Posttraumatic Stress Disorder and Cannabis Use:

An In-Depth Examination of a Nationally Representative Sample

by

Jessa M. Hogarth

University of Manitoba

This thesis was submitted to the Faculty of Graduate Studies at the University of Manitoba

In partial fulfillment of the requirements of the degree of

DOCTOR OF PHILOSOPHY

Department of Psychology, University of Manitoba, Winnipeg

Abstract

Cannabis is among the top substances used by individuals with PTSD. Research regarding the effects of cannabis use on PTSD symptomatology is largely contradictory and unclear, claiming both the improvement and worsening of PTSD symptoms concurrently. Furthermore, cannabis use disorder (CUD) is increasing in prevalence, due to recent legalization of recreational cannabis use across much of North America. To date, relatively little is known about correlates of comorbid PTSD and CUD (PTSD-CUD), as well as the impact of comorbid PTSD-CUD on various areas of mental health functioning. Individuals with PTSD routinely experience barriers to acceptable and effective treatment, which may be further exacerbated by the co-occurrence of CUD. Three distinct research studies utilized a nationally representative sample of adult civilians (≥18 years) collected during the National Epidemiologic Survey on Alcohol and Related Conditions III (NESARC-III; N = 36,309) in 2012-2013. The aims of the proposed project were threefold: (1) to examine the sociodemographic profile of individuals with PTSD-CUD, (2) to identify distinct cannabis use profiles among individuals with PTSD, and (3) to examine rates of mental healthcare utilization among individuals with PTSD who use cannabis. This nationally representative sample provides the opportunity to examine the complex relationships between PTSD and cannabis use in comprehensive detail. Comorbid PTSD-CUD represents an increasingly frequent disorder combination that appears to impact treatment course and outcome. Improved understanding regarding the relations between PTSD and cannabis use is fundamental to reduce disorder durations, resolve healthcare disparities, and improve treatment interventions for this complex population.

Keywords: Posttraumatic Stress Disorder, PTSD, Cannabis Use Disorder, Cannabis, Marijuana, Mental Healthcare Utilization, Latent Mixture Model, Mental Health Comorbidities.

Acknowledgements

This manuscript was completed under the supervision of my advisors Dr. Matthew Keough and Dr. Natalie Mota, in partial fulfillment of the requirements for the degree of Doctorate in Philosophy at the University of Manitoba. I would like to sincerely thank my advisors for their collaboration, patience, and countless hours of assistance in completing this dissertation research. Your support as well as your clinical expertise have been truly invaluable, and I am truly humbled and grateful that I had the opportunity to work with and learn from you both. Special thanks to Dr. Kristin Reynolds, Dr. Pamela Holens, and Dr. Christopher Fries for their gracious dedication, support, patience, and valuable contributions as members of my thesis committee. Further appreciation to the Department of Psychology Graduate Fellowship, as well as the Liquor, Gaming and Cannabis Association of Manitoba for funding and supporting this dissertation research.

I would also like to express my gratitude and indebtedness to my parents, Sara and James Hogarth, for both supporting me and pushing me (rather insistently) to pursue academia when I had no interest in it myself. Further appreciation to my maternal grandparents, Paul and Doreen Bromley, as well as my paternal grandparents, Jaqueline and Jim Glen, who supported me financially and encouraged me to continue in my studies throughout all these years. I would not have gotten here without any of you.

Contribution of Authors

I, Ms. Jessa Hogarth, am the primary author for studies 1, 2, and 3, as well as the introductory and discussion chapters. In working collaboratively with my co-advisors, Dr. Natalie Mota and Dr. Matt Keough, I was responsible for study design and hypothesis formation, literature review, ethics and data access submissions, data cleaning and preparation, primary and secondary data analyses, and manuscript preparation. The final written document is entirely my own written work. My co-advisors provided me with valuable input into data procurement, study design and analyses, as well as written edits on the dissertation document throughout the research process. My committee members, Dr. Kristin Reynolds, Dr. Pamela Holens, and Dr. Christopher Fries, also provided feedback on the completed document. This work was partially supported by the Liquor, Gaming and Cannabis Authority Graduate Scholarship, as well as the University of Manitoba James Gordon Fletcher Research Award.

Table of Contents

List of Tables

Chapter One: Introduction

Posttraumatic Stress Disorder

The concept of trauma is rooted in the Greek word for “injury” or “wound” (Ford & Gomez, 2015). Our understanding of trauma has evolved over time, transitioning from referring solely to physical injury to encompassing psychological injury, as well. Ford and colleagues emphasize that the key difference between physical and psychological traumas lies not in differing etiology, but rather the addition of stress to an individuals’ psychological processing. Traumatic stress, therefore, is highly pertinent to the topic of psychological trauma.

Posttraumatic stress disorder (PTSD) is a debilitating mental health condition that involves distressing symptoms following exposure to a traumatic event. Posttraumatic stress disorder was introduced in 1980 as a mental health disorder in the *Diagnostic and Statistical Manual of Mental Disorders Third Edition* (*DSM–III*; American Psychiatric Association, 1980), and diagnostically has continued to evolve with notable revisions in each subsequent edition of the *DSM*. Previously classified as an anxiety disorder in *DSM-IV* (American Psychiatric Association, 1994), PTSD was transitioned into the newly formed category of "trauma and stressor related disorders" in *DSM-5* (American Psychiatric Association, 2013). All 17 symptoms of PTSD from *DSM-IV* were maintained in *DSM-5*, with the addition of three new symptom criteria and phrasing of criteria reworked. The categorical transition of PTSD in *DSM-5* attempted to address criticisms of PTSD primarily characterized as an anxiety disorder. Many of the symptoms experienced by individuals with PTSD extend beyond symptoms of anxiety disorders, such as guilt, shame, and anger (Pai et al., 2017; Phillips, 2015). Furthermore, many of the symptoms experienced as sequelae of traumatic exposure were not previously included in the diagnostic criteria in *DSM-IV* (Friedman et al., 2014). As such, modifications in categorization and

symptom criterion in *DSM-5* attempt to address more comprehensively the symptoms of traumatic stress experienced by individuals with PTSD.

In *DSM-5*, PTSD is now comprised of eight diagnostic criteria following "exposure to actual or threatened death, serious injury, or sexual violence" through direct experiencing, witnessing, or second-hand experiencing with a family member, close friend, or graphic exposure (Criterion A; Appendix A; American Psychiatric Association, 2013). Criterion B through E represent further specificity of disorder symptomatology, including intrusive symptoms (e.g., distressing memories, dissociation), avoidance symptoms (e.g., avoiding memories, thoughts, or external reminders of the trauma), negative alterations in cognitions and mood (e.g., persistent distorted cognitions and negative emotional state), as well as alterations in arousal or reactivity (e.g., irritability, hypervigilance, recklessness; American Psychiatric Association, 2013). Remaining criterion F-H echo other *DSM-5* categories, specifying symptoms that last for at least one month, cause significant impairment in one or more areas, and are not attributable to substance use or other medical conditions (Appendix A; American Psychiatric Association, 2013).

There are several inherent complexities unique to PTSD in *DSM*-5. First, the diagnostic criterion for PTSD is lengthy and comprised of several categories of symptom criteria, which facilitates 636,120 possible symptom combinations for PTSD. Second, although the symptom categories of PTSD have been shown to be highly correlated with one another (e.g., Chen et al., 2017), there is also significant variability in terms of the number of PTSD symptoms an individual may endorse. Within DSM-5 diagnostic criteria, individuals with PTSD may experience a range of 6-20 symptoms, where higher number of symptoms endorsed may be considered indicative of increased disorder severity (e.g., Rehder & Bowen, 2019). Previous

research by Palm and colleagues (2009) illustrated that DSM-IV PTSD symptoms can be combined to assess a single dimension of PTSD severity, providing support for a continuum of symptom severity. Furthermore, there have been differences observed in PTSD symptomatology among latent classes of individuals with PTSD, which vary along dimensions of symptom severity (Breslau et al., 2005; Campbell et al., 2020). As such, there may be significant variability and differences in clinical presentation of PTSD symptomatology, depending on the interaction between symptom endorsement and symptom severity.

Posttraumatic Stress Disorder affects approximately 8-10% of the population across the lifespan (Kessler et al., 1995; Van Ameringen et al., 2008), with past year prevalence in *DSM-5* projected around 3.5% (American Psychiatric Association, 2013). Posttraumatic stress disorder is among the most common and enduring mental health disorders (e.g., Shalev, 2009), with low remission rates in the first 3-7 years and high rates of enduring lifetime pathology (Armenta et al., 2019; Steinert et al., 2015; Zlotnick et al., 1999; Zlotnick et al., 2004; De Jong et al., 2001; Goldstein et al., 2016; Friedman, 2007; Kessler et al., 1995). Sociodemographic correlates of PTSD include sex, age, education, marital status, and household income (Pietrzak et al. 2011; Breslau et al., 2004), with higher prevalence seen among young females, previously married, with lower income, and greater than a high school education (Goldstein et al., 2016; de Vries & Olff, 2009; Kessler et al., 1995). Posttraumatic stress disorder is known to occur alongside many other physical and mental health disorders, with complex associations, common risk factors, and bidirectional etiology that are not easily identified or well understood (e.g., Tripp et al., 2020; Stander et al., 2014; Jacob et al., 2019).

PTSD and Comorbidities

Comorbidity, or the co-occurring diagnosis of two or more disorders within the same

person, is increasingly common within clinical populations. Mental health comorbidities have been associated with increased symptom complexity (i.e., symptom overlap and variety) and severity (Helle et al., 2020; Najt et al., 2011; Schafer & Najavits, 2007), increased functional impairment (e.g., Shalev et al., 2017), and decreased treatment effectiveness (e.g., Newman et al., 1998). Posttraumatic stress disorder presents with high rates of mental health comorbidities (e.g., Goldstein et al., 2016), with approximately 80 percent of individuals with PTSD meeting criteria for at least one comorbid mental health disorder (Grinage, 2003; Kessler et al., 1995). Additionally, PTSD is associated with many different types of comorbid mental health disorders, including depressive disorders (e.g. Dore et al., 2012; Angelakis & Nixon, 2015; Stander et al., 2014), anxiety disorders (e.g. Goldstein et al., 2016; Smith et al., 2016a), personality disorders (e.g. Pagura et al., 2010; Smith et al., 2016a), as well as substance use disorders (SUDs; Brady et al., 2000; Dore et al., 2012; Galatzer-Levy et al., 2013; Ruglass et al., 2021; Goldstein et al., 2016; Bryan et al., 2021; Emerson et al., 2017; Tripp et al., 2019; Tripp et al., 2020).

The prevalence of SUDs among individuals with PTSD is high (Brady et al., 2000; Dore et al., 2012; Galatzer-Levy et al., 2013; Ruglass et al., 2021; Goldstein et al., 2016; Bryan et al., 2021; Emerson et al., 2017; Tripp et al., 2019; Tripp et al., 2020). Previous research has documented co-occurrence rates ranging from 34%– 52% (Mills et al, 2006; Vujanovic et al, 2016), with individuals with PTSD approximately five times more likely to have a coexisting SUD than those without PTSD (e.g., Kessler et al., 1995; Mills et al.). The most commonly used substances among individuals with PTSD are alcohol, tobacco, and cannabis (e.g., Contractor et al., 2019; Kearns et al., 2020; Turna & MacKillop, 2021; Mills et al.), with risk of severe and disordered use patterns associated with each type. Individuals with comorbid PTSD-SUDs frequently present with increasingly severe symptomatology (e.g., Papastavrou et al., 2011), and

have been associated with several other adverse mental health outcomes (e.g., Goldstein et al., 2016).

PTSD and Cannabis Use

Cannabis use has been increasing over the past decade, following legalization of recreational cannabis use in Canada and much of North America in 2018 (e.g., Patton, 2020; Fisher et al., 2017), contributing to subsequent normalization of cannabis use overall. Cannabis use has been associated with increased symptom complexity, poorer functioning, and increased associations with co-occurring mental health conditions (Compton et al., 2016; Hasin et al., 2019). Research regarding the relationship between cannabis use and PTSD symptomatology has been observed to be contradictory (e.g., Shishko et al., 2018), claiming both the improvement (Greer et al., 2014; Elms et al., 2019; Cameron et al., 2014) and worsening (Boden et al., 2013; Wilkinson et al., 2015; Hinojosa et al., 2023; Manhapra et al., 2015; Metrik et al., 2016) of PTSD symptoms concurrently. In addition to contradictory evidence regarding perceived benefits and harms associated with cannabis use, there is inconclusive evidence on the benefits of cannabis use for PTSD symptomatology overall. A systematic review by O'Neil and colleagues (2017) concluded that there is insufficient evidence to draw definitive conclusions about perceived benefits and harms of cannabis use for individuals with PTSD. Furthermore, a recent review by Bedard-Gilligan and colleagues (2022) noted "the only randomized controlled trial to date found cannabis had no greater effect on PTSD symptoms than placebo" (p.1). These findings illustrate both a lack of conclusive evidence regarding the efficacy of cannabis for the treatment of PTSD, as well as the limited amount of definitive evidence regarding the causal relationship between cannabis use and PTSD symptom severity.

Posttraumatic stress disorder remains one of the top presenting concerns among individuals

using medicinal cannabis (e.g., Bowles, 2012). In the United States, PTSD has been approved in at least 16 states as a qualifying condition for a medicinal cannabis prescription (Shishko et al., 2018; Wilkinson et al., 2015). Medicinal cannabis use has been associated with lower physical quality of life and a higher prevalence of medical conditions compared to individuals who use cannabis without a medical prescription (Wall et al., 2019). There appears to be no clear, conclusive evidence thus far that medicinal cannabis is helpful for managing PTSD symptomatology, as illustrated by several recent reviews that noted contradictory and inconclusive findings (Shishko et al., 2018), limited evidence regarding safety and efficacy (Orsolini et al., 2019), and lack of support overall (Sarris et al., 2020). Furthermore, research by Fischer and colleagues (2010) illustrated that medicinal cannabis use is often associated with more severe cannabis use profiles. In combination, it appears that medicinal cannabis use is often associated with more severe use patterns that have a higher likelihood of escalating to cannabis use disorder.

PTSD and Cannabis Use Disorder

Cannabis use disorder (CUD) in *DSM-5* requires at least two of eleven substance use symptoms (e.g., craving, tolerance, withdrawal) within a 12-month period (Appendix B), with higher scores indicating more severe disordered use (American Psychiatric Association, 2013). Cannabis use disorder occurs in approximately 1.5% of the general population (American Psychiatric Association), and it is estimated that approximately one in ten individuals who use cannabis will develop cannabis use disorder (e.g., Hasin, et al., 2015b; American Psychiatric Association, 2013). Continuous cannabis usage has also been associated with more severe tolerance and dependence patterns indicative of CUD (Aquino et al., 2018). Moreover, CUD has been associated with a variety of other mental health conditions, including anxiety disorders,

psychotic symptoms and disorders, mood disorders, personality disorders, trauma and stressor related disorders, other substance use disorders, as well as suicidality (Buckner et al., 2012; Leadbeater et al., 2019, Livne et al., 2018; Hasin & Walsh, 2021; Hasin et al., 2016; Stinson et al., 2006; Hayley et al., 2017; Ford & Gomez, 2015).

Posttraumatic stress disorder has been consistently associated with CUD (Cornelius et al., 2010; Kevorkian et al., 2015; Bordieri et al., 2014), and at higher rates than the general population (9.4% compared to 2.2%; Bilevicius et al., 2019). Posttraumatic stress disorder has also been demonstrated to be a risk factor for CUD, whereby PTSD was predictive of past year CUD but not the reverse (Metrik et al., 20019). Furthermore, higher PTSD symptom severity has been associated with higher rates of CUD (Bordieri et al., 2014; Livingston et al., 2022; Boden et al., 2013), suggestive that severe patterns of cannabis use are associated with worsening of PTSD symptomatology. During treatment, co-occurring CUD has been shown to be predictive of lower rates of PTSD symptom improvement (Bonn-Miller et al., 2013). Therefore, individuals with PTSD who also have CUD appear to be at increased risk for increased PTSD symptom severity and functional impairment. Due to high rates of comorbidity between PTSD and CUD, it is important to understand underlying etiology and motivations for cannabis use among individuals with PTSD.

Motives for Cannabis Use

Individuals with PTSD may engage in cannabis use for a variety of therapeutic and recreational motives, including enhancement, expansion, coping, relaxation, pain management, conformity, and socialization (e.g., Anthenien et al., 2021; Bresin & Mekawi, 2019; Reilly et al., 1998; Simons et al., 2000; Bonn-Miller et al., 2014a; Bonn-Miller et al., 2010; Lake et al., 2020). Several theoretical models have been proposed to explain the relationship between PTSD and

cannabis use motives. The self-medication model (Khantzian, 1997), the tension reduction model (Conger, 1956), the avoidance coping model (Litman, 2006; Roth & Cohen, 1986) and the stress coping model (e.g., Hyman & Sinha, 2009) remain centered around the principle that cannabis use is rooted in alleviating or avoiding negative states and affect, and/or increasing positive affect.

The self-medication model posits that PTSD leads individuals to use substances, such as cannabis, to cope with negative internal experiences (Khantzian, 1997). To date, the self-medication model has received the most support in terms of illustrating why individuals with PTSD so frequently engage in substance use (Danovitch, 2016; Hawn et al., 2020; Loflin et al., 2017; Metrik et al., 2018; Schafer & Najavits, 2007). Other similar theories, including the tension-reduction model and the stress-coping model, postulate that individuals engage in cannabis use to reduce unpleasant cognitive and emotional states (Wills & Hirky, 1996). Studies have shown that tension reduction motives are often linked to more frequent cannabis use patterns. Grant and colleagues (2015) found that individuals with PTSD that had a higher expectancy of relaxation and tension reduction from cannabis use were more likely to report cannabis use within the past month. Other research has suggested that the tension-reduction model helps explain the relationship between cannabis use and anxiety, postulating that cannabis is used to reduce anxiety and tension. This is supported by the fact that cannabis use is often prevalent among those seeking treatment for anxiety disorders (Ouellette et al., 2019). Alternatively, the stress coping model suggests that individuals use cannabis as a means of managing stress, which is particularly relevant to individuals in high stress states following traumatic exposure. The relationship between stress and cannabis use has been well established (Goeders, 2003; 2004; Sinha, 2001; 2005; Turner & Lloyd, 2003; Wills, 1990). Overall, the

stress coping model postulates that stress places individuals at greater risk for substance use disorders (Hyman & Sinha, 2009).

Alternatively, other pertinent theories such as the common factors model (Wolf et al., 2010), the mutual maintenance model (Stewart et al., 1998), and the susceptibility model (Chilcoat & Breslau, 1998) focus on varying pathways that drive and maintain substance use. The common factors model speculates that shared (common) factors significantly increase the risk of cannabis use, as well as contribute to the maintenance of use (Danovitch, 2016; Hawn et al., 2020). Alternatively, the mutual maintenance model posits that several mutual pathways between PTSD and cannabis use produce a combination of risk factors for problem use, and maintenance factors for continued use (Stewart et al., 1998). Lastly, the susceptibility model elucidates that cannabis use may lead to the development of PTSD, either through social or physiological pathways (Chilcoat & Breslau, 1998; Danovitch, 2016).

Evidently, there are many theories postulating potential motivations for cannabis use among individuals with PTSD. Since no model has been able to account for the relationship between PTSD and cannabis use in its entirety, it is likely that a multifactorial model exists, whereby multiple models account for a proportion of the symptomatology among individuals with PTSD (as discussed by Ruglass et al., 2014). Thereby, it stands to reason that differing motivations for cannabis use produce a variety of differential consequences and clinical outcomes.

As many more individuals with PTSD are now experimenting with cannabis than ever before, understanding the motivations for cannabis use and the relationships between cannabis use and PTSD symptomatology are both urgent and important. There is a critical need to provide both policy makers and the public with pertinent information regarding the effects of cannabis

consumption on various facets of health. Individuals with PTSD are widely understood to frequently use cannabis, however the effects of cannabis consumption on PTSD symptomatology are generally inconclusive and unclear. These contradictory findings may suggest overall heterogeneity within cannabis use variables, with differing typologies or profiles of cannabis use associated with more or less severe clinical profiles. Individuals with PTSD remain at high risk for CUD, due to personal attempts to self-medicate and manage their undesirable symptoms. Furthermore, individuals with mental health comorbidities are frequently more difficult to treat, due to severe symptom profiles and enhanced treatment needs. Therefore, it is pertinent to the study of PTSD to understand not only how cannabis use contributes to symptom severity, but also how cannabis use relates to treatment seeking behaviors and clinical outcomes among individuals with PTSD.

The Present Research and Contributions to the Literature

Three distinct research studies were conducted to examine the complex, nuanced associations between PTSD and cannabis use, using a nationally representative sample of adult civilians (≥18 years) that was collected during the National Epidemiologic Survey on Alcohol and Related Conditions III (NESARC-III; N = 36,309) in 2012-2013. The goal of study one was to examine sociodemographic and clinical correlates for individuals with comorbid PTSD-CUD. There is limited prior research regarding the relationships between comorbid PTSD-CUD and other sociodemographic and clinical correlates. At first glance, sociodemographic correlates for PTSD and CUD independently appear to share some commonalities, however also present with unique influences. This makes it difficult to ascertain relevant populations with higher likelihood of comorbid PTSD-CUD. A series of multinomial logistic regressions were run to compare individuals with comorbid PTSD-CUD to individuals having neither of these disorders, as well

as individuals having PTSD alone. By comparing comorbid PTSD-CUD to PTSD alone, associations between PTSD symptom severity and each of the groups could be examined. Epidemiological findings regarding pertinent risk factors for comorbid PTSD-CUD are beneficial to improve our understanding regarding the complex profile of individuals with comorbid PTSD-CUD, with the goal of improving prevention efforts and reducing duration of the disorders.

The goal of study two was to utilize latent mixture modelling (LMM) to identify distinct cannabis use profiles that vary on measures of cannabis use severity (age of onset of use, frequency of use, quantity of use, medicinal use, disordered use) among individuals with PTSD. Utilizing the R3STEP method, each participant was assigned to their most likely group membership, and then the cannabis use classes were subsequently compared along clinical outcomes. Previous research on cannabis use among individuals with PTSD has historically approached cannabis use patterns homogeneously, despite several research studies demonstrating heterogeneity of cannabis use and calling for the examination of types of cannabis use patterns. Two previous studies have examined typologies of substance users among a PTSD sample (Kearns et al., 2020; Contractor et al., 2019). No prior research to my knowledge has examined different typologies of cannabis use profiles among a PTSD sample. By comparing different subgroups of individuals who use cannabis along dimensions of severity of use indicators, results illustrated if differing cannabis use patterns were associated with higher or lower scores in PTSD symptom severity. Due to meaningful clinical differences between PTSD and other population groups, as well as cannabis use compared to other substance use, this novel comparison illustrates if there are differential findings between high versus low substance use severity groups. These findings may be used to address the observed disparity in clinical research

postulating cannabis as both helpful and harmful, by further examining which types of cannabis use patterns are associated with desirable versus undesirable outcomes.

Finally, the goal of study three was to examine rates of mental healthcare utilization among individuals with comorbid PTSD-CUD, compared to individuals with PTSD who do not use cannabis and individuals that have less severe (non-disordered) cannabis use patterns. This study examined whether having comorbid PTSD-CUD is associated with decreased rates of mental healthcare utilization, which may provide further support for various theoretical models explaining persistent substance use among individuals with PTSD, many of which have not been examined for cannabis use among a PTSD sample specifically (e.g., Bonn-Miller et al., 2014a). As individuals with comorbid mental health and substance use disorders typically present with more severe symptomatology and greater treatment avoidance and resistance, it is important to understand the relationship between cannabis use and mental healthcare treatment utilization. Furthermore, there has been limited research investigating differences between disordered versus non-disordered cannabis use, which may produce distinct differences in clinical outcomes. This comparison represents a meaningful addition to the existing literature that is fundamental to understanding how more severe patterns of cannabis use are associated with differing clinical outcomes and rates of mental healthcare treatment utilization.

In combination, these three research studies provide important comparisons between comorbid PTSD-CUD versus PTSD alone, disordered versus non-disordered cannabis use patterns, as well as variations among relevant cannabis use variables (e.g., frequency, quantity, age of first use) that may produce distinct clinical outcomes. This included examining how individuals with medicinal versus recreational cannabis use were associated with different cannabis use severity profiles. The large scale, nationally representative adult civilian sample

used for this project provided the opportunity to examine the complex relationship between PTSD and cannabis use in comprehensive and nuanced detail. As the majority of previous research on comorbid PTSD-CUD has been conducted on veteran populations, it is increasingly important to examine PTSD and cannabis use among civilian populations. Although veterans represent an important, vulnerable population that have higher likelihood of developing PTSD, there are many other population groups that have higher likelihood of developing PTSD (such as low-income groups or those in war frequent countries). Furthermore, while veterans may have higher likelihood of certain types of traumatic exposure, civilian populations may have higher likelihood of other types of traumatic exposure that may produce differing clinical outcomes. Therefore, utilizing a sample of civilian adults to examine different types of traumatic exposure and experiences provided the opportunity to ascertain sociodemographic and clinical outcomes for adult civilians with PTSD.

PTSD remains one of the most enduring and debilitating mental health disorders, whereby individuals with PTSD experience notable barriers to acceptable, accessible, and effective care. Comorbid PTSD-CUD represents a frequent disorder combination that severely affects etiology, treatment course, and clinical outcomes. Improved understanding of the nuances in the relationships between PTSD and cannabis use can be used to improve public messaging around high-risk cannabis use patterns, with the goal of reducing barriers to effective PTSD treatment. As previously noted by Borodovsky and Budney (2018), “it is necessary to begin building a body of scientific knowledge that can be used to design cannabis regulations that protect those with or predisposed to developing mental disorders” (p. 17).

Chapter Two:

Epidemiology of Comorbid Posttraumatic Stress Disorder and Cannabis Use Disorder in a Nationally Representative Sample

Jessa M. Hogarth[1], Matthew Keough[2], & Natalie Mota[3]

(1) Department of Psychology, University of Manitoba

(2) Department of Psychology, York University

(3) Department of Clinical Health Psychology, University of Manitoba

Abstract

The relationships between Posttraumatic Stress Disorder (PTSD) and Cannabis Use Disorder (CUD) are not well understood. The aim of the present research was to examine sociodemographic and clinical correlates of PTSD-CUD, compared to having neither of these conditions or PTSD alone. Data was analyzed from a nationally representative sample of adult civilians (≥18 years), the National Epidemiologic Survey on Alcohol and Related Conditions III (NESARC-III; N = 36,309), which was collected using face-to-face interviews in 2012-2013. Sociodemographic correlates (age, sex, education, marital status, household income) and clinical correlates (adverse childhood experiences, traumatic exposure, physical and mental health comorbidities) were examined across a four-group dependent variable (PTSD, CUD, PTSD-CUD, Neither) using cross-tabulations and multinomial regressions, respectively. Individuals had higher odds of PTSD-CUD if they were single or never married (compared to married/cohabiting), Alaskan Native/American Indian or Black (compared to White), as well as having a household income under $20K (compared to over $70K). The PTSD-CUD group was associated with increased odds of reporting adverse childhood experiences and specific types of traumatic exposure (sexual assault, physical assault), compared to individuals with neither disorder. The comorbid group appeared to display the most severe clinical outcomes overall, with highest odds of past year mental health disorders, physical health conditions, drug use disorders, and alcohol use disorder, compared to having neither disorder. When comparing PTSD-CUD to individuals with PTSD alone, PTSD-CUD was associated with increased likelihood of having another mental health disorder, substance use disorder, as well as increased odds of certain traumatic experiences. Evidence suggests that individuals with PTSD-CUD appear to present with more severe symptomatology that is further complicated by additional

comorbidities and may require non-traditional treatment approaches. This study represents an important first step to improving our understanding of comorbid PTSD-CUD and how it may differ from PTSD alone.

Keywords: Posttraumatic Stress Disorder, PTSD, Cannabis, Cannabis Use Disorder, Marijuana, Substance Use Disorders.

Introduction

Posttraumatic stress disorder is a persistent mental health disorder that is associated with significant impairment, complex symptom heterogeneity, and significant mental health comorbidities across the lifespan (e.g., Sareen, 2018; Goldstein et al., 2016). Cannabis is frequently used by individuals with PTSD for self-medication of their symptoms (e.g., Khantzian, 2007) among other motives, with both recreational use and disordered use increasing in frequency across North America (e.g., Hasin et al., 2016). Individuals living with comorbid disorders often present with extended chronicity of symptoms, as well as other mental and physical health problems (e.g., Newman et al., 1998) that have large societal and economic impacts. However, research regarding the impact of co-occurring PTSD-CUD has been limited to date, with the majority of prior research focusing on PTSD and other substance use disorders (SUDs) broadly. Cannabis use disorder presents with unique elements from other SUDs, due to: (1) mixed reports of potential benefits and harms associated with use, (2) medicinal cannabis being prescribed for management of various mental health symptoms (as discussed by Borodovsky & Budney, 2019), and (3) producing differential clinical outcomes than other substances (Bonn-Miller et al., 2011). With the prevalence of CUD further increasing following legalization of cannabis in Canada, and decreases in treatment utilization for CUD observed and expected (Mennis et al., 2023), there is an inherent need to understand the nuanced relationship between comorbid PTSD-CUD in greater detail. The proposed research examined sociodemographic and clinical correlates of comorbid PTSD-CUD to illustrate meaningful clinical relationships and symptom presentations that are associated with this comorbidity. This information can be used to increase information for the public and healthcare providers regarding additional challenges associated with PTSD-CUD, as well as target prevention efforts to avoid

detrimental health outcomes for individuals with PTSD.

Posttraumatic Stress Disorder

Posttraumatic stress disorder involves distressing symptoms following variations of direct or indirect exposure to a traumatic event (American Psychiatric Association, 2013). In the *Diagnostic and Statistical Manual of Mental Disorders Fifth Edition* (*DSM-5*), PTSD is comprised of eight diagnostic criteria, including intrusive symptoms, avoidance symptoms, negative alterations in cognitions and mood, as well as alterations in arousal or reactivity (Appendix A).

Research estimates that 70% or more of individuals worldwide have been exposed to traumatic events, with approximately one third of those individuals' reporting exposure to three or more traumatic events (Kessler et al., 2017). In previous research using the NESARC-III, past year PTSD has been demonstrated to have a prevalence of 4.7%, while lifetime PTSD has a prevalence of 6.1% (Goldstein et al., 2016; Sommer et al., 2018). Approximately 80 percent of individuals with PTSD have at least one comorbid mental health disorder (e.g., Grinage, 2003), which are often associated with increased challenges to treatment planning, issues with treatment compliance, and complications in delivery of treatment (e.g., Newman et al., 1998). In clinical populations, approximately 25–50% of individuals with PTSD have a comorbid substance use disorder (SUD; Schafer & Najavits, 2007). Lifetime PTSD has been significantly associated with CUD (Kevorkian et al., 2016), with higher PTSD symptom severity associated with greater likelihood of CUD (Bordieri et al., 2014).

