investigate the use of edibles as a potential harm reduction strategy, as this method of administration should have no negative respiratory effects due to the oral route of administration. However, more research is needed to understand fully the health risks associated with edible use (e.g., accidental consumption of more than intended [Barrus et al., 2016; Hudak, Severn, & Nordstrom, 2015 Lewis et al., 2020]). Another harm reduction strategy related to these findings for negative respiratory symptoms could involve the use financial incentives (e.g., discounts, price caps, etc.) to consumers to purchase or manufacturers/retailers to sell cannabis administration methods that do not cause respiratory harm, such as edibles. These incentives could be enforced at a local or state-level where cannabis sales are legal. Lastly, these results also warrant further investigation of other possible factors related to respiratory symptoms or respiratory health among cannabis users, including co-use of other inhaled products (e.g., cigarettes or nicotine vaping), cannabis forms (e.g., dried cannabis vs. concentrates), and other cannabis constituents (e.g., contaminants such as mold or other cannabinoids). Importantly, although the US Centers for Disease Control and Prevention identified that the cannabis concentrate additive, vitamin E acetate, was largely responsible for the EVALI outbreak in 2019, unanswered questions still remain regarding the potential negative effects of inhaling other cannabis concentrate additives on pulmonary health (Centers for Disease Control and Prevention, 2019).

There were several other unexpected findings from the current study including main effects of week and interactions of week by day of week. There was a main effect of week for respiratory symptoms, which were higher during week 1 compared to week 2 and a main effect of week for number of cannabis administration methods used, which shared a similar pattern (e.g., higher reports during week 1 compared to week 2). These results were unexpected and have not been reported or observed in previous literature. There is a possibility that these main effects of week may diminish if four weeks of EMA data were collected. This same explanation is applicable for the interactions of week by day of week observed in the current study. Across study results, there were interactions of week by day of week observed for cannabis use frequency, number of cannabis administration methods used, and cannabis-related intoxication symptoms. Among these three previous outcomes, two similar patterns emerged. There were higher reports of cannabis use frequency, number of cannabis administration methods used, and cannabis-related intoxication symptoms reported on Thursday of week 1 compared to week 2. There were also lower reports of cannabis use frequency, number of cannabis administration methods used, and cannabis-related intoxication symptoms reported on Sunday of week 1 compared to week 2. One possible reason for higher reports on Sunday of week 2 compared to week 1 is an over-reporting from participants on the final day of data collection. Higher reports at the end of the study compared to the beginning of the study also could be a result of multiple sources of bias. Subject bias is when, instead of research participants responding or acting in a true manner, the participants act or respond in a way that they think is helpful to the research goal (Lester, 1969; McCambridge, Kypri, & Elbourne, 2014). Another bias that may have affected study results is reactivity. As a result of being observed for the research study, participants may have altered their normal patterns of behavior in the second week due to the observations in the first week of data collection.

There were several limitations to the current study. One limitation to the current study was the geographical area where the study was conducted. The data was collected at one study site in the Mid-Atlantic US region, in a US state where cannabis was illegal to use recreationally but was permitted to use for limited medicinal purposes. As such, current study results may only represent a small sub-group of cannabis users. If the study were to have taken place in a legalized cannabis policy environment where different types of cannabis products and administration methods are easier to access, we may have recruited more cannabis users who exclusively used non-combusted administration methods, and we may have been able to conduct our intended analyses for Aim 2. Another limitation to the current study was the spread of the infectious virus, SARS-CoV-2 (COVID-19), during data collection. Data was collected over a two-month period from the end of January 2020 to the end of March 2020, and the first reported cases of COVID-19 in the geographic area occurred during early March. Therefore, COVID-19 could have affected 11 participants who were currently engaged in data collection during this time. Another limitation to the current study was that participants who used other illicit substances in the past 30 days were excluded from the study, and study results indicated that many users who were excluded were more dependent on cannabis, had used cannabis for a longer period of time, and were older than the sample included in the study. Therefore, the excluded group of participants was unique and warrants further examination. Future studies, which include participants who recently used other illicit substances, may reveal how other illicit substance and cannabis use patterns interact, as well as identify potential health risks related to the use of multiple substances. Another limitation to the current study was the inability to meet the intended sample size to detect day of week and time of day effects. There was sufficient power (0.90) to detect a moderate effect for time of day. However, there was insufficient power to detect a moderate effect for day of week (related to Aim 1); however, the use of a longer data collection period (e.g., four weeks) may offset the need for a larger sample size. Another limitation was the use of text message-based EMA, as opposed to other types of EMA, such as Interactive Voice Response or paper diaries. We encountered some problems with sending text messages to participants (e.g., technological issues and failed message deliveries). The use of text message-based EMA also limited our recruitment to participants who had cellular data capabilities on their cell phones. The inability to use the frequency of edible use data during analysis was another limitation. For the current study, cannabis use frequency was measured in hits, and edibles use frequency was quantified in number of edibles consumed. Hits frequency and number of edibles consumed are not synonymous measures. Hits are inhaled, whereas edibles are ingested. This difference in consumption would have affected the main outcomes of the study (i.e., respiratory and intoxication symptoms). Previous research indicates cannabis consumed orally is associated with delayed intoxication onset and stronger intoxication effects compared to inhaled cannabis (Schlienz et al., 2020; Spindle et al., 2018). As such, the choice was made to remove the frequency of edible use data from the current analyses. However, one way to examine cannabis edibles and inhaled administration methods and intoxication effects in the same study would be to gather samples of participants' cannabis products and test the samples for THC concentration. Understanding THC concentration across products would provide a common variable to compare with subjective intoxication effects associated with various cannabis use behaviors among cannabis users.

Conclusions

In sum, daily cannabis use patterns and related acute health effects are not well understood. Results from the current study indicated that cannabis use frequency, number of cannabis administration methods used, and intoxication symptoms were highest or most severe during the evenings, which has implications for cannabis interventionists. Intoxication symptoms were higher among high frequency combination administration method users compared to high frequency combusted administration method users. Future research should measure cannabis-related intoxication effects in different ways using biological and behavioral measures in clinical and natural settings. Finally, results indicated that cannabis-related respiratory symptoms were similar across heavy cannabis users, regardless of use frequency or administration method used. These results are informative for interventionists, public health officials, and policymakers. More research is needed to address gaps in knowledge regarding cannabis use behaviors and the effects on intoxication and respiratory symptoms.

References

Advokat, C. C., JE; Julien, RM. (2014). *Julien's primer of drug action: a comprehensive guide to the actions, uses, and side effects of psychoactive drugs* (13th ed.). New York: Worth Publishers.

Aldington, S., Williams, M., Nowitz, M., Weatherall, M., Pritchard, A., McNaughton, A., . . . Beasley, R. (2007). Effects of cannabis on pulmonary structure, function and symptoms. *Thorax*, *62*(12), 1058-1063. doi:10.1136/thx.2006.077081

Ameri, A. (1999). The effects of cannabinoids on the brain. *Prog Neurobiol, 58*(4), 315-348.

Anderson, R. P., & Zechar, K. (2019). Lung injury from inhaling butane hash oil mimics pneumonia. *Respir Med Case Rep, 26*, 171-173. doi:10.1016/j.rmcr.2019.01.002

APA, American Psychological Association. (2013). Substance-related and addictive disorders. Diagnositc and statistical manual of mental disorders (5th ed.). Washington, DC. doi: 10.1176/appi.books.9780890425596.dsm16

Arria, A. M., Caldeira, K. M., Bugbee, B. A., Vincent, K. B., & O'Grady, K. E. (2015). The academic consequences of marijuana use during college. *Psychol Addict Behav, 29*(3), 564-575. doi:10.1037/adb0000108

Asbridge, M., Duff, C., Marsh, D., & Erickson, P. (2014). Probelms with the identification of "problematic" cannabis use: Examining the issues of frequency, quantity, and drug use environment. *Eur Addict Res*, *10*(5), 243-267. doi:10.1159/000360697

Barrus, D. G., Capogrossi, K. L., Cates, S. C., Gourdet, C. K., Peiper, N. C., Novak, S. P., . . . Wiley, J. L. (2016). Tasty THC: Promises and Challenges of Cannabis Edibles. *Methods Rep RTI Press, 2016*. doi:10.3768/rtipress.2016.op.0035.1611

BehaveNet. (2016). Substance-Related Disorders. Retrieved from http://behavenet.com/substance-related-disorders

Bidwell, L. C., Mueller, R., YorkWilliams, S. L., Hagerty, S., Bryan, A. D., & Hutchison, K. E. (2018). A Novel Observational Method for Assessing Acute Responses to Cannabis: Preliminary Validation Using Legal Market Strains. *Cannabis Cannabinoid Res, 3*(1), 35-44. doi:10.1089/can.2017.0038

Bonar, E. E., Goldstick, J. E., Collins, R. L., Cranford, J. A., Cunningham, R. M., Chermack, S. T., . . . Walton, M. A. (2017). Daily associations between cannabis motives and consumption in emerging adults. *Drug Alcohol Depend, 178*, 136-142. doi:10.1016/j.drugalcdep.2017.05.006

Buckner, J. D., Heimberg, R. G., & Schmidt, N. B. (2011). Social anxiety and marijuana-related problems: the role of social avoidance. *Addict Behav, 36*(1-2), 129-132. doi:10.1016/j.addbeh.2010.08.015

Buckner, J. D., Zvolensky, M. J., Crosby, R. D., Wonderlich, S. A., Ecker, A. H., & Richter, A. (2015). Antecedents and consequences of cannabis use among racially diverse cannabis users: an analysis from Ecological Momentary Assessment. *Drug Alcohol Depend, 147*, 20-25. doi:10.1016/j.drugalcdep.2014.12.022

Buckner, J. D., Zvolensky, M. J., & Ecker, A. H. (2013). Cannabis use during a voluntary quit attempt: an analysis from ecological momentary assessment. *Drug Alcohol Depend, 132*(3), 610-616. doi:10.1016/j.drugalcdep.2013.04.013

Buckner, J. D., Zvolensky, M. J., Smits, J. A., Norton, P. J., Crosby, R. D., Wonderlich, S. A., & Schmidt, N. B. (2011). Anxiety sensitivity and marijuana use: an analysis from ecological momentary assessment. *Depress Anxiety, 28*(5), 420-426. doi:10.1002/da.20816

Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res*, *28*(2), 193-213.

Carlini, E. A., & Cunha, J. M. (1981). Hypnotic and antiepileptic effects of cannabidiol. *J Clin Pharmacol*, *21*(8-9 Suppl), 417S-427S.

Cavazos-Rehg, P. A., Krauss, M. J., Sowles, S. J., Floyd, G. M., Cahn, E. S., Chaitan, V. L., & Ponton, M. (2018). Leveraging user perspectives for insight into cannabis concentrates. *Am J Drug Alcohol Abuse*, *44*(6), 628-641. doi:10.1080/00952990.2018.1436179

CBHSQ, Center for Behavioral Health Statistics and Quality. (2018). *Results from the 2017 National Survey on Drug Use and Health: Detailed Tables*. Rockville, MD.

Centers for Disease Control and Prevention. (2019). Outbreak of lung injury associated with e-cigarette use, or vaping. Retrieved from https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html

Cerda, M., Wall, M., Feng, T., Keyes, K. M., Sarvet, A., Schulenberg, J., . . . Hasin, D. S. (2017). Association of State Recreational Marijuana Laws With Adolescent Marijuana Use. *JAMA Pediatr*, *171*(2), 142-149. doi:10.1001/jamapediatrics.2016.3624

Cerda, M., Wall, M., Keyes, K. M., Galea, S., & Hasin, D. (2012). Medical marijuana laws in 50 states: investigating the relationship between state legalization of medical marijuana and marijuana use, abuse and dependence. *Drug Alcohol Depend*, *120*(1-3), 22-27. doi:10.1016/j.drugalcdep.2011.06.011

Chandra, S., Radwan, M. M., Majumdar, C. G., Church, J. C., Freeman, T. P., & ElSohly, M. A. (2019). New trends in cannabis potency in USA and Europe during the last decade (2008-

2017). *Eur Arch Psychiatry Clin Neurosci, 269*(1), 5-15. doi:10.1007/s00406-019-00983-5

Cohn, A., Hagman, B. T., Moore, K., Mitchell, J., & Ehlke, S. (2014). Does negative affect mediate the relationship between daily PTSD symptoms and daily alcohol involvement in female rape victims? Evidence from 14 days of interactive voice response assessment. *Psychol Addict Behav, 28*(1), 114-126. doi:10.1037/a0035725

Collins, R. L., Kashdan, T. B., & Gollnisch, G. (2003). The feasibility of using cellular phones to collect ecological momentary assessment data: application to alcohol consumption. *Exp Clin Psychopharmacol, 11*(1), 73-78.

Corroon, J., & Kight, R. (2018). Regulatory Status of Cannabidiol in the United States: A Perspective. *Cannabis Cannabinoid Res, 3*(1), 190-194. doi:10.1089/can.2018.0030

Corroon, J., & Phillips, J. A. (2018). A Cross-Sectional Study of Cannabidiol Users. *Cannabis Cannabinoid Res, 3*(1), 152-161. doi:10.1089/can.2018.0006

Crean, R. D., Crane, N. A., & Mason, B. J. (2011). An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. *J Addict Med, 5*(1), 1-8. doi:10.1097/ADM.0b013e31820c23fa

Cuttler, C., & Spradlin, A. (2017). Measuring cannabis consumption: Psychometric properties of the Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory (DFAQ-CU). *PLoS One, 12*(5), e0178194. doi:10.1371/journal.pone.0178194

Daniulaityte, R., Lamy, F. R., Barratt, M., Nahhas, R. W., Martins, S. S., Boyer, E. W., . . . Carlson, R. G. (2017). Characterizing marijuana concentrate users: A web-based survey. *Drug Alcohol Depend, 178*, 399-407. doi:10.1016/j.drugalcdep.2017.05.034

Dilley, J. A., Richardson, S. M., Kilmer, B., Pacula, R. L., Segawa, M. B., & Cerda, M. (2019). Prevalence of Cannabis Use in Youths After Legalization in Washington State. *JAMA Pediatr, 173*(2), 192-193. doi:10.1001/jamapediatrics.2018.4458

Earleywine, M., & Barnwell, S. S. (2007). Decreased respiratory symptoms in cannabis users who vaporize. *Harm Reduct J, 4*, 11. doi:10.1186/1477-7517-4-11

El-Alfy, A. T., Ivey, K., Robinson, K., Ahmed, S., Radwan, M., Slade, D., . . . Ross, S. (2010). Antidepressant-like effect of delta9-tetrahydrocannabinol and other cannabinoids isolated from Cannabis sativa L. *Pharmacol Biochem Behav, 95*(4), 434-442. doi:10.1016/j.pbb.2010.03.004

ElSohly, M. A., Mehmedic, Z., Foster, S., Gon, C., Chandra, S., & Church, J. C. (2016). Changes in Cannabis Potency Over the Last 2 Decades (1995-2014): Analysis of Current Data in the United States. *Biol Psychiatry, 79*(7), 613-619. doi:10.1016/j.biopsych.2016.01.004

Emboden, W. (1974). Cannabis - a polytypic genus. *Economic Botany, 28*(304). doi:10.1007/BF02861427

Everhart, R. S., Smyth, J. M., Santuzzi, A. M., & Fiese, B. H. (2010). Validation of the Asthma Quality of Life Questionnaire with momentary assessments of symptoms and functional limitations in patient daily life. *Respir Care, 55*(4), 427-432.

Filbey, F., & Yezhuvath, U. (2013). Functional connectivity in inhibitory control networks and severity of cannabis use disorder. *Am J Drug Alcohol Abuse, 39*(6), 382-391. doi:10.3109/00952990.2013.841710

Franz, C. A., & Frishman, W. H. (2016). Marijuana Use and Cardiovascular Disease. *Cardiol Rev, 24*(4), 158-162. doi:10.1097/CRD.0000000000000103

Ganz, O., Johnson, A. L., Cohn, A. M., Rath, J., Horn, K., Vallone, D., & Villanti, A. C. (2018). Tobacco harm perceptions and use among sexual and gender minorities: findings from a national sample of young adults in the United States. *Addict Behav, 81*, 104-108. doi:10.1016/j.addbeh.2018.01.032

Gerberich, S. G., Sidney, S., Braun, B. L., Tekawa, I. S., Tolan, K. K., & Quesenberry, C. P. (2003). Marijuana use and injury events resulting in hospitalization. *Ann Epidemiol, 13*(4), 230-237.