Cannabis Use Disorder

Cannabis Use Disorder is classified in *DSM-5* as requiring at least two of eleven substance use symptoms (e.g., tolerance, withdrawal, craving) within a 12-month period, with a higher

number of symptoms endorsed indicating more severely disordered use (Appendix B; American Psychiatric Association, 2013). It is estimated that approximately one in ten individuals who use cannabis will develop cannabis use disorder (e.g., Wagner & Anthony, 2002), with PTSD being a pertinent risk factor of CUD (Blanco et al., 2016; Cougle et al., 2011). Posttraumatic Stress Disorder is associated with both past year and lifetime CUD (*OR* = 4.3, 3.8), with associations between PTSD and CUD increasing with CUD severity (Hasin et al., 2016). Previous research has demonstrated that PTSD is predictive of past year CUD, however CUD is not predictive of past year PTSD (Metrik et al., 2019; Chilcoat & Breslau, 1998). These findings suggest that PTSD tends to precede CUD (Jacobsen et al., 2001), providing support for various self-medication and stress coping hypotheses. Furthermore, there can be worse clinical outcomes for comorbid mental health and substance use disorders in instances where the mental health disorder pre-existed the substance use disorder (Najt et al., 2011). Therefore, individuals with PTSD who develop CUD may be at greater risk for increased symptom severity and increased mental health comorbidities. The present study examined sociodemographic and clinical correlates of PTSD-CUD to examine complex symptom presentations that are associated with this mental health comorbidity.

Demographic Correlates

There is relatively little information regarding the sociodemographic correlates of comorbid PTSD-CUD. Independently, PTSD presents at higher rates among individuals who are younger, female, widowed/separated/divorced, have lower education, lower household income, and are of racial minorities including Black or Native American descent (e.g., Alegría et al., 2013; Breslau, 2009; Goldstein et al., 2016; Pietrzak et al., 2011; Last, 2020; Weaver & Etzel, 2003). Individuals of Asian and Latino descent typically have lower prevalence rates of PTSD

(Alegría et al., 2013; Roberts et al., 2011). Previously research by Kessler and colleagues (1995) found that war or combat exposure, childhood neglect, and childhood physical abuse were associated with the highest likelihood of subsequent PTSD among men, while sexual molestation, physical attacks, being threatened with a weapon, and childhood physical abuse were associated with the highest likelihood among women. Some research suggests that females are at higher risk for developing PTSD due increased susceptibility to certain types of traumatic exposure and methods of coping (Breslau, 2009; Tolin & Foa, 2006). Specifically, females are more likely to experience certain types of traumatic exposure that are highly correlated with PTSD, including sexual assault, intimate partner violence, and childhood abuse (Breslau, 2009; Tolin & Foa, 2006). These types of traumatic exposure tend to have a higher risk of resulting in PTSD compared to other types of traumatic events. Females may also face repeated instances of trauma, and cumulative trauma exposure has been shown to significantly increase the likelihood of PTSD (Kessler et al., 1995).

Alternatively, prominent risk factors for CUD often include similar factors of younger age, lower income, and Black or Native American descent (Kerridge et al., 2018; Hasin et al., 2016). However, there has been limited research overall investigating differences in CUD prevalence among specific racial minorities (Montgomery et al., 2022), as well as mixed findings regarding sex as a risk factor for CUD (Secades-Villa & Fernández-Artamendi, 2017). Higher rates of cannabis use are often observed among females than males (Hayatbakhsh et al., 2009; Looby & Earleywine, 2007), while males often present with more cannabis use severity indicators, as well as higher rates of CUD (Hayatbakhsh et al., 2009; Hasin et al., 2016; Looby & Earleywine, 2007). Males may be more prone to developing CUD due to increased engagement in risk-taking behaviors (e.g., Khan et al., 2013), or increased social acceptance of substance use (e.g., Becker

& Hu, 2008). A "telescoping effect" has often been observed among females, whereby the progression from initial cannabis use to CUD is accelerated in comparison to males (Kerridge et al., 2018; Khan et al., 2013; Secades-Villa & Fernández-Artamendi, 2017). Other risk factors for cannabis use and CUD include changes in maternal marital status, maternal smoking, child school performance, childhood sexual abuse, early adolescence smoking and alcohol consumption, and adolescent aggression/delinquency were strongly associated with young adult cannabis use and use disorder, with exposure to multiple risk factors increasing the likelihood of cannabis use and CUD (Hayatbakhsh et al., 2009).

In synthesis, several risk correlates are shared amongst the individual groups of PTSD and CUD, including higher rates observed among individuals with lower income, younger age, from racial minorities of Black and Native American descent. This overlap between disorders suggests these particular sociodemographic groups may have a higher likelihood of comorbid PTSD-CUD, although this has not yet been established. Whether sex is a correlate of PTSD-CUD is unclear, as females are at higher risk for developing PTSD, while males are at higher risk for developing CUD. However, given the theoretical model that CUD presents following PTSD, it appears possible that the greater susceptibility of females toward developing PTSD would facilitate greater likelihood of developing PTSD-CUD.

Clinical Correlates

Only a subsection of individuals exposed to traumatic events subsequently develop PTSD. It remains difficult to determine which individuals are at higher risk for developing severe and enduring posttraumatic symptoms, as the severity of the traumatic event alone does not entirely account for the development of PTSD symptoms. As Bromet and colleagues (2018) outline, "the clinical and public health challenge is how to identify those individuals at greatest risk in

comparison to the resilient others who will not develop PTSD" (pg. xiii). Furthermore, it is unclear how the severity of the traumatic event, as well as the severity of the posttraumatic symptoms, influence the relationship between PTSD and cannabis use.

Types of Traumatic Exposure

Research has begun to investigate potential differences in clinical symptomatology and outcomes among varying *types* of traumatic exposure. The World Mental Health surveys identify the most frequently reported types of traumatic exposure are accidents and injuries, automobile accidents, interpersonal violence, and life-threatening illness and injuries (as discussed by Bromet et al., 2018). Different types of traumatic exposure (e.g., sexual assault, natural disaster, physical abuse) have been associated with differing clinical outcomes. Sexual assault has often been associated with the highest risk for developing subsequent PTSD among both men and women (e.g., Kessler et al., 1995). Previous studies have found an association between amount and type of traumatic exposure and physical health conditions (e.g., Atwoli et al., 2016; Husarewycz et al., 2014; Sommer et al., 2018) as well as mental health conditions (e.g., Kaltman et al., 2005; Piper & Berle, 2019). In a latent class analysis by Campbell and colleagues (2020), individuals with high PTSD symptoms had higher odds of childhood sexual abuse and war history, while individuals with low PTSD symptoms had lower odds of childhood sexual abuse but higher odds of other trauma. Specific types of traumatic exposure, including sexual trauma and non-sexual physical violence, have also been associated with increased PTSD symptom severity (Smith et al., 2016b). In combination, these findings appear to suggest that different types of traumatic exposure are associated with significant differences in symptom presentation. Therefore, grouping all traumatic experiences into one homogenous category likely neglects distinct clinical differences between varying types of traumatic exposure.

Relevant to the present study, the relationship between comorbid PTSD-CUD and specific types of traumatic exposures is, to my knowledge, yet to be examined. Understanding whether certain types of traumatic exposure are associated with comorbid PTSD-CUD may help explain which individuals are more likely to develop PTSD and co-occurring substance use disorders, in comparison to individuals with PTSD alone. Furthermore, since individuals with comorbid PTSD-CUD typically present with more severe, highly comorbid clinical profiles, it is important for prevention and treatment of PTSD-CUD to understand factors that may be contributing to etiology and maintenance of disorder symptomatology.

Adverse and Traumatic Experiences (ACEs)

Research has also examined potential differences in clinical symptomatology and outcomes among varying *amounts* of traumatic exposure. Kessler and colleagues (1995) found prevalence rates of PTSD approximately doubled among both men and women that had experienced previous traumatic exposure prior to a subsequent traumatic event. Furthermore, research has consistently established a significant relationship between adverse childhood experiences (ACEs), or traumatic exposure during childhood, and undesirable clinical outcomes. Adverse childhood experiences have been associated with poorer general health (Crouch et al., 2017), premature death (Brown et al., 2009), mental health comorbidities (Evans et al., 2020), substance use disorders (Tang et al., 2020; Khoury et al., 2010; Davis et al., 2023) and increased rates of suicide attempts (Dube et al., 2001; LeBouthillier et al., 2015; Merrick et al., 2017; Turner et al., 2017). Traumatic exposure during childhood is associated with a variety of undesirable clinical outcomes, including impairment of social functioning, cognitive functioning (memory, learning), as well as mental health and emotional functioning (Anda et al., 2006; Teicher & Samson, 2016; Watson 2019). Furthermore, exposure to traumatic experiences during childhood has also been

identified as a risk for subsequent traumatic exposure as well as enduring symptoms of traumatic stress (Briere & Elliott, 2003; Cloitre et al., 2009; Felitti et al., 1998; Wyatt et al., 1992). In the WHO survey, instances of physical abuse during childhood were associated with enduring episodes of PTSD longer than 11 years (Kessler et al., 2017). Evidently, exposure to traumatic events during the developmental period is often associated with poorer physical and mental health outcomes. Moreover, the more instances of traumatic exposure a person experiences, the greater the risk of detrimental outcomes. Previous research has illustrated a significant relationship between ACEs and the development of PTSD (Frewen et al., 2019; Layne et al., 2014). A recent retrospective review by Frewen and colleagues (2019) found that ACEs predicted increased trauma and stressor-related symptoms, even after accounting for other lifetime traumatic stress. Furthermore, the cumulative impact of repeated exposure to ACEs have been associated with increased risk of PTSD, SUDs, suicide attempts, and poly-drug use (Brockie et al., 2015). Therefore, it is important to consider previous exposure to traumatic events when examining individuals with PTSD, in order to understand pertinent clinical risk factors for developing PTSD.

There is also a significant relationship between ACEs and substance use disorders. There is a higher prevalence of ACEs among individuals with SUDs than in the general population, as well as a significant association between ACEs and the severity of SUDs (Dube et al., 2003; Felitti et al., 1998; Leza et al., 2021; Merrick et al., 2017; Khoury et al., 2010). Previous ACEs among individuals with CUD are also predictive of more severe symptomatology and earlier onset of comorbid mental health disorders compared to individuals with CUD without prior ACEs (Trovani et al., 2023; Smith & Graham, 2020). Furthermore, ACEs also increase the likelihood of individuals with CUD utilizing other substances in addition to cannabis. A recent

latent class analysis on ACEs by Smith and colleagues (2023) identified that individuals in classes of interpersonal abuse and harm had increased odds for lifetime, past month, and medicinal cannabis use relative to those in the low adversity class. Additionally, individuals in the high adversity class had higher odds of medicinal cannabis use. Therefore, the association between childhood traumatic experiences and subsequent SUDs appear relatively strong. Although I am not aware of any research investigating the role of ACEs in comorbid PTSD-CUD, increased risk for PTSD and SUD independently would suggest that ACEs may be a pertinent risk factor for comorbid PTSD and CUD.

Severity of Posttraumatic Symptoms

Akin to the influence of amount and type of traumatic exposure, it appears likely that the *severity* of traumatic symptoms may vary significantly among individuals with PTSD and potentially impact the relationship between PTSD and cannabis use. One way to examine severity of PTSD symptoms is through calculating PTSD symptom count, whereby a higher number of PTSD symptoms is considered indicative of increased disorder severity. A previous latent class analysis by Campbell and colleagues (2020) found that classes of high and low PTSD symptoms produced differential clinical outcomes. Specifically, the high PTSD symptom class was at higher risk for an increased number of mental health comorbidities, as well as poorer mental and physical health (as indicated by the SF-12). It appears that individuals with a higher number of PTSD symptoms present with more severe clinical profiles, which could lead to increased risk for substance use and subsequently substance use disorders. As we do not currently understand factors driving subsamples of individuals with PTSD to substance use disorders, it is important to explore these clinical correlates in more detail.

Health Comorbidities

Individuals with PTSD-CUD present with increased rates of physical and mental health comorbidities (e.g., Brady et al., 2000; Ohayon & Shapiro, 2000; Scherrer et al., 2019; Grinage, 2003). Mental and physical health comorbidities are frequently associated with increased symptom severity and complexity, as well as higher odds of negative health outcomes (e.g., Scott et al., 2016; Walker et al., 2015).

Mental Health Comorbidities

Independently, previous research has demonstrated strong associations between PTSD and other mental health comorbidities (e.g., Ohayon & Shapiro, 2000), most commonly depressive disorders, anxiety disorders, and substance use disorders (Brady et al., 2000; Galatzer-Levy et al., 2013; Dore et al., 2012; Pietrzak et al., 2011; Flory & Yehuda, 2015), as well as personality disorders, including antisocial personality disorder, borderline personality disorder and schizotypal personality disorder (Goldstein et al., 2016; Pagura et al., 2010). PTSD and substance use have also been associated with impulsivity (e.g., Morris et al., 2020), which may partially explain the relationship between PTSD, substance use, and borderline personality disorder (e.g., Cloitre et al., 2014). PTSD is also significantly associated with suicide (Gradus et al., 2010; Krysinska & Lester, 2010), with multiple traumatic experiences further increasing the risk of suicidal ideation and attempts (LeBouthillier et al., 2015; Panagioti et al., 2009). These comorbidities contribute to greater symptom severity, increased functional impairment, and poorer treatment outcomes (e.g., Gros et al., 2012; Sareen et al., 2007).

Individuals with CUD are also at greater risk for co-occurring mental disorders, with previous research demonstrating mental health comorbidities at rates over 95% among males and females with CUD (Khan et al., 2013). Prior research has established that cannabis use is

associated with increased depression, anxiety, and psychosis (Leadbeater et al., 2018; Hasin et al., 2017; Bahorik et al., 2018; Volkow et al., 2017). A recent review by Hasin and Walsh (2020) supported strong associations between cannabis use and CUD with other drug use, psychosis, mood disorders, anxiety disorders, and personality disorders. Furthermore, Gorelick (2019) discusses how mental health comorbidities are especially significant in CUD, as they are often associated with a poorer prognosis for CUD, the co-occurring disorders, or both. Cannabis use disorder is also independently associated with increased suicidal behaviors (e.g., Ilgen et al., 2009; Pedersen, 2008; Gobbi et al., 2019), with chronic cannabis use predictive of suicidality (Borges et al., 2016). Additionally, previous research on cannabis use has also demonstrated that cannabis use is associated with increased risk of dying by suicide (Kung et al., 2003; Kung et al, 2005).

Both PTSD and CUD are independently associated with heterogeneous symptom complexity and increased rates of mental health comorbidities (e.g., Hasin and Walsh, 2020). The most common mental health disorders associated with both these conditions are depressive disorders, anxiety disorders, and substance use disorders (Brady et al., 2000; Galatzer-Levy et al., 2013), as well as suicidality. Therefore, it appears increasingly likely that individuals with comorbid PTSD and CUD experience increased rates of mental health comorbidities, as well as increasingly complex symptomatology, although this remains to be examined.

Physical Health Comorbidities

Previous research has established a relationship between PTSD and physical health conditions (e.g., Boscarino, 2014; El-Gabalawy et al., 2018; Sommer et al., 2021; Ryder et al., 2018; Pacella et al., 2013), with significant associations observed between PTSD and cardiovascular diseases, respiratory diseases, chronic pain conditions, gastrointestinal illnesses,

and cancer (e.g., Sareen et al., 2007; Krantz et al., 2022). A prior research study utilizing the NESARC-III by Sommer and colleagues (2018) examined associations between specific clusters of PTSD symptoms and physical health conditions. They found that re-experiencing symptoms were associated with cardiovascular and endocrine/metabolic conditions, while negative alterations in mood/cognition were associated with sleep disorders. These findings appear to suggest that different classifications of PTSD symptoms are associated differentially with physical health conditions.

Cannabis use is also a risk factor for both chronic and acute physical health problems. Acute problems may include myocardial infarction (Desai et al., 2017) and ischemic stroke (Rumalla et al., 2016), while chronic problems may include neurocognitive impairments (Karila et al., 2014), cardiovascular disease (e.g., Hall & Degenhardt, 2009), and respiratory disease (e.g., Aldington et al., 2008; Tetrault et al., 2007). Severe patterns of cannabis use, like in CUD, are also associated with detrimental health outcomes like acute limb ischemia (McGuinness et al., 2022).

Although both PTSD and cannabis use have been associated with detrimental physical health problems, research regarding physical health conditions among individuals with comorbid PTSD-CUD is scarce. To my knowledge, only one prior study conducted by Bilevicius and colleagues (2019) examined the relationship between PTSD, CUD, and physical health. Specifically, the study examined whether PTSD was associated with elevated rates and severity of CUD for a variety of physical health, chronic pain conditions, including musculoskeletal pain (fibromyalgia, osteoporosis, arthritis), digestive pain (pancreatitis, irritable bowel syndrome/inflammatory bowel disease), and nerve pain conditions (sympathetic dystrophy/complex regional pain syndrome, other nerve pain in legs, arms, or back), compared

to individuals without PTSD. They found that the odds of CUD were greater for PTSD and specific types of pain, including digestive pain, nerve pain, and chronic pain overall, compared to having neither PTSD nor chronic pain. However, this study did not investigate the presence of other physical health conditions outside the scope of chronic pain, nor did it examine comorbid PTSD-CUD as a distinct comparison group. Therefore, there remains an absence of evidence regarding the relationship between comorbid PTSD-CUD and physical health conditions, despite evidence in the PTSD research that may suggest a potential relationship. Furthermore, due to the fact that medicinal cannabis is prescribed to manage some physical health conditions as well as PTSD, it is important to understand if individuals with comorbid PTSD-CUD are experiencing an improvement or worsening of their symptoms.

The Present Study

Cannabis is among the most commonly used substances by individuals with PTSD. Presently, it is unclear how various sociodemographic and clinical correlates influence the relationship between PTSD and cannabis use. Independently, sociodemographic correlates for PTSD and CUD appear to indicate higher risk among individuals who are younger, with lower income, from specific racial minorities (including Black or Native American descent; Kerridge et al., 2018; Hasin et al., 2016). There is limited research overall investigating differences in CUD prevalence among specific racial minorities (Montgomery et al., 2022), as well as mixed findings regarding sex as a risk factor for both PTSD and CUD independently (e.g., Secades-Villa & Fernández-Artamendi, 2017). Research regarding clinical correlates among individuals with PTSD and CUD is scarce. It is unclear how amount and type of traumatic exposure, as well as severity of traumatic symptoms influence the strength and direction of the relationship between PTSD and CUD. Evidently, more research specific to PTSD-CUD is needed, in order to

understand which sociodemographic factors may influence the course and development of PTSD-CUD.

Individuals with PTSD-CUD present with highly comorbid symptom profiles that are not well documented. It is important to understand the relationship between PTSD-CUD and other physical and mental health disorders, to account for various moderating and mediating factors that may alter overall symptomatology and clinical profiles, impacting treatment outcomes. Due to the fact that additional health comorbidities may contribute to increased symptom severity, complexity, or alter treatment recommendations, it is important to understand the psychological profile of individuals with comorbid PTSD-CUD in more detail.

The information gained through the present study will improve our ability to theorize if cannabis use (in the context of cannabis use disorder) may be helpful or harmful for managing PTSD symptoms. This is particularly relevant for driving treatment recommendations regarding the potential use of medicinal cannabis for treatment of PTSD.

Research Objectives

Using a cross-sectional nationally representative sample of adults in the USA, the present research examined sociodemographic and clinical correlates, as well as health comorbidities, among individuals with comorbid PTSD and CUD, relative to individuals having neither disorder. In secondary analyses, individuals with PTSD-CUD were also compared to individuals having PTSD only. There were three primary objectives of the present study.

First, the associations between comorbid PTSD-CUD and sociodemographic correlates (including age, sex, race, marital status, education, household income), as well as clinical correlates (including ACEs, type of traumatic exposure, and posttraumatic symptom severity) were examined, relative to having neither disorder. Based on prior research (e.g., Last, 2020), I

predicted that PTSD-CUD would be more prevalent among individuals that are young, single, of racial minorities, and with lower income. I also hypothesized that comorbid PTSD-CUD would occur approximately equally in males and females, due to the fact that PTSD often presents more highly in females and CUD more highly in males (e.g., Weaver & Etzel, 2003). Based on prior research, I hypothesized that individuals with PTSD-CUD would be more likely to report physical assault, sexual assault, or childhood abuse, compared to those with PTSD alone (Smith et al., 2023; Kessler et al., 1995; Breslau, 2009; Kilpatrick et al., 2013). Lastly, I predicted that individuals with comorbid PTSD-CUD would display with higher rates of ACEs and higher rates of traumatic exposure compared to individuals having neither disorder (e.g., Breslau et al, 1999; Smith et al., 2023).

Second, I examined the relationship between comorbid PTSD-CUD and various other health comorbidities, including mental health and physical health comorbidities, as well as substance use disorder comorbidities. I examined potential co-occurring mental health disorders, including depressive disorders, anxiety disorders, eating disorders, and personality disorders, predicting that individuals with PTSD-CUD would display higher rates of mental health comorbidities, compared to individuals having neither disorder. I also examined the association between PTSD-CUD and other substance use disorders, including alcohol use disorder as well as drug use disorders overall. Based on prior literature (e.g., Turna & MacKillop, 2021), I predicted that individuals with PTSD-CUD would present with higher rates of other drug use disorders, as well as alcohol use disorder, compared to individuals with neither disorder. I also examined the relationship between PTSD-CUD and physical health conditions, by examining associations with a variety of past year medical diagnoses of 32 physical health conditions. I predicted that individuals with PTSD-CUD would display with higher rates of physical health comorbidities

compared to those having neither disorder.

Method

Participants

The present study utilized data from the National Epidemiological Survey for Alcohol and Related Conditions Wave Three (NESARC-III), collected by the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The NESARC-III was conducted from April 2012 through June 2013 using multistage probability sampling, with detailed recount of data collection protocols described elsewhere (e.g., Grant et al., 2014). The NESARC-III includes a civilian sample of noninstitutionalized adults living in the United States of America, including veterans but excluding active service members in order to maintain confidentiality (Grant et al., 2014). Additionally, Black, Hispanic, and Asian adults were sampled at a higher rate than the remainder of the population intentionally, in order to increase power and reliability of the information provided by these marginalized groups. The target sample size was determined based upon prior NESARC wave designs, in order to provide sufficient power with a cutoff of 80% and a minimum effect size greater than 3% (Cudjoe, 2019).

A total of 44,931 individuals were selected to participate in the NESARC-III, however 1,567 were ineligible for interview due to exclusion criteria. Of the remaining 43,364 eligible individuals, 36,309 participated in the NESARC-III, while 7,055 declined to respond. This yielded an overall response rate of 60.1 percent (Cudjoe, 2019; Grant et al., 2014). Missing data across measures excluded participants from analyses.

Procedure

To administer the NESARC-III survey, approximately 1,000 trained lay interviewers visited the addresses previously selected through multistage probability sampling in the US.

Participants were asked general questions about their background, health, and lifestyle, such as age, education, alcohol consumption, mood, anxiety, behavior, personality, and medical conditions through computer-assisted, semi-structured diagnostic interviews. Further details about this process are described by Grant and colleagues (2014).

In order to gain access to the NESARC-III, a request for data acquisition was sent to the NESARC-III Data Access Committee (NIAAA), and ethics approval was obtained from the University of Manitoba Bannatyne Research Ethics Board. The NESARC-III dataset was then downloaded in a secure, encrypted format to a password protected, secure computer (as outlined by the Procedures for Obtaining Dataset found at https://www.niaaa.nih.gov/research/nesarc-iii/nesarc-iii-data-access/procedures-obtaining-dataset). Consent was obtained during primary data collection by the owners of the data, the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

Measures

The NESARC-III utilized the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5; National Institute on Alcohol Abuse and Alcoholism, 2015), in order to assess for the presence of mental health disorders. The AUDADIS-5 was designed to assess alcohol, drug use and mental health disorders during past year and lifetime periods, according to *DSM-5* diagnostic criteria (Grant et al, 2015). The AUDADIS-5 has been demonstrated to have good to excellent validity for CUD (Hasin et al., 2015) as well as good reliability for CUS (Grant et al., 2015). The AUDADIS-5 also has as well as fair to good reliability for DSM-5 disorders, including good to excellent reliability specifically for PTSD, mood, and anxiety disorders (Grant et al., 2015).

Posttraumatic Stress Disorder

During the semi-structured interview, participants were asked about 20 potentially traumatic events they may have directly experienced during their lifetime (e.g., serious life-threatening injury or illness, natural disasters, sexual abuse or assault), as well as 14 events they may have witnessed or been indirectly exposed to (as described by Hale et al., 2018). Participants who reported experiencing at least one traumatic event (i.e., Criterion-A; Appendix A) were subsequently asked about PTSD symptoms following the most traumatic or stressful event they had experienced. These questions were designed in order to operationalize the 20 PTSD symptoms from *DSM-5* (Criteria B–E), including five questions for criterion B (intrusion), two questions for criterion C (avoidance), seven questions for criterion D (altered cognition/mood), and six questions for criterion E (arousal; Chen et al., 2017; Goldstein et al., 2016). Furthermore, as per *DSM-5* diagnostic criteria, participants had to indicate if symptoms persisted greater than one month, as well as indicate the degree of clinically significant impairment or distress. Posttraumatic stress disorder was assessed dichotomously, with 0 = no PTSD and 1 = PTSD, using past year *DSM-5* diagnostic criteria for PTSD (see Appendix A).

Type of Traumatic Exposure

Participants were asked to report their most stressful or traumatic exposure (used in the present study) in accordance with 34 potential response categories, which were further collapsed into seven categories (as previously done by Sommer et al., 2018): (1) sexual assaultive trauma (sexually abused before age 18, sexually assaulted as an adult), (2) physical assaultive trauma (physically abused before age 18, beaten up by spouse/ romantic partner, beaten up by someone else), (3) life-threatening illness (serious or life-threatening illness), (4) life-threatening injury (serious or life-threatening injury, injured in a terrorist attack), (5) psychological trauma (saw a

dead body or body parts, kidnapped/held hostage, stalked, mugged/held up/threatened with a weapon), (6) witnessed any trauma, and (7) other traumatic experiences (natural disaster, active military combat, peacekeeper/relief worker, civilian in a war zone, refugee, prisoner of war, juvenile detention/jail, other).

Previous Adverse and Traumatic Experiences (ACEs)

Participants were asked a number of questions about their family and developmental history, which discussed ACEs they may have experienced. The present study utilized 29 questions from the NESARC-III that mapped onto 10 categories of adverse childhood experiences, which were collapsed into three main categories of abuse, neglect, and household dysfunction (as done by Roos et al., 2013, Tang et al., 2020). ACE questions were entered dichotomously, with responses over a certain frequency threshold (reported below) coded as the presence (= 1) or absence (= 0) of that subtype of ACE.

Abuse. Abuse was collapsed to encapsulate three categories of childhood abuse, including: (1) emotional abuse (e.g., how often did a parent/other adult living in your home swear at or insult you or say hurtful things), (2) physical abuse (e.g., how often did a parent/other adult living in your home push, grab, shove, slap or hit you), and (3) sexual abuse (e.g., how often did an adult/other person have you touch their body in a sexual way when you didn't want to or were too young to know what was happening). These items were based on a 5-point scale (never, almost never, sometimes, fairly often, or very often.) Respondents were considered to have experienced physical abuse if they responded "sometimes" or more when asked how often a parent or other adult living in the respondent's home had (1) pushed, grabbed, shoved, slapped, or hit the respondent, or (2) hit the respondent so hard it left marks or bruises or caused an injury. As previously done by Roos and colleagues (2013), a respondent was considered to have

experienced emotional abuse if they answered “fairly often” or “very often” to any of the following scenarios that asked about how often a parent or other adult living in the respondent’s home: (1) swore at, insulted, or said hurtful things to the respondent; (2) threatened to hit or throw something at the respondent (but did not); or (3) acted in any other way that made respondents afraid that they would be physically hurt or injured. The presence of sexual abuse was defined as any response more often than “never” (on the aforementioned 5-point scale) to any of 4 questions regarding sexual abuse. These questions investigated the occurrence of uninvited sexual advances during childhood.

Neglect. Neglect was collapsed to include two categories of childhood neglect: (1) physical neglect (e.g., how often did a parent/other adult living in your home make you go hungry or not prepare regular meals), and (2) emotional neglect (e.g., my family was a source of strength and support; reverse scored). Participants were asked questions related to physical neglect based on a 5-point scale (never, almost never, sometimes, fairly often, or very often.) An alternative 5-point scale was used for questions regarding emotional neglect (never true, rarely true, sometimes true, often true, or very often true). As the AUDADIS-5 included only 4 of the original 5 questions about neglect, the distribution of summed responses to all physical neglect questions in the NESARC data set was examined and distributed, as done by Roos and colleagues. Emotional neglect was considered present if the respondent had a reversed-scored sum total of 15 or greater from the 5 relevant questions, as was also consistent with previous research based on the Child Trauma Questionnaire (Dube et al., 2003).

Household Dysfunction. Household dysfunction was collapsed to encapsulate five categories, including: (1) household physical violence (e.g., how often did your father/other adult male push, grab, slap or throw something at your mother/other adult female), (2) household

substance abuse (e.g., parent/other adult living in home was a problem drinker/ alcoholic), (3) household mental illness (e.g., parent/other adult living in home attempted suicide), (4) parental separation or divorce (e.g., did biological or adoptive parents get divorced or permanently stop living together before respondent was 18), and (5) household member incarcerated (e.g., parent/other adult living in home went to jail or prison). Participants were asked to answer questions about perceived maternal abuse (from household dysfunction) on a 5-point scale. Perceived maternal abuse was assessed by asking whether a respondent's father, stepfather foster or adoptive father, or mother's boyfriend had ever done any of the following things to the respondent's mother, stepmother, foster or adoptive mother, or father's girlfriend: (1) pushed, grabbed, slapped, or threw something at her; (2) kicked, bit, hit with a fist, or hit her with something hard; (3) repeatedly hit her for at least a few minutes; or (4) threatened to use or actually used a knife or gun on her. All other questions regarding household dysfunction required a yes or no answer (as described by Roos et al., 2013).

Cannabis Use Disorder

The AUDADIS-5 was also used to assess cannabis use (e.g., quantity, frequency, duration) as well as disordered cannabis use in the past year and lifetime periods. The present study assessed past year CUD dichotomously, with 0 = No CUD and 1 = CUD. CUD was classified using *DSM-5* diagnostic criteria, requiring at least two of eleven substance use symptoms (e.g., tolerance, withdrawal, craving) within a 12-month period to obtain a diagnosis (Appendix B; American Psychiatric Association, 2013).

Demographic Correlates

As done in previous NESARC research by Mota and colleagues (2018) and Goldstein and colleagues (2016), sociodemographic correlates assessed included six variables: age

(continuous), sex (male, female), race/ethnicity (White, Black, American Indian/Alaska Native, Asian/Native Hawaiian/Other Pacific Islander, Hispanic), education (less than high school, high school or equivalent, some post-secondary or completed), marital status (married or common law, widowed/separated/divorced, or never married), and household income ($0–$19,999, $20,000–$34,999, $35,000–$69,999, $70,000+).

Mental Health Comorbidities

The AUDADIS-5 was used to assess other mental health disorders according to *DSM-5* criteria. I examined the following dichotomous mental health variables: (1) mood disorders (including major depressive disorder, dysthymia, bipolar disorder); (2) anxiety disorders (including generalized anxiety disorder, social phobia, agoraphobia, specific phobias and panic disorder); (3) personality disorders (including borderline personality disorder, antisocial personality disorder, schizotypal personality disorder). The AUDADIS-5 has been deemed to have overall good reliability and validity for mental health disorders (e.g., Grant et al., 2015).

Other Substance Use Disorders

The AUDADIS-5 was also used to assess *DSM-5* alcohol, tobacco, and drug use disorders, including cocaine, crack, hallucinogens, opioids, sedatives, inhalants/solvents, heroin, club drugs, stimulants and ‘other drug’ use disorders. Cannabis use disorder was excluded from this category. Drug use disorders were entered dichotomously, with 0 = no DUD and 1 = DUD.