Ghasemiesfe, M., Ravi, D., Vali, M., Korenstein, D., Arjomandi, M., Frank, J., . . . Keyhani, S. (2018). Marijuana Use, Respiratory Symptoms, and Pulmonary Function: A Systematic Review and Meta-analysis. *Ann Intern Med, 169*(2), 106-115. doi:10.7326/M18-0522

Green, B., Kavanagh, D., & Young, R. (2003). Being stoned: a review of self-reported cannabis effects. *Drug Alcohol Rev, 22*(4), 453-460. doi:10.1080/09595230310001613976

Grotenhermen, F. (2003). Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet, 42*(4), 327-360. doi:10.2165/00003088-200342040-00003

Hall, W., & Degenhardt, L. (2009). Adverse health effects of non-medical cannabis use. *Lancet, 374*(9698), 1383-1391. doi:10.1016/S0140-6736(09)61037-0

Hasin, D., AL, S., Cerda, M., Keyes, K., Galea, S., & Wall, M. (2017). *U.S. illicit cannabis use, cannabis use disorders, and medical marijuana laws, 1991-1991 to 2012-2013*. Paper presented at the Annual Meeting of the College on Problems of Drug Dependence, Montreal, Canada.

Hasin, D. S., Sarvet, A. L., Cerda, M., Keyes, K. M., Stohl, M., Galea, S., & Wall, M. M. (2017). US Adult Illicit Cannabis Use, Cannabis Use Disorder, and Medical Marijuana Laws:

1991-1992 to 2012-2013. *JAMA Psychiatry, 74*(6), 579-588. doi:10.1001/jamapsychiatry.2017.0724

Heishman, S. J., Huestis, M. A., Henningfield, J. E., & Cone, E. J. (1990). Acute and residual effects of marijuana: profiles of plasma THC levels, physiological, subjective, and performance measures. *Pharmacol Biochem Behav, 37*(3), 561-565. doi:10.1016/0091-3057(90)90028-g

Howden, M. L., & Naughton, M. T. (2011). Pulmonary effects of marijuana inhalation. *Expert Rev Respir Med, 5*(1), 87-92. doi:10.1586/ers.10.87

Hudak, M., Severn, D., & Nordstrom, K. (2015). Edible Cannabis-Induced Psychosis: Intoxication and Beyond. *Am J Psychiatry, 172*(9), 911-912. doi:10.1176/appi.ajp.2015.15030358

Hughes, J. R., Fingar, J. R., Budney, A. J., Naud, S., Helzer, J. E., & Callas, P. W. (2014). Marijuana use and intoxication among daily users: an intensive longitudinal study. *Addict Behav, 39*(10), 1464-1470. doi:10.1016/j.addbeh.2014.05.024

Hughes, J. R., Naud, S., Budney, A. J., Fingar, J. R., & Callas, P. W. (2016). Environmental cues and attempts to change in daily cannabis users: An intensive longitudinal study. *Drug Alcohol Depend*, *161*, 15-20. doi:10.1016/j.drugalcdep.2015.09.033

Jacobus, J., & Tapert, S. F. (2014). Effects of cannabis on the adolescent brain. *Curr Pharm Des, 20*(13), 2186-2193.

Karl, T., Garner, B., & Cheng, D. (2016). The therapeutic potential of the phytocannabinoid cannabidiol for Alzheimer's disease. *Behav Pharmacol*. doi:10.1097/FBP.0000000000000247

Kelly, B. C. (2005). Bongs and blunts: notes from a suburban marijuana subculture. *J Ethn Subst Abuse, 4*(3-4), 81-97. doi:10.1300/J233v04n03_04

Kwok, O. M., Underhill, A. T., Berry, J. W., Luo, W., Elliott, T. R., & Yoon, M. (2008). Analyzing Longitudinal Data with Multilevel Models: An Example with Individuals Living with Lower Extremity Intra-articular Fractures. *Rehabil Psychol, 53*(3), 370-386. doi:10.1037/a0012765

Lafaye, G., Karila, L., Blecha, L., & Benyamina, A. (2017). Cannabis, cannabinoids, and health. *Dialogues Clin Neurosci, 19*(3), 309-316.

Lariscy, J. T., Hummer, R. A., Rath, J. M., Villanti, A. C., Hayward, M. D., & Vallone, D. M. (2013). Race/Ethnicity, nativity, and tobacco use among US young adults: results from a nationally representative survey. *Nicotine Tob Res, 15*(8), 1417-1426. doi:10.1093/ntr/nts344

Lee, D. C., Crosier, B. S., Borodovsky, J. T., Sargent, J. D., & Budney, A. J. (2016). Online survey characterizing vaporizer use among cannabis users. *Drug Alcohol Depend, 159*, 227-233. doi:10.1016/j.drugalcdep.2015.12.020

Leo, A., Russo, E., & Elia, M. (2016). Cannabidiol and epilepsy: Rationale and therapeutic potential. *Pharmacol Res, 107*, 85-92. doi:10.1016/j.phrs.2016.03.005

Lester, D. (1969). The subject as a source of bias in psychological research. *J Gen Psychol, 81*(2d Half), 237-248. doi:10.1080/00221309.1969.9711289

Lewis, B., Fleeger, T., Judge, B., Riley, B., & Jones, J. S. (2020). Acute toxicity associated with cannabis edibles following decriminalization of marijuana in Michigan. *American Journal of Emergency Medicine, YAJEM-159447*.

Lippiello, P., Balestrini, S., Leo, A., Coppola, A., Citraro, R., Elia, M., . . . De Sarro, G. (2016). From cannabis to cannabidiol to treat epilepsy, where are we? *Curr Pharm Des*.

Loflin, M., & Earleywine, M. (2014). A new method of cannabis ingestion: the dangers of dabs? *Addict Behav, 39*(10), 1430-1433. doi:10.1016/j.addbeh.2014.05.013

Loflin, M. J. E., Earleywine, M., Farmer, S., Slavin, M., Luba, R., & Bonn-Miller, M. (2017). Placebo Effects of Edible Cannabis: Reported Intoxication Effects at a 30-Minute Delay. *J Psychoactive Drugs, 49*(5), 393-397. doi:10.1080/02791072.2017.1354409

Macdonald, S., Hall, W., Roman, P., Stockwell, T., Coghlan, M., & Nesvaag, S. (2010). Testing for cannabis in the work-place: a review of the evidence. *Addiction, 105*(3), 408-416. doi:10.1111/j.1360-0443.2009.02808.x

Malouff, J. M., Rooke, S. E., & Copeland, J. (2014). Experiences of marijuana-vaporizer users. *Subst Abus, 35*(2), 127-128. doi:10.1080/08897077.2013.823902

Marijuana Policy Project. (2019). Know the law. Retrieved from https://www.consumeresponsibly.org/law/

Martinasek, M. P., McGrogan, J. B., & Maysonet, A. (2016). A Systematic Review of the Respiratory Effects of Inhalational Marijuana. *Respir Care*. doi:10.4187/respcare.04846

Matsuda, L. A., Lolait, S. J., Brownstein, M. J., Young, A. C., & Bonner, T. I. (1990). Structure of a cannabinoid receptor and functional expression of the cloned cDNA. *Nature, 346*(6284), 561-564. doi:10.1038/346561a0

McCambridge, J., Kypri, K., & Elbourne, D. (2014). Research participation effects: a skeleton in the methodological cupboard. *J Clin Epidemiol, 67*(8), 845-849. doi:10.1016/j.jclinepi.2014.03.002

McMahon, M. J., Bhatt, N. A., Stahlmann, C. G., & Philip, A. I. (2016). Severe Pneumonitis after Inhalation of Butane Hash Oil. *Ann Am Thorac Soc, 13*(6), 991-992. doi:10.1513/AnnalsATS.201602-101LE

Mehl, M., & Conner, T. (Eds.). (2012). *Handbook of Research Methods for Studying Daily Life*. New York, NY: The Guildford Press.