The AUDADIS-5 was also used to assess alcohol use as well as alcohol use disorder in the past year and lifetime periods. Participants were asked during the face-to-face interview about their patterns of alcohol consumption. Past year alcohol use disorder was entered dichotomously, with 0 = no AUD and 1 = AUD.

Physical Health Comorbidities

Participants self-reported on 32 medical conditions from the past year, and were asked whether they had been diagnosed by a physician. These conditions included: digestive (irritable bowel syndrome/inflammatory bowel disease, stomach ulcer, pancreatitis, cirrhosis of the liver, other liver disease), cardiovascular (angina, myocardial infarction, arteriosclerosis, hypertension, other heart disease), musculoskeletal (arthritis, osteoporosis, fibromyalgia), endocrine/metabolic (high triglycerides, high cholesterol, diabetes), infectious (sexually transmitted disease, human immunodeficiency virus/acquired immune deficiency syndrome, tuberculosis), cancer (breast cancer, liver cancer, cancer of the mouth/tongue/throat/esophagus, other cancer), respiratory (chronic bronchitis/emphysema/ pneumonia/influenza), neurologic (stroke, reflex sympathetic dystrophy/complex regional pain syndrome, traumatic brain injury, epilepsy, other nerve problems), sleep disorder, and anemia. Physical health comorbidities were entered continuously and mean centered as a composite score, ranging from 0-32.

Data Analysis

Past year PTSD and CUD dichotomous variables in the NESARC-III were used to create a four-group dependent variable: (1) neither PTSD nor CUD, (2) PTSD alone, (3) CUD alone, and (4) comorbid PTSD and CUD. Cross-tabulations were used to calculate the prevalence of sociodemographic correlates (age, sex, education, marital status, household income), clinical correlates (previous adverse and traumatic experiences, type of traumatic exposure, severity of posttraumatic symptoms) and health comorbidities (other mental health disorders, other drug use disorders, alcohol use disorder, physical health comorbidities) across the four-group dependent variable. All analyses utilized STATA version 15 (StataCorp, 2017) and were weighted to ensure representativeness of the sample.

Differences between the four groups with regards to correlates and comorbidities were examined using a series of independent, bivariate multinomial logistic regression analyses, with the four group variable entered as the dependent variable and each correlate entered as the independent variable in separate regressions. Relative risk ratios (RRR) were calculated for the association of each correlate with having PTSD alone, CUD alone, or comorbid PTSD and CUD, when compared to the neither disorder group. In secondary parallel analyses, multinomial logistic regressions were conducted comparing individuals with PTSD-CUD to individuals with PTSD alone.

Results

Cross-tabulations were used to calculate prevalence. Past year comorbid PTSD-CUD was present among 0.4% of the total sample (n = 155). Results of the unadjusted multinomial logistic regression analyses are presented in Table 1 (demographic correlates) and Table 2 (clinical correlates and health comorbidities). Primary comparisons used the neither PTSD or CUD disorder group as a reference group (Table 1 and 2), with secondary comparisons using the PTSD alone group as a reference group (Table 3).

Demographic Correlates

Individuals in the PTSD alone group were slightly younger (*M* = 43.0 years), female (69.0%), White (69.9%), married/cohabiting (47.7%), with some post-secondary education (58.5%), and household income <20K (29.1%) compared to those in the neither PTSD or CUD reference group. Individuals in the CUD alone group were primarily younger (*M* = 31 years), male (70.1%), White (59.2%), single/never married (57.6%), with some post-secondary education (52.7%), and household income <20K (34.9%) compared to those in the neither PTSD or CUD group.

Individuals with comorbid PTSD-CUD were significantly younger (M = 32) than those with neither PTSD or CUD (M = 47). Females did not have significantly higher or lower odds of comorbid PTSD-CUD than males. Black individuals and American Indian/Alaska Native individuals had higher likelihood of PTSD-CUD than White individuals (RRR= 2.35-5.19, all $p<0.01$ or better). Hispanics and Asian/Hawaiian/Pacific Islander individuals did not have significantly higher or lower likelihood of PTSD-CUD than White individuals. Individuals who were single/never married had 4.37 times the likelihood of PTSD-CUD than individuals who were married/cohabiting. Individuals who were widowed/separated/divorced did not have significantly higher or lower likelihood of PTSD-CUD than individuals who were married/cohabiting. Individuals with high school/GED education or less than high school education did not have significantly higher or lower likelihood for PTSD-CUD than those with post-secondary education. Individuals in the 0-19,999 household income group had 7.35 times the likelihood of PTSD-CUD than individuals with household income over 70K. Individuals with household income of 20-34,999 and 35-69,999 did not have significantly higher or lower likelihood of PTSD-CUD compared to those with household income over 70K.

Table 1
Multivariate Analysis of Sociodemographic Correlates for PTSD, CUD, and Comorbid PTSD-CUD

	Neither (*n*=33,713, 92.9%)		**PTSD Alone** (*n*=1624, 4.5%)		**CUD Alone** (*n*=817, 2.3%)		**PTSD - CUD** (*n*=155, 0.4%)	
Variable	*M (SE)*	*RRR*	*M (SE)*	*RRR*	*M (SE)*	*RRR*	*M (SE)*	*RRR*
Age (years)	47.11 (0.20)	1.00	43.33 (0.42)	**0.99 (0.98-0.99)*** **	30.80 (0.61)	**0.93 (0.92-0.94)*** **	31.82 (1.35)	**0.94 (0.92-0.95)*** **
	n (%)	*RRR*	*n (%)*	*RRR*	*n (%)*	*RRR*	*n (%)*	*RRR*
Sex								
Male	14785 (48.4%)	1.00	457 (31.0%)	1.00	553 (70.1%)	1.00	67 (47.1%)	1.00
Female	18928 (51.6%)	1.00	1167 (69.0%)	**2.08 (1.80-2.40)*** **	264 (29.9%)	**0.40 (0.32-0.50)*** **	88 (52.9%)	1.05 (0.71-1.58)
Race/Ethnicity								
White	17815 (66.2%)	1.00	937 (69.9%)	1.00	376 (59.2%)	1.00	66 (53.5%)	1.00
Black	7136 (11.6%)	1.00	315 (11.0%)	0.90 (0.74-1.09)	266 (20.5%)	**1.98 (1.60-2.47)*** **	49 (21.9%)	**2.35 (1.29-4.25)** **
American Indian/Alaska Native	433 (1.4%)	1.00	56 (4.1%)	**2.81 (1.85-4.26)*** **	13 (2.7%)	2.18 (0.96-4.94)	9 (5.8%)	**5.19 (2.74-9.84)*** **
Asian/Hawaiian/Pacific Islander	1745 (6.0%)	1.00	30 (2.1%)	**0.34 (0.20-0.56)*** **	23 (2.8%)	**0.52 (0.33-0.84)** **	3 (3.0%)	0.63 (0.18-2.13)
Hispanic	6584 (14.8%)	1.00	286 (12.9%)	**0.83 (0.70-0.98)***	139 (14.8%)	1.12 (0.90-1.38)	28 (15.7%)	1.31 (0.80-2.13)
Marital Status								
Married/Cohabiting	15927 (59.1%)	1.00	610 (47.7%)	1.00	214 (28.8%)	1.00	43 (31.4%)	1.00
Widowed/Div/Sep	8692 (19.4%)	1.00	581 (29.4%)	**1.88 (1.66-2.13)*** **	122 (13.5%)	**1.43 (1.02-2.01)***	28 (18.6%)	1.81 (0.98-3.33)
Single/Never Married	9094 (21.6%)	1.00	433 (22.8%)	**1.31 (1.11-1.55)** **	481 (57.6%)	**5.47 (4.45-6.71)*** **	84 (50.1%)	**4.37 (2.66-7.18)*** **
Education								
Post-Secondary	19595 (61.6%)	1.00	916 (58.5%)	1.00	431 (52.7%)	1.00	78 (55.2%)	1.00
High School or GED	9071 (25.7%)	1.00	437 (25.2%)	1.03 (0.89-1.19)	250 (31.6%)	**1.44 (1.19-1.73)*** **	41 (26.6%)	1.15 (0.65-2.03)
Less than High School	5047 (12.8%)	1.00	271 (16.4%)	**1.35 (1.16-1.57)*** **	136 (15.7%)	**1.44 (1.13-1.83)** **	36 (18.2%)	1.59 (0.97-2.61)
Household Income (USD)								
>70K	8376 (33.6%)	1.00	252 (21.7%)	1.00	131 (20.7%)	1.00	12 (12.1%)	1.00
35-69,999	9209 (28.1%)	1.00	402 (27.7%)	**1.53 (1.30-1.79)*** **	189 (23.7%)	**1.37 (1.05-1.79)***	33 (20.7%)	2.04 (0.82-5.08)
20-34,999	7207 (18.5%)	1.00	361 (21.5%)	**1.80 (1.48-2.18)*** **	180 (20.7%)	**1.81 (1.36-2.40)*** **	24 (14.7%)	2.20 (0.88-5.49)
0-19,999	8921 (19.8%)	1.00	609 (29.1%)	**2.28 (1.91-2.72)*** **	317 (34.9%)	**2.86 (2.22-3.68)*** **	86 (52.5%)	**7.35 (3.07-17.59)*** **

Note. PTSD = Post Traumatic Stress Disorder, CUD = Cannabis Use Disorder, RRR = Relative Risk Ratio at 95% Confidence Interval. *p<0.05; **p<0.01; ***p<0.001.

Table 2
Multivariate Analysis of Health Comorbidities and Clinical Correlates for PTSD, CUD, and Comorbid PTSD-CUD Compared to Neither Disorder

	Neither (*n*=33,713, 92.9%)		**PTSD Alone** (*n*=1624, 4.5%)		**CUD Alone** (*n*=817, 2.3%)		**PTSD - CUD** (*n*=155, 0.4%)	
Variable	*M (SE)/ n (%)*	*RRR*	*M (SE)/ n (%)*	*RRR*	*M (SE)/ n (%)*	*RRR*	*M (SE)/ n (%)*	*RRR*
Clinical Correlates								
Previous Adverse Childhood Experiences (ACEs)								
Abuse	8104 (24.0%)	1.00	978 (61.0%)	**4.95 (4.37-5.60)*****	318 (36.5%)	**1.82 (1.54-2.14)*****	108 (70.0%)	**7.36 (4.41-12.28)*****
Neglect	11504 (36.0%)	1.00	948 (60.4%)	**2.72 (2.44-3.02)*****	405 (54.1%)	**2.09 (1.76-2.49)*****	102 (69.3%)	**4.01 (2.35-6.84)*****
Household Dysfunction	13334 (39.7%)	1.00	1014 (64.4%)	**2.75 (2.43-3.12)*****	499 (63.0%)	**2.58 (2.14-3.12)*****	127 (83.8%)	**7.83 (3.85-15.95)*****
Type of Traumatic Exposure								
Sexual Assault	1589 (4.5)	1.00	452 (26.1%)	**7.55 (6.57-8.67)*****	59 (7.1%)	**1.62 (1.16-2.27)****	49 (35.9%)	**11.95 (7.94-18.0)*****
Physical Assault	1551 (4.2%)	1.00	217 (12.0%)	**3.14 (2.52-3.90)*****	63 (8.2%)	**2.06 (1.52-2.81)*****	21 (12.3%)	**3.21 (1.83-5.63)*****
Life Threatening Illness	1867 (6.2%)	1.00	89 (6.2%)	1.00 (0.75-1.33)	37 (4.4%)	0.69 (0.46-1.05)	13 (9.9%)	1.68 (0.80-3.52)
Life Threatening Injury	1532 (4.8%)	1.00	125 (7.7%)	**1.64 (1.31-2.06)*****	34 (4.7%)	0.97 (0.60-1.57)	7 (3.6%)	0.73 (0.30-1.80)
Psychological Trauma	3305 (9.7%)	1.00	210 (12.5%)	**1.32 (1.11-1.56)****	115 (12.4%)	**1.31 (1.03-1.68)***	21 (13.6%)	1.46 (0.90-2.38)
Witnessed Trauma	9363 (30.4%)	1.00	355 (24.2%)	**0.73 (0.63-0.85)*****	270 (35.0%)	**1.23 (1.01-1.51)***	36 (21.2%)	0.61 (0.37-1.01)
Other Trauma	2193 (6.9%)	1.00	169 (11.3%)	**1.73 (1.42-2.12)*****	70 (8.3%)	1.24 (0.91-1.67)	7 (3.6%)	0.50 (0.20-1.25)
PTSD Symptom Severity	3.82 (0.05)	1.00	18.42 (0.13)	**1.56 (1.52-1.60)*****	6.30 (0.25)	**1.09 (1.08-1.12)*****	18.76 (0.50)	**1.59 (1.48-1.70)*****
Health Comorbidities								
Other Mental Health Disorders	8225 (24.0%)	1.00	1342 (81.1%)	**13.64 (11.74-15.86)*****	471 (58.4%)	**4.45 (3.73-5.31)*****	150 (96.8%)	**94.84 (37.56-239.44)*****
Other Drug Use Disorders	403 (1.2%)	1.00	112 (6.0%)	**5.41 (4.24-6.90)*****	106 (13.3%)	**13.03 (9.64-17.61)*****	38 (24.9%)	**28.18 (18.08-43.92)*****
Alcohol Use Disorder	4172 (12.3%)	1.00	367 (20.6%)	**1.84 (1.61-2.11)*****	495 (58.9%)	**10.18 (8.61-12.02)*****	99 (62.1%)	**11.67 (7.84-17.38)*****
Physical Health Conditions	1.37 (0.02)	1.00	2.73 (0.09)	**1.25 (1.22-1.28)*****	0.80 (0.06)	**0.81 (0.76-0.86)*****	1.94 (0.27)	**1.13 (1.03-1.23)****

Note. PTSD = Post Traumatic Stress Disorder, CUD = Cannabis Use Disorder, RRR = Relative Risk Ratio at 95% Confidence Interval. Health Comorbidities were examined for past year. Other Mental Health Disorders did not include PTSD. Other drug use disorders did not include CUD. Physical Health Conditions were measured continuous, all other variables are categorical. *p<0.05; **p<0.01; ***p<0.001.

Clinical Correlates

Individuals in the comorbid group displayed the highest number of PTSD symptoms, indicative of the highest PTSD symptom severity compared to individuals with neither disorder. The comorbid group was associated with increased odds of ACEs, including childhood abuse, neglect, and household dysfunction (RRR= 4.01-7.83, all $p<0.001$) compared to individuals with neither disorder. Lastly, PTSD-CUD was associated with increased odds of specific traumatic exposures, including sexual assault and physical assault (RRR= 5.21-6.95, all $p<0.001$) compared to individuals with neither disorder.

Results of the unadjusted multinomial logistic regression analyses comparing PTSD-CUD to PTSD alone (reference group) among clinical correlates and health comorbidities are displayed in Table 3. In secondary comparisons using PTSD alone as the reference group, individuals in the PTSD-CUD group presented with higher odds of specific traumatic exposure, including household dysfunction during childhood, as well as sexual assault (RRR range= 1.58-2.85, all p's<0.05). Individuals in the comorbid group presented with decreased odds of other traumatic exposures when compared to the PTSD alone group (RRR=0.29, $p<0.01$).

Health Comorbidities

Regarding mental health comorbidities, The PTSD alone group was associated with increased odds of any past year mental health disorders, a higher number of physical health conditions, any drug use disorder, and alcohol use disorder, compared to those having neither disorder (RRR range= 1.25-13.64, all $p<0.001$).

The CUD alone group was associated with higher odds of past year mental health disorders, drug use disorders, as well as alcohol use disorder, compared to having neither disorder (RRR range= 4.45-13.03, $p<0.001$). CUD alone was also associated with decreased

odds of physical health conditions compared to having neither disorder (RRR= 0.81, p<0.01).

Lastly, the comorbid group was strongly associated with higher odds of past year mental health disorders, physical health conditions, drug use disorders, and alcohol use disorder (RRR= 1.13 - 94.84, p < 0.01), compared to having neither disorder.

Table 3

Multivariate Analysis Comparing Comorbid PTSD-CUD to PTSD Alone

	PTSD Alone (*n*=1624, 4.5%)		**PTSD - CUD** (*n*=155, 0.4%)	
Variable	*M (SE)/ n (%)*	*RRR*	*M (SE)/ n (%)*	*RRR*
Clinical Correlates				
Previous Adverse Childhood Experiences (ACEs)				
Abuse	978 (61.0%)	1.00	108 (70.0%)	1.49 (0.87-2.53)
Neglect	948 (60.4%)	1.00	102 (69.3%)	1.48 (0.86-2.54)
Household Dysfunction	1014 (64.4%)	1.00	127 (83.8%)	**2.85 (1.38-5.86)****
Type of Traumatic Exposure				
Sexual Assault	452 (26.1%)	1.00	49 (35.9%)	**1.58 (1.05-2.38)***
Physical Assault	217 (12.0%)	1.00	21 (12.3%)	1.02 (0.56-1.85)
Life Threatening Illness	89 (6.2%)	1.00	13 (9.9%)	1.68 (0.75-3.74)
Life Threatening Injury	125 (7.7%)	1.00	7 (3.6%)	0.45 (0.18-1.10)
Psychological Trauma	210 (12.5%)	1.00	21 (13.6%)	1.10 (0.66-1.87)
Witnessed Trauma	355 (24.2%)	1.00	36 (21.2%)	0.84 (0.50-1.42)
Other Trauma	169 (11.3%)	1.00	7 (3.6%)	**0.29 (0.11-0.74)****
PTSD Symptom Severity	18.42 (0.13)	1.00	18.76 (0.50)	1.02 (0.95-1.09)
Health Comorbidities				
Other Mental Health Disorders	1342 (81.1%)	1.00	150 (96.8%)	**6.95 (2.67-18.08)*****
Other Drug Use Disorders	112 (6.0%)	1.00	38 (24.9%)	**5.21 (3.34-8.13)*****
Alcohol Use Disorder	367 (20.6%)	1.00	99 (62.1%)	**6.34 (4.19-9.58)*****
Physical Health Conditions	2.73 (0.09)	1.00	1.94 (0.27)	**0.90 (0.82-0.99)***

Note. PTSD = Post Traumatic Stress Disorder, CUD = Cannabis Use Disorder, RRR = Relative Risk Ratio at 95% Confidence Interval. Health Comorbidities were examined for past year. Other Mental Health Disorders does not include PTSD. Other drug use disorders does not include CUD. Physical Health Conditions were measured continuously, all other variables are categorical. *p<0.05; **p<0.01; ***p<0.001.

Discussion

The present study examined the sociodemographic and clinical profile of individuals with comorbid PTSD-CUD in a nationally representative sample of civilian adults. The primary aim was to highlight pertinent correlates associated with higher likelihood of having comorbid PTSD-CUD, with the ultimate goal of improving our understanding of the nuanced relationship between PTSD and CUD. A four-group model was used, in order to highlight meaningful differences between varying PTSD alone, CUD alone, and PTSD-CUD, in comparison to individuals who do not have PTSD or CUD. Results of the primary and secondary analyses illustrate that individuals with comorbid PTSD-CUD typically present with more severe pathology, when compared to individuals with neither disorder.

Demographic Correlates

Regarding sociodemographic correlates, findings illustrate that individuals with comorbid PTSD-CUD have higher odds of being younger in age, lower income (0-19,999), being single or never married, as well as being of Black or American Indian/Alaska Native descent. These findings are in support of hypothesis that PTSD-CUD would be more prevalent in populations that are young, single, racial minorities, and with lower income. These findings are in line with previous research that illustrated higher likelihood of PTSD and CUD independently among individuals who are younger, with lower income, and from specific racial minorities, including Black or Native American descent (e.g., Kerridge et al., 2018; Hasin et al., 2016).

Females were more than twice as likely to have PTSD than males, while having less than half of the likelihood of CUD than males. There was no significant relationship observed between the comorbid group and sex, likely due to different sex differences for PTSD and CUD independently. These findings supported the hypothesis that PTSD-CUD would occur

approximately equally in males and females, consistent with previous research identifying males had increased likelihood of CUD (e.g., Leadbater et al., 2019; Weaver & Etzel, 2003) and females had increased likelihood of PTSD, independently (e.g., Kessler et al., 1995; Breslau 2009; Secades-Villa & Fernández-Artamendi, 2017). These findings suggest that treatment interventions should consider sex differences in motivations and rates of cannabis use among individuals with PTSD (Khan et al., 2013; Cooper et al., 2017). Tailoring treatment approaches to account for sex differences could help reduce the progression of cannabis use to CUD, particularly among men who are more likely to use cannabis in social or recreational contexts. It could also help to screen women who may be more at risk for developing PTSD and deliver earlier, more timely interventions. Understanding the complex interactions between PTSD and CUD across sexes works to support more nuanced treatment models that can improve clinical outcomes.

Clinical Correlates

All three mental health disorder groups of PTSD, CUD, and PTSD-CUD illustrated increased odds of reporting ACEs (including abuse, neglect, and household dysfunction) compared to individuals having neither PTSD nor CUD. These findings suggest that traumatic experiences during childhood are associated with both posttraumatic stress and cannabis use in adulthood, consistent with past research on PTSD and CUD independently showing higher prevalence of ACEs among individuals with SUDs (Leza et al., 2021; Trovani et al., 2023). Individuals in the comorbid PTSD-CUD group displayed the highest risk ratio for abuse, neglect, and household dysfunction compared to individuals having neither disorder, supporting the prediction that individuals with PTSD-CUD would display with higher rates of ACEs. In comparing individuals with PTSD-CUD to PTSD alone, individuals in the comorbid group

displayed increased odds of experiencing household dysfunction in childhood. These findings are in line with previous research suggesting that traumatic experiences during childhood significantly contribute to both mental health and substance use disorders later in life (e.g., Anda et al., 2006, Felitti et al., 1998). These findings are important because they highlight the strong link between ACEs and both PTSD and cannabis use in adulthood. The fact that the PTSD-CUD group displayed the highest risk ratios for abuse, neglect, and household dysfunction further emphasizes the impact of childhood trauma on the development of these comorbid conditions.

In regards to types of traumatic exposure, I predicted higher rates of traumatic exposure for PTSD-CUD compared to having neither disorder. This hypothesis was partially supported, as individuals with PTSD-CUD had higher likelihood of two types of traumatic exposure, sexual and physical assault. It is important to note that all three mental health groups of PTSD, CUD, and PTSD-CUD were associated with increased likelihood of sexual assault and physical assault, with the comorbid group displaying the highest risk ratio of all three groups. These findings are also consistent with previous research by Campbell and colleagues (2020) wherein the high PTSD symptom group was associated with childhood sexual abuse. Previous research by Foa and colleagues (1992) suggests that physical and sexual assault significantly disrupt an individual's basic assumptions of safety, control, and predictability in the world, which likely contributes to the development of PTSD. In other words, the unpredictability of assault combined with the loss of control experienced can make it challenging for individuals to regain a sense of normalcy and safety following an assault. These results suggest that certain types of traumatic experiences place individuals at higher risk for developing mental health disorders and drug disorders, which is pertinent for understanding who is at higher risk for developing PTSD or CUD following a traumatic experience. Understanding the specific types of traumatic events

that increase the risk of PTSD is fundamental to improving prevention and treatment efforts, placing more focus on individuals who are most at risk for PTSD-CUD.

Furthermore, individuals in the comorbid group displayed the highest risk ratio for PTSD symptom severity of any of the three groups, although increased prevalence of PTSD symptom severity was not significantly greater than those in the PTSD alone group. Understanding differences in PTSD symptom severity is important as individuals with more severe PTSD symptomatology tend to have worse and distinct clinical outcomes compared to those with lower PTSD symptom severity (Campbell et al., 2020). Identifying and treating those with both PTSD and CUD, especially individuals with high severity symptoms, would likely be beneficial to improve treatment outcomes. These findings illustrate the need for more nuanced approaches to comorbid disorder treatment that account for complexities of the interactions between PTSD and CUD.

There is still much clinical debate on whether cannabis use is helpful for managing PTSD symptomatology. This study contributes meaningful information on the comparison of PTSD symptomatology among individuals with comorbid PTSD-CUD versus PTSD alone, to examine whether individuals with the comorbidity are experiencing an increase or reduction in their PTSD symptoms. As there was no significant difference observed in PTSD symptom severity was observed between the comorbid PTSD-CUD and PTSD alone groups, it appears as though cannabis use (in the context of disordered use) is not associated with an improvement of PTSD symptoms. These findings provide further evidence that the relationship between PTSD and CUD needs further investigation, in order to understand meaningful clinical differences between different types of cannabis use patterns. Overall, this research is necessary in order to drive appropriate treatment recommendations and protocols for individuals with comorbid PTSD and

CUD.

Health Comorbidities

Individuals with a higher number of PTSD symptoms have been previously associated with an increased number of mental health comorbidities, as well as poorer mental and physical health (Campbell et al., 2020). Therefore, I predicted that individuals with PTSD-CUD would display higher rates of mental health comorbidities, compared to having neither disorder. Comorbid PTSD-CUD was associated with approximately 95 times higher odds of other mental health comorbidities, compared to individuals having neither disorder. PTSD-CUD was also associated with approximately 7 times higher odds of mental health comorbidities when compared to individuals with PTSD alone. These findings are highly important, as they illustrate that individuals with PTSD-CUD are experiencing significantly more mental health challenges compared to individuals with PTSD who do not have CUD. This suggests that disordered cannabis use may be increasing the mental health challenges associated with PTSD, rather than helping to manage PTSD symptoms. This information is imperative for both the public and clinicians to better identify and treat individuals with PTSD who are using cannabis, offering psychoeducation on risks associated with cannabis use and potentially more tailored interventions for individuals with PTSD using cannabis.

I also examined the association between PTSD-CUD and other substance use disorders, including alcohol use disorder as well as drug use disorders overall. Based on prior literature, I predicted that individuals with PTSD-CUD would present with higher rates of other drug use disorders, as well as alcohol use disorder, compared to individuals with neither disorder. These hypotheses were supported as the PTSD-CUD group was associated with approximately 28 times higher odds of other drug use disorders compared to those with neither PTSD or CUD. They also

had approximately 5 times higher likelihood of other drug use disorders than those with PTSD alone. Individuals with PTSD-CUD had approximately 12 times higher likelihood of AUD (compared to neither) as well as approximately 6 times higher likelihood of AUD compared to individuals with PTSD. This is in line with previous research (e.g., Turna & MacKillop, 2021) that alcohol and cannabis use tend to co-occur. These findings suggest that individuals with the comorbidity have significantly higher likelihood of AUD compared to individuals with PTSD alone, who maintain a relatively high likelihood of AUD as is. These findings appear to suggest greater likelihood of polysubstance use among individuals with comorbid PTSD-CUD, highlighting the increased risk for developing alcohol and other drug use disorders compared to those with PTSD alone. This information is important for clinicians to be aware of in this population and to screen for polysubstance use during treatment. By understanding this heightened risk, interventions can be better tailored to address not only PTSD and cannabis use but also the likelihood of co-occurring substance use disorders, leading to more comprehensive and effective care.

The hypothesis that individuals with PTSD-CUD would display higher rates of physical health comorbidities when compared to individuals with neither disorder was also supported. Interestingly, when compared to individuals with PTSD alone, individuals with PTSD-CUD had less odds of physical health comorbidities. One possible explanation for these findings is that individuals who use cannabis tend to be younger, which might account for fewer physical health issues compared to older individuals with PTSD alone (e.g., Hasin et al., 2016). Another possible explanation is that after using cannabis, individuals may be less cognitively alert and therefore may notice their physical health problems less. It is also possible that the addition of cannabis use (associated with CUD) may be beneficial for physical health comorbidities. Cannabis use

could potentially alleviate pain, distress, or other physical symptoms, leading these individuals to experience fewer comorbid physical health conditions or perceive them as less severe (Ware et al., 2010). Another possibility is that individuals with PTSD-CUD might be less likely to access medical care overall, due to avoidance behaviors, fear of judgement or stigma, or beliefs that cannabis is effectively addressing their health concerns (e.g., Walsh et al., 2017). This may result in fewer diagnosed physical health conditions. Evidently, further research is needed to determine specifically if there are potential benefits to any physical health conditions with cannabis use, as well as distinguishing severity of use measures for cannabis use to determine helpful versus potentially harmful impacts of various usage patterns.

Strengths and Limitations

The present study presented with notable strengths as well as limitations. First, utilizing data collected by the NIAAA for secondary data analysis allowed a large sample to be examined with limited resources. The large sample size also improved the overall generalizability and reliability of the results, as well as providing the opportunity for more detailed subgroup analyses that likely would have not been possible with a smaller sample size. However, as the dataset was cross-sectional in design, no causal relationships between variables could be established. Second, as most variables in the NESARC (including substance use, adverse childhood experiences, and traumatic exposure) are self-reported by participants, responses are subject to recall and memory biases that increase in likelihood over time. This is especially relevant for reported substance use and history of traumatic exposure, which are experiences in themselves that may worsen memory recall. In addition to challenges with memory, individuals with a history of traumatic experiences may experience more shame about their substance use that may lead them to be intentionally dishonest with themselves or others. Individuals with a history of traumatic exposure during

childhood often experienced higher rates of shame that are associated with higher rates of substance use and substance use problems (e.g., Dearing et al., 2005; Bhuptani et al., 2024; Koenig, 2021). Furthermore, shame has been demonstrated to be both an antecedent and consequence of substance use in various contexts (Luoma et al., 2019). Therefore, increased experiences of shame among individuals with substance use may lead them to conceal or underreport their substance use. They may find it difficult to be honest or self-reflect about their patterns of substance use, as it may bring up painful emotions. This may have led individuals to underreport their usage and be classified incorrectly to group membership. Third, as the dataset was collected in 2012-2013, it is possible that the findings presented here are now somewhat outdated. This is of particular relevance, as since legalization of recreational cannabis across sixteen jurisdictions from 2012-2020 (Patton, 2020), it is possible that patterns of use have changed over this time. Lastly, due to the fact that some population segments were not able to be interviewed for the NESARC-III (such as homeless individuals, prisoners, those in hospital, etc.), the estimates presented may underestimate the true prevalence of substance use disorders.

Future Directions

Further research is needed in order to identify which mental health and drug use disorders occur most often alongside comorbid PTSD-CUD, as well as establishing effective treatment for individuals in this highly comorbid group. Due to the high rates of mental health comorbidities and substance use disorders among individuals with PTSD-CUD, future research should also examine a potential relationship between PTSD-CUD and suicidal behaviors. Future research may also continue to examine additional clinical correlates of traumatic experience to further illustrate which individuals may be at higher risk for severe posttraumatic symptoms, as more severe posttraumatic symptoms appear to place them at higher risk for PTSD-CUD. Due to the

prominent worsening of mental health correlates associated with PTSD-CUD, as well as the increased accessibility of cannabis in North America, this understanding is relevant to direct prevention efforts amongst the general population. Furthermore, additional research should also aim to separate or classify different types of cannabis use patterns, in order to more accurately understand the role of cannabis as it contributes to PTSD symptomatology. This may involve studying cannabis use more broadly, and expanding the present research beyond disordered use to other types of cannabis use patterns.

Results indicate that individuals with PTSD-CUD have lower odds of physical health comorbidities compared to those with PTSD alone. Future research can determine whether this is an age related effect as well as continue to examine whether cannabis use may improve certain areas of physical health, provide temporary relief from symptoms, or have a placebo effect. It is also possible that individuals may be reporting fewer physical health symptoms if their cannabis use is masking their symptoms. This could delay necessary medical care, potentially leading to worse outcomes down the road. Research has indicated that while cannabis can offer temporary symptom relief, it might also facilitate an increase in avoidance behaviors, that may ultimately reduce effective treatment seeking behaviors (e.g., Bonn-Miller et al., 2011). It would be beneficial for clinicians to openly discuss cannabis use with their patients, doing their best to foster a nonjudgemental approach that encourages individuals to share their experiences with the shared goal of improved care. It is possible that some individuals may be missing critical opportunities for formal care and interventions that may be more suitable to their needs and goals. Moreover, further research is needed to examine how different aspects of cannabis use, including method of delivery, dosage, frequency of use, and type of cannabis product used, impact both PTSD symptoms and physical health. These findings would help to illustrate if

certain patterns of cannabis use are beneficial or harmful for symptomatology (e.g., Yehuda et al., 2015).