Mehmedic, Z., Chandra, S., Slade, D., Denham, H., Foster, S., Patel, A. S., . . . ElSohly, M. A. (2010). Potency trends of Delta9-THC and other cannabinoids in confiscated cannabis preparations from 1993 to 2008. *J Forensic Sci, 55*(5), 1209-1217. doi:10.1111/j.1556-4029.2010.01441.x

Millar, S. A., Stone, N. L., Yates, A. S., & O'Sullivan, S. E. (2018). A Systematic Review on the Pharmacokinetics of Cannabidiol in Humans. *Front Pharmacol, 9*, 1365. doi:10.3389/fphar.2018.01365

Moir, D., Rickert, W. S., Levasseur, G., Larose, Y., Maertens, R., White, P., & Desjardins, S. (2008). A comparison of mainstream and sidestream marijuana and tobacco cigarette smoke produced under two machine smoking conditions. *Chem Res Toxicol, 21*(2), 494-502. doi:10.1021/tx700275p

Munro, S., Thomas, K. L., & Abu-Shaar, M. (1993). Molecular characterization of a peripheral receptor for cannabinoids. *Nature, 365*(6441), 61-65. doi:10.1038/365061a0

National Academies of Sciences, Engineering, and Medicine. (2017). *The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research*. Retrieved from Washington, DC: doi: 10.17226/24625.

National Center for Chronic Disease Prevention and Health Promotion, Center for Disease Control and Prevention. (2018). *Behavioral Risk Factor Surveillance System*. Retrieved from: https://www.cdc.gov/brfss/annual_data/annual_2017.html

National Conference of State Legislatures. (2018a, 12/14/2018). Marijuana Overview.

National Conference of State Legislatures. (2018b, 11/8/2018). State Medical Marijuana Laws. Retrieved from http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx

National Institute on Drug Abuse. (2012). Resource guide: Screening for drug use in general medical settings. Retrieved from https://www.drugabuse.gov/publications/resource-guide-screening-drug-use-in-general-medical-settings/nida-quick-screen

National Institute on Drug Abuse. (2012). The NIDA Quick Screen. *Resource Guide: Screening for Drug Use in General Medical Settings.* Retrieved from https://www.drugabuse.gov/publications/resource-guide-screening-drug-use-in-general-medical-settings/nida-quick-screen

National Institute on Drug Abuse Clincal Trials Network. (2015). NIDA CTN Common Data Elements. Retrieved 7/30/2019 https://cde.drugabuse.gov/

Nazarian, D., Smyth, J. M., & Sliwinski, M. J. (2006). A naturalistic study of ambulatory asthma severity and reported avoidant coping styles. *Chronic Illn, 2*(1), 51-58. doi:10.1177/17423953060020010101

Newmeyer, M. N., Swortwood, M. J., Barnes, A. J., Abulseoud, O. A., Scheidweiler, K. B., & Huestis, M. A. (2016). Free and Glucuronide Whole Blood Cannabinoids' Pharmacokinetics after Controlled Smoked, Vaporized, and Oral Cannabis Administration in Frequent and Occasional Cannabis Users: Identification of Recent Cannabis Intake. *Clin Chem, 62*(12), 1579-1592. doi:10.1373/clinchem.2016.263475

Nguyen, T., Li, J. X., Thomas, B. F., Wiley, J. L., Kenakin, T. P., & Zhang, Y. (2017). Allosteric Modulation: An Alternate Approach Targeting the Cannabinoid CB1 Receptor. *Med Res Rev, 37*(3), 441-474. doi:10.1002/med.21418

Niaura, R., Rich, I., Johnson, A. L., Villanti, A. C., Romberg, A. R., Hair, E. C., . . . Abrams, D. B. (2019). Young Adult Tobacco and E-cigarette Use Transitions: Examining Stability using Multi-State Modeling. *Nicotine Tob Res*. doi:10.1093/ntr/ntz030

Oomen, P. P., van Hell, H. H., & Bossong, M. G. (2018). The acute effects of cannabis on human executive function. *Behav Pharmacol, 29*(7), 605-616. doi:10.1097/FBP.0000000000000426

Patti, F., Messina, S., Solaro, C., Amato, M. P., Bergamaschi, R., Bonavita, S., . . . group, S. F. s. (2016). Efficacy and safety of cannabinoid oromucosal spray for multiple sclerosis spasticity. *J Neurol Neurosurg Psychiatry, 87*(9), 944-951. doi:10.1136/jnnp-2015-312591

Pew Research Center. (2015). Demographic Questions - Web or Mail Mode. Washington, DC: Pew Research Center.

Phillips, K. T., Phillips, M. M., Lalonde, T. L., & Prince, M. A. (2018). Does social context matter? An ecological momentary assessment study of marijuana use among college students. *Addict Behav*. doi:10.1016/j.addbeh.2018.01.004

Phillips, K. T., Phillips, M. M., Lalonde, T. L., & Tormohlen, K. N. (2015). Marijuana use, craving, and academic motivation and performance among college students: An in-the-moment study. *Addict Behav, 47*, 42-47. doi:10.1016/j.addbeh.2015.03.020

Phillips, M. M., Phillips, K. T., Lalonde, T. L., & Dykema, K. R. (2014). Feasibility of text messaging for ecological momentary assessment of marijuana use in college students. *Psychol Assess, 26*(3), 947-957. doi:10.1037/a0036612

Preston, K. L., Kowalczyk, W. J., Phillips, K. A., Jobes, M. L., Vahabzadeh, M., Lin, J. L., . . . Epstein, D. H. (2018). Exacerbated Craving in the Presence of Stress and Drug Cues in Drug-Dependent Patients. *Neuropsychopharmacology, 43*(4), 859-867. doi:10.1038/npp.2017.275

Prochaska, J. O., & Velicer, W. F. (1997). The transtheoretical model of health behavior change. *Am J Health Promot, 12*(1), 38-48. doi:10.4278/0890-1171-12.1.38

Raber, J. C., Elzinga, S., & Kaplan, C. (2015). Understanding dabs: contamination concerns of cannabis concentrates and cannabinoid transfer during the act of dabbing. *J Toxicol Sci, 40*(6), 797-803. doi:10.2131/jts.40.797

Rath, J. M., Villanti, A. C., Abrams, D. B., & Vallone, D. M. (2012). Patterns of tobacco use and dual use in US young adults: the missing link between youth prevention and adult cessation. *J Environ Public Health, 2012*, 679134. doi:10.1155/2012/679134

Ribeiro, L. I., & Ind, P. W. (2016). Effect of cannabis smoking on lung function and respiratory symptoms: a structured literature review. *NPJ Prim Care Respir Med, 26*, 16071. doi:10.1038/npjpcrm.2016.71

Rieder, S. A., Chauhan, A., Singh, U., Nagarkatti, M., & Nagarkatti, P. (2010). Cannabinoid-induced apoptosis in immune cells as a pathway to immunosuppression. *Immunobiology, 215*(8), 598-605. doi:10.1016/j.imbio.2009.04.001

Rivera-Olmos, V. M., & Parra-Bernal, M. C. (2016). [Cannabis: Effects in the Central Nervous System. Therapeutic, societal and legal consequences]. *Rev Med Inst Mex Seguro Soc, 54*(5), 626-634.

Rogeberg, O., & Elvik, R. (2016). The effects of cannabis intoxication on motor vehicle collision revisited and revised. *Addiction, 111*(8), 1348-1359. doi:10.1111/add.13347

Rudy, A. K. (2018). *A survey of cannabis consumption and implications of an experimental policy manipulation among young adults.* (Masters Thesis), Virginia Commonwealth University.