These findings also illustrate the need for public psychoeducation and knowledge dissemination, especially as cannabis has become more widely used and socially accepted. There is a real need for public health campaigns to address the complexities of cannabis use in populations at risk for PTSD, highlighting both the potential risks and benefits of working with a clinician for optimal care. Emphasizing professional treatment over self-medication could reduce the risks associated with dependence and support healthier coping mechanisms. Additionally, the observed relationship between PTSD, cannabis use, and fewer reported physical health issues suggests the need for integrated treatment approaches. Interventions that address both PTSD and substance use simultaneously could be particularly beneficial to improve treatment outcomes (e.g., Back et al., 2014; McGovern et al., 2011).

Overall, these findings emphasize the importance of holistic, patient-centered care that considers the interaction between mental health and physical health. Social determinants, including socioeconomic status, access to healthcare, and perceived stigma, may all influence how cannabis use and PTSD impact one another (e.g., Breslau, 2009). Understanding these factors in greater detail would likely be beneficial in developing more targeted public health interventions to support those most at risk. Research regarding the relationship between PTSD and cannabis use disorder is imperative now more than ever in order to guide best practice guidelines for both the public and practitioners.

Chapter Three:

Cannabis Use Profiles Among Individuals with Posttraumatic Stress Disorder: A Latent Mixture Model

Jessa M. Hogarth[1], Matthew Keough[2], & Natalie Mota[3]

(1) Department of Psychology, University of Manitoba

(2) Department of Psychology, York University

(3) Department of Clinical Health Psychology, University of Manitoba

Abstract

Among individuals with PTSD, research ascertains both perceived therapeutic benefits and harms associated with cannabis use. This reported disparity may be explained by differing types of cannabis use patterns that are associated with distinct clinical outcomes. The present study utilized latent mixture modelling (LMM) to identify cannabis use profiles among individuals with lifetime PTSD who endorsed lifetime cannabis use (N = 1145), in a large sample of adult civilians from the National Epidemiologic Survey on Alcohol and Related Conditions III (NESARC-III). The LMM was run in Mplus using the R3STEP method. Five cannabis use variables were inputted into the LMM, including: (1) age of first use, (2) quantity of use, (3) frequency of use, (4) medicinal cannabis use, and (5) disordered cannabis use (CUD). Four distinct cannabis use classes were identified, including: *moderate severity* (mid-teen onset, moderate quantity, high frequency daily use), *low stable use* (adult onset, low quantity and frequency use), *low variable use* (late-teen onset, low quantity, moderate frequency use), and *high severity* (early teen onset, daily use, high quantity, high frequency). Moderate and high severity classes had earlier age of first use, significantly more medicinal use, and increased odds of past year CUD (OR = 0.15-0.43, all $p<0.001$). Participants in the low variable use class were significantly older than those in the moderate severity class, while the high severity class had significantly more males than any of the other three classes. The high severity class was the only class associated with increased odds of PTSD symptom severity (OR = 0.78-0.81, $p<0.05$). Tobacco use disorder was associated with increased odds among the moderate and high severity classes compared to both low severity classes (OR = 0.26-0.49, $p<0.05$ or lower). Results illustrate key differences among cannabis use patterns that are imperative to improving our understanding regarding the relationship between PTSD and cannabis use.

Keywords: Posttraumatic Stress Disorder, PTSD, Cannabis, Marijuana, Cannabis Use Disorder, Latent Mixture Model, Substance Use Disorder, Comorbid Disorders.

Introduction

Posttraumatic stress disorder (PTSD) is a mental health disorder characterized by intrusion, avoidance, cognitive, mood, arousal, and reactivity symptoms, following exposure to death, serious injury, or sexual violence (American Psychiatric Association, 2013). The relationships between PTSD and substance use have been well established. Cannabis and alcohol are the most commonly used substances among individuals with PTSD (e.g., Turna & MacKillop, 2021; Mills et al., 2006; Anthenien et al., 2021), for a variety of reasons, including enhancement, expansion, coping, relaxation, conformity, and socialization motives (Anthenien et al., 2021; Bresin & Mekawi, 2019; Reilly et al., 1998; Simons et al., 2000; Bonn-Miller et al., 2014a; Bordieri et al., 2014). There are more than 104 different types of cannabinoids (ElSohly & Gul, 2014), including delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), as well as a number of synthetic cannabinoids (e.g., nabilone) that have been developed in capsule form (National Academies of Sciences, Engineering & Medicine, 2017). Although widely understood that cannabis is frequently used by individuals with PTSD, the interaction between cannabis use and PTSD symptomatology is not well understood, with research on the topic described as “sparse and inconclusive” (O’Neil et al., 2017).

There are inconsistent, mixed findings regarding the therapeutic use of cannabis for symptom management among individuals with PTSD. Some individuals self-report that cannabis is beneficial for reducing PTSD symptoms (Greer et al., 2014; Elms et al., 2019; Cameron et al., 2014), as well as improving secondary issues of sleep, mood, anxiety, and stress (Fraser, 2009; Cameron et al.; Bonn-Miller et al., 2014a; Jetly et al., 2015). Cannabis has been self-reported as “moderately” to “quite a bit” helpful among individuals with PTSD using medicinal cannabis, despite simultaneously reporting a high number of cannabis use problems (e.g., Bonn-Miller et

al., 2014a). Greer and colleagues compared individuals who do not use cannabis to individuals who were prescribed medicinal cannabis for treatment of PTSD. They reported a greater than 75% reduction in intrusion, avoidance, and negative alteration PTSD symptoms, however the sample was limited to individuals who had already found cannabis helpful for PTSD symptom management. Alternatively, a clinical trial by Fraser examined the effectiveness of nabilone in treatment resistant nightmares among individuals with PTSD. They reported a 72% reduction or elimination of nightmares, with 28% discontinuing nabilone due to side effects. However, only 9% of participants experienced successful discontinuation of nabilone after 4-12 months of pharmacotherapy (i.e., their nightmares returned if nabilone was stopped).

Alternatively, some individuals with PTSD experience no improvement (Bonn-Miller et al., 2014a; Johnson et al., 2016) or worsening of their PTSD symptoms (Wilkinson et al., 2015; Hinojosa et al., 2023; Manhapra et al., 2015; Metrik et al., 2016) with cannabis use. Wilkinson and colleagues conducted a comprehensive, longitudinal study of 2,276 veterans to examine four groups of individuals with PTSD, including those with no cannabis use at admission or discharge, those who used cannabis at admission but not after discharge, those who used cannabis at admission and after discharge, and those using cannabis after discharge but not at admission. They found that cannabis use was significantly associated with negative outcomes in PTSD symptom severity, violent behavior, and concurrent alcohol/drug use. Interestingly, they also found that at follow up, those who had never used or had stopped using cannabis at discharge had the lowest levels of PTSD symptoms, while those who had started use after discharge had the highest levels of violent behavior. These findings appear to suggest that cannabis use is associated with more severe PTSD symptomatology, as well as other undesirable behaviors. Boden and colleagues (2013) examined the association between PTSD and cannabis

use (nonspecific type) among 94 veterans with cannabis dependence (now CUD) immediately before cannabis cessation. They found that compared to participants without PTSD, participants with PTSD endorsed significantly higher coping motives, and reported increased rates of craving and withdrawal symptoms. These findings continue to suggest a complex, nuanced relationship between PTSD symptoms and cannabis use. Evidently, further research is needed to examine the relationships between PTSD symptomatology and motives for cannabis use. A more recent study by Hinojosa and colleagues (2023) examined the association between different types of cannabis users and PTSD symptoms, among females who experienced a recent criterion A traumatic event. They found that among all three groups of cannabis users (low, increasing, and high cannabis use), cannabis use (nonspecific type) was associated with increased PTSD symptomatology at both time points of 8 and 12 weeks. These findings appear to suggest that cannabis use after traumatic exposure is associated with worsening of PTSD symptomatology. Collectively, these studies highlight the potential risks associated with cannabis use among individuals with PTSD, suggesting that cannabis use may potentially worsen symptoms rather than provide symptom relief.

Heterogeneity of Cannabis Use

As there are inconsistent and inconclusive findings regarding the therapeutic use of cannabis among individuals with PTSD, it appears likely that the disparity observed between helpful and harmful therapeutic uses may be at least partially attributable to assessing cannabis use homogenously. Examining patterns of cannabis use homogenously appears to neglect meaningful differences between varying patterns of cannabis use, as previous research on cannabis use often does not regulate or report specific types of cannabis products used, frequency of cannabis use, or quantity and duration of use (e.g., Bonn-Miller et al., 2014b;

Johnson et al., 2016; Elms et al., 2019; Greer, et al., 2014).

To this point, recent research on comorbid PTSD and substance use disorders has emphasized the fundamental importance of addressing heterogeneity within substance use patterns (e.g., Contractor et al., 2019). A meta-analysis by Pearson (2019) noted that cannabis use presents with significant heterogeneity related to negative consequences, that are not explained by a single factor of cannabis use. Furthermore, Kroon and colleagues (2020) conducted a systematic review that highlighted potential moderators of CUD in the brain, including age of use onset, heaviness of use, CUD severity, the ratio of 9-tetrahydrocannabinol to cannabidiol, and the severity of comorbid disorders. These findings suggests that additional factors of cannabis use must be taken into account to portray the effects of cannabis use among individuals with PTSD accurately.

In determining which severity of use indicators appear to be most influential, Canada's lower-risk cannabis use guidelines discuss age of first cannabis use, choice of cannabis product (i.e., high versus low THC and CBD), method of consumption (i.e., smoking, edibles), frequency of use, intensity of use, and genetic risk factors as severity of use indicators that place individuals at higher risk for consequences of cannabis consumption (as discussed by Fisher et al., 2017). Frequency is arguably the most robust and widely used measure of cannabis use severity, with "substantial evidence for a statistical association between increases in cannabis use frequency and the progression to developing problem cannabis use" (National Academies of Sciences, Engineering & Medicine, 2017, p.337). In a previous latent class analysis of cannabis use, Fischer and colleagues (2009) found that earliest age of first use and highest frequency of use was associated with higher risk of harm among individuals with CUD. Among individuals with PTSD, higher frequency of cannabis use has been consistently linked to increased symptom

severity. Bonn-Miller et al. (2014b) found that individuals with PTSD who used cannabis more frequently reported more severe PTSD symptoms over time. Similarly, studies have shown that increased frequency of cannabis use is associated with worse overall clinical outcomes, including greater anxiety, depressive symptoms, and reduced functional ability among individuals with PTSD (Yehuda et al., 2015; Wilkinson et al., 2015). Leadbeater et al. (2018) also demonstrated that high cannabis use frequency is associated with increased psychotic and depressive symptoms, which co-occur with PTSD.

The majority of previous research on cannabis use has neglected to investigate the impact of quantity of cannabis consumption (i.e., amount of cannabis consumed) on health outcomes (as discussed by Callaghan et al., 2020), despite research that cannabis use quantity is associated with cannabis related problems (e.g., Zeisser et al., 2012). In fact, low risk guidelines on cannabis use caution individuals to avoid daily use, however make no mention on quantity of use (Fischer et al., 2017). Zeisser and colleagues discuss how this may be partially due to the fact that there is no easy way to standardize quantity of cannabis consumption, in comparison to alcohol which has a "standard size drink."

Furthermore, any amount of cannabis use inherently comes with the risk of developing CUD, including symptoms of cannabis dependence and tolerance. While some individuals who use cannabis report low frequency, low quantity of use that is associated with lower risk of CUD, others report high frequency, high quantity use patterns that may facilitate development of CUD (e.g., Leung et al., 2020). Previous reviews and research have examined the relationship between frequency of cannabis use and progression to disordered cannabis use (i.e., CUD; Robinson et al., 2022; Callaghan et al., 2020; Schuster et al., 2019; Leung et al., 2020), illustrating that CUD is significantly associated with increased quantity of cannabis use, frequency of cannabis use,

and the quantity-by-frequency interaction (Callaghan et al., 2020). Schuster and colleagues (2019) found that frequency of cannabis use, beliefs about use, perceived cognitive abilities, and reported anxiety were all associated with increased CUD severity in young adults with regular cannabis use patterns.

Additionally, there may be significant differences in clinical outcomes between medicinal and recreational cannabis use. Medicinal cannabis use has been associated with higher rates of cannabis use and PTSD symptomatology compared to recreational cannabis use (Loflin et al., 2017). Findings by Wall and colleagues (2019) demonstrated that individuals who use cannabis for both medical and recreational motives, as well as medical only users demonstrate higher prevalence of medical conditions and lower physical quality of life. Moreover, medicinal cannabis use has been associated with more severe cannabis use profiles (Fischer et al., 2010), and there is some evidence to suggest that medicinal cannabis use has been previously shown to be higher among people with CUD (Choi et al., 2017). There is minimal research overall examining differences between recreational and medicinal cannabis use, partially due to the fact that cannabis was an illegal substance until recent years.

Recent systematic reviews have noted contradictory, inconclusive, and limited findings regarding safety and efficacy of medicinal cannabis for the treatment of PTSD (Shishko et al., 2018; Orsolini et al., 2019). Shishko and colleagues reviewed five studies evaluating the use of medicinal cannabis for PTSD, including three studies that discussed potential benefits of medicinal cannabis use and two that discouraged medicinal cannabis use. Orsolini and colleagues reviewed 12 studies examining four types of cannabis and CBD use (Nabilone, CBD, THC, or combined CBD+THC) for PTSD symptom management. Their findings were mixed, with studies reporting reduction in PTSD symptom severity (5 studies; all four types), some

reporting no change (2 studies; CBD+THC, THC), and some reporting worsening of PTSD symptom severity (1 study; CBD+THC). Five studies reported improvement in insomnia and reduction of nightmares (Nabilone, CBD+THC, THC). They reported health risks and chronic use risk associated with cannabis use. Therefore, it appears that medicinal cannabis use may be associated with more severe use patterns that are likely associated with undesirable clinical outcomes, or may develop into problematic use patterns.

It is fundamentally important to the study of PTSD and cannabis use to investigate variability in cannabis use severity patterns, such as quantity of use, frequency of use, age of first use, medicinal use, disordered use, and polydrug use (e.g., Callaghan et al., 2020; Pearson, 2019), in order to provide evidence-based recommendations for PTSD treatment.

Latent Mixture Modelling

Person-centered analytic approaches, such as latent class analysis and mixture modelling, are useful in differentiating large-scale, heterogeneous groups into distinctive subpopulations. This is accomplished by identifying relationships or patterns between pertinent variables (Dean & Raftery, 2010; Collins & Lanza, 2010; McCutcheon, 2002; McCutcheon, 1987; Hochheimer et al., 2020). Prior research utilizing latent mixture modelling for substance use disorders among individuals with PTSD has produced three-class solutions (Anderson et al., 2017; Contractor et al., 2017; Contractor et al., 2019; Tomczyk et al., 2016) as well as five-class solutions (Kearns et al., 2020), although the latter incorporated variables of coping strategy utilization that likely affected the number of classes identified. Research by Contractor and colleagues (2019) investigated latent classes of substance use (SU) among individuals with PTSD. They utilized PTSD symptoms, alcohol use, and drug use responses in order to classify different subgroups of individuals with PTSD who used substances. They found three distinct classes, including low

PTSD symptoms and SU, moderate PTSD symptoms/drug use and high alcohol use, and high PTSD symptoms and SU. These three groups primarily differed on measures of symptom severity, and produced differential outcomes on measures of depression and reckless behavior. This illustrates that severity of use patterns tend to produce differing clinical outcomes among people with PTSD. Second, Kearns and colleagues (2020) examined latent classes of substance use among individuals who had experienced at least one *DSM-5* Criterion A traumatic event. By examining PTSD symptom severity and endorsement of substances, they identified five classes that they classified as: (1) asymptomatic PTSD/low substance, (2) asymptomatic PTSD/high substance, (3) low PTSD/low substance, (4) moderate PTSD/moderate substance; and (5) high PTSD/moderate substance. The term "asymptomatic PTSD" was used to denote individuals with relatively few PTSD symptoms who had still been exposed to a *DSM-5* Criterion A traumatic event. This illustrates that higher PTSD symptom severity scores tend to be associated with higher substance use, however does not speak to cannabis use specifically.

Previous class analysis of cannabis use patterns among the general population has identified important cannabis severity use measures that produce differential clinical outcomes. Research by Fischer and colleagues (2017) on typologies of cannabis users among a Canadian adult sample utilized six cannabis use variables for latent mixture modelling, including: (1) age of first use, (2) frequency past 30 days, (3) frequency past three months, (4) quantity consumed past year, (5) medicinal use, and (6) with whom used. The study identified a four-class solution for the data, whereby early age of first use and highest frequency of use were associated with poor clinical outcomes, including other illicit drug use, health problems, and cannabis use problems. This study can be used to frame pertinent cannabis use severity measures (i.e., frequency, quantity, age of first use, medicinal use) that are important in class analysis.

Two novel research studies (Contractor et al., 2019; Kearns et al., 2020) have utilized latent class analysis to examine substance use typologies among individuals with PTSD, however did not isolate cannabis use from overall substance use profiles. Cannabis may present with unique consumption patterns and differential clinical outcomes in comparison to other substances. Previous research has demonstrated that differing substances are associated distinctly with different PTSD symptoms (e.g., Avant et al., 2011; Jakupcak et al., 2010; Khoury et al., 2010). Additionally, due to the fact that medicinal cannabis is prescribed for the treatment of PTSD, it is important to examine the relationship between cannabis use and PTSD specifically, in order to better ascertain helpful versus harmful patterns of use.

To my knowledge, only one recent study by Hinojosa and colleagues (2023) utilized latent mixture modelling to examine the associations between different types of cannabis use patterns (low, high, and increasing use) and PTSD symptoms, among females who experienced a recent criterion A traumatic event. Albeit these individuals did not have a formal PTSD diagnosis. They found that among all three groups of individuals who used cannabis, cannabis use was associated with increased PTSD symptomatology at follow up week 8 and 12 time points. However, this study did not have a comparison group of individuals without cannabis use, making it difficult to differentiate if the worsening of symptoms is specific to cannabis use, or would have occurred following the traumatic event alone.

Treating cannabis use as a unified construct negates the importance of widely recognized substance use severity indicators, such as frequency of use, quantity of use, age of onset of use, number of years of use, and medicinal use that are associated with disordered use patterns (e.g., Callaghan et al., 2020). Previous research has often neglected to examine specific subtypes of cannabis products and specific patterns of cannabis use that may be associated with differential

clinical outcomes. Information regarding which cannabis use profiles are associated with various severity of use indicators is beneficial in order to develop more tailored treatment interventions that address specific risk factors and needs of each subgroup, with the goal of reducing adverse effects (e.g., CUD), disorder symptomatology, and functional impairment. Furthermore, improved understanding of heterogeneity of cannabis use patterns can be used to make sense of the body of research that ascertains both perceived advantages and harms of cannabis use for individuals with PTSD.

The Present Study

Using a cross-sectional large sample of adults in the United States, the present research utilized latent mixture modelling to identify unique cannabis use profiles among individuals with lifetime PTSD. Five main cannabis use variables were inputted into the latent mixture model, including: (1) quantity of use, (2) frequency of use, (3) age of first use, (4) disordered use, and (5) medicinal cannabis use. (See Appendix D). Once I identified distinct cannabis use profiles, selecting the model with the best fit, I then examined the relationship between the cannabis use profiles and PTSD symptom severity, as well as other sociodemographic and clinical correlates. Due to the fact that cannabis use appears heterogeneous and presents with varied clinical presentation, I expected that the LMM would produce three to five distinct profiles of cannabis usage, in line with a previous LMM examining PTSD and SUD (Contractor et al., 2019; Kearns et al., 2020). I predicted the cannabis use profiles would differ on measures of overall severity, with certain classes presenting with more severe use patterns.

The primary goal of the study was to differentiate between high and low risk patterns of cannabis use among individuals with PTSD. I expected to find at least one high risk group, characterized by early onset use, high frequency and quantity of cannabis use, as well as at least

one low risk group, characterized by later age of first use, as well as low frequency and quantity of use.

Prior research by Wilkinson and colleagues (2015) indicated that cannabis use was associated with worse PTSD symptom severity among individuals with PTSD. Therefore, I predicted there would be an association between more severe cannabis use classes (high frequency, high quantity, early age of first use) and increased PTSD symptom severity. I also expected to find that more severe cannabis use classes would be associated with substance use disorders, including alcohol use disorder and tobacco use disorder, based on previous research on PTSD and AUD co-occurrence (e.g., Turna & MacKillop, 2021), as well as PTSD and tobacco co-occurrence (e.g., Estey et al., 2021).

Lastly, both cannabis use and cannabis use disorder have been associated with reduced quality of life in the general population (Lev-Ran et al., 2012; Goldenberg et al., 2017), with lowest scores among individuals who used cannabis heavily or met criteria for CUD. Therefore, the present study hypothesized that cannabis use would be associated with reduced mental and physical quality of life among individuals with PTSD. Specifically, I predicted that high severity profiles (early age of first use, high frequency, high quantity) would be associated with the lowest quality of life scores.

Method

Participants

The present study utilized data from the National Epidemiological Survey for Alcohol and Related Conditions Wave Three (NESARC-III), collected by the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The NESARC-III was conducted from April 2012 through June 2013 using multistage probability sampling, with detailed recount of data collection

protocols detailed elsewhere (e.g., Grant et al., 2014). The NESARC-III includes a civilian sample of noninstitutionalized adults living in the United States of America, including inactive veterans, excluding active service members to maintain confidentiality (Grant et al., 2014). Additionally, Black, Hispanic, and Asian adults were sampled at a higher rate than the remainder of the population intentionally to increase power and reliability of the information provided by these marginalized groups. The target sample size was determined based upon prior NESARC wave designs to provide sufficient power with a cutoff of 80% and a minimum effect size greater than 3% (Cudjoe, 2019).

A total of 44,931 individuals were selected to participate in the NESARC-III, however 1,567 were ineligible for interview due to exclusion criteria. Of the remaining 43,364 eligible individuals, 36,309 participated in the NESARC-III, while 7,055 declined to respond. This yielded an overall response rate of 60.1 percent (Grant et al., 2014). The present study utilized a subsample of participants endorsing lifetime PTSD who also endorsed lifetime cannabis use (N = 1145). This subsample allowed for comparisons along varying cannabis use dimensions to examine patterns of use.

Procedure

To administer the NESARC-III survey, approximately 1,000 trained interviewers visited the addresses previously selected through multistage probability sampling in the United States. Participants were then given the opportunity to participate, and were asked general questions about their background, health, and lifestyle. Further details about this process are described by Grant et al. (2014).

Ethics approval was obtained from the University of Manitoba Bannatyne Research Ethics Board, followed by data acquisition from the NESARC-III Data Access Committee with the

NIAAA. Consent was obtained during primary data collection by the owners of the data, the National Institute on Alcohol Abuse and Alcoholism (NIAAA).

Measures

The NESARC-III employed a semi-structured diagnostic interview in order to collect information using the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5; National Institute on Alcohol Abuse and Alcoholism, 2015). The AUDADIS-5 was designed to assess alcohol, drug use and mental health disorders according to *DSM-5* criteria in the general population (Grant et al, 2001).

Posttraumatic Stress Disorder

During the semi-structured interview, participants were asked about 20 potentially traumatic events they may have directly experienced during their lifetime (e.g., serious life-threatening injury or illness), as well as 14 they may have witnessed or been indirectly exposed to (as described by Hale et al., 2018). Participants who reported experiencing at least one type of traumatic event (i.e., Criterion-A; Appendix A) were subsequently asked 33 questions about their symptoms following the most traumatic or stressful event they had experienced. A subset of these questions were used assess the 20 PTSD symptoms from *DSM-5* (Criteria B–E) in different ways, including five questions for criterion B (intrusion), two questions for criterion C (avoidance), seven questions for criterion D (altered cognition/mood), and six questions for criterion E (arousal; Chen et al., 2017; Goldstein et al., 2016). Furthermore, as per *DSM-5* diagnostic criteria, participants had to indicate if symptoms persisted greater than one month, as well as indicate clinically significant impairment or distress. For the present study, participants were included in the sample if they met *DSM-5* diagnostic criteria for lifetime PTSD (see Appendix A). Key sociodemographic characteristics of the lifetime PTSD sample are reported

below in Table 4.

Cannabis Use Variables

Age of First Use. Participants were asked to report how old they were when they first used cannabis. This was entered as a continuous variable in the LMM.

Frequency. Participants were asked two questions about their frequency of cannabis use, including their average frequency of use over the past year and their highest frequency of use over their lifetime. The present study utilized peak use as a measure of frequency, in order to remain consistent with the other lifetime cannabis use variables in the LMM, as well as to utilize highest severity of use as a meaningful indicator of substance use severity. Participants were asked *"when you were using marijuana the most, about how often did you use marijuana*?" Participants were asked to choose from ten response categories, including: (1) every day, (2) nearly every day, (3) 3–4 times a week, (4) 1–2 times a week, (5) 2–3 times a month, (6) once a month, (7) 7–11 times in the last year, (8) 3–6 times in the last year, (9) two times in the last year, and (10) once in the last year. Frequency was initially coded continuously, with daily = 1, through once in the past year = 10. It was re-coded so that 1=once in the past year through 10=daily so that higher scores represented higher frequency of use.

Quantity. Participants were asked two questions about the quantity of cannabis they consumed, investigating average consumption over the past year and highest consumption across the lifespan. The present study again utilized peak use, in order to retain lifetime cannabis use variables in the LMM, as well as to utilize highest severity of use as a meaningful indicator of substance use severity. Participants were asked *"on the days that you used marijuana the most, about how many joints did you usually smoke in a single day."* Participants reported the number of joints, which resulted in a range of 0-40. Quantity was entered continuously.

Medicinal Cannabis Use. Participants were asked if they had used medicinal cannabis in the last 12 months and/or before 12 months ago. Participants that endorsed past year or prior use were considered to meet criteria for lifetime medicinal cannabis use, with medicinal use entered categorically into the latent mixture model.

Cannabis Use Disorder (Dichotomous). Participants were asked a series of questions during the interview to assess past year and lifetime *DSM-5* criteria for CUD. Cannabis use disorder was entered categorically into the LMM, based on lifetime DSM-5 criteria whereby 0 = *no use*, and 1 = *CUD*.

Predictors of Class Membership

Age. Participants were asked to provide their age in years, ranging 18 years and older. Age was entered continuously.

Sex. Participants were asked to identify their biological sex assigned at birth as male or female. Responses were categorically coded, whereby 0 = *male*, 1 = *female*.

PTSD Symptom Severity. I computed a composite variable delineating total PTSD symptom count as an indicator of PTSD symptom severity. This was calculated by summarizing the individual symptom criteria for intrusion, avoidance, cognition/mood and arousal/reactivity, producing a composite score ranging from 0-30, with PTSD threshold in the range of 6-30 (see Appendix F). This did not include the questions for *DSM-5* Criterion A, F, or G regarding exposure to the traumatic event, duration of the disturbance, or impairment. Posttraumatic stress disorder symptom severity was entered continuously and mean centered. Reliability of PTSD overall using the AUDADIS-5 has been shown to be good (Grant et al., 2015).

Past Year CUD (continuous). I created a continuous composite variable of past year CUD symptom count, ranging from 0-11. This was used to assess the number of CUD symptoms

endorsed by each class (See Appendix E).

Alcohol Use Disorder. The AUDADIS-5 was used to assess alcohol use as well as alcohol use disorder in the past year and lifetime periods. Participants were asked during the face-to-face interview about their patterns of alcohol consumption. Lifetime alcohol use disorder was entered dichotomously, whereby 0 = no AUD and 1 = lifetime AUD.

Tobacco Use Disorder. The AUDADIS-5 was used to assess tobacco use as well as tobacco use disorder in the past year and lifetime periods. Participants were asked during the face to face interview about their patterns of tobacco use. Lifetime tobacco use disorder was entered dichotomously, whereby 0 = no TUD and 1 = lifetime TUD.

Quality of Life. The 12-Item Short-Form Health Survey (SF-12) was used in the NESARC-III as a global measure of quality of life. It is a shortened version of the 36-Item Short Form Health Survey (SF-36), which was created to assess eight main areas of functioning, including: (1) physical function, (2) mental health, (3) role functioning (emotional), (4) role functioning (physical), (5) social functioning, (6) bodily pain, (7) vitality, and (8) general health (Ware et al., 1996). As described in the NESARC-III data notes, for participants who had a missing response on the SF-12 that could be imputed based on their responses to other questions, their missing response was imputed. More specifically, participants who reported a valid (non-missing) response for the item on general health but were missing values for one to four of the other component variables, the missing data was imputed on the basis of the response to general health. For participants who had missing data for the question on general health but valid responses to all of the other items, their score on general health was imputed on the basis of their score for the other 11 remaining items. Imputation flag variables were used to indicate cases with imputed values. Participants with missing scores in excess of what is described here were left

unimputed and this resulted in missing values. The SF-12 has been demonstrated to be highly correlated with the components of SF-36, while still discriminating between pertinent variables of physical and mental health. Therefore, the SF-12 produces a summary score in the two domains of mental health (Mental Component Summary; MCS) and physical health (Physical Component Summary; PCS). Scoring is continuous and norm based with a mean of 50 (SD = 10), whereby higher scores indicate increased quality of life. The SF-12 has been demonstrated to possess good reliability and validity in both general and clinical populations (Ware et al., 1996; Salyers et al., 2000). It also has been demonstrated as suitable for the assessment of quality of life in trauma patients (Kiely et al., 2006).

Analyses

Latent mixture modelling (LMM) is a person-centered statistical approach used to separate latent classes of homogenous groups from a larger heterogeneous sample. I utilized LMM using MPlus version 8.7 (Muthén and Muthén, 1998-2017) in order to identify latent profiles of cannabis use among individuals with lifetime PTSD. The latent mixture model was run using a R3STEP method (as described by Asparouhov & Muthén, 2014; Dermody, 2018), which allowed for estimation of class portion, as well as comparisons utilizing follow up multinomial logistic regressions. The latent class model was determined based on the five cannabis use variables, including: (1) age of first use, (2) frequency of use, (3) quantity of use, (4) medicinal cannabis use, and (5) disordered cannabis use (see Appendix D). Each participant was assigned to their most likely group membership, based on the distribution from step one. Regression analyses were used to predict the most likely group membership based on the cannabis use variables. Predictors of interest were entered, including age, sex, PTSD symptom severity, past year CUD, as well as AUD, TUD, and quality of life.

To determine the optimal number of latent classes underlying the data, I ran the LMM multiple times increasing the class number systematically, discontinuing when model fit was observed to decline (as done by Contractor et al., 2019; Sommer et al., 2018). Three primary information criteria were used to aid in model selection, including Akaike Information Criterion (AIC; Raftery, 1995), the sample size-adjusted Bayesian information criterion (BIC; Schwartz, 1978). The adjusted BIC has been shown to be more consistent than AIC in model selection (e.g., Padgett & Tipton, 2020; Morgan, 2015; Nylund et al., 2007), however I ran both for comparison. I used a drop of greater than ten points to determine a superior model fit with the addition of k+1 classes. I also conducted the adjusted Lo-Mendell-Rubin likelihood ratio test (aLMR; Lo et al., 2001), which is a significance test utilizing a cutoff score of less than 0.05, designed to test the null hypothesis that the model with less classes fits the data as well as the model with more classes. The aLMR has been demonstrated to be highly consistent indicators and is recommended across mixture models used for class analysis (Padgett & Tipton, 2020; Nylund et al., 2007). Lastly, the entropy statistic (Raftery, 1995) was used to estimate how distinct each class is from one another. The entropy statistic is used to provide an indication of the classification quality, with values near 1 indicating a better model fit. Typically, a cut off score of 0.8 is used as an indicator of good accuracy. Average classification probability was examined as a measure of quality of classification, ensuring high scores in the retaining model.

Once the optimal number of classes were determined, the classes were compared on other severity predictors, including PTSD symptom severity, alcohol use disorder, and tobacco use disorder. Other drug use disorders could not be examined, due to too small of a sample size among some classes to make suitable comparisons. The classes were also compared along physical and mental disability as a measure of quality of life.

Results

Table 4 illustrates descriptive statistics for the subsample of participants with lifetime PTSD who endorsed lifetime cannabis use, which were used in the latent mixture model (N = 1145). The subsample was observed to be primarily female (66.5%), White (59%), married/cohabiting (35.8%), with low income (0-19,999; 40.3%) and have some post-secondary education (58.8%). The average age was 40.08 years old, and the average age of first cannabis use was 16.78 years old. A total of 93 participants endorsed lifetime medicinal cannabis use (8.1%), and 400 (34.9%) met criteria for lifetime CUD. 755 met criteria for lifetime tobacco use disorder (65.9%), and 803 met criteria for lifetime alcohol use disorder (70.1%). The average PTSD symptom count (indicative of PTSD symptom severity) was 19.15/24 symptoms, while the average past year CUD symptom count was 1.25/11.

Table 4
Descriptive Statistics of Cannabis Use Variables (N = 1145).

Variables	N (%)	M	SD	Range
Age		40.08	13.50	18-90
Sex	761 F (66.5%)			
PTSD Symptom Severity	--	19.15/24	3.02	10-24
PY CUD Symptom Severity	--	1.25/11	1.97	0-11
Age of First Use	--	16.78	5.16	10-75
LT Peak Quantity (joints/day)	--	3.41	4.22	1-40
LT Peak Frequency	--	7.16	3.20	1-10
SF-12 PDS	--	45.23/72	12.87	9.8-71.3
SF-12 MDS	--	40.62/72	12.89	3.8-72
LT AUD	803 (70.1%)	--		
LT TUD	755 (65.9%)	--		
LT Medicinal Use	93 (8.1%)	--		
LT CUD	400 (34.9%)	--		

Note. Frequency was measured categorically, with 1 = once per year, 2 = 2 times per year, 3 = 3-6 times per year, 4 = 7-11 times per year, 5 = once per month, 6 = 2-3 times per month, 7 = 1-2 times per week, 8 = 3-4 times per week, 9 = nearly every day, and 10 = daily. *p<0.05; **p<0.01; ***p<0.001. PY = past year, LT = lifetime.

The four-class solution was demonstrated to be the best fit for the data (Table 5). Although the five-class solution had the smallest aBIC and AIC, the aLMRT indicated that the model with five classes was not significantly beneficial over the model with four classes. Alternatively, the four-class solution maintained lower AIC, aBIC, and entropy statistics over the three-class solution, while still maintaining significant benefit over the three-class model as indicated by the aLMRT. The four-class solution was also consistent with previous research, indicating a 3-5 class solution would likely be the best fit for the data. Therefore, the four-class model was retained, as it was the best overall fit for the data. It maintained support from the aLMR and entropy statistics, as well as high classification probabilities for all four classes. Lastly, the four-model solution made sense based on theoretical interpretation, and was generally consistent with past research differentiating low from high severity classes.

Table 5

Model Fit Indices for Cannabis Use Variables Among Individuals with Lifetime PTSD (*N* = 1145).

Number of Classes	Entropy	aLMRT	p-value	AIC	aBIC
1	--	--	--	21357.7	21372.7
2	0.921	987.4	0.000	20359.0	20385.1
3	0.946	675.6	0.013	19679.4	19716.7
4	**0.942**	**560.5**	**0.012**	**19117.6**	**19166.2**
5	0.927	342.4	0.315	18779.1	18838.9

Note: PTSD = Posttraumatic Stress Disorder. AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion, aBIC = sample size adjusted BIC, LMRT = Lo-Mendell-Rubin Test.

Among the four-class solution, there were notable differences observed between cannabis use variables for each class (Table 6). Class one was a moderate severity group, comprised of a mid-adolescent onset (*M* = 15.6 years), moderate quantity of use (4.3 joints per day), high frequency of use (daily use), relatively moderate rates of medicinal use (12.9%) and high rates of CUD (53.5%). Class two was a low stable use group with the latest age of first use (*M* = 19.1

years), low quantity of use (1.2 joints per day), low frequency of use (twice per year), low rates of CUD (5.2%) and low medicinal use (1.6%). Class three was a low variable use group, comprised of late adolescent onset (*M* = 17.4 years), low quantity of use (1.7 joints per day), high frequency of use (1-2 times per week), low CUD (2.2%) and low medicinal use (3.7%). Lastly, class four was a high severity group, comprised of the earliest age of first use (*M* = 13.2 years), high quantity use (22.7 joints per day average), high frequency (daily use), highest rates of CUD (63.7%), and highest rates of medicinal use (14.3%).

Table 6

Means (SE) and Percentages (SE) of Cannabis Use Variables by Class (*N* = 1145).

Variables	1 (Moderate Severity: Mid-Teen Onset, Moderate Daily Use)	2 (Low Stable Use; Adult Onset, Low Quantity and Frequency Use)	3 (Low Variable Use; Late-Teen Onset, Low Quantity Moderate Frequency)	**4 (High Severity; Early-Teen Onset, Daily Use, High Quantity and Frequency)**
N (%)	576 (50.3%)	262 (22.9%)	279 (24.4%)	**28 (2.4%)**
Avg Classification Probability	96.9	98.3	93.3	**98.0**
	M (SE)	*M (SE)*	*M (SE)*	*M (SE)*
Age of First Use	15.6 (0.21)	19.1 (0.36)	17.4 (0.30)	**13.2 (0.51)**
Quantity (joints/day)	4.3 (0.15)	1.2 (0.05)	1.7 (0.08)	**22.7 (2.22)**
Frequency	9.6 (0.03)	1.9 (0.07)	6.6 (0.10)	**9.9 (0.07)**
	% (SE)	*% (SE)*	*% (SE)*	*% (SE)*
Medicinal Use	12.9% (0.01)***	1.6% (0.01)*	3.7% (0.01)**	**14.3% (0.07)***
CUD	53.5% (0.02)***	5.2% (0.02)***	2.2% (0.03)***	**63.7%(0.09)*****

Note. Frequency was measured categorically, with 1 = once per year, 2 = 2 times per year, 3 = 3-6 times per year, 4 = 7-11 times per year, 5 = once per month, 6 = 2-3 times per month, 7 = 1-2 times per week, 8 = 3-4 times per week, 9 = nearly every day, and 10 = daily. *p<0.05; **p<0.01; ***p<0.001.

Step three involved performing regression analyses, where the cannabis use variables were used to predict the most likely group membership. Predictors of interest, including age, sex, PTSD symptom severity, past year CUD, as well as AUD, TUD, and quality of life were then

entered into the analyses. A series of multinomial regression analyses were utilized through the R3STEP procedure described above, which allowed for comparisons between the cannabis use classes (DV; categorical) in regards to predictors, including: (1) current age (continuous), and (2) sex (categorical), (3) past year PTSD symptom severity (IV; continuous), (4) alcohol use disorder (IV; categorical), (5) tobacco use disorder (IV; categorical), as well as (6) past year CUD (IV; continuous), (7) SF-12 physical disability scale (IV; continuous), and (8) SF-12 mental disability scale (IV; continuous). Results are displayed in Table 7. Odds ratio with a 95% confidence interval was used to interpret how each variable related to increased or decreased likelihood of membership in one class compared to others.

Individuals who were older had increased odds of being in the low variable use class than those in the moderate severity class. There were no other significant differences between the classes for age. Being male increased the odds of being in the severe use class compared to all other classes. Having CUD and TUD increased the likelihood of being in the moderate and high severity classes compared to the low severity classes, with no significant difference between the moderate and high severity classes. Higher PTSD symptom severity scores increased the odds of being in the high severity class, relative to all three other classes. There were no significant differences associated with alcohol use disorder between any of the classes. Higher SF-12 Physical Disability scores decreased the odds of being in the high severity class, relative to all three other classes. Higher SF-12 Mental Disability scores increased the odds of being in the moderate severity class, compared to the low variable use class.

Table 7
Group Comparisons on Sociodemographic and Clinical Correlates – Odds Ratios (Confidence Intervals).

Predictor	Moderate Severity vs Low Stable Use	Moderate Severity vs Low Variable Use	Moderate Severity vs High Severity	Low Stable Use vs Low Variable Use	Low Stable Use vs High Severity	Low Variable Use vs High Severity
Age	1.01 (0.99-1.02)	**1.02 (1.00-1.03)***	0.98 (0.94-1.02)	1.01 (1.00-1.02)	0.98 (0.94-1.02)	0.97 (0.93-1.01)
Sex	1.25 (0.83-1.89)	1.21 (0.81-1.82)	**0.17 (0.06-0.51)****	0.97 (0.63-1.49)	**0.14 (0.04-0.42)****	**0.14 (0.05-1.43)****
PTSD Symptom Severity	0.97 (0.91-1.03)	0.99 (0.93-1.06)	**1.24 (1.03-1.49)***	1.03 (0.96-1.09)	**1.28 (1.06-1.55)***	**1.25 (1.03-1.51)***
AUD	0.84 (0.57-1.25)	0.83 (0.56-1.23)	1.34 (0.42-4.27)	0.98 (0.66-1.46)	1.59 (0.49-5.17)	1.63 (0.51-5.23)
TUD	**0.49 (0.33-0.73)*****	**0.41 (0.28-0.60)*****	1.55 (0.51-4.72)	0.83 (0.57-1.22)	**3.15 (1.01-9.87)***	**3.80 (1.22-11.86)***
Past Year CUD	**0.16 (0.10-0.26)*****	**0.43 (0.30-0.62)*****	1.10 (0.92-1.32)	**2.72 (1.65-4.51)*****	**6.92 (4.18-11.45)*****	**2.54 (1.71-3.77)*****
SF-12 Physical Disability	1.01 (0.99-1.02)	1.01 (0.99-1.02)	**0.95 (0.92-0.99)****	1.00 (0.99-1.02)	**0.94 (0.91-0.98)****	**0.94 (0.91-0.98)****
SF-12 Mental Disability	1.00 (0.99-1.02)	**1.02 (1.00-1.03)***	1.01 (0.97-1.05)	1.02 (1.00-1.03)	1.01 (0.97-1.05)	1.00 (0.96-1.04)

Note. PTSD = Posttraumatic Stress Disorder, AUD = Alcohol Use Disorder, CUD = Cannabis Use Disorder. First group listed was used as reference group. *p<0.05; **p<0.01; ***p<0.001

Discussion

The present study aimed to advance our understanding regarding the relationships between PTSD and cannabis use. Specifically, it aimed to: (1) illustrate heterogeneity of cannabis use variables by examining differing profiles of cannabis use, and (2) examine the relationship between cannabis use profiles and PTSD symptom severity.

A four-class solution from the LMM was demonstrated to be the best fit for the data. The classes varied in regard to measures of cannabis use severity, ranging from low occasional use to high heavy use. Generally, earlier age of first use was associated with higher severity ratings, as indicated by earliest ages in the moderate and severe classes. These findings are in line with previous research, illustrating that earlier age of first substance use is associated with greater risk for SUD (e.g., Behrendt et al., 2009). Furthermore, that earlier age of first use is associated with more mental health challenges and traumatic experiences in youth (Hawke et al., 2020). Interestingly, one low severity class postulated low quantity but moderate frequency of use (1-2 times per week) and slightly more individuals with medicinal cannabis use compared to the other low quantity and low frequency class (1-2 times per year). This appears to suggest that some individuals are able to use cannabis, either medicinally or recreationally, without developing problematic usage patterns. Furthermore, the low severity class with the moderate frequency of use postulated the lowest CUD ratings of all four classes. In itself, this suggests that moderate frequency of use of 1-2 times per week may not be a risk factor for CUD or increased PTSD symptom severity, and could potentially contribute positively to overall symptomatology. These findings are generally in line with Canada's lower-risk cannabis use guidelines, which discuss age of first cannabis use, frequency of use, and intensity of use as factors that place individuals at higher risk for consequences of cannabis consumption (Fisher et al., 2017). Both the moderate

and severe use classes reported on average daily cannabis use. There was a substantial difference in quantity of use between the moderate and severe classes, with an average of 4.3 joints compared to 22.7 joints, respectively. However, even at an average of 4.3 joints per day, the moderate use class still maintained high rates of CUD. There were no significant differences observed in rates of CUD between the moderate and severe classes. Although the moderate severity class was associated with higher rates of CUD than the low severity classes, it was not associated with higher likelihood of PTSD symptom severity compared to any of the classes. On the other hand, the high severity class was associated with the highest rates of CUD, as well as increased odds of higher PTSD symptom severity compared to any of the other three classes. These findings are in line with previous research by Kearns and colleagues (2020) and Contractor and colleagues (2019), whereby higher PTSD symptom severity scores was associated with higher substance use severity measures. Interestingly, medicinal cannabis use was generally low among all classes (ranging 1.6-14.3%), however remained highest in the moderate and severe use classes (12.9% and 14.3% respectively). These findings are in line with prior research by Fischer and colleagues (2010) that illustrated medicinal use is often associated with more severe cannabis use profiles. Unlike previous research (e.g., Contractor et al.) alcohol use was not associated with higher likelihood of membership in any of the classes. However, individuals with TUD had increased likelihood of being in the moderate and high severity classes compared to the low severity classes, in line with previous research among the general population (i.e., individuals without PTSD) that cannabis use and CUD are associated with TUD (Wittchen et al., 2007; Patton et al., 2005).

Implications and Future Directions

These results have important clinical implications. First, distinct types of low, moderate,

and high severity use classes were identified in the present study, illustrating several homogenous classes that were contributing to overall heterogeneity of cannabis use in the sample. The classes differed in severity use patterns, including frequency and quantity of use, and were associated with different outcomes, such as variations in CUD and PTSD symptom severity. Consistent with previous research, earlier age of first cannabis use may be associated with higher likelihood of severe use patterns and disordered use patterns later on in life. These findings suggest that examining cannabis use homogenously may neglect meaningful clinical differences in usage types that likely contributes to underlying confusion of cannabis as helpful or harmful for PTSD. Future research should continue to distinguish between usage patterns and severity indicators identified in Canada's lower-risk cannabis use guidelines (Fisher et al., 2017), improve our understanding regarding the complex relationship between cannabis use and PTSD. Future research should also continue to examine and identify types of cannabis being examined, which was unfortunately not possible in the present study.

Second, results illustrate that higher severity of use is associated with greater PTSD symptom severity, and medicinal cannabis use was associated with the highest severity classes. These findings have important clinical implications for the utilization of medicinal cannabis for treatment of PTSD. High quantity, high frequency cannabis use was associated with higher likelihood of PTSD symptom severity, replicating previous research (Kearns et al., 2020; Contractor et al., 2019). These findings illustrate the need for physicians and treatment providers to carefully monitor and assess cannabis use among individuals with PTSD, as high severity use patterns may potentially exacerbate or worsen PTSD symptoms. Future directions may involve examining the relationship between cannabis use severity and specific PTSD symptoms to better understand if certain PTSD symptoms are more or less influenced by certain cannabis use

patterns. Furthermore, identifying the threshold between potentially beneficial and harmful medicinal cannabis use is of critical importance to improving treatment outcomes. Evidently, more research is needed to differentiate helpful versus harmful usage patterns of cannabis among individuals with PTSD to ensure evidence-based, accurate recommendations for patients and providers.

Limitations

The present study also presented with some discernable limitations and strengths. First, the present study utilized a large sample who completed a cross-sectional survey in 2012-2013. Therefore, the findings cannot be used to determine causal relationships between variables, and may present as somewhat outdated. More specifically, since legalization of cannabis occurred across much of North America in 2018, it is possible that patterns of use have changed over this time. Second, the participant self-report methods may introduce potential response or memory bias. Specifically, individuals may not accurately recall the number of joints they had per day, especially for individuals consuming larger quantities. Therefore, the self-report of cannabis consumption may have introduced measurement error. Third, as the dataset was pre-determined, I was unable to add additional variables of interest to the research. Although I would have liked to include a measure of duration or number of years in the cannabis use variables, regrettably there was not a measure of that in the dataset. I also would have liked to ask participants about other relevant cannabis use variables, such as number of hits, ratio of THC to CBD, or type of cannabis products. Lastly, due to the fact that some population segments were not covered by the NESARC-III (e.g., homeless individuals, prisoners, and most treated individuals), estimates presented may underestimate the true prevalence of AUD and other DUD.

Conclusion

The present study illustrates important findings regarding the heterogeneity of cannabis use among individuals with PTSD. The four-class model of the data illustrates pertinent differences in cannabis use variables, including frequency and quantity of use, as well as age of first use, which are associated with varying rates of CUD and PTSD symptom severity. Further research is needed regarding quantity and frequency of use, in order to replicate these findings, as well as further determine which range of quantity and frequency of use contributes significant risk for physical and mental health disability, as well as CUD. Future research may also investigate other potential cannabis use variables, such as length or duration of cannabis use, in order to determine if the effects of cannabis change over time.

Chapter Four:

Associations Between Cannabis Use and Mental Healthcare Utilization Among Individuals with Posttraumatic Stress Disorder

Jessa M. Hogarth[1], Matthew Keough[2], & Natalie Mota[3]

(1) Department of Psychology, University of Manitoba

(2) Department of Psychology, York University

(3) Department of Clinical Health Psychology, University of Manitoba

Abstract

Mental health treatment utilization among individuals with posttraumatic stress disorder (PTSD) is low among both veteran and civilian populations. As cannabis is viewed as a viable treatment for PTSD, individuals self-medicating with recreational cannabis or receiving medicinal cannabis prescriptions may be less likely to pursue further treatment. The present study used a nationally representative sample of adults (≥18 years) from the third wave of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-III) in 2012-2013, examining reported use of mental healthcare utilization services among individuals with past year PTSD (N = 1779). A three-group model was used to compare individuals with past year PTSD who did not use cannabis (PTSD-NoCU), to those with PTSD who used cannabis but did not report disordered use patterns (PTSD-CU) and those with comorbid PTSD and CUD (PTSD-CUD). Logistic regressions were used to compare the three groups on four dimensions of mental healthcare utilization (professional help, prescription medication and drugs, self-help, emergency care) for PTSD specifically, as well as for other mental health disorders (depressive, anxiety, and eating disorders). Results illustrate that individuals in the PTSD-CUD group presented with decreased odds of professional help utilization and prescription medication use for PTSD, as well as decreased odds of professional help across all mental health disorders compared to individuals with PTSD-NoCU (OR = 0.49-0.64, all $p<0.05$). Interestingly, individuals in the PTSD-CU group presented with increased odds of professional help utilization for anxiety disorders compared to those with PTSD-NoCU (OR = 1.59). Future research may investigate potential barriers to treatment for comorbid PTSD-CUD, as well as implement targeted treatment approaches for this comorbid group.

Keywords: Posttraumatic Stress Disorder, PTSD, Cannabis Use Disorder, Marijuana,

Mental Healthcare Utilization, PTSD Treatment, Substance Use Disorders

Introduction

Posttraumatic stress disorder (PTSD) is an enduring mental health disorder with high rates of mental health comorbidities and associated functional impairment (e.g., Shalev et al., 2017; Kondev et al., 2021; Sareen, 2014). Symptoms of PTSD have been shown to persist for an average of six years across varying types of traumatic exposure, with certain types of traumatic exposure associated with symptoms lasting over 13 years (Kessler et al., 2017). Previous research has demonstrated more than one third of individuals with PTSD do not meet criteria for recovery after many years of impairment (e.g., Kessler et al., 1995), and many individuals continue to experience residual PTSD symptoms even if they no longer meet the minimum symptom threshold for a PTSD diagnosis (e.g., Bradley et al., 2005; Schnurr et al., 2019). However, effective pharmacological treatments (i.e., tricyclic antidepressants, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors) and psychological treatments (e.g., Cognitive Processing Therapy, Prolonged Exposure Therapy) have been developed for PTSD, and many individuals who receive psychological treatment for PTSD do recover or see an improvement to their symptoms (as discussed by Bradley et al., 2005). Therefore, it appears likely that individuals with persistent symptoms of PTSD are often those who do not receive adequate treatment, or those who are not able to or choose not to utilize treatment services.

Rates of treatment utilization for PTSD are lower across both civilian and veteran populations compared to treatment for other disorders (Grekin et al., 2021; Ranney et al., 2023; Johnson & Possemato, 2019; Stecker et al., 2007), with civilian populations displaying even lower rates of treatment utilization for PTSD than veteran populations (Ranney et al., 2023). This disparity may be explained by specific educational and environmental advantages within veteran populations, including: (1) increased screening for PTSD symptoms and diagnosis, (2), increased

awareness of traumatic symptoms and their effects, (3) greater promotion and discussion of treatment services available, (4) increased treatment accessibility, including better health coverage and more programs offered, and (5) increased treatment acceptability, including increased social support and discussion of services among veterans (Ranney et al., 2023; Shen et al., 2003). Furthermore, there appears to be lower desirability for treatment of PTSD specifically compared to other mental health disorders. Twenty percent of veterans with symptoms of PTSD indicate they would not even consider treatment for PTSD (Gutner et al., 2018). This treatment resistance appears to be partially attributable to PTSD symptomatology in and of itself, in other words, symptoms of traumatic avoidance and hyperarousal that are within the *DSM-5* diagnostic criteria for PTSD (Kazlauskas, 2017). Previous research by Blais and colleagues (2014) found that higher avoidance symptoms predicted lower rates of treatment utilization among veterans with PTSD. Treatment avoidance may also be related to additional barriers of disorder stigmatization (e.g., Corrigan, 2004; Mittal et al., 2013; Kantor et al., 2017; Stecker et al., 2007), cost and limited accessibility of services (Kantor et al., 2017; Reisman, 2016; Hale et al., 2018), timing of services (Strecker et al., 2007), lack of knowledge and mental health literacy (Kantor et al., 2017), low treatment acceptability, as well as past negative or failed attempts at treatment (Possemato et al., 2018; Brown et al., 1995). Evidently, individuals with PTSD experience many types of physiological, psychological, and environmental barriers that may facilitate a reduction in utilization of treatment services.

Relatively little is known about how cannabis use influences treatment utilization among individuals with PTSD. Cannabis is utilized as a medicinal treatment for a variety of mental health conditions in North America, potentially facilitating initiation and continuation of cannabis use among those with mental health disorders (Borodovsky & Budney, 2018).

However, cannabis use among veterans with PTSD has been shown to present with similar symptom severity to other substances (including alcohol, cocaine, opiates). Manhapra and colleagues (2016) found that cannabis use was associated with similar symptom burden to other substances, and subsequent abstinence from cannabis use was associated with symptom improvement comparable to individuals abstaining from alcohol or other substance use. Therefore, despite that cannabis is prescribed as a medicinal treatment in most of the United States (Patton, 2020), it is discernably unclear to both the public as well as healthcare professionals if cannabis use is helpful for mental health symptoms overall, as well as specifically which symptoms and conditions it can be helpful for (e.g., Borodovsky & Budney, 2018; National Academies of Sciences, Engineering, & Medicine, 2017). It is likely based on current messaging that individuals with PTSD may very reasonably believe they are treating their symptoms with cannabis, especially if they have a medicinal cannabis prescription for PTSD. These beliefs may facilitate a reduction in other formal medication use, and/or enable rationalization of substance use (as discussed by Borodovsky & Budney, 2018). Indeed, cannabis has been self-reported as "moderately" to "quite a bit" helpful among individuals with PTSD using medicinal cannabis, despite simultaneously reporting a high number of cannabis use problems (Bonn-Miller et al., 2014a).

Furthermore, as individuals with PTSD experience a high degree of functional impairment (Jellestad et al., 2021), hyperarousal and avoidance inherent to diagnostic symptoms (e.g., Kazlauskas, 2017; Blais et al., 2014), and mental health disorder comorbidities (e.g., Hasin et al., 2016), it is understandable that they have increased difficulty accessing traditional, institutional treatments. Mental health treatment can be physically and emotionally taxing, as well as demanding of resources, such as time and finances (e.g., Kantor et al., 2017). Evidently, there is

not only mixed messaging regarding if cannabis is helpful or harmful for PTSD treatment, but also limited understanding of how cannabis use may reduce likelihood of seeking formal treatment services. Therefore, research is needed to determine if individuals with PTSD-CUD are utilizing treatment for PTSD or other mental health problems at similar rates to individuals with PTSD who are not using cannabis. Prompt treatment of PTSD is imperative, in order to shorten duration of illness, reduce psychological distress and functional impairment, as well as reduce likelihood of disorder chronicity (Kessler et al., 1995; as discussed by Gavrilovic et al., 2005).

PTSD Treatments and Efficacy

Treatment for PTSD often includes a combination approach of pharmacological and psychological treatments (e.g., Foa et al., 2010; Nobles et al., 2017), to address both biological and psychological components that may be contributing to PTSD symptomatology.

Pharmacological Treatment

Pharmacological treatments for PTSD may include tricyclic antidepressants, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, as well as anti-adrenergic agents, anticonvulsants, benzodiazepines, or atypical antipsychotics (e.g., Albucher & Liberzon, 2002; Ravindran & Stein, 2009). In their PTSD prevention and treatment guidelines, the International Society for Traumatic Stress Studies (ISTSS) recommends prescription medication including Fluoxetine, Paroxetine, Sertraline, Venlafaxine, and Quetiapine for PTSD after three months (as discussed by Bisson et al., 2019). Goals of pharmacological treatment often include reducing intrusive thoughts, anxiety/fear, avoidance, hyperarousal, hypervigilance, irritability, anger, and/or improving depressed mood (e.g., Stein et al., 2015). The efficacy of pharmacological interventions is notably modest, with most drugs producing small effect sizes (Hoskins et al., 2015). This begins to highlight the need for further interventions and treatment options for

PTSD. Ravindran and Stein (2009) discuss that challenges with pharmacological treatment of PTSD symptoms may result from multiple facets of dysregulation and variation in biological pathways, making it challenging to account for genetic variations and heterogeneity of symptoms simultaneously.

Furthermore, pharmacological interventions in the presence of substance use disorders for individuals with PTSD are often contraindicated (e.g., Brady et al., 2004), although medicinal cannabis is at times prescribed for pharmacological treatment by physicians. Overall, research regarding the efficacy of medicinal cannabis for PTSD is inadequate and underwhelming (e.g., O'Neil et al., 2017; Wilkinson et al., 2016), with no conclusive evidence that medicinal cannabis is helpful in the long term for managing PTSD symptomatology (Shishko et al., 2018). Previous systematic reviews by Steencamp and colleagues (2017) and Black and colleagues (2019) have found that current evidence for the efficacy of cannabis for PTSD treatment is largely lacking and inconclusive.

Psychological Treatments

Trauma specific psychological treatments appear to have the strongest empirical support and are often considered first-line treatment for PTSD (Forbes et al., 2020). Evidence-based psychological interventions used for the treatment of PTSD include Cognitive Processing Therapy (CPT; Resick et al., 2008), Eye Movement Desensitization and Reprocessing Therapy (EMDR; Shapiro, 2001), Prolonged Exposure Therapy (Foa et al., 2007), and Trauma-Focused Cognitive-Behavioral Therapy (tf-CBT; Bisson et al., 2013). The International Society for Traumatic Stress Studies recommends various trauma specific treatments (e.g., CPT, EMDR) within the first three months of a traumatic event (as discussed by Bisson et al., 2019).

The majority of interventions specific to PTSD and trauma treatment include some form of

trauma processing and guided exposure (e.g., Roberts et al., 2016). However, a substantial number of individuals with PTSD have symptoms that appear to be resistant to treatment (Stein, 2021), prolonging duration of the disorder. Furthermore, many studies evaluating the effectiveness of therapeutic interventions for PTSD frequently exclude individuals with comorbid SUD (e.g., Bradley et al., 2005; Gerger et al., 2014), making it difficult to ascertain the effectiveness of PTSD treatments for individuals with co-occurring SUDs.

PTSD and Treatment Utilization

Despite available pharmacological and psychological treatments and their reported effectiveness, rates of treatment utilization for PTSD are significantly lower than other mental health disorders (Grekin et al., 2021; Ranney et al., 2023; Johnson & Possemato, 2019; Stecker et al., 2007). There have been many psychological, physiological, and environmental factors hypothesized to explain why, including disorder stigmatization (Corrigan, 2004; Mittal et al., 2013; Kantor et al., 2017; Stecker et al., 2007; Mueller et al., 2008; Kazlauskas, 2017), cost and accessibility of services (Kantor et al., 2017; Reisman, 2016; Kazlauskas, 2017; Hale et al., 2018), timing of services (Strecker et al., 2007; Maguen et al., 2012), lack of knowledge and mental health literacy (Kantor et al., 2017), co-occurring symptom complexities (Stein, 2021; Spinazzola et al., 2005) as well as past negative attempts at treatment (Possemato et al., 2018; Brown et al., 1995). Furthermore, symptoms of PTSD likely facilitate treatment avoidance in and of itself, due to inherent symptoms of avoidance of traumatic stimuli (e.g., Trusz et al., 2011; Kantor et al., 2017; Kazlauskas, 2017)) as well as increased distress associated with hyperarousal (e.g., Tull & Roemer, 2003; Tull et al., 2016). There may also be a lack of specific treatment for co-occurring problems and disorders (Spinazzola et al., 2005).

In combination, this may lead individuals with PTSD to maintain a strong preference for

self-help and self-directed treatment options (Stecker et al., 2007; Kantor et al., 2017). Self-directed treatments could provide increased flexibility regarding timing of treatment delivery (i.e., various times in the day), less triggers associated with hyperarousal, as well as a sense of control over their own treatment program that may be particularly desirable following the uncontrollable experience of traumatic events. Unfortunately, options for self-help and self-directed treatment for PTSD appear notably scarce and limited. As such, individuals with PTSD may be more frequently motivated to use substances for self-medication (e.g., Hawn et al., 2020; Kazlauskas, 2017), among which the most commonly used are typically alcohol, tobacco, and cannabis (e.g., Turna & MacKillop, 2021; Schafer & Najavits, 2007). Indeed, cannabis appears to be among the limited options for self-directed PTSD treatment. There is also a growing perception of cannabis as helpful versus harmful, due to legalization of cannabis across much of North America over the past decade (e.g., Patton, 2020; Fisher et al., 2017). Furthermore, many individuals are aware that cannabis is used for medicinal treatment of PTSD, thereby giving the impression it is helpful for PTSD symptom management.

There may be further motivations that make cannabis a desirable self-help treatment for individuals with PTSD. As cannabis impacts learning and various stages of memory (e.g., Kroon et al., 2021; Ranganathan & D'Souza, 2006), cannabis use may potentially reduce the acuity of traumatic memories. Furthermore, previous research has documented that cannabis can be helpful for dampening arousal (Tull et al., 2016), which is a persistent challenge and can be a source of significant distress among individuals with PTSD. Many individuals with PTSD also intentionally or unintentionally display avoidance of traumatic stimuli, which can exacerbate or facilitate substance use and self-medication (e.g., Schafer & Najavits, 2007). Therefore, it appears likely that many individuals with PTSD may experience some benefits from cannabis

use for managing symptoms of PTSD, illustrating why they may perceive cannabis to be a helpful treatment (e.g., Bonn-Miller et al., 2014a). However, it also seems likely that individuals with PTSD experience difficulties associated with cannabis use, including long-term worsening of PTSD symptoms overall (e.g., Hinojosa et al., 2023). In combination, it is difficult to ascertain whether cannabis is helpful or harmful for PTSD symptoms overall, and how cannabis use may interact with other formal treatment services.