Rusby, J. C., Westling, E., Crowley, R., Mills, K. L., & Light, J. M. (2019). Associations between marijuana use and anxious mood lability during adolescence. *Addict Behav, 92*, 89-94. doi:10.1016/j.addbeh.2018.12.029

Russell, C., Rueda, S., Room, R., Tyndall, M., & Fischer, B. (2018). Routes of administration for cannabis use - basic prevalence and related health outcomes: A scoping review and synthesis. *Int J Drug Policy, 52*, 87-96. doi:10.1016/j.drugpo.2017.11.008

Russo, E. B., & Marcu, J. (2017). Cannabis Pharmacology: The Usual Suspects and a Few Promising Leads. *Adv Pharmacol, 80*, 67-134. doi:10.1016/bs.apha.2017.03.004

Sarvet, A. L., Wall, M. M., Keyes, K. M., Olfson, M., Cerda, M., & Hasin, D. S. (2018). Self-medication of mood and anxiety disorders with marijuana: Higher in states with medical marijuana laws. *Drug Alcohol Depend, 186*, 10-15. doi:10.1016/j.drugalcdep.2018.01.009

Sawler, J., Stout, J. M., Gardner, K. M., Hudson, D., Vidmar, J., Butler, L., . . . Myles, S. (2015). The Genetic Structure of Marijuana and Hemp. *PLoS One, 10*(8), e0133292. doi:10.1371/journal.pone.0133292

Schauer, G. L., King, B. A., Bunnell, R. E., Promoff, G., & McAfee, T. A. (2016). Toking, Vaping, and Eating for Health or Fun: Marijuana Use Patterns in Adults, U.S., 2014. *Am J Prev Med, 50*(1), 1-8. doi:10.1016/j.amepre.2015.05.027

Schlienz, N. J., Spindle, T. R., Cone, E. J., Herrmann, E. S., Bigelow, G. E., Mitchell, J. M., . . . Vandrey, R. (2020). Pharmacodynamic dose effects of oral cannabis ingestion in healthy adults who infrequently use cannabis. *Drug Alcohol Depend, 211*, 107969. doi:10.1016/j.drugalcdep.2020.107969

Schrot, R. J., & Hubbard, J. R. (2016). Cannabinoids: Medical implications. *Ann Med, 48*(3), 128-141. doi:10.3109/07853890.2016.1145794

Schulenberg, J., Johnston, L., O'Malley, P., Bachman, J., Miech, R. A., & Patrick, M. (2018). *Monitoring the Future national survey results on drug use, 1975-2017: Volume II, College students and adults ages 19-55*. Ann Arbor: Institute for Social Research: The University of Michigan Retrieved from http://www.monitoringthefuture.org//pubs/monographs/mtf-vol2_2017.pdf.

Schuster, R. M., Mermelstein, R. J., & Hedeker, D. (2016). Ecological momentary assessment of working memory under conditions of simultaneous marijuana and tobacco use. *Addiction, 111*(8), 1466-1476. doi:10.1111/add.13342

Schwope, D. M., Bosker, W. M., Ramaekers, J. G., Gorelick, D. A., & Huestis, M. A. (2012). Psychomotor performance, subjective and physiological effects and whole blood Delta(9)-tetrahydrocannabinol concentrations in heavy, chronic cannabis smokers following acute smoked cannabis. *J Anal Toxicol, 36*(6), 405-412. doi:10.1093/jat/bks044

Sewell, R. A., Poling, J., & Sofuoglu, M. (2009). The effect of cannabis compared with alcohol on driving. *Am J Addict, 18*(3), 185-193. doi:10.1080/10550490902786934

Sexton, M., Cuttler, C., Finnell, J. S., & Mischley, L. K. (2016). A Cross-Sectional Survey of Medical Cannabis Users: Patterns of Use and Perceived Efficacy. *Cannabis Cannabinoid Res, 1*(1), 131-138. doi:10.1089/can.2016.0007

Sharma, P., Murthy, P., & Bharath, M. M. (2012). Chemistry, metabolism, and toxicology of cannabis: clinical implications. *Iran J Psychiatry, 7*(4), 149-156.

Shiffman, S. (2009). Ecological momentary assessment (EMA) in studies of substance use. *Psychol Assess, 21*(4), 486-497. doi:10.1037/a0017074

Shrier, L. A., Walls, C. E., Kendall, A. D., & Blood, E. A. (2012). The context of desire to use marijuana: momentary assessment of young people who frequently use marijuana. *Psychol Addict Behav, 26*(4), 821-829. doi:10.1037/a0029197

Slavet, J. D., Stein, L. A., Colby, S. M., Barnett, N. P., Monti, P. M., Golembeske, C., Jr., & Lebeau-Craven, R. (2006). The Marijuana Ladder: measuring motivation to change marijuana use in incarcerated adolescents. *Drug Alcohol Depend, 83*(1), 42-48. doi:10.1016/j.drugalcdep.2005.10.007

Small, E., & Marcus, D. (2002). Hemp: A new crop with new uses for North America. In J. Janick & A. Whipkey (Eds.), *Trends in new crops and new uses* (pp. 284-326). Alexandria, VA: ASHS Press.

Spindle, T. R., Cone, E. J., Schlienz, N. J., Mitchell, J. M., Bigelow, G. E., Flegel, R., . . . Vandrey, R. (2018). Acute Effects of Smoked and Vaporized Cannabis in Healthy Adults Who Infrequently Use Cannabis: A Crossover Trial. *JAMA Netw Open, 1*(7), e184841. doi:10.1001/jamanetworkopen.2018.4841

Stogner, J. M., & Miller, B. L. (2015). The Dabbing Dilemma: A Call for Research on Butane Hash Oil and Other Alternate Forms of Cannabis Use. *Subst Abus, 36*(4), 393-395. doi:10.1080/08897077.2015.1071724

Tashkin, D. P., & Roth, M. D. (2019). Pulmonary effects of inhaled cannabis smoke. *Am J Drug Alcohol Abuse*, 1-14. doi:10.1080/00952990.2019.1627366

Testa, M., Wang, W., Derrick, J. L., Brown, W. C., & Collins, R. L. (2019). Does morning affect contribute to daily Cannabis use? *Addict Behav, 95*, 64-69. doi:10.1016/j.addbeh.2019.03.001

Tetrault, J. M., Crothers, K., Moore, B. A., Mehra, R., Concato, J., & Fiellin, D. A. (2007). Effects of marijuana smoking on pulmonary function and respiratory complications: a systematic review. *Arch Intern Med, 167*(3), 221-228. doi:10.1001/archinte.167.3.221

The National Organization for the Reform of Marijuana Laws. (2019). Virginia laws and penalties. *State Laws.* Retrieved from https://norml.org/laws/item/virginia-penalties-2

Treloar Padovano, H., & Miranda, R. (2018). Subjective cannabis effects as part of a developing disorder in adolescents and emerging adults. *J Abnorm Psychol, 127*(3), 282-293. doi:10.1037/abn0000342

U.S. Department of Health and Human Services. (2004). Marinol. (Vol. NDA 18-651/S-021). Rockville, MD. Retrieved from https://www.accessdata.fda.gov/drugsatfda_docs/label/2005/018651s021lbl.pdf

U.S. Department of Health and Human Services. (2014). *The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General*. Retrieved from Atlanta:

U.S. Food and Drug Administration. (2018). FDA approves first drug comprised of an active ingredient derived from marijuana to treat rare severe forms of epilepsy. U.S. Food and

Drug Administration Retrieved from https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-comprised-active-ingredient-derived-marijuana-treat-rare-severe-forms.

U.S. Food and Drug Administration. (2019a). FDA regulation of cannabis and cannabis-derived products: Questions and answers. Retrieved from https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-questions-and-answers#whatare

U.S. Food and Drug Administration. (2019b). Statement from FDA Commissioner Scott Gottlieb, M.D., on new steps to advance agency's continued evaluation of potential regulatory pathways for cannabis-containing and cannabis-derived products [Press release]. Retrieved from https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-new-steps-advance-agencys-continued-evaluation

Agriculture Improvement Act of 2018, S. 3042 C.F.R. (2018).

U.S. Substance Abuse and Mental Health Data Archive. (2019). National Survey on Drug Use and Health (NSDUH). Retrieved from https://www.datafiles.samhsa.gov/study-series/national-survey-drug-use-and-health-nsduh-nid13517

University of Michigan, Institute for Social Research. (2007). *Panel Study of Income Dynamics*.