PTSD, Cannabis Use, and Treatment Utilization

Although accepted that individuals with PTSD experience barriers to effective treatment services, relatively little is known about how cannabis use influences treatment utilization for individuals with PTSD. There appear to be several possibilities to explain why individuals with PTSD who are using cannabis may experience additional barriers to treatment utilization, compared to other individuals with PTSD who do not use cannabis.

First, many individuals who use cannabis to cope with PTSD symptoms may not be open to or feel they are able to reduce their cannabis use. It is possible they may not be able to reduce their cannabis use, as cannabis may be helpful for reducing arousal (e.g. Tull et al., 2016) and improving sleep (e.g., Bonn-Miller et al., 2014a; Fraser, 2009; Jetly et al., 2015; Cameron et al., 2014), which are central difficulties among individuals with PTSD. As individuals with PTSD experience significant mental health symptoms and comorbidities (e.g. Hasin et al., 2016) associated with a high degree of functional impairment (e.g. Jellestad et al., 2021), they may be more desperate for symptom relief and reliant on coping mechanisms to reduce symptomatology. A qualitative study by Bujarski and colleagues (2016) of clinician and patient reported factors discussed significant clinician endorsement that many patients do not want to stop using cannabis, as well as the fact that they are not open to treatment for CUD. Indeed, a study of

substance use among veterans with PTSD illustrated that individuals using cannabis only to cope with PTSD symptoms (compared to polysubstance use) were associated with the lowest rates of abstinence following treatment (Manhapra et al., 2015). Therefore, any programs that require individuals to stop using cannabis, or programs that are highly suggestive of reducing substance use, may be undesirable or unhelpful for some individuals with PTSD.

Second, individuals with PTSD who are using cannabis are at risk for increased cannabis use over time, as well as potential long-term harms associated with cannabis use and cannabis use disorder. Comorbid PTSD and CUD (PTSD-CUD) has been consistently associated with worse PTSD symptomatology (e.g. Wilkinson et al., 2015), and comorbid mental health and substance use disorders are widely considered more difficult to treat (e.g. Blakey & Bowers, 2014; as discussed by Salas et al., 2021; Brown et al., 1995). Many individuals with PTSD present with treatment resistance (e.g., Bujarski et al., 2016), whereby they require varied or tailored treatments to achieve a desirable clinical response (Stein, 2021). Evidence-based treatment for co-occurring disorders among individuals with PTSD remain largely ineffective and underdeveloped, with significant systemic and psychological barriers to integrated PTSD and SUD treatment (Blakey & Bowers, 2014). Previously, it was considered standard of care to treat SUD prior to commencing treatment for PTSD (e.g., Becker et al., 2004; Pitman et al., 1991). Alternatively, treatment for PTSD has been associated with improvements in SUD (e.g., Hien et al., 2010), and increased PTSD symptom severity and impairment can facilitate increased substance use in a cyclical manner (e.g., Contractor et al., 2019; Jacobson et al., 2001). Evidently, the co-occurrence of both PTSD and SUDs complicates both interventions and protocols, by increasing treatment complexity, reducing treatment acceptability, and contributing more clinical factors for providers to balance during treatment. To date, best practice guidelines

regarding comorbid PTSD and CUD are scarce and unclear, leading to confusion and frustration among patients and clinicians (as discussed by Roberts et al., 2016).

Third, individuals with PTSD with comorbid SUDs often face greater challenges in treatment adherence, as substance use can become a coping mechanism that reduces perceived need for formal care (McCauley et al., 2012). Rates of mental healthcare utilization overall among individuals with PTSD are notably low (e.g., Brown et al., 1999; Grekin et al., 2021), with reduced rates observed for both initial treatment seeking as well as treatment completion. Close to half of individuals typically attend an initial visit (Hoge et al., 2004; DeViva, 2014; Nobles et al., 2017), with only a small number of individuals attending the full number or a large number of treatment sessions (Hoge et al., 2004; DeViva, 2014; Seal et al., 2010). Previous research has also demonstrated notable barriers in treatment seeking for veterans, with one study illustrating an average of more than two years following traumatic exposure until the first mental health visit (Maguen et al., 2012). Among individuals who believe they are self-medicating their symptoms for PTSD, they may be less likely to seek out additional treatment services that extend beyond initial barriers to PTSD treatment.

Fourth, stigma related to mental health disorders and treatment services are often one of the main reasons for avoidance of help-seeking (Schnyder et al., 2017). Many individuals with both PTSD and CUD independently experience perceived stigmatization (e.g. Kulesza et al., 2015). Fear of stigma has been illustrated as a barrier for CUD treatment (Kerridge et al., 2017; Gates & Copeland, 2017) as well as for individuals with comorbid PTSD and CUD (Kulesza et al., 2015; Bujarski et al., 2016). Based on potential stigmatization of both disorders, it appears likely that individuals with PTSD-CUD may experience significantly more stigmatization than either disorder alone. Furthermore, higher perceived stigma at treatment seeking has been significantly

associated with lower rates of treatment utilization among veterans (Kulesza et al., 2015). Comorbid PTSD and CUD may present with higher rates of substance use relapse that require more intensive treatment (as discussed by Brown et al., 1995), and continued cannabis use may facilitate ongoing financial strain that can further limit access to treatment and resources. In synthesis, it appears that individuals with comorbid PTSD and CUD likely experience more stigmatization than either disorder alone, hypothetically reducing motivation for formal treatment services.

The impact of comorbid PTSD and CUD on treatment utilization has been vastly understudied, with the majority of prior research typically involving veteran populations specifically, as well as substance use disorders broadly. In unison with other substance use disorders, higher perceived stigma of treatment seeking has been shown to be significantly associated with lower rates of mental healthcare utilization among veterans with a variety of mental health disorders (Kulesza et al., 2015). Similarly, although rates of adequate PTSD treatment are notably already very low (6.8%), rates of combined PTSD and SUD therapy are almost nonexistent (less than 1%; Greckin, 2021) suggesting a further decrease in treatment utilization for those with comorbid SUDs. Furthermore, psychiatric comorbidities overall were associated with decreased odds of treatment in general. However, previous research by Bujarski and colleagues (2016) discussed the importance of CUD specific education and information for the treatment of PTSD, based on differential findings compared to other SUDs. Therefore, it is important to study the relationship between comorbid PTSD-CUD and treatment utilization specifically, in order to observe differential patterns and clinical outcomes from other SUDs.

The Present Study

It is imperative to understand how cannabis use impacts mental healthcare utilization for

individuals with PTSD, in order to increase utilization of treatment services and ultimately improve functioning and quality of life. Examining meaningful differences in mental healthcare utilization between individuals with comorbid PTSD-CUD compared to PTSD alone may provide useful information in determining if there are potential barriers to treatment that could be investigated in future research.

I utilized a three-group variable as the independent variable, including: (1) past year PTSD no cannabis use (PTSD-NoCU; reference group), (2) past year PTSD and cannabis use (non-disordered; PTSD-CU), and (3) comorbid PTSD and CUD (PTSD-CUD). Disorder type was entered categorically with mental healthcare utilization entered as the dependent variable (categorical).

The main objective of the proposed research project was to examine the association between cannabis use and mental healthcare utilization among individuals with PTSD. Specifically, I was interested to know if individuals with comorbid PTSD-CUD presented with decreased odds of treatment utilization, in comparison to individuals with PTSD who do not use cannabis.

First, the three groups were compared on the likelihood of having other past year mental health disorders. I examined how individuals with comorbid PTSD-CUD differ in regard to sociodemographic correlates (age, sex, education, marital status, household income) and mental health comorbidities (depressive disorders, anxiety disorders, eating disorders) across the three groups. I predicted that the comorbid PTSD-CUD group would have higher rates of mental health comorbidities than the PTSD-NoCU group, consistent with previous research (Kessler et al., 1995; Hasin et al., 2016).

Second, I utilized a series of logistic regressions in order to compare mental healthcare

utilization estimates for PTSD among the three-group variable. Mental healthcare utilization was assessed along four domains of: (1) professional help, (2) prescription medication or drugs, (3) self-help, (4) emergency care. I predicted that comorbid PTSD-CUD would be associated with lower rates of mental healthcare utilization, compared to non-disordered use. I also examined mental healthcare utilization for any mental health disorder, due to high prevalence rates of comorbidities among individuals with PTSD. Mental healthcare utilization included treatment for mood disorders, anxiety disorders, and eating disorders. I predicted that comorbid PTSD-CUD would be associated with significantly lower rates of mental healthcare utilization for other mental health disorders, compared to non-disordered use or no cannabis use.

Method

Participants

The present study utilized data from the National Epidemiological Survey for Alcohol and Related Conditions Wave Three (NESARC-III), collected by the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The NESARC-III was conducted from April 2012 through June 2013 using multistage probability sampling, with detailed recount of data collection protocols detailed elsewhere (e.g., Grant et al., 2014). The NESARC-III includes a civilian sample of noninstitutionalized adults living in the United States of America, including inactive veterans, excluding active service members in order to maintain confidentiality (Grant et al., 2014). It was reported that Black, Hispanic, and Asian adults were sampled at a higher rate than the remainder of the population intentionally, to increase sample size of important marginalized groups.

A total of 44,931 individuals were selected to participate in the NESARC-III, however 1,567 were ineligible for interview due to exclusion criteria, while 7,055 declined to respond.

This yielded an overall response rate of 60.1 percent and a total sample size of 36,309 participants, (Cudjoe, 2019; Grant et al., 2014). The present study used a subsample of these participants (N = 1779) who met criteria for past year PTSD. One participant was excluded from the analyses, as they did not respond to questions about if they had used cannabis, or their frequency of use. Therefore, the total sample size was 1778. Missing data across measures excluded the participant from those specific analyses. All other participants had missing data within a 2% range and were included in the analyses. The NESARC-III uses imputation when missing responses can be inferred from other responses. Imputed responses are coded separately from valid responses.

Procedure

Approximately 1,000 trained lay interviewers visited previously selected addresses through multistage probability sampling in the United States of America to administer the NESARC-III. Further details about this process are described by Grant et al. (2014). The NESARC-III employed a computer-assisted, semi-structured diagnostic interview, the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5; National Institute on Alcohol Abuse and Alcoholism, 2015), in order to assess mental health disorders.

In order to gain access to the NESARC-III, a request was submitted to the University of Manitoba Bannatyne Research Ethics Board. Upon receiving their approval, the request for data acquisition was sent to the NESARC-III Data Access Committee (NIAAA) for their approval. The NESARC-III dataset was then downloaded in a secure, encrypted format to a password protected, secure computer (as outlined by the Procedures for Obtaining Dataset found at https://www.niaaa.nih.gov/research/nesarc-iii/nesarc-iii-data-access/procedures-obtaining-dataset). Consent was obtained during primary data collection by the owners of the data, the

National Institute on Alcohol Abuse and Alcoholism (NIAAA).

Measures

The Alcohol Use Disorder and Associated Disabilities Interview Schedule–5 (AUDADIS-5) was used to assess a variety of psychological conditions for the NESARC-III. These included depression, anxiety, panic, bipolar, substance use disorders, PTSD, as well as personality disorders, among others. The AUDADIS-5 was designed to assess alcohol, drug use and mental health disorders during past year and lifetime periods, according to DSM-5 diagnostic criteria (Grant et al, 2001).

Posttraumatic Stress Disorder

During the semi-structured interview, participants were asked about 20 potentially traumatic events they may have directly experienced during their lifetime (e.g., serious life threatening injury or illness, sexual assault, natural disasters), as well as 14 events that they may have witnessed or been indirectly exposed to (as described by Hale et al., 2018). Participants who reported experiencing at least one type of traumatic event (i.e., Criterion-A; Appendix A) were subsequently asked 33 questions about their symptoms following the most traumatic or stressful event they had experienced. These questions were designed in order to operationalize the 20 PTSD symptoms from *DSM-5* (Criteria B–E), including five questions for criterion B (intrusion), two questions for criterion C (avoidance), seven questions for criterion D (altered cognition/mood), and six questions for criterion E (arousal; Chen et al., 2017; Goldstein et al., 2016). Furthermore, as per *DSM-5* diagnostic criteria, participants had to indicate if symptoms persisted greater than one month, as well as indicate clinically significant impairment or distress. For the present study, PTSD was assessed using *DSM-5* diagnostic criteria for past year PTSD (see Appendix A). Reliability of trauma and stress related disorders ranged from fair to good for

the NESARC-III (Grant et al., 2015).

Cannabis Use

A three-group variable was created in order to compare individuals with past year PTSD along dimensions of past year cannabis use, including: (1) PTSD with no past year cannabis use (PTSD-NoCU); (2) PTSD with past year cannabis use (PTSD-CU; endorsed using cannabis at least once in the past year, but did not meet CUD criteria); and (3) comorbid PTSD and CUD (PTSD-CUD; endorsed using cannabis at least once in the past year, met criteria for CUD). Sociodemographic information for the three groups is displayed in Table 8.

The AUDADIS-5 was used to assess overall cannabis use, as well as disordered cannabis use in the past year and lifetime periods. Participants were asked during the face-to-face interview if they had ever used marijuana before, as well as if it was during the past 12 months, prior to the past 12 months, or both. Participants were subsequently asked on average how many joints they consumed over the past year, selecting from ten response categories ranging from once per year to daily. Participants that reported consuming any cannabis over the past year (one joint per year or more) were classified as individuals who used cannabis for analyses. Any participants that also meet criteria for CUD were excluded from the cannabis use (non-disordered) group.

Cannabis use disorder was classified using *DSM-5* diagnostic criteria, requiring at least two of the eleven symptoms within a 12-month period to obtain a diagnosis (Appendix B; American Psychiatric Association, 2013). Individuals who meet criteria for past year CUD were included in the comorbid PTSD and CUD group. Cannabis use and cannabis use disorder were entered categorically. The AUDADIS-5 has been demonstrated to have good to excellent validity for CUD (Hasin et al., 2015) as well as fair to good reliability (Grant et al., 2015).

Other Mental Health Disorders

Due to the high rates of comorbidity with PTSD and other mental health disorders, the present research also assessed the presence of other mental health conditions including: (1) depressive disorders, including major depressive disorder and dysthymia; (2) anxiety disorders, including generalized anxiety disorder, social phobia, specific phobia, panic disorder, as well as agoraphobia; and (3) eating disorders, including anorexia nervosa, bulimia, as well as binge eating disorder. A summary variable was created, looking at any mental health disorder overall (excluding PTSD). Establishing the presence of other mental health disorders is pertinent to examine treatment for other mental health conditions alongside PTSD.

Mental Healthcare Utilization

Mental healthcare utilization was examined in multiple modules of the NESARC-III. Using a semi-structured interview, the AUDADIS-5, participants were asked questions about mental healthcare utilization related to substance use disorders. They were also asked about mental healthcare utilization for various mental health disorders, including PTSD, depressive disorders (major depressive disorder, dysthymia), anxiety disorders (generalized anxiety (GAD), specific phobia, social phobia, panic attacks, and agoraphobia), and eating disorders (anorexia nervosa, bulimia nervosa, binge eating disorder). Treatment for mental health disorders compared to substance use disorders was assessed differently in the NESARC-III, making it not possible to draw comparisons between the two groups of conditions.

The present study focused primarily on mental health treatment specifically for PTSD, as it is most pertinent to the study of comorbid PTSD-CUD. However, due to the fact that PTSD-CUD presents with high rates of comorbidity with other mental health disorders, and the fact that individuals with PTSD symptoms may be inclined to seek treatment for other problems over

PTSD, mental healthcare utilization for other areas of mental health was also assessed as a secondary measure (including depressive disorders, anxiety disorders, and eating disorders). Lastly, all treatment for mental health disorders was summarized into a dichotomous treatment variable. This characterization of mental healthcare utilization allowed for examination of both broad and specific treatment utilization for individuals with PTSD, providing a more nuanced and comprehensive understanding of treatment services utilized by individuals with PTSD.

For each mental health disorder, participants were asked five questions about mental healthcare utilization: (1) if they ever sought professional treatment (i.e., talk to any health professional like a psychiatrist, other medical doctor, psychologist, social worker or any other kind of counselor or therapist); (2) participated in self-help programs (i.e., attended self-help or support groups or online chat rooms); (3) were hospitalized overnight, (4) visited an emergency room, or (5) were prescribed prescription medication or drugs by a doctor. Hospital and emergency room visits were collapsed to form one category of emergency care, and all responses were coded dichotomously (*no utilization vs utilization)*. Therefore, mental healthcare utilization for all mental health disorders was assessed along four domains of: (1) professional treatment, (2) prescription medication or drugs, (3) self-help, and (4) emergency care.

Sociodemographic Measures

Age, sex, race/ethnicity, education, marital status, and household income were examined as sociodemographic correlates to contextualize the sample. They were assessed based on prior research utilizing the NESARC-III (e.g., Sommer et al., 2018; Goldstein et al., 2016; Reynolds et al., 2015). Age was entered continuously, while biological sex was coded categorically as male or female. Ethnicity was collapsed into five categories of: (1) White, (2) Black, (3) American Indian or Alaska Native, (4) Asian, Hawaiian, or Pacific Islander, and (5) Hispanic, 14 response

options for education were collapsed into three categories of: (1) less than high school, (2) high school diploma or GED, and (3) post- secondary education. Six categories of potential marital status were collapsed into three categories of married/cohabiting, widowed/divorced/separated, and single/never married, as done in prior NESARC research. Lastly, household income for the past year was reported categorically using 21 categories (ranging from less than $5000 to $200,000 or more). Categories were further collapsed into four categories of 0–19,999; 20,000–34,999; 35,000–69,999; and ≥70,000.

Analyses

All analyses utilized STATA version 15 (StataCorp, 2017) to account for the NESARC-III's complex sampling design, in order to generate the appropriate variance and standard error estimates. All analyses in STATA were weighted to ensure national representativeness. Among the total sample of individuals in the NESARC-III (n = 36,309), a sub-sample of individuals that met DSM-5 diagnostic criteria for past year PTSD were selected for analyses. Past year PTSD was used in order to examine current episodes of PTSD and increase the likelihood that PTSD and cannabis use was occurring within the same timeframe, reducing the likelihood of drawing conclusions between instances of unrelated PTSD and cannabis use across the lifespan.

Within the sample of individuals that met DSM-5 criteria for past year PTSD, I created a three-group variable as the independent variable: (1) PTSD with no cannabis use (PTSD-NoCU), (2) PTSD and cannabis use without disordered use patterns (PTSD-CU), and (3) comorbid PTSD and CUD (PTSD-CUD). Mental healthcare utilization and other mental disorders were examined as dependent variables (categorical).

Cross-tabulations and frequencies were used to calculate the prevalence or means of sociodemographic correlates (age, sex, education, marital status, household income) across the

three groups of PTSD-NoCU (reference group), PTSD-CU, and comorbid PTSD-CUD. Cross tabulations were also used to examine the prevalence of other mental disorders and mental healthcare utilization across the three groups.

Bivariate logistic regressions were then used to examine the relationship between the three group PTSD/cannabis variable and other mental disorders separately, including depressive disorders (major depressive disorder, dysthymia); anxiety disorders (generalized anxiety disorder, social phobia, specific phobia, panic disorder, agoraphobia); and eating disorders (anorexia nervosa, bulimia, binge eating disorder). Logistic regressions were used to examine the associations between the three-group variable and mental healthcare utilization for PTSD across four types of mental healthcare services (professional help, prescription medication or drugs, self-help, and emergency care). The reference groups was individuals with PTSD who did not use cannabis. Mental healthcare utilization was also examined for other mental health disorders, including depressive, anxiety, and eating disorders, across the same four types of mental healthcare service use.

Results

Table 8 displays the sociodemographic descriptive statistics of the sample. Past year PTSD was prevalent among 4.7% of the total database (N = 1779), with one participant excluded due to missing data (i.e., they did not answer questions about past year cannabis use), for a sample of N = 1778. This left n = 1388 in the PTSD-NoCU group (78.0%), n = 235 in the PTSD-CU group (13.4%), and n = 155 in the comorbid PTSD-CUD group (8.6%), illustrating relatively high rates of comorbidity.

Individuals in the PTSD-NoCU group were primarily older (M = 44.4 years), female (70.0%), White (69.8%), married/cohabiting (50.4%), with some post-secondary education

(59.2%), and household income ranging $35K-$69,999 (29.5%). Individuals in the PTSD-NoCU group had not used cannabis at all in the past year.

Individuals in the PTSD-CU group were primarily middle age (*M* = 36.2 years), female (62.1%), White (70.1%), single/never married (39.5%), with some post-secondary education (53.2%), and low household income (<20K; 46.1%). Individuals in the PTSD-CU group reported cannabis use patterns that included less than monthly use (*n* = 88; 37.4%), monthly use (*n* = 48; 20.4%), weekly use (*n* = 40; 17%), to daily or close to daily use (*n* = 59; 25.1%) in the past year. Individuals in the PTSD-CU group often reported relatively high co-occurrence rates with other mental health disorders (87.7%), including depressive disorders (53.1%), anxiety disorders (54.5%), and eating disorders (7.6%). The PTSD-CU group was associated with increased odds of past year other mental health disorders (*OR* = 1.77) compared to individuals in the PTSD-NoCU group.

Individuals in the PTSD-CUD group were primarily younger (*M* = 31.8 years), female (52.9%), White (53.5%), single or never married (50.1%), with some post-secondary education (55.2%), and low household income (<20K; 52.5%). Individuals in the PTSD-CUD group reported cannabis use patterns that included less than monthly use (*n* = 15; 9.7%), monthly use

Table 8

Sociodemographic Characteristics of the Three Group PTSD and Cannabis Use Variables.

	PTSD-NoCU (*n* = 1388)		**PTSD-CU** (*n* =235)		**PTSD-CUD** (*n* =155)	
Variable	*M (SE)*	*RRR*	*M (SE)*	*RRR*	*M (SE)*	*RRR*
Age (years)	44.4 (0.49)	1.00	36.2 (0.99)	**0.96 (0.95-0.97)*** **	31.8 (1.35)	**0.93 (0.91-0.95)*** **
	N (%)	*OR*	*N (%)*	*OR*	*N (%)*	*OR*
Sex						
Male	373 (30.0%)	1.00	84 (37.9%)	1.00	67 (47.1%)	1.00
Female	1015 (70.0%)	1.00	151 (62.1%)	**0.70 (0.51-0.97)***	88 (52.9%)	**0.48 (0.33-0.71)*** **
Race/Ethnicity						
White	797 (69.8%)	1.00	139 (70.1%)	1.00	66 (53.5%)	1.00
Black	268 (11.1%)	1.00	47 (9.8%)	0.87 (0.57-1.34)	49 (21.9%)	**2.57 (1.41-4.70)** **
Hispanic/Other	323 (19.0%)	1.00	49 (20.1%)	1.05 (0.68-1.63)	40 (24.5%)	**1.68 (1.04-2.72)***
Marital Status						
Married/Cohabiting	556 (50.4%)	1.00	53 (30.3%)	1.00	43 (31.4%)	1.00
Widowed/Divorced/Separated	501 (29.3%)	1.00	80 (30.2%)	**1.71 (1.11-2.65)***	28 (18.6%)	1.02 (0.54-1.90)
Single/Never Married	331 (20.3%)	1.00	102 (39.5%)	**3.24 (1.93-5.43)*** **	84 (50.1%)	**3.96 (2.44-6.43)*** **
Education						
Post-Secondary	793 (59.2%)	1.00	122 (53.2%)	1.00	78 (55.2%)	1.00
High School or GED	366 (24.5%)	1.00	71 (29.7%)	1.35 (0.90-2.02)	41 (26.6%)	1.16 (0.64-2.10)
Less than High School	229 (16.2%)	1.00	42 (17.2%)	1.18 (0.68-2.04)	36 (18.2%)	1.20 (0.70-2.08)
Household Income						
>70K	224 (22.5%)	1.00	28 (16.6%)	1.00	12 (12.1%)	1.00
35-69,999	367 (29.5%)	1.00	35 (16.3%)	0.75 (0.44-1.27)	33 (20.7%)	1.30 (0.50-3.41)
20-34,999	309 (21.5%)	1.00	51 (21.0%)	1.32 (0.77-2.26)	24 (14.7%)	1.26 (0.47-3.37)
0-19,999	488 (26.5%)	1.00	121 (46.1%)	**2.35 (1.41-3.93)*** **	86 (52.5%)	**3.67 (1.46-9.23)** **
Other Mental Health Disorders (Excludes DUD)	1133 (80.1%)	1.00	208 (87.7%)	**1.77 (1.16-2.69)** **	150 (96.8%)	**7.42 (2.85-19.34)*** **
Depressive Disorders	665 (46.4%)	1.00	129 (53.1%)	1.31 (0.94-1.82)	108 (70.7%)	**2.79 (1.85-4.19)*** **
Anxiety Disorders	677 (49.3%)	1.00	126 (54.5%)	1.23 (0.93-1.64)	95 (63.5%)	**1.79 (1.14-2.81)***
Eating Disorders	71 (5.9%)	1.00	15 (7.6%)	1.33 (0.64-2.75)	11 (6.5%)	1.13 (0.50-2.51)

Note: Other Mental Health Disorder was assessed for past year. OR = Odds Ratio. RRR = Relative Risk Ratio. OR and RRR both display 95% Confidence Interval in parentheses.

(*n* = 14; 9.0%), weekly use (*n* = 29; 18.7%), or daily or close to daily use (*n* = 97; 62.6%) in the past year. Individuals in the comorbid PTSD-CUD group reported extremely high co-occurrence with other mental health disorders (96.8%), including depressive disorders (70.7%), anxiety disorders (63.5%), and eating disorders (6.5%). Results illustrate that the PTSD-CUD group presented with higher odds of depressive disorders (*OR* = 2.79), anxiety disorders (*OR* = 1.79), and mental health disorders overall (*OR* = 7.42) compared to individuals in the PTSD-NoCU group.

Table 9 displays results from the bivariate logistic regression models examining the relationship between the three-group PTSD/cannabis use variable and mental healthcare utilization, across four types of services (professional help, prescription medication or drugs, self-help, and emergency care). Among individuals with past year PTSD, individuals with comorbid PTSD-CUD presented with decreased odds of utilizing professional help for PTSD (*OR* = 0.48), as well as decreased odds of utilizing prescription medication or drugs for PTSD (*OR* = 0.56) compared to individuals with PTSD who do not use cannabis. They also presented with decreased odds of mental healthcare utilization overall (*OR* = 0.64) compared to individuals with PTSD who do not use cannabis. Individuals in the cannabis use group presented with increased odds of professional help for anxiety disorders (*OR* = 1.59), as well as increased odds of past year treatment for anxiety disorders overall (*OR* =1.40). No other significant differences were found.

Individuals who used cannabis but did not report disordered use patterns (PTSD-CU) presented with increased odds of utilizing professional help for anxiety disorders (*OR* = 1.59), as well as increased odds of past year treatment for an anxiety disorder (*OR* = 1.40) compared to individuals with PTSD who did not use cannabis (PTSD-NoCU). There were no other significant

differences found between the PTSD-CU group compared to PTSD-NoCU.

Table 9

Logistic Regressions of Associations between Past Year PTSD, Cannabis Use, and Treatment Utilization.

	PTSD-NoCU (*n* = 1388)		**PTSD-CU** (*n* =235)		**PTSD-CUD** (*n* =155)	
Variable	*N (%)*	*OR*	*N (%)*	*OR*	*N (%)*	*OR*
PTSD						
Professional Help	806 (59.3%)	1.00	140 (62.0%)	1.12 (0.83-1.52)	60 (41.1%)	**0.48 (0.32-0.73)*** **
Prescription Medication or Drugs	520 (39.1%)	1.00	85 (39.2%)	1.01 (0.66-1.53)	36 (26.6%)	**0.56 (0.33-0.96)***
Self-Help	249 (18.3%)	1.00	45 (19.0%)	1.05 (0.67-1.65)	22 (18.9%)	1.04 (0.55-2.00)
Emergency Care	241 (16.8%)	1.00	47 (24.4%)	1.59 (0.95-2.68)	26 (15.8%))	0.93 (0.50-1.73)
Past year Tx	424 (30.9%)	1.00	68 (31.0%)	1.01 (0.69-1.47)	35 (24.6%)	0.73 (0.44-1.21)
Depressive Disorders						
Professional Help	805 (59.8%)	1.00	147 (65.5%)	1.28 (0.91-1.79)	84 (56.8%)	0.89 (0.61-1.29)
Prescription Medication or Drugs	737 (54.6%)	1.00	127 (54,7%)	1.00 (0.73-1.38)	71 (50.9%)	0.86 (0.55-1.36)
Self-Help	298 (21.0%)	1.00	50 (22.2%)	1.07 (0.69-1.68)	35 (22.9%)	1.12 (0.69-1.80)
Emergency Care	312 (22.2%)	1.00	65 (26.1%)	1.24 (0.83-1.84)	39 (25.2%)	1.18 (0.75-1.85)
Past year Tx	493 (35.4%)	1.00	93 (39.1%)	1.17 (0.80-1.71)	58 (44.0%)	1.43 (0.92-2.22)
Anxiety Disorders						
Professional Help	601 (43.4%)	1.00	122 (54.9%)	**1.59 (1.18-2.15)****	67 (42.7%)	0.97 (0.65-1.45)
Prescription Medication or Drugs	529 (39.4%)	1.00	95 (44.1%)	1.21 (0.83-1.77)	57 (37.5%)	0.92 (0.61-1.41)
Self-Help	186 (13.0%)	1.00	31 (11.7%)	0.89 (0.53-1.49)	23 (12.2%)	0.94 (0.50-1.76)
Emergency Care	227 (15.3%)	1.00	30 (13.1%)	0.84 (0.50-1.39)	30 (15.8%)	1.04 (0.59-1.85)
Past year Tx	551 (39.2%)	1.00	106 (47.4%)	**1.40 (1.00-1.96)***	66 (41.1%)	1.08 (0.70-1.65)
Eating Disorders						
Professional Help	71 (6.1%)	1.00	14 (6.0%)	0.99 (0.45-2.20)	7 (5.6%)	0.91 (0.40-2.07)
Prescription Medication or Drugs	28 (1.6%)	1.00	5 (3.3%)	2.06 (0.60-7.04)	2 (1.9%)	1.19 (0.21-6.79)
Self-Help	25 (2.4%)	1.00	2 (0.56%)	0.23 (0.04-1.17)	2 (2.2%)	0.90 (0.17-4.83)
Emergency Care	20 (1.7%)	1.00	0	--	2 (2.2%)	1.31 (0.26-6.70)
Past year Tx	66 (5.6%)	1.00	13 (5.7%)	1.01 (0.43-2.38)	5 (4.3%)	0.76 (0.33-1.76)
Any Mental Health						
Professional Help	1052 (77.6%)	1.00	190 (83.3%)	1.43 (0.93-2.21)	103 (69.0%)	**0.64 (0.43-0.95)***
Prescription Medication or Drugs	884 (66.4%)	1.00	156 (67.5%)	1.05 (0.74-1.50)	85 (57.3%)	0.68 (0.44-1.05)
Self-Help	426 (30.9%)	1.00	72 (29.5%)	0.94 (0.66-1.33)	47 (32.3%)	1.07 (0.66-1.72)
Emergency Care	471 (33.9%)	1.00	91 (39.4%)	1.27 (0.85-1.89)	54 (31.4%)	0.89 (0.57-1.40)
Past year Tx	759 (54.7%)	1.00	133 (57.7%)	1.13 (0.84-1.52)	84 (56.2%)	1.06 (0.71-1.58)

Note: PTSD = Posttraumatic Stress Disorder, CUD = Cannabis Use Disorder, CU = Cannabis Use, Tx = Treatment, OR = Odds Ratio with 95% Confidence Interval in parentheses.