Van Dam, N. T., & Earleywine, M. (2010). Pulmonary function in cannabis users: Support for a clinical trial of the vaporizer. *Int J Drug Policy, 21*(6), 511-513. doi:10.1016/j.drugpo.2010.04.001

van de Donk, T., Niesters, M., Kowal, M. A., Olofsen, E., Dahan, A., & van Velzen, M. (2019). An experimental randomized study on the analgesic effects of pharmaceutical-grade cannabis in chronic pain patients with fibromyalgia. *Pain, 160*(4), 860-869. doi:10.1097/j.pain.0000000000001464

van der Molen, T., Willemse, B. W., Schokker, S., ten Hacken, N. H., Postma, D. S., & Juniper, E. F. (2003). Development, validity and responsiveness of the Clinical COPD Questionnaire. *Health Qual Life Outcomes, 1*, 13.

Volkow, N. D., Baler, R. D., Compton, W. M., & Weiss, S. R. (2014). Adverse health effects of marijuana use. *N Engl J Med, 370*(23), 2219-2227. doi:10.1056/NEJMra1402309

Wachtel, S. R., ElSohly, M. A., Ross, S. A., Ambre, J., & de Wit, H. (2002). Comparison of the subjective effects of Delta(9)-tetrahydrocannabinol and marijuana in humans. *Psychopharmacology (Berl), 161*(4), 331-339. doi:10.1007/s00213-002-1033-2

Walden, N., & Earleywine, M. (2008). How high: quantity as a predictor of cannabis-related problems. *Harm Reduct J, 5*, 20. doi:10.1186/1477-7517-5-20

Wen, H., Hockenberry, J. M., & Cummings, J. R. (2015). The effect of medical marijuana laws on adolescent and adult use of marijuana, alcohol, and other substances. *J Health Econ, 42*, 64-80. doi:10.1016/j.jhealeco.2015.03.007

World Health Organization. (2018). *Cannabidiol: Critical Review Report*. Retrieved from Geneva: https://www.who.int/medicines/access/controlled-substances/CannabidiolCriticalReview.pdf

Youth Risk Behavior Survey Questionnaire. (2015). Retrieved from: www.cdc.gov/yrbs

Zalesky, A., Solowij, N., Yucel, M., Lubman, D. I., Takagi, M., Harding, I. H., . . . Seal, M. (2012). Effect of long-term cannabis use on axonal fibre connectivity. *Brain, 135*(Pt 7), 2245-2255. doi:10.1093/brain/aws136

Zeiger, J. S., Haberstick, B. C., Corley, R. P., Ehringer, M. A., Crowley, T. J., Hewitt, J. K., . . . Rhee, S. H. (2012). Subjective effects for alcohol, tobacco, and marijuana association with cross-drug outcomes. *Drug Alcohol Depend, 123 Suppl 1*, S52-58. doi:10.1016/j.drugalcdep.2012.02.014

Zhang, Z., Zheng, X., Zeng, D. D., & Leischow, S. J. (2016). Tracking Dabbing Using Search Query Surveillance: A Case Study in the United States. *J Med Internet Res, 18*(9), e252. doi:10.2196/jmir.5802

Appendix A. Aim 1 untransformed, transformed, and estimated marginal means and standard deviations or standard errors for Models 1-4.

		Model 1: Cannabis hits frequency			Model 2: Number of cannabis administration methods used		
		Untransformed M (SD)	Transformed M (SD)	Estimated marginal M (SE)	Untransformed M (SD)	Transformed M (SD)	Estimated marginal M (SE)
Time of day							
	Morning	3.52 (5.52)	1.25 (1.40)	1.26 (0.14)	0.63 (0.71)	0.56 (0.56)	0.56 (0.05)
	Afternoon	2.26 (3.86)	0.93 (1.18)	0.95 (0.14)	0.48 (0.58)	0.46 (0.52)	0.46 (0.05)
	Evening	3.62 (4.83)	1.41 (1.28)	1.42 (0.14)	0.71 (0.62)	0.66 (0.52)	0.66 (0.05)
Day of week							
	Monday	3.55 (5.23)	1.31 (1.36)	1.35 (0.16)	0.66 (0.66)	0.61 (0.54)	0.61 (0.06)
	Tuesday	2.57 (4.14)	1.05 (1.22)	1.07 (0.16)	0.57 (0.64)	0.53 (0.54)	0.53 (0.06)
	Wednesday	2.91 (4.56)	1.17 (1.25)	1.20 (0.16)	0.61 (0.62)	0.57 (0.54)	0.57 (0.06)
	Thursday	2.79 (4.19)	1.13 (1.23)	1.15 (0.16)	0.61 (0.67)	0.55 (0.55)	0.56 (0.06)
	Friday	3.13 (4.67)	1.21 (1.30)	1.25 (0.16)	0.59 (0.65)	0.55 (0.54)	0.57 (0.06)
	Saturday	3.81 (5.71)	1.34 (1.43)	1.33 (0.16)	0.64 (0.69)	0.58 (0.55)	0.58 (0.06)
	Sunday	3.02 (4.84)	1.14 (1.31)	1.11 (0.16)	0.54 (0.59)	0.52 (0.53)	0.51 (0.06)
Week							
	Week 1	3.20 (4.60)	1.25 (1.28)	1.26 (0.14)	0.64 (0.64)	0.59 (0.54)	0.59 (0.05)
	Week 2	3.02 (5.00)	1.13 (1.32)	1.16 (0.14)	0.57 (0.65)	0.52 (0.54)	0.53 (0.05)
Day of week X week							
Week 1	Monday	4.34 (6.00)	1.51 (1.44)	1.56 (0.18)	0.76 (0.70)	0.68 (0.55)	0.68 (0.07)
	Tuesday	2.54 (3.14)	1.15 (1.11)	1.18 (0.18)	0.69 (0.69)	0.62 (0.56)	0.62 (0.07)
	Wednesday	3.05 (4.43)	1.25 (1.23)	1.27 (0.18)	0.68 (0.65)	0.62 (0.55)	0.62 (0.07)
	Thursday	3.31 (4.26)	1.33 (1.25)	1.35 (0.18)	0.71 (0.66)	0.65 (0.54)	0.65 (0.07)
	Friday	3.01 (4.03)	1.23 (1.23)	1.25 (0.18)	0.60 (0.59)	0.57 (0.53)	0.57 (0.07)
	Saturday	3.69 (5.37)	1.33 (1.40)	1.31 (0.18)	0.61 (0.62)	0.57 (0.54)	0.56 (0.07)
	Sunday	2.51 (4.39)	0.95 (1.28)	0.91 (0.18)	0.44 (0.55)	0.42 (0.51)	0.41 (0.07)
Week 2	Monday	2.81 (4.28)	1.12 (1.26)	1.14 (0.18)	0.57 (0.62)	0.54 (0.53)	0.54 (0.07)
	Tuesday	2.61 (4.96)	0.95 (1.31)	0.96 (0.18)	0.45 (0.55)	0.43 (0.51)	0.43 (0.07)
	Wednesday	2.76 (4.73)	1.08 (1.27)	1.13 (0.18)	0.53 (0.58)	0.51 (0.53)	0.52 (0.07)
	Thursday	2.25 (4.06)	0.92 (1.20)	0.95 (0.19)	0.51 (0.67)	0.46 (0.55)	0.46 (0.07)
	Friday	3.26 (5.31)	1.18 (1.37)	1.26 (0.19)	0.59 (0.71)	0.53 (0.56)	0.56 (0.07)
	Saturday	3.93 (6.06)	1.35 (1.46)	1.36 (0.18)	0.67 (0.76)	0.59 (0.58)	0.59 (0.07)
	Sunday	3.52 (5.23)	1.33 (1.33)	1.32 (0.18)	0.64 (0.61)	0.61 (0.52)	0.60 (0.07)

Appendix A (continued). Aim 1 untransformed, transformed, and estimated marginal means and standard deviations or standard errors for Models 1-4.

		Model 3: Intoxication scores			Model 4: Respiratory scores		
		Untransformed M (SD)	Transformed M (SD)	Estimated marginal M (SE)	Untransformed M (SD)	Transformed M (SD)	Estimated marginal M (SE)
Time of day							
	Morning	0.89 (1.63)	0.49 (0.81)	0.50 (0.09)	2.22 (3.15)	1.03 (1.08)	1.03 (0.15)
	Afternoon	1.28 (1.88)	0.69 (0.89)	0.70 (0.09)	1.87 (2.77)	0.91 (1.02)	0.92 (0.15)
	Evening	2.10 (2.26)	1.06 (1.00)	1.06 (0.09)	2.09 (2.89)	1.00 (1.04)	1.02 (0.15)
Day of week							
	Monday	1.27 (1.80)	0.71 (0.88)	0.72 (0.10)	2.05 (2.86)	1.01 (1.02)	1.02 (0.15)
	Tuesday	1.44 (2.16)	0.72 (0.96)	0.72 (0.10)	2.12 (2.98)	1.02 (1.05)	1.03 (0.16)
	Wednesday	1.53 (2.11)	0.79 (0.96)	0.79 (0.10)	2.13 (2.91)	1.02 (1.05)	1.04 (0.15)
	Thursday	1.32 (1.84)	0.72 (0.90)	0.72 (0.11)	2.04 (2.85)	0.99 (1.03)	1.02 (0.16)
	Friday	1.69 (2.16)	0.87 (0.97)	0.88 (0.11)	2.17 (3.10)	1.01 (1.07)	1.00 (0.16)
	Saturday	1.45 (2.04)	0.76 (0.94)	0.75 (0.11)	2.20 (3.19)	0.99 (1.11)	0.97 (0.16)
	Sunday	1.31 (1.92)	0.71 (0.91)	0.69 (0.11)	1.65 (2.66)	0.81 (1.00)	0.82 (0.16)
Week							
	Week 1	1.46 (2.03)	0.77 (0.93)	0.77 (0.09)	2.12 (2.70)	1.06 (1.00)	1.07 (0.15)
	Week 2	1.40 (2.00)	0.74 (0.93)	0.74 (0.09)	1.98 (3.16)	0.89 (1.09)	0.91 (0.15)
Day of week X week							
Week 1	Monday	1.16 (1.61)	0.69 (0.84)	0.71 (0.12)	2.18 (2.76)	1.11 (0.98)	1.12 (0.17)
	Tuesday	1.47 (2.01)	0.77 (0.94)	0.77 (0.12)	2.27 (2.67)	1.13 (1.00)	1.16 (0.17)
	Wednesday	1.49 (2.17)	0.75 (0.97)	0.76 (0.12)	2.05 (2.43)	1.05 (0.98)	1.06 (0.17)
	Thursday	1.63 (1.91)	0.89 (0.93)	0.88 (0.13)	2.45 (2.76)	1.22 (0.98)	1.24 (0.17)
	Friday	1.87 (2.26)	0.95 (0.99)	0.96 (0.12)	2.26 (2.94)	1.10 (1.03)	1.09 (0.17)
	Saturday	1.52 (2.21)	0.78 (0.96)	0.75 (0.12)	2.01 (2.75)	1.01 (1.01)	1.01 (0.17)
	Sunday	1.07 (1.89)	0.55 (0.88)	0.54 (0.12)	1.65 (2.60)	0.82 (0.99)	0.79 (0.17)
Week 2	Monday	1.38 (1.97)	0.72 (0.93)	0.73 (0.12)	1.92 (2.95)	0.92 (1.05)	0.93 (0.17)
	Tuesday	1.41 (2.31)	0.67 (0.99)	0.66 (0.12)	1.97 (3.28)	0.90 (1.09)	0.89 (0.17)
	Wednesday	1.58 (2.05)	0.84 (0.94)	0.83 (0.12)	2.22 (3.36)	0.98 (1.13)	1.03 (0.17)
	Thursday	1.01 (1.73)	0.55 (0.85)	0.56 (0.13)	1.61 (2.90)	0.76 (1.03)	0.81 (0.17)
	Friday	1.49 (2.04)	0.77 (0.95)	0.80 (0.13)	2.07 (3.28)	0.92 (1.12)	0.91 (0.17)
	Saturday	1.38 (1.87)	0.75 (0.92)	0.75 (0.12)	2.40 (3.61)	0.98 (1.21)	0.93 (0.17)
	Sunday	1.55 (1.93)	0.86 (0.91)	0.84 (0.12)	1.65 (2.74)	0.80 (1.01)	0.85 (0.17)

Note: “M” indicates mean, “SD” indicates standard deviation, and “SE” indicates standard error.

ALYSSA RUDY

Department of Psychology
Virginia Commonwealth University

Personal

Home address: 4944 Benzie Highway, Benzonia, MI 49616
Telephone: 262-353-1583
Email: rudya@vcu.edu

Education

Ph.D. — Degree in Psychology, Anticipated December 2020
Virginia Commonwealth University, Richmond, VA, USA
Dissertation: Characterizing patterns of cannabis use and related health effects among young adults using ecological momentary assessment
Dissertation Chair: Caroline O. Cobb, Ph.D.

M.S. — Degree in Health Psychology, Awarded May 2018
Virginia Commonwealth University, Richmond, VA, USA
Thesis: A survey of cannabis consumption and implications of an experimental policy manipulation among young adults
Thesis Chair: Caroline O. Cobb, Ph.D.

B.S. — Degree in Psychology and Spanish, Awarded May 2014, *Magna Cum Laude*
University of Wisconsin – Whitewater, Whitewater, WI, USA

Research Experience

Research Assistant — Center for the Study of Tobacco Products – U54, Virginia Commonwealth University
Supervisors: Alison Breland, Ph.D.; Caroline O. Cobb, Ph.D.
Focus: Impact analysis of regulatory policies on electronic cigarette products as well as a population level assessment of electronic cigarette regulatory policies.
Duties: Study coordination, data management, study recruitment and participant retention, IRB application coordination/compliance, communication/coordination between study personnel.
Dates of employment: January 2019-Present

Research Assistant — Virginia Foundation for Healthy Youth/Behavioral Health Research Laboratory, Virginia Commonwealth University
Supervisors: Caroline O. Cobb, Ph.D.; Andrew J. Barnes, Ph.D.
Focus: Content analysis and experimental cross-sectional survey regarding electronic cigarette advertisements' effects on youth susceptibility to and intentions to use tobacco products; clinical laboratory evaluation of e-cigarette flavors and nicotine content
Duties: IRB application coordination/compliance, instrument development and implementation, data quality management, research staff training, communication/coordination between study personnel, abstract and manuscript preparation/submission; data collection; participant recruitment and enrollment
Dates of employment: August 2015-August 2018

Research Assistant — Center for the Study of Tobacco Products – Project 3: Randomized Controlled Clinical Trial, Virginia Commonwealth University
Supervisor: Caroline Cobb, Ph.D.
Focus: Effects of novel tobacco products on toxicant exposure, disease

risk, adverse events, and use of other tobacco products.
Duties: participant recruitment and enrollment/randomization, on-site data collection, data input.
Dates of employment: June 2017-August 2017; June 2018-August 2018

Research Assistant University of Wisconsin – Whitewater
Supervisor: Michael Oldani, Ph.D.
Focus: Anthropological analysis of a pilot mental health court.
Duties: conducted historical analyses, literature reviews, annotation of court proceedings.
Dates of employment: May 2014-August 2015

Research Assistant American Lung Association
Supervisor: Katie Halverson
Focus: Promoting smoke-free campuses across the University of Wisconsin System.
Duties: completed IRB forms, established/maintained transdisciplinary communication between study personnel
Dates of employment: February 2014-August 2015

Research Assistant University of Wisconsin – Whitewater
Supervisor: Sasha Karnes, Ph.D.
Focus: Effects of online Motivational Interviewing modules on weight loss.
Duties: conducted literature reviews, built online modules, completed IRB forms.
Dates of employment: January 2014-August 2015

Research Interests

General: Cannabis use patterns and health effects, tobacco control and prevention, and tobacco and cannabis policy
Specific: Cannabis methods of administration, respiratory and intoxication effects. Alternative tobacco products (little cigars, electronic cigarettes), trends in tobacco use prevalence.