Discussion

The present research attempts to improve our understanding regarding the nuanced relationship between PTSD, cannabis use, and mental healthcare utilization. To my knowledge, this represents one of the first studies to examine rates of treatment utilization among individuals with comorbid PTSD-CUD. Findings demonstrate that comorbid PTSD-CUD presents at rates of 8.6% among individuals with past year PTSD, which is over five times the prevalence rates of 1.5% in the general population cited in *DSM-5* (American Psychiatric Association, 2013).

Individuals in the PTSD-CUD group presented with increased odds of comorbid depressive and anxiety disorders, compared to individuals with PTSD who were not using cannabis. This suggests that individuals with PTSD and CUD are experiencing worse mental health functioning overall compared to individuals with PTSD who are not using cannabis. Individuals in the PTSD-CUD group presented with decreased odds of utilizing professional help and prescription medication or drugs for PTSD, compared to individuals with PTSD alone. Furthermore, individuals in the comorbid group also presented with decreased odds of professional treatment for any mental health disorder overall, compared to individuals with PTSD alone. In combination, these findings suggest that individuals using cannabis with severe use patterns present with increased rates of resistance and/or avoidance to help seeking overall, in comparison to already low rates of mental healthcare utilization for PTSD. This is consistent with previous research showing low treatment engagement among people with PTSD (Hoge et al., 2004; Maguen et al., 2012).

Findings appear to support the self-medication hypothesis as well as the avoidance coping model, predicting that individuals with PTSD may use cannabis to self-medicate and/or avoid negative emotional states (Khantzian, 1997; Hyman & Sinha, 2009; Conger, 1956; Litman, 2006;

Roth & Cohen, 1986). Utilizing cannabis for self-medication may temporarily alleviate some PTSD symptoms, but may also reinforce avoidance behaviors that reduce the likelihood of engaging with more effective, long-term treatment options. Patterns of short-term coping and avoidance are likely to perpetuate the chronicity of the disorder, leading to continued functional impairment over time. These findings illustrate the need for psychoeducation for both the general public as well as treatment providers regarding the relationship between cannabis use and PTSD treatment seeking and symptom improvement.

Interestingly, individuals in the PTSD-CU group presented with increased odds of professional help seeking and past year treatment for anxiety disorders, compared to individuals with PTSD who do not use cannabis. Previous research has illustrated that individuals with frequent cannabis use have a higher prevalence of anxiety disorders, and individuals with anxiety disorders have relatively high rates of cannabis use (Crippa et a., 2009). These findings may suggest that individuals with PTSD who use cannabis are experiencing an increase in anxiety symptoms that increases their odds of seeking treatment. Evidently, further research is needed to examine the causality and directionality of these relationships.

Contributions

Currently, there are notable gaps in the literature regarding the relationships between comorbid PTSD-CUD and mental healthcare utilization. The present study illustrated that comorbid PTSD and CUD is associated with decreased odds of professional help and medication use for PTSD, compared to individuals with PTSD alone. Prior research on cannabis use motives have ascertained potential self-medication, tension reduction, stress coping, and avoidance coping motives to cannabis use (Khantzian, 1997; Hyman & Sinha, 2009; Conger, 1956; Litman, 2006; Roth & Cohen, 1986; Bonn-Miller et al., 2014a). These motives are relevant for PTSD

symptom management, where individuals may turn to cannabis to improve sleep, reduce acuity and emotional distress, or avoid trauma-related memories. However, research examining rates of mental healthcare utilization amongst individuals with comorbid PTSD-CUD is sparse, limiting our ability to understand the unique challenges associated with treatment engagement in this population. Given that both PTSD and SUDs are recognized as highly debilitating and enduring disorders (e.g., Shalev, 2009), it is of particular importance to identify and reduce barriers to effective care within the comorbid population. Understanding the role of cannabis use in treatment avoidance and its impact on the efficacy of traditional PTSD interventions will be essential for developing more tailored and integrated approaches to care.

Additionally, there has been limited research investigating outcome differences between disordered versus non-disordered cannabis use patterns. These novel comparisons provide valuable insights into how patterns of cannabis use interact with mental health outcomes and treatment engagement. Understanding these distinctions is crucial, as disordered cannabis use, particularly among individuals with PTSD, may lead to more severe mental health outcomes and treatment avoidance when compared to non-disordered use. It is also important to investigate potential differences between non-disordered cannabis use and abstinence from cannabis, in order to understand the full scope of cannabis use and how it interacts with PTSD symptomatology. Comparisons in the present study between non-disordered, disordered, and abstinent cannabis use represent a significant addition to the literature that is critical to improve our understanding of how patterns of cannabis use and severity of use patterns are associated with differing clinical outcomes and rates of mental healthcare utilization. By examining these distinctions, we can better identify the risks associated with cannabis use and tailor treatment approaches accordingly. Improved understanding regarding how cannabis use and disordered use

is associated with rates of mental healthcare utilization can help reduce barriers to treatment and improve the delivery of effective care.

Furthermore, research on cannabis use among individuals with PTSD has historically approached cannabis use homogeneously. However, it is important to compare individuals who use cannabis along several dimensions of use, in order to examine meaningful differences amongst clinical outcomes. This study is one of the first to my knowledge to compare individuals who use cannabis with individuals who meet criteria for CUD, which is beneficial for improving our understanding regarding the heterogeneity of cannabis use and separating helpful from harmful clinical outcomes. These findings may be useful in order to address the mixed findings on cannabis use outcomes by differentiating between high versus low severity groups.

Finally, there is limited information available regarding the relationship between comorbid PTSD-CUD and other sociodemographic and clinical correlates. There were increased odds of depressive and anxiety disorders among individuals with comorbid PTSD-CUD, compared to individuals with PTSD alone. Interestingly, individuals who used cannabis but did not meet criteria for CUD presented with increased odds of professional treatment for anxiety disorders. One possible explanation for these findings may be that individuals with mild to moderate cannabis use patterns experience an increase in anxiety symptoms, however, with less severe use patterns do not experience the same barriers to seeking treatment for these anxiety symptoms. These findings highlight the complex interaction between cannabis use and mental health symptomatology, suggesting there is likely an interaction between severity of use patterns and mental health symptomatology.

Implications and Future Directions

There are several directions suitable for future research. First, further examination of the

discrepancy between mental healthcare utilization and comorbid PTSD-CUD in comparison to individuals with PTSD alone should be replicated, as well as extended with the use of other methods (i.e., RCTs, longitudinal study) and potentially other populations of comparison. Second, due to notable heterogeneity in cannabis use patterns, future research could also differentiate cannabis use patterns based on severity of use indicators, in order to assess potential meaningful differences in treatment outcomes. This may include comparing individuals with more severe or highly disordered use patterns, to individuals with less frequent or severe use. It would be interesting to investigate if any other relationships between PTSD and cannabis use emerged when separating by severity of use, rather than cannabis use dichotomously. Third, although I was able to compare rates of mental healthcare utilization for individuals with PTSD, I was unable to assess specific barriers to treatment, length of treatment, acceptability and accessibility of treatments, or efficacy of treatments for comorbid PTSD-CUD. Therefore, future research investigating varying facets of treatment for comorbid PTSD and CUD would be helpful in illustrating *why* individuals with the comorbidity have been associated with decreased utilization of treatment services. It still remains poorly understood why individuals with PTSD do not seek out treatment services, with no shortage of possible etiologies. Fourth, future research should investigate the potential relationship between PTSD symptom severity and mental healthcare utilization among individuals with comorbid PTSD-CUD. For example, it would be interesting to examine if PTSD symptom severity has a mediating or moderating effect on mental healthcare utilization. It stands to reason that individuals with comorbid PTSD-CUD may not be able to utilize treatment, if their PTSD symptoms are worsened by CUD.

Limitations

The present study presented with some notable limitations. Due to the fact that the present

study utilized a large nationally representative sample, the study was cross-sectional in design and therefore no causal relationships between variables could be established. Therefore, future longitudinal research and randomized control trials further examining the relationship between PTSD-CUD and treatment is warranted. Second, as the NESARC-III dataset was pre-determined, I was unable to add additional variables of interest to the research. Although I was able to examine rates of treatment utilization for PTSD and anxiety, depressive, and eating disorders, I would have liked to examine treatment utilization for any mental health disorders, in order to ensure that individuals with PTSD weren't pursuing treatment for other disorders. Furthermore, ideally the research study would have investigated not only rates of mental healthcare utilization, but also reported barriers to mental healthcare utilization as well, in order to more comprehensively examine mental health treatment as a whole. Third, as mental healthcare utilization was self-reported by participants, it is possible that this may have introduced elements of participant response or memory bias. For example, it is possible that due to potential stigmatization, participants may not have felt comfortable reporting mental healthcare utilization even if they recalled accessing services. Lastly, due to the fact that substance use disorders were assessed differently than mental health disorders in the NESARC-III, I was unable to examine rates of SUD treatment and include SUD treatment in our treatment analyses. Ideally, as I was interested in comorbid PTSD and CUD, I would have preferred to examine treatment for CUD alongside PTSD.

Conclusion

Posttraumatic stress disorder remains one of the most enduring and debilitating mental health disorders in the modern world. Individuals with PTSD continue to experience notable barriers to acceptable, accessible, and effective care. Despite growing awareness of patterns of

cannabis use among individuals with PTSD, relatively little is known about how comorbid CUD impacts treatment utilization among individuals with PTSD. Lack of effective integration between PTSD and SUD treatments appear, in other research, to be a barrier to care, potentially contributing to treatment avoidance. Knowledge translation programs educating the public on the risk of comorbidity for PTSD and CUD, as well as options for isolated or combined PTSD-SUD treatments may potentially improve rates of mental healthcare utilization for this population. Understanding differences in mental healthcare utilization for individuals with comorbid PTSD-CUD may also aid treatment providers in reducing barriers to effective care and improve clinical outcomes for individuals with PTSD.

Chapter Five: Discussion

Posttraumatic stress disorder has been consistently identified as a both a public health issue and priority (e.g., Magruder, et al., 2017; Watson, 2019), as it is associated with significant financial costs and functional impairment at an individual, interpersonal, and societal level. Traumatic experiences are common worldwide, and a subset of individuals continue to experience severe and disabling traumatic symptoms for many years following traumatic exposure (e.g., Kessler et al., 2017). With the recent legalization of cannabis across much of North America, there is an urgent need to provide both policy makers and the public with pertinent information regarding the effects of cannabis consumption on various facets of mental health. Comorbid mental health conditions are frequently associated with increased symptom severity (Helle et al., 2020; Najt et al., 2011; Schafer & Najavits, 2007), increased functional impairment (e.g., Shalev et al., 2017), increased odds of psychological comorbidities (e.g., Goldstein et al., 2016; Grinage, 2003), as well as decreased treatment effectiveness (e.g., Newman et al., 1998) that may extend the duration of disorders and lead to undesirable clinical outcomes. Individuals with PTSD who use cannabis may experience potential benefits or harms with use that are nuanced and not well understood. The present research examined multiple facets of the symptom profile of individuals with PTSD who use cannabis, in an attempt to explain the observed disparity in research regarding perceived harms and benefits associated with cannabis use. Novel comparisons between disordered versus non-disordered cannabis use, as well as variations among cannabis use severity measures all contribute to the clinical significance of the present research.

Summary of Findings

Three distinct research studies were conducted using a nationally representative sample of

adult civilians collected during the National Epidemiologic Survey on Alcohol and Related Conditions III (NESARC-III; N = 36,309) in 2012-2013. Study one utilized a series of multinomial logistic regressions to examine sociodemographic and clinical correlates of individuals with comorbid PTSD-CUD, compared to having neither disorder or PTSD alone. Findings illustrate that risk correlates of comorbid PTSD-CUD include low income (0-19,999), being single or never married, as well as being of Black or American Indian or Alaska Native descent. Comorbid PTSD and CUD was also associated with increased odds of other mental and physical health comorbidities, as well as other substance use disorders, compared to individuals having neither disorder. Furthermore, individuals in the comorbid group displayed the highest risk ratio for PTSD symptom severity of any of the three groups, when compared to individuals in the neither condition. This appears to suggest that individuals who have comorbid PTSD-CUD are experiencing worsening of their PTSD symptoms. Alternatively, in comparing PTSD-CUD to PTSD alone, individuals with the comorbidity presented with higher odds of other mental and drug use disorders, as well as higher rates of alcohol use disorder. Interestingly, they presented with decreased odds of physical health conditions. Individuals in the comorbid PTSD-CUD group presented with the highest odds of all three types of adverse childhood experiences, including abuse, neglect, and household dysfunction, compared to individuals with neither disorder. Individuals with PTSD-CUD also presented with the highest odds of sexual assault and physical assault of all three comparison groups, when compared to individuals with neither disorder. In combination, the study findings demonstrate that individuals with comorbid PTSD-CUD present with more severe symptom profiles along several facets of health, compared to individuals without the comorbidity.

Study two utilized latent mixture modelling to identify distinct subtypes of cannabis use

patterns among individuals with PTSD, based on various cannabis use severity indicators (age of onset, frequency, quantity, medicinal cannabis use, disordered cannabis use) and predictors of age, sex, PTSD symptom severity, past year CUD, alcohol use disorder, tobacco use disorder, as well as mental and physical quality of life. A four class-solution that differed on measures of substance use severity was identified, including a moderate use group, a severe use group, as well as two low use groups. Early age of first use, high frequency, high quantity, as well as increased rates of medicinal use and disordered use were all associated with higher severity use profiles. Results indicated that participants in the low severity classes were significantly older than those in the moderate severity class, while the high severity class had significantly more males than any of the other classes. Moderate and high severity classes were associated with increased odds of CUD compared to the low severity classes, while the high severity class was associated with increased odds of PTSD symptom severity relative to all three other groups. Tobacco use disorder was associated with increased odds of being in the moderate and high severity classes compared to both low severity groups. Lastly, the high severity group was associated with decreased rates of physical quality of life compared to all three other groups, while individuals in the moderate severity group presented with increased odds of mental quality of life compared to one of the low severity groups. Examining subtypes of cannabis use patterns among individuals with PTSD Overall, it appears the four-class solution contributes meaningful information in order to differentiate distinct subgroups of cannabis use patterns and outcomes.

Lastly, study three examined rates of mental healthcare utilization for four types of treatment (professional help, prescription medication or drugs, self-help, and emergency care) among individuals with PTSD, along three dimensions of cannabis use (no use, disordered use, non-disordered use). Individuals with comorbid PTSD-CUD presented with decreased odds of

utilizing professional help and prescription medication or drugs for PTSD, compared to individuals with PTSD alone. Furthermore, individuals with the comorbidity also presented with decreased odds of mental healthcare utilization overall, compared to individuals with PTSD alone. Interestingly, individuals in the non-disordered group presented with increased odds of professional help utilization for anxiety disorders compared to individuals with PTSD alone. Overall, this study demonstrates that individuals with comorbid PTSD-CUD utilize significantly less professional and mental health treatment services than individuals with PTSD alone.

Theoretical Contributions

The present research projects contributed meaningful information to the study of PTSD and cannabis use along several facets. First, it contributed novel information regarding the relationship between PTSD, cannabis use, and PTSD symptomatology, that has been notably inconsistent and contradictory in prior research. Study one demonstrated that comorbid PTSD-CUD is associated with higher rates of PTSD symptom severity, compared to individuals with neither disorder. Study two, alternatively, illustrated that a high severity cannabis use profile was associated with increased rates of PTSD symptom severity, compared to all three other low and moderate severity use groups. In combination, these findings illustrate that disordered cannabis use and high severity cannabis use profiles are associated with increased rates of PTSD symptom severity. These findings are relevant for investigating the complex relationship between PTSD and cannabis use, as it is related to treatment recommendations utilizing medicinal cannabis use for the treatment of PTSD.

Second, the present research contributed meaningful information regarding comorbid PTSD-CUD and an assortment of sociodemographic and clinical correlates. In study one, comorbid PTSD-CUD was noted to be associated with low income (0-19,999), being single or

never married, as well as being of Black or American Indian or Alaska Native descent, in comparison to individuals with neither disorder. Furthermore, comorbid PTSD-CUD was also presented with increased rates of co-occurrence with other health conditions, including mental health, physical health, and substance use disorders, compared to individuals having neither disorder. In study three, comorbid PTSD-CUD was associated with increased rates of depressive and anxiety disorders, and mental health disorders overall in comparison to individuals with PTSD alone. This illustrates that individuals with comorbid PTSD-CUD present with increasingly comorbid, complex clinical profiles that may complicate treatment. Information regarding rates of comorbidity may help improve treatment recommendations and outcomes for this high-risk group.

Another significant contribution of the present research is the support for a multifactorial theoretical model that integrates multiple pathways for cannabis use among individuals with PTSD. The present research provides support for the self-medication hypothesis (Khantzian, 1997), demonstrating that individuals with comorbid PTSD-CUD experience more severe PTSD symptomatology (i.e., anxiety, hypervigilance, and negative mood alterations), and therefore it appears likely that they use cannabis in an attempt to alleviate these negative emotional states. However, motives for cannabis use cannot be summarized by the self-medication model alone. Theories such as the mutual maintenance model (Stewart et al., 1998) and the susceptibility model (Chilcoat & Breslau, 1998) are particularly relevant in understanding how PTSD and cannabis use can perpetuate one another. The present research appears to provide support for these models by illustrating that individuals with higher PTSD symptom severity, especially those who experienced more types of traumatic exposures like sexual or physical assault, were more likely to develop severe cannabis use profiles. These findings provide further support that

cannabis use and PTSD symptomatology are mutually reinforcing. Furthermore, there is also support for the common factors model (Wolf et al., 2010) that certain shared risk factors underlie both PTSD and substance use disorders. Study one identified ACEs as a common antecedent for both PTSD and cannabis use, where individuals with comorbid PTSD-CUD were more likely to report higher rates of ACEs. These findings are in line with previous research by Breslau (2009) and Goldstein and colleagues (2016) demonstrating that childhood traumatic exposure significantly increased the likelihood of developing PTSD and substance use disorders, suggesting that shared risk factors early on in life are precedents for both disorders, supporting the idea that common underlying vulnerabilities contribute to the observed comorbidity.

The variability of cannabis use profiles among individuals with PTSD provides further evidence that cannabis use should not be studied homogenously. Earlier studies (e.g., Bonn-Miller et al., 2010; Lake et al., 2020) often treated cannabis use as a dichotomous behavior among individuals with PTSD. The present research was the first of my knowledge to examine specific subtypes of cannabis use patterns among individuals with PTSD. Utilizing latent mixture modelling, study two produced four cannabis use classes that differed primarily on severity of use patterns (low, moderate, and severe). Findings were consistent with prior research with other substance use disorders that illustrated age of first use, quantity of use, frequency of use, disordered use, and medicinal use are all associated with higher severity use profiles. Cannabis use classes were also noted to differ in regard to certain predictors, including PTSD symptom severity, physical quality of life, as well as tobacco use disorder and past year CUD. While some individuals who use cannabis may self-report a reduction or alleviation in PTSD symptoms associated with cannabis use, others may experience a worsening of PTSD symptoms. This disparity in results suggests that the therapeutic or detrimental impact of cannabis may depend on

factors like type of cannabis used, in addition to the quantity and frequency of use. Examining heterogeneity within cannabis use is imperative in order to differentiate more and less severe patterns of cannabis use that may contribute to differing clinical outcomes.

The present research also utilized novel comparisons between individuals with PTSD who do not use cannabis, with those who use cannabis, as well as those who meet criteria for CUD, in order to examine potential differences between disordered versus non-disordered cannabis use. This comparison represents a significant addition to the literature that is critical to understanding how patterns of use are associated with differing clinical outcomes. Additionally, comparing individuals with comorbid PTSD-CUD to those with PTSD alone revealed meaningful results that highlight the nuances of the PTSD-CUD comorbidity. Findings that individuals with comorbid PTSD-CUD were associated with decreased rates of professional treatment and prescription medication or drugs provides support for theoretical modules postulating cannabis is used for self-medication. Improved understanding regarding how cannabis use and disordered use is associated with rates of mental healthcare utilization can help reduce barriers to treatment and improve effective care.

Findings from the present research also contribute to the ongoing debate about the role of medicinal versus recreational cannabis use among individuals with PTSD. The present research illustrates that the therapeutic potential of cannabis for PTSD remains unclear. These findings are in line with prior research postulating both perceived benefits, including improved sleep or reduced anxiety with cannabis use (Greer et al., 2014; Elms et al., 2019), as well as negative effects, including worsening of symptoms like hyperarousal and avoidance (Boden et al., 2013; Wilkinson et al., 2015). The present research providers further support that the medicinal use of cannabis should be approached with caution, which is particularly relevant as cannabis is

sometimes prescribed by physicians for individuals with PTSD (e.g., Shishko et al., 2018; Wilkinson et al., 2015).

Another contribution of the present research is the exploration of mental healthcare utilization among individuals with comorbid PTSD-CUD. Cannabis use has previously been shown to be a barrier to PTSD treatment, illustrating lower rates of symptom improvement during PTSD interventions (Bonn-Miller et al., 2013). Results show that individuals with PTSD-CUD are less likely to utilize formal mental health treatment services compared to those with PTSD alone. Reduced treatment seeking may result from a combination of several factors, including perceived stigma, financial barriers, or limited availability of integrated care services, all of which have been previously documented as contributors to healthcare disparities in PTSD and SUD populations (Najt et al., 2011; Schafer & Najavits, 2007). The observed reduced rates of healthcare utilization continue to highlight the need to for treatment models that consider both PTSD and substance use treatment concurrently. Thus, treatment models should incorporate components like harm reduction and skills training for alternative coping mechanisms, rather than relying solely on abstinence-based substance use models.

The present research emphasizes the necessity of moving towards a multidimensional model of the interactions between cannabis use and PTSD that incorporates individual factors (e.g., symptom severity, motivations for use), social factors (e.g., healthcare accessibility, stigma), and cannabis-specific variables (e.g., dosage, type), to develop a more comprehensive understanding of the etiology of comorbid PTSD-CUD. This understanding will provide a more evidence-based, accurate framework for both researchers and clinicians to better tailor prevention and treatment approaches for this complex and heterogeneous population.

Future Directions

Continued efforts to develop evidence-based recommendations for the use and contraindicated use of cannabis for various mental health disorders should be a top economic priority. It is important to further investigate the effects of specific variations of cannabis use among individuals with PTSD. Evidently, varying cannabis use profiles contribute to meaningful clinical differences in PTSD symptomatology. Although the present research was able to analyze certain cannabis use variables (such as estimated frequency and quantity), other pertinent variations such as duration of use, cannabis strain (i.e., THC to CBD ratio), and more controlled calculated quantity and frequency of use were unable to be examined. These additional variables would likely prove highly relevant for ascertaining harms and benefits of cannabis for individuals with PTSD.

Randomized Controlled Trials

There is a significant lack of randomized controlled trials (RCTs) for PTSD and cannabis use. Given the mixed findings regarding cannabis as a treatment for PTSD, RCTs are urgently needed to examine the therapeutic efficacy of cannabis, particularly in comparison to traditional PTSD interventions. Randomized controlled trials would also be beneficial to compare various types of cannabis products, including products with differing THC to CBD ratios, to determine whether specific formulations provide increased symptom relief without increasing the risk of CUD or other negative health consequences. For example, CBD has been suggested to have anti-inflammatory properties that would likely benefit individuals with PTSD without the psychoactive effects of THC. Future RCTs should also consider examining different PTSD populations, (i.e., civilians, veterans, and individuals with specific types of traumatic exposure), as well as different socioeconomic groups to examine any differences in perceived effectiveness

of cannabis use for PTSD symptomatology. Fortunately, RCTs should be more feasible and accessible following legalization of recreational cannabis in Canada in 2018.

Cannabis Use Typologies

One of the significant contributions of this research was the identification of distinct cannabis use typologies among individuals with PTSD using latent mixture modeling. Future research should seek to validate these typologies using independent datasets and longitudinal methods to understand how these and other cannabis use profiles evolve and change over time. Future research could also investigate whether these cannabis use profiles predict differential treatment outcomes. For example, individuals in the high-severity groups may require more comprehensive or integrated interventions that simultaneously address PTSD symptoms and cannabis dependence.

Although both medicinal and recreational cannabis use was present within the present sample, there were limited opportunities for comparison between the two. However, among latent classes of individuals who use cannabis within the lifetime PTSD sample, the highest rates of medicinal cannabis use were present in the most severely disordered cannabis use group. This is in line with previous research, whereby medicinal cannabis use was associated with higher rates of cannabis use and PTSD symptomatology compared to recreational cannabis use (e.g., Loflin et al., 2017). It is important for future research to examine the directional relationship between these two factors. In other words, it is possible that more severe PTSD symptomatology is facilitating an increase in medicinal cannabis use, however it is also possible that more severe use is facilitating increased PTSD symptomatology, or both.

The current research was limited by the absence of detailed data on the type, potency, and administration method of cannabis used by participants. Given the increasing variability in

cannabis products available today, future research should explicitly examine how these factors influence the relationship between PTSD and cannabis use. For example, cannabis products high in THC content may exacerbate symptoms of hyperarousal and anxiety, while cannabis products high in CBD could have differential, perhaps more stabilizing effects on mood.

Future studies should also investigate the impact of different modes of administration (e.g., smoking, vaping, edibles) on PTSD symptomatology. For example, previous research by Hasin and colleagues (2016) suggested that higher THC levels are associated with increased CUD severity. Additionally, method of administration of cannabis could potentially influence the experience of cannabis use. These factors must be carefully documented in future studies to improve our understanding of how cannabis use contributes to PTSD symptom severity.

Symptom Severity

Additionally, future research regarding the complex relationship between PTSD symptom severity and cannabis use among individuals with PTSD is warranted. As noted by the National Academies of Sciences, Engineering, and Medicine (2017) "from a cannabis therapeutics perspective, blinded, randomized, placebo-controlled studies in patients with PTSD need to be conducted to evaluate any potential therapeutic benefits of cannabis on PTSD symptoms and course" (p.323). I attempted to examine meaningful differences in PTSD symptom severity for differing cannabis use patterns in all three studies, with particular focus on examining differential clinical outcomes between low and high severity cannabis use patterns. Although able to compare PTSD symptom severity between individuals with different cannabis use patterns in study two, regrettably there was not a cannabis abstinent group for comparison. Therefore, future research should compare individuals with differing types of cannabis use to individuals who do not use cannabis, to investigate potential important differences in PTSD symptomatology and

better elucidate whether cannabis presents with helpful qualities among lower severity of use profiles, or whether harmful effects of cannabis use present for other severity of use groups as well.

Barriers to Treatment Utilization

Findings from study three illustrate that individuals with comorbid PTSD-CUD were significantly less likely to engage in mental health services, suggesting a need for future research to develop strategies that enhance healthcare accessibility for this population. Future research should explore integrative approaches to PTSD treatment, improving treatment acceptability by providing individuals with self-directed or clinician-led treatment programs to offer more autonomy and flexibility to this struggling population. Furthermore, individuals with PTSD may also benefit from online interventions that they can do from the comfort of their own home, reducing barriers of accessibility.

Although I was able to compare rates of mental healthcare utilization for individuals with PTSD, I regrettably did not have data in our sample with regards to specific barriers to treatment, preference for treatment type and format, or treatment efficacy or acceptability ratings. Therefore, future research that investigates specific barriers to treatment for comorbid PTSD and CUD would be helpful in illustrating *why* individuals with the comorbidity are utilizing less treatment services. This information is critically important in order to reduce barriers to care for individuals with PTSD. Other pertinent factors, such as duration of treatment, type of treatment, as well as willingness to engage in treatment may also be beneficial to examine.

Furthermore, findings from study one emphasize the sociodemographic disparity among individuals with PTSD-CUD, particularly among marginalized groups such as Black, Alaskan Native/American Indian, and lower-income individuals. Future research should focus on

developing culturally informed and trauma-informed interventions that are sensitive to the unique experiences and needs of these populations. This could include interventions that incorporate peer support from individuals with shared cultural backgrounds or their own previous experience of trauma. It would also be beneficial for community health workers to understand who may be most at risk for developing PTSD following a traumatic event. Future research could investigate potential differential effects of culturally specific interventions.

Longitudinal Research

Longitudinal research on co-occurring PTSD and CUD is notably non-existent, and critically necessary in order to determine how PTSD and cannabis use influence each other over time. A significant limitation of the present research was its cross-sectional design, which restricted the ability to establish causal pathways between PTSD and cannabis use. Longitudinal research could help to clarify whether cannabis use serves as a precursor to PTSD in certain contexts or if it predominantly emerges as a coping mechanism post-traumatic exposure, or both. It could also be used to examine both acute and long term effects of cannabis use on PTSD symptomatology over time. Longitudinal studies could also help explore how different types of traumatic exposure differentially impact subsequent cannabis use. Future research could use prospective cohorts to follow young people with high levels of adverse childhood experiences (ACEs) to see if they are more likely to develop both PTSD and CUD. This approach would help validate the common factors model (Wolf et al., 2010) by providing real-world data on how early life stressors set the stage for subsequent psychopathologies. Furthermore, longitudinal studies should include repeated measures of cannabis use (e.g., frequency, potency, method of administration) and PTSD symptomatology to explore how changes in one affect the course of the other over time. With CUD increasing in prevalence following legalization (e.g., Aletraris et

al., 2023), it is important to investigate longitudinal changes in symptomatology, severity, and chronicity in order to more accurately depict the impact of comorbid PTSD and CUD over time.

Implications of Research

These research findings have several implications to clinical practice, policy formation, and public health initiatives. Understanding the nuanced relationship between PTSD and cannabis use is important in order to make informed decisions about the development of targeted interventions and mental health treatment overall.

Information regarding the unique sociodemographic profile of individuals with comorbid PTSD and CUD can be used to better understand the nuances between comorbid PTSD and CUD compared to those without the comorbidity. The proposed research attempts to illustrate pertinent sociodemographic and clinical correlates unique to the comorbidity, as well as potential relationships between the comorbidity and other facets of mental health functioning.

Second, information regarding cannabis use variables (i.e., frequency, quantity) as well as cannabis use profiles among individuals with PTSD can be used to differentiate unique clinical outcomes among individuals with PTSD. Investigating meaningful differences among cannabis use variables is fundamental in order to better understand the unique, varying effects of cannabis use on PTSD symptomatology. These findings can be used to determine if there are potential symptom profiles that may benefit or suffer from cannabis use, as well as if these distinct classes may suggest distinct clinical interventions.

Third, improved understanding regarding the relationship between PTSD, cannabis use, and mental healthcare utilization is fundamental in order to improve treatment seeking behavior, direct treatment recommendations, increase treatment effectiveness, and decrease symptom severity for individuals with PTSD. Furthermore, comparisons between CUD, non-disordered

use, and no cannabis use among individuals with PTSD help characterize the relationship between cannabis use and treatment seeking behaviors in the areas of professional help, prescription medication or drugs, self-help, and emergency care.

The synthesis of these findings produce significant clinical implications for the long-term effects of cannabis use among individuals with PTSD, especially given the increased availability of cannabis and potential increase in utilization patterns in North America. They may be used to direct future research, as well as treatment recommendations for cannabis use for individuals with PTSD.