Grant Applications

F31 Ruth L. Kirschstein National Research Service Award (NRSA) Individual
Dates: August 2018
Project Title: “Characterizing patterns of cannabis use and related health effects among young adults using ecological momentary assessment”
Role: PI
Total Costs: $31,310.00
Status: Not Funded

F31 Ruth L. Kirschstein National Research Service Award (NRSA) Individual (Resubmission)
Dates: April 2019
Project Title: “Characterizing patterns of cannabis use and related health effects among young adults using ecological momentary assessment”
Role: PI
Total Costs: $31,310.00
Status: Not Funded

Administrative and Revision Supplements to Expand Vaping Research and Understand EVALI (NOT-HL-19-724)
Dates: February 2020
Project Title: “Respiratory Effects of THC and Nicotine E-Cigarettes: A Prospective Study”
Role: Research Assistant, Co-Author
Status: Funded

Publications (N=14)

Hoetger, C., Wall, C.S.J., Braxton, D., Cogley, J., Khan, M., Sey, S., Bhatt, S., **Rudy, A.K.**, Barnes, A.J., & Cobb, C.O. (2020). TV and online electronic cigarette video advertising: Thematic content and spend characteristics. *Journal of Public Health.* In press.

Cobb, C.O., Lester, R., **Rudy, A.K.**, Hoetger, C., Scott, M.A., Austin, M., Graham, A.L., Lipato, T., Montpetit, A., & Eissenberg, T. (2020). Behavior and toxicant exposure associated with dual use of cigarettes and electronic cigarettes. *Experimental and Clinical Psychopharmacology*. In press.

Nicksic, N.E., Bono, R.S., **Rudy, A.K.**, Cobb, C.O., & Barnes, A.J. (2020). Smoking status and racial/ethnic disparities in youth exposure to tobacco advertising. *Journal of Ethnicity in Substance Abuse,* doi: 10.1080/15332640.2020.1815113

Hardesty, J.J., Li, K.A., Cohen, J.E., Kennedy, R.D., Breland, A.B., **Rudy, A.K.,** & Eissenberg, T.E. A deceptive marketing strategy: An early warning of industry behavior after the premarket tobacco application deadline? *Nicotine and Tobacco Research*. In press.

Barnes, A.J., Bono, R.S., **Rudy, A.K.,** Hoetger, C. Nicksic, N.E., & Cobb, C.O. Effect of e-cigarette advertisement themes on hypothetical e-cigarette purchasing in price-responsive adolescents. *Addiction*, in press. doi: 10.1111/add.15084.

Eissenberg, T., Soule, E., Shihadeh, A., & the **CSTP Nicotine Flux Work Group**. 'Open-System' electronic cigarettes cannot be regulated effectively. *Tobacco Control, 2020 Mar 17: tobaccocontrol-2019-055499.* doi: 10.1136/tobaccocontrol-2019-055499.

Rudy, A.K., Nicksic, N.E., Morlett-Paredes, A., Barnes, A.J., & Cobb, C.O. (2019). Electronic cigarette print and online advertisements: Content characteristics, and marketing strategies by brand and media source. *Tobacco Regulatory Science.* In press.

Rudy, A.K., Barnes, A.J., Cobb, C.O., & Nicksic, N.E. (2019). Attitudes about and correlates of cannabis legalization policy among U.S. young adults. *Journal of American College Health.* In press. doi: 10.1080/07448481.2020.1713135

Cobb, C.O., Lopez, A.A., Soule, E.K., Yen, M.S., Rumsey, H.E., Lester-Scholtes, R., **Rudy, A.K.,** Lipato, T., Guy, M.C., & Eissenberg, T. (2019). Influence of electronic cigarette liquid flavors and nicotine content on subjective measures of abuse liability. *Drug and Alcohol Dependence, 203*, 27-34. doi: 10.1016/j.drugalcdep.2019.05.024.

Cobb, C.O., Soule, E.K., **Rudy, A.K.**, & Cohn, A.M. (2018). Patterns and correlates of tobacco and cannabis co-use by tobacco product type: Findings from the Virginia Youth Survey. *Substance Use and Misuse, 53*(14), 2310-2319*.* doi: 10.1080/10826084.2018/1473437

Sutter, M.E., Everhart, R.S., Miadich, S., **Rudy, A.K**., Nasim, A., & Cobb, C.O. (2018). Patterns and profiles of adolescent tobacco users: Results from the Virginia Youth Survey. *Nicotine and Tobacco Research, 1-9.* doi: 10.1093/ntr/nty032.

Rudy, A.K., Leventhal, A.M., Goldenson, N.I., & Eissenberg, T. (2017). Assessing electronic cigarette effects and regulatory impact: Challenges with user self-reported device power. *Drug and Alcohol Dependence, 179*, 337-340. doi: 10.1016/j.drugalcdep.2017.07.031

Nicksic, N.E., Snell, L.M., **Rudy, A.K.**, Cobb, C.O., & Barnes, A.J. (2017). Tobacco marketing, e-cigarette susceptibility, and perceptions among adults. *American Journal of Health Behaviors, 41*(5), 579-590. doi: 10.5993/AJHB.41.5.7

Soule, E.K., Maloney, S.F., Spindle, T.R., **Rudy, A.K.,** Hiler, M.M., & Cobb, C.O. (2016). Electronic cigarette use and indoor air quality in a natural setting. *Tobacco Control, 26*(1), 109-112*.* doi: 10.1136/tobaccocontrol-2015-052772

Manuscripts Under Review/Preparation (N=1)

Rudy, A.K., Cohn, A.M., & Cobb, C.O. Cannabis consumption and administration methods among young adults: A latent class analysis. In preparation.

Oral Presentations

Invited Speaker – Social Psychology, 4/19/2018

Invited Speaker – Center for the Study of Tobacco Products Scientific Seminar, 12/7/2017

Awards/Honors

University of Wisconsin - Whitewater Dean's List (3.5 or higher GPA); 2010 – 2014

VCU Psychology Department Conference Travel Award; 2015-2019

VCU Graduate School's Outstanding Master's Thesis Award; 2018

University Service

Capstone Project Judge for History of Psychology 2015-2018

Participated in "Building Community through Intra-Departmental Dialogues"; 2016-2017

Participated in a promotional video for the Health Psychology graduate program; Spring 2017

Coordinated the Health Psychology Colloquium 2018-2019

Student Representative on a Promotion and Tenure Committee in the VCU Psychology department, 2019

Teaching Experience

Adjunct Faculty — Virginia Commonwealth University, Richmond, VA, USA
- PSYC-317 Research Methods, Summer 2019

Teaching Assistant — Virginia Commonwealth University, Richmond, VA, USA
- PSYC-451 History of Psychology, Spring 2016
- PSYC-317 Research Methods, Fall 2018
- PSYC-317 Research Methods, Spring 2019

Relevant Coursework — Virginia Commonwealth University, Richmond, VA, USA
- Teaching Practicum, PSYC-795, Spring 2018

Undergraduate Mentorship — Virginia Commonwealth University, Richmond, VA, USA
- Destini Braxton, Fall 2016-Spring 2017
- Jacquelyn Cogley, Fall 2016-Spring 2017
- Rafa Khan, Fall 2017-Spring 2018
- Marwa Eltaib, Fall 2017-Spring 2018
- Michaela Blankenship, Fall 2017- Spring 2019
- Joshua Hackney, Spring 2019
- Savannah Cook, Summer 2019-Spring 2020
- Sohee Ha, Spring 2020
- Cindy Miranda, Spring 2020

Association Memberships

American Psychological Association (APA); APA Division 28: Psychopharmacology & Substance Abuse; 2017-present
American Psychological Association (APA); APA Division 38: Health Psychology; 2017-present
Society for Research on Nicotine and Tobacco (SRNT); 2015-present
  SRNT Adolescent Network – Communications Subcommittee; 2017-2019
National Center for Faculty Development & Diversity; 2017-present
CSTP Nicotine Flux Work Group; Center for the Study of Tobacco Products; 2019-present

Professional Service

Ad Hoc Reviewer: *American Journal of Preventive Medicine*

Reviewer: *Journal of Adolescent Health*

Drug and Alcohol Dependence