Clinical Practice Implications

The identification of distinct cannabis use profiles among individuals with PTSD highlights the need for personalized treatment approaches that acknowledge varying motivations, severities, and patterns of cannabis use. Clinicians working with individuals with PTSD who use cannabis may benefit from exploring the primary reasons for use, which may include symptom relief, recreational use, or as a coping strategy for pain. Tailoring interventions to these motives is likely critical for treatment adherence and efficacy. Considering the high prevalence of comorbidities among individuals with PTSD, specifically anxiety, depressive, and other substance use disorders, integrated treatment programs that address both PTSD and substance use simultaneously should be prioritized. This is in line with recommendations of prior research.

There is also a need for comprehensive psychoeducation programs for individuals with PTSD and their families. Many individuals with PTSD turn to cannabis under the assumption that it will provide relief from their symptoms without understanding the potential for substance dependence and exacerbation of PTSD symptoms. Educating individuals and their support networks about the risks associated with cannabis use, its potential impact on mental health, and

the benefits of evidence-based alternatives could reduce harmful use patterns and help individuals to make more informed decisions about their health and wellbeing.

Policy Implications

The findings of the present research also have important implications to policy development. PTSD is one of the most common reasons cited for medicinal cannabis use. As such, policy makers need to regulate and establish clear guidelines around the prescription of cannabis for PTSD. These policies should encourage practitioners to conduct a thorough clinical interview that includes a detailed history of challenges. Clinicians may also want to consider recommending alternative treatments before considering cannabis as a treatment, and ensure that patients are well-informed about the potential risks and benefits associated with cannabis use for PTSD.

Individuals with PTSD-CUD were found to have lower mental healthcare utilization rates, possibly due to barriers such as stigma, financial constraints, or accessibility issues. Policy makers should work towards reducing these barriers by expanding insurance coverage for mental health services, increasing funding for community-based mental health programs, and ensuring that vulnerable populations, such as racial minorities and those with low income, have equitable access to comprehensive PTSD treatment. Additionally, initiatives aimed at reducing stigma surrounding both PTSD and substance use are crucial in fostering an environment where individuals feel empowered to seek help without fear of judgment.

There is evidently a clear need for improved messaging and warnings on cannabis products regarding the potential risks associated with use, particularly for individuals with a history of traumatic exposure. Product packaging could include warnings similar to those on tobacco or alcohol, specifically alerting individuals to the potential exacerbation of mental health

symptoms, including anxiety, paranoia, and worsening PTSD symptoms. Public information campaigns could also highlight these risks, especially focusing on individuals with pre-existing mental health conditions.

Public Health Implications

The findings of this research also highlight several areas where public health initiatives can make meaningful changes. Public health initiatives can create awareness campaigns specifically targeted at populations most at risk of comorbid PTSD-CUD, particularly marginalized racial groups and those with lower socioeconomic status. These campaigns should aim to inform these groups about the potential risks of cannabis use as a coping mechanism for PTSD and provide information on alternative resources for managing symptoms. This may include other resources such as peer support groups, crisis services, or pro-bono or low cost mental health therapy.

Incorporating mental health education within primary care and general healthcare settings is also essential. Public health and treatment providers can also improve care by prioritizing early screening for cannabis use among individuals with PTSD, similar to how first responders and individuals known to have high exposure to traumatic events are screened for symptoms of PTSD following traumatic exposure. By integrating mental health and substance use screenings into the general population, healthcare providers can identify at-risk individuals earlier and refer them to appropriate services. Furthermore, by educating individuals about the risks associated with cannabis use, particularly for those with PTSD or other mental health disorders, healthcare providers can play a proactive role in preventing the escalation from use to disorder.

There is also a clear public health need for the development and training of healthcare professionals in recognizing the complexities of the PTSD-CUD comorbidity. Providers should be equipped not only with the skills to assess both PTSD and substance use but also to

understand other factors influencing cannabis use. This training could include guidance on non-judgmental communication, which is key to ensuring that individuals feel comfortable discussing their substance use without fear of stigma or repercussions.

Societal Implications

These findings also have broader implications for society as a whole. The dual stigma surrounding both PTSD and substance use can prevent individuals from seeking necessary treatment. At present, the portrayal of both PTSD and cannabis use in the media is likely exacerbating barriers to effective treatment. For example, recent research by Mennis and colleagues (2023) illustrates how rates of treatment utilization for CUD have been decreasing across the US following legalization. They discuss more tolerant attitudes and greater social acceptance towards cannabis use, as well as reduced perception of frequent cannabis use as problematic as potential contributing factors to decreased rates of treatment utilization. Media efforts should be targeted to reduce stigmatization and enhance empathy and understanding of individuals struggling with PTSD and substance use. Utilizing mental health campaigns such as *Bell Let's Talk* to increase understanding and even provide treatment recommendations for subpopulations that may be particularly resistant or avoidant to treatment (i.e., individuals with PTSD) can aid knowledge translation efforts tremendously. By promoting narratives of compassion and understanding that reflect the complexity of self-medication behaviors and the challenges faced by individuals with PTSD-CUD, the media can play a role in reducing societal stigma and supporting individuals in accessing care. Furthermore, introducing mental health psychoeducational and literacy programs that discuss trauma, substance use, and coping mechanisms in schools and universities can help reduce the risk of CUD among individuals with PTSD. These programs can teach students healthier coping skills, emphasize the importance of

seeking help, and inform them about the potential dangers of self-medicating with substances like cannabis.

The present research underscores the importance of community-based support networks in mitigating the need for cannabis use as a coping mechanism for PTSD. Programs that foster peer support groups, community mental health initiatives, or trauma-informed community outreach can provide individuals with alternative sources of support that reduce reliance on substances for symptom management. Providing options for care and reinforcing autonomy in care decisions is particularly important for individuals with PTSD who have experienced a loss of control and autonomy during traumatic exposure. Empowering communities and community agencies to take an active role in providing non-judgmental, trauma-informed care will have a positive impact on reducing the need for more formal mental health services.

The key takeaway from the present research is the need for nuanced, personalized approaches that respect the complex motivations and circumstances underlying cannabis use in individuals with PTSD. Whether through targeted clinical interventions, policy reform, public health initiatives, or societal changes in attitude, the aim should be to provide a supportive environment that mitigates the risks associated with cannabis use, enhances treatment accessibility, and ultimately improves quality of life for individuals struggling with PTSD and CUD. This comprehensive approach ensures that interventions do not merely target symptoms but address the broader factors contributing to the comorbidity. As the use of cannabis continues to change and evolve following legalization, we must continue to refine our approach to care for these vulnerable populations.

Strengths and Limitations

The proposed research project presents with a number of discernable strengths. First,

utilizing data collected by the NIAAA for secondary data analysis provides increased efficiency in order to study a large number of people with the limited resources of the University of Manitoba. Second, utilizing data that has already been collected allows the research project to focus time and resources solely on creating detailed hypotheses, analyses, and publishing conclusions, as well as manage the restrictions for data collection due to the COVID-19 pandemic. Third, using a large-scale cross-sectional data allows for increased power that facilitates improved confidence in research findings and greater generalization to society overall. Fourth, a large proportion of past research regarding comorbid PTSD-CUD has been conducted on veteran populations. Therefore, the present study presented with notable strength in examining a civilian population of considerable size. Last, increased power as well as the large number of variables studied in the national sample allows for intricacies between variables to be observed and assessed. This provides increased detail and understanding that is ultimately fundamental for studying a complex population, individuals with PTSD.

The proposed research does present with some notable limitations. First, the NESARC-III is a cross-sectional survey collected in 2012-2013, and therefore cannot be used to determine causal relationships between variables and may present somewhat outdated findings. Utilizing a previously collected dataset also means that research variables cannot be altered for the current project. Therefore, although there may be other variables or instruments of interest to the researchers, regrettably they were not be able to be introduced. For the latent mixture model, ideally there would have been additional measures of cannabis use severity (such as duration of cannabis use) or utilized more specific indicators of quantity and frequency of use. For example, the measure of cannabis consumption in the NESARC-III is typically in regard to “the number of joints smoked per day”, however this measurement is somewhat vague and does not account for

differences such as joint size, potency, number of hits, or consumption of other cannabis products. Furthermore, it is possible that individuals may not accurately recall the number of joints they had per day, especially for individuals consuming larger quantities. Therefore, the self-report of cannabis consumption may have introduced measurement error, albeit consistently between participants. Regarding mental healthcare utilization, ideally I would have liked to assess substance use disorder treatment in combination with mental health disorder treatment, in order to obtain a comprehensive picture of mental healthcare utilization overall.

Potential study limitations also include differences in some aspects of survey measures translating from *DSM-IV* to *DSM-5*, as well as less than ideal reliability for a few diagnoses other than AUD. Due to the fact that some population segments were not covered (e.g., homeless individuals, prisoners), estimates presented may underestimate the true prevalence of AUD and other DUD. Lifetime comorbid associations with AUD may be subject to recall bias and bias in variation of associations by ages at onset of comorbid disorders. However, these concerns are not relevant to 12-month comorbidity associations that demonstrated similar direction and magnitude as comorbid lifetime associations. Similarly to other large US surveys, the NESARC-III did not assess all mental health disorders.

Conclusion

The present research provided a comprehensive examination of the nuanced and intricate relationships between posttraumatic stress disorder (PTSD) and cannabis use, utilizing a nationally representative dataset from the National Epidemiologic Survey on Alcohol and Related Conditions III (NESARC-III). Through three distinct but interconnected studies, this dissertation addressed several key questions about the sociodemographic and clinical correlates of PTSD-CUD, the diversity in cannabis use behaviors among those with PTSD, and the patterns

of mental healthcare utilization in this population. The findings not only advance our understanding of PTSD and cannabis use but also pose significant theoretical, clinical, and policy-related implications for future research and practice.

Comorbid PTSD-CUD represents a frequent disorder combination that severely affects etiology, treatment course and clinical outcomes. The present research demonstrates that individuals with comorbid PTSD-CUD present with more severe, high comorbid profiles that are associates with negative clinical outcomes (PTSD symptom severity, reduced quality of life) as well as high rates of other mental health and substance use disorders. Future research is needed in order to examine barriers to treatment and improve clinical outcomes. Improved understanding regarding the impact of cannabis use on PTSD is fundamental in order to tailor treatment recommendations for medicinal cannabis use for PTSD, contribute to low-risk cannabis use guidelines for individuals with PTSD, as well as reduce treatment barriers and tailor more effective clinical interventions for this struggling population.

References

Albucher, R. C., & Liberzon, I. (2002). Psychopharmacological treatment in PTSD: a critical review. *Journal of psychiatric research*, *36*(6), 355-367

Aldington, S., Harwood, M., Cox, B., Weatherall, M., Beckert, L., Hansell, A., ... & Beasley, R. (2008). Cannabis use and risk of lung cancer: a case–control study. *European Respiratory Journal*, *31*(2), 280-286.

Alegría, M., Fortuna, L. R., Lin, J. Y., Norris, L. F., Gao, S., Takeuchi, D. T., ... & Valentine, A. (2013). Prevalence, risk, and correlates of posttraumatic stress disorder across ethnic and racial minority groups in the US. *Medical care*, *51*(12), 1114.

Aletraris, L., Graves, B. D., & Ndung'u, J. J. (2023). Assessing the impact of recreational cannabis legalization on cannabis use disorder and admissions to treatment in the United States. *Current addiction reports*, *10*(2), 198-209.

American Psychiatric Association. (1980). *Diagnostic and Statistical Manual of Mental Disorders*, (3rd ed.). Washington, DC: American Psychiatric Association.

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders,* (4th ed.). Washington, DC: American Psychiatric Association.

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders,* (5th ed.). Arlington, VA: American Psychiatric Association.

Anda, R. F., Felitti, V. J., Bremner, J. D., Walker, J. D., Whitfield, C., Perry, B. D., Dube, S. R., & Giles, W. H. (2006). The enduring effects of abuse and related adverse experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience, 256*(3), 174-186.

Anthenien, A., Prince, M., Wallace, G., Jenzer, T., & Neighbors, C. (2021). Cannabis outcome expectancies, cannabis use motives, and cannabis use among a small sample of frequent

using adults. *Cannabis*, *4*(1), 69-84.

Anderson, R.E., Hruska, B., Boros, A.P., Richardson, C.J., & Delahanty, D.L. (2017). Patterns of co-occurring addictions, posttraumatic stress disorder, and major depressive disorder in detoxification treatment seekers: Implications for improving detoxification treatment outcomes. *Journal of Substance Abuse Treatment, 86,* 45–51.

Angelakis, S., & Nixon, R. D. The comorbidity of PTSD and MDD: Implications for clinical practice and future research. *Behaviour Change*, *32*(1), 1-25.

Armenta, R. F., Walter, K. H., Geronimo-Hara, T. R., Porter, Stander, V. A., & LeardMann, C. 2019). Longitudinal trajectories of comorbid PTSD and depression symptoms among US service members and veterans. *BMC psychiatry*, *19*(1), 1-12.

Avant, E. M., Davis, J. L., & Cranston, C. C. (2011). Posttraumatic stress symptom clusters, trauma history, and substance use among college students. *Journal of Aggression, Maltreatment & Trauma*, *20*(5), 539-555.

Bahorik, A. L., Sterling, S. A., Campbell, C. I., Weisner, C. M., & Ramo, D. E. (2018). Medical and non-medical cannabis use among psychiatry patients with depression, anxiety, and post-traumatic stress disorder. *Journal of Substance Abuse Treatment, 85*, 36-44.

Behrendt, S., Wittchen, H. U., Höfler, M., Lieb, R., & Beesdo, K. (2009). Transitions from first substance use to substance use disorders in adolescence: is early onset associated with a rapid escalation?. *Drug and alcohol dependence*, *99*(1-3), 68-78.

Bedard-Gilligan, M., Lehinger, E., Cornell-Maier, S., Holloway, A., & Zoellner, L. (2022). Effects of Cannabis on PTSD Recovery: Review of the Literature and Clinical Insights. *Current Addiction Reports*, 1-14.

Bhuptani, P. H., Zhang, Y., Danzey, L., Bali, A., Langdon, K., & Orchowski, L. M. (2024).

Interpersonal trauma, shame, and substance use: a systematic review. *Drug and alcohol dependence*, 111253.

Bilevicius, E., Sommer, J. L., Asmundson, G. J., & El-Gabalawy, R. (2019). Associations of PTSD, chronic pain, and their comorbidity on cannabis use disorder: Results from an American nationally representative study. *Depression and anxiety*, *36*(11), 1036-1046.

Bisson, J. I., Berliner, L., Cloitre, M., Forbes, D., Jensen, T. K., Lewis, C., ... & Shapiro, F. (2019). The international society for traumatic stress studies new guidelines for the prevention and treatment of posttraumatic stress disorder: Methodology and development process. *Journal of traumatic stress,* 32(4), 475-483.

Bisson, J. I., Roberts, N. P., Andrew, M., Cooper, R., & Lewis, C. (2013). Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults. *Cochrane database of systematic reviews*, (12).

Black, N., Stockings, E., Campbell, G., Tran, L. T., Zagic, D., Hall, W. D., Farrell, M., & Degenhardt, L. (2019)."Cannabis use in the management of pain and anxiety: A systematic review." *Journal of Clinical Psychiatry*, 80(4), 18r12563.

Blais, R. K., Hoerster, K. D., Malte, C., Hunt, S., & Jakupcak, M. (2014). Unique PTSD clusters predict intention to seek mental health care and subsequent utilization in US veterans with PTSD symptoms. *Journal of Traumatic Stress*, *27*(2), 168-174.

Blakey, J. M., & Bowers, P. H. (2014). Barriers to integrated treatment of substance abuse and trauma among women. *Journal of Social Work Practice in the Addictions*, *14*(3), 250-272.

Blanco, C., Hasin, D. S., Wall, M. M., Flórez-Salamanca, L., Hoertel, N., Wang, S., ... & Olfson, M. (2016). Cannabis use and risk of psychiatric disorders: prospective evidence from a US national longitudinal study. *JAMA psychiatry*, *73*(4), 388-395.

Boden, M. T., Babson, K. A., Vujanovic, A. A., Short, N. A., & Bonn-Miller, M. O. (2013). Posttraumatic stress disorder and cannabis use characteristics among military veterans with cannabis dependence. *The American Journal on Addictions*, *22*(3), 277-284.

Bonn-Miller, M. O., Babson, K. A., & Vandrey, R. (2014a). Using cannabis to help you sleep: heightened frequency of medical cannabis use among those with PTSD. *Drug and alcohol dependence*, *136*, 162-165.

Bonn-Miller, M. O., Boden, M. T., Bucossi, M. M., & Babson, K. A. (2014b). Self-reported cannabis use characteristics, patterns and helpfulness among medical cannabis users. *The American journal of drug and alcohol abuse*, *40*(1), 23-30.

Bonn-Miller, M. O., Babson, K. A., Vujanovic, A. A., & Feldner, M. T. (2010). Sleep problems and PTSD symptoms interact to predict marijuana use coping motives: A preliminary investigation. *Journal of Dual Diagnosis*, *6*(2), 111-122.

Bonn-Miller, M. O., Boden, M. T., Vujanovic, A. A., & Drescher, K. D. (2013). Prospective investigation of the impact of cannabis use disorders on posttraumatic stress disorder symptoms among veterans in residential treatment. *Psychological Trauma: Theory, Research, Practice, and Policy*, *5*(2), 193

Bonn-Miller, M. O., Moos, R. H., Boden, M. T., Long, W. R., Kimerling, R., & Trafton, J. A. (2015). The impact of posttraumatic stress disorder on cannabis quit success. *The American journal of drug and alcohol abuse*, *41*(4), 339-344.

Bonn-Miller, M. O., Vujanovic, A. A., Boden, M. T., & Gross, J. J. (2011). Posttraumatic stress, difficulties in emotion regulation, and coping-oriented marijuana use. *Cognitive behaviour therapy*, *40*(1), 34-44.

Bordieri, M. J., Tull, M. T., McDermott, M. J., & Gratz, K. L. (2014). The moderating role of

experiential avoidance in the relationship between posttraumatic stress disorder symptom severity and cannabis dependence. *Journal of contextual behavioral science*, *3*(4), 273-278.

Borodovsky, J. T., & Budney, A. J. (2018). Cannabis regulatory science: Risk–benefit considerations for mental disorders. *International Review of Psychiatry*, *30*(3), 183-202.

Bradley, R., Greene, J., Russ, E., Dutra, L., & Westen, D. (2005). A multidimensional meta-analysis of psychotherapy for PTSD. *American journal of Psychiatry*, *162*(2), 214-227.

Brady, K. T., Back, S. E., & Coffey, S. F. (2004). Substance abuse and posttraumatic stress disorder. *Current directions in psychological science*, *13*(5), 206-209.

Brady, K. T., Killeen, T. K., Brewerton, T., & Lucerini, S. (2000). Comorbidity of psychiatric disorders and posttraumatic stress disorder. *The Journal of Clinical Psychiatry*.

Breslau, N. (2009). The epidemiology of trauma, PTSD, and other posttrauma disorders. *Trauma, Violence, & Abuse*, *10*(3), 198-210.

Breslau, N., Davis, G. C., Andreski, P., Peterson, E. L., & Schultz, L. R. (1997). Sex differences in posttraumatic stress disorder. *Archives of general psychiatry*, *54*(11), 1044-1048

Breslau, N., Lucia, V. C., & Davis, G. C. (2004). Partial PTSD versus full PTSD: an empirical examination of associated impairment. *Psychological medicine*, *34*(7), 1205.

Breslau, N., Reboussin, B. A., Anthony, J. C., & Storr, C. L. (2005). The structure of posttraumatic stress disorder: latent class analysis in 2 community samples. *Archives of General Psychiatry, 62*(12), 1343-1351.

Briere, J., & Elliott, D. M. (2003). Prevalence, characteristics, and long-term sequelae of natural disaster exposure in children: Research findings. *Child Abuse & Neglect, 27*(2), 223-240.

Bromet, E. J., Karam, E. G., Koenen, K. C., & Stein, D. J. (Eds.). (2018). *Trauma and*

posttraumatic stress disorder: Global perspectives from the WHO world mental health surveys. Cambridge University Press.

Brown, P. J., Recupero, P. R., & Stout, R. (1995). PTSD substance abuse comorbidity and treatment utilization. *Addictive behaviors*, *20*(2), 251-254.

Brown, P. J., Stout, R. L., & Mueller, T. (1999). Substance use disorder and posttraumatic stress disorder comorbidity: Addiction and mental health treatment rates. *Psychology of Addictive Behaviors*, *13*(2), 115.

Bryan, J. L., Hogan, J., Lindsay, J. A., & Ecker, A. H. (2021). Cannabis use disorder and post-traumatic stress disorder: The prevalence of comorbidity in veterans of recent conflicts. *Journal of substance abuse treatment*, *122*, 108254.

Buckner, J. D., Heimberg, R. G., Schneier, F. R., Liu, S. M., Wang, S., & Blanco, C. (2012). The relationship between cannabis use disorders and social anxiety disorder in the National Epidemiological Study of Alcohol and Related Conditions (NESARC). *Drug and alcohol dependence*, *124*(1-2), 128-134.

Bujarski, S. J., Galang, J. N., Short, N. A., Trafton, J. A., Gifford, E. V., Kimerling, R., ... & Bonn-Miller, M. O. (2016). Cannabis use disorder treatment barriers and facilitators among veterans with PTSD. *Psychology of Addictive Behaviors*, *30*(1), 73.

Callaghan, R. C., Sanches, M., & Kish, S. J. (2020). Quantity and frequency of cannabis use in relation to cannabis-use disorder and cannabis-related problems. *Drug and Alcohol Dependence*, *217*, 108271.

Cameron, C., Watson, D., & Robinson, J. (2014). Use of a synthetic cannabinoid in a correctional population for posttraumatic stress disorder–related insomnia and nightmares, chronic pain, harm reduction, and other indications: a retrospective evaluation. *Journal of*

clinical psychopharmacology, *34*(5), 559.

Campbell, S. B., Shields, G. S., & Slavich, G. M. (2019). Inflammation-related genes are associated with the association between posttraumatic stress disorder and chronic health conditions: A systematic review. *Neuroscience & Biobehavioral Reviews, 107*, 122-137.

Campbell, S. B., Trachik, B., Goldberg, S., & Simpson, T. L. (2020). Identifying PTSD symptom typologies: A latent class analysis. *Psychiatry Research*, *285*, 112779.

Chen, C. M., Yoon, Y. H., Harford, T. C., & Grant, B. F. (2017). Dimensionality of DSM-5 posttraumatic stress disorder and its association with suicide attempts: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. *Social psychiatry and mental health epidemiology*, *52*(6), 715-725.

Chilcoat, H. D., & Breslau, N. (1998). Investigations of causal pathways between PTSD and drug use disorders. *Addictive behaviors*, *23*(6), 827-840.

Chilcoat, H. D., & Menard, C. (2003). Epidemiological investigations: Comorbidity of posttraumatic stress disorder and substance use disorder.

Choi, N. G., DiNitto, D. M., & Marti, C. N. (2017). Nonmedical versus medical marijuana use among three age groups of adults: associations with mental and physical health status. The American Journal on Addictions, 26(7), 697-706.

Cloitre, M., Stolbach, B. C., Herman, J. L., van der Kolk, B., Pynoos, R., Wang, J., & Petkova, E. (2009). A developmental approach to complex PTSD: Childhood and adult cumulative trauma as predictors of symptom complexity. *Journal of Traumatic Stress, 22*(5), 399-408.

Collins, L. M., & Lanza, S. T. (2010). *Latent class and latent transition analysis: With applications in the social, behavioral, and health sciences*. New York, NY: Wiley.

Compton, W. & Baler, R. (2016). The epidemiology of DSM-5 cannabis use disorders among

US adults: science to inform clinicians working in a shifting social landscape. *The American Journal of Psychiatry*. Published Online. https://doi.org/10.1176/appi.ajp.2016.16030314

Conger, J. J. (1956). II. Reinforcement theory and the dynamics of alcoholism. *Quarterly journal of studies on alcohol*, *17*(2), 296-305.

Contractor, A. A., Caldas, S., Weiss, N. H., & Armour, C. (2018). Examination of the heterogeneity in PTSD and impulsivity facets: A latent profile analysis. *Personality and Individual Differences*, *125*, 1–9. https://doi.org/10.1016/j.paid.2017.12.022

Contractor, A. A., Roley-Roberts, M. E., Lagdon, S., & Armour, C. (2017). Heterogeneity in patterns of DSM-5 posttraumatic stress disorder and depression symptoms: Latent profile analyses. *Journal of Affective Disorders*, *212*, 17-24.

Contractor, A. A., Weiss, N. H., Dixon-Gordon, K. L., & Blumenthal, H. (2019). Heterogeneity in the co-occurrence of substance use and posttraumatic stress disorder: a latent class analysis approach. *Journal of dual diagnosis, 15*(2), 105-117.

Cornelius, J. R., Kirisci, L., Reynolds, M., Clark, D. B., Hayes, J., & Tarter, R. (2010). PTSD contributes to teen and young adult cannabis use disorders. *Addictive behaviors*, *35*(2), 91-94.

Corrigan, P. (2004). How stigma interferes with mental health care. *American psychologist*, *59*(7), 614.

Cougle, J. R., Hakes, J. K., Macatee, R. J., Chavarria, J., & Zvolensky, M. J. (2015). Resnick, H., & Kilpatrick, D. G. (2009). Quality of life and risk of mental health disorders among regular users of alcohol, nicotine, and cannabis: An analysis of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC). *Journal of mental*

health research, 66, 135-141.

Cougle, J. R., Resnick, H., & Kilpatrick, D. G. (2009). PTSD, depression, and their comorbidity in relation to suicidality: cross-sectional and prospective analyses of a national probability sample of women. *Depression and Anxiety*, *26*(12), 1151-1157.

Crippa, J. A., Zuardi, A. W., Martín-Santos, R., Bhattacharyya, S., Atakan, Z., McGuire, P., & Fusar-Poli, P. (2009). Cannabis and anxiety: a critical review of the evidence. *Human Psychopharmacology: Clinical and Experimental*, *24*(7), 515-523.

Cudjoe, T. R. (2019). Exploring Predictors of Drug Use Disorders and Drug Treatment Services in a National Sample of Women. Retrieved from https://mdsoar.org/bitstream/handle/11603/17683/Cudjoe_2019.pdf?sequence=1

Davis, J. P., Pedersen, E. R., Tucker, J., Dunbar, M., Rodriguez, A., Seelam, R., & D'Amico, E. J. (2023). Childhood adversity and developmental trajectories of alcohol and cannabis co-use. *Child Abuse & Neglect*, *141*, 106238.

De Jong, J., Komproe, T.V. Ivan, H., von Ommeren, M., El Masri, Araya, Khaled, N.,van de Put, W., & Somasundarem, D.J. (2001). Lifetime events and Posttraumatic Stress Disorder in 4 postconflict settings. *Journal of the American Medical Association*, 286, 555-562.

De Vries, G. J., & Olff, M. (2009). The lifetime prevalence of traumatic events and posttraumatic stress disorder in the Netherlands. Journal of Traumatic Stress: Official Publication of The International Society for Traumatic Stress Studies, 22(4), 259-267.

Dean, N., & Raftery, A. E. (2010). Latent class analysis variable selection. *Annals of the Institute of Statistical Mathematics*, *62*(1), 11.

Dearing, R. L., Stuewig, J., & Tangney, J. P. (2005). On the importance of distinguishing shame from guilt: Relations to problematic alcohol and drug use. *Addictive behaviors*, *30*(7),

1392-1404.

Desai, R., Patel, U., Sharma, S., Amin, P., Bhuva, R., Patel, M. S., ... & Kumar, G. (2017). Recreational marijuana use and acute myocardial infarction: insights from nationwide inpatient sample in the United States. *Cureus*, *9*(11).

Dore, G., Mills, K., Murray, R., Teesson, M., & Farrugia, P. (2012). Post-traumatic stress disorder, depression and suicidality in inpatients with substance use disorders. *Drug and Alcohol Review*, *31*(3), 294-302.

Dube, S. R., Anda, R. F., Felitti, V. J., Chapman, D. P., Williamson, D. F., & Giles, W. H. (2001). Childhood abuse, household dysfunction, and the risk of attempted suicide throughout the life span: findings from the Adverse Childhood Experiences Study. *Jama*, *286*(24), 3089-3096.

Dube, S. R., Felitti, V. J., Dong, M., Chapman, D. P., Giles, W. H., & Anda, R. F. (2003). Childhood abuse, neglect, and household dysfunction and the risk of illicit drug use: the adverse childhood experiences study. *Pediatrics*, *111*(3), 564-572.

Elms, L., Shannon, S., Hughes, S., & Lewis, N. (2019). Cannabidiol in the treatment of post-traumatic stress disorder: a case series. *The Journal of Alternative and Complementary Medicine*, *25*(4), 392-397.

ElSohly, M., & Gul, W. (2014). Constituents of Cannabis sativa. *Handbook of cannabis*, *3*(1093), 187-188.

Emerson, M. A., Moore, R. S., & Caetano, R. (2017). Association between lifetime posttraumatic stress disorder and past year alcohol use disorder among American Indians/Alaska Natives and Non-Hispanic Whites. *Alcoholism: Clinical and Experimental Research*, *41*(3), 576-584.

Estey, D., Platt, J., Goodwin, R. D., & Weinberger, A. H. (2021). Relationship of trauma exposure and PTSD to cigarette smoking prevalence, frequency, and quantity: Data from a nationally representative sample of US adults. *Psychological Trauma: Theory, Research, Practice, and Policy*, *13*(2), 231.

Evans, E. A., Goff, S. L., Upchurch, D. M., & Grella, C. E. (2020). Childhood adversity and mental health comorbidity in men and women with opioid use disorders. *Addictive behaviors*, *102*, 106149.

Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., Koss, M. P., & Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults: The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine, 14*(4), 245-258.

Fischer, B., Rehm, J., Irving, H., Ialomiteanu, A., Fallu, J. S., & Patra, J. (2010). Typologies of cannabis users and associated characteristics relevant for public health: a latent class analysis of data from a nationally representative Canadian adult survey. *International journal of methods in mental health research, 19*(2), 110-124.

Fischer, B., Russell, C., Sabioni, P., van den Brink, W., Le Foll, B., Hall, W., Rehm, J. & Room, R. (2017). Lower-Risk Cannabis Use Guidelines (LRCUG): An evidence-based update. *American Journal of Public Health, 107*(8). DOI: 10.2105/AJPH.2017.303818.

Flory, J. D., & Yehuda, R. (2015). Comorbidity between post-traumatic stress disorder and major depressive disorder: Alternative explanations and treatment considerations. *Dialogues in Clinical Neuroscience, 17*(2), 141-150.

Foa, E. B., Hembree, E. A., & Rothbaum, B. O. (2007). *Prolonged exposure therapy for PTSD: Emotional processing of traumatic experiences: Therapist guide*. Oxford, UK: Oxford

University Press.

Foa, E. B., Keane, T. M., Friedman, M. J., & Cohen, J. A. (Eds.). (2010). *Effective treatments for PTSD: practice guidelines from the International Society for Traumatic Stress Studies*. Guilford Press.

Foa, E. B., Zinbarg, R., & Rothbaum, B. O. (1992). Uncontrollability and unpredictability in post-traumatic stress disorder: an animal model. *Psychological bulletin*, *112*(2), 218

Forbes, D., Bisson, J., Monson, C., & Berliner, L. (2020). *Effective Treatments for PTSD Third Edition: Practice Guidelines from the International Society for Traumatic Stress Studies. Guilford Publications.*

Ford, J. D., & Gómez, J. M. (2015). The relationship of psychological trauma and dissociative and posttraumatic stress disorders to nonsuicidal self-injury and suicidality: A review. *Journal of Trauma & Dissociation*, *16*(3), 232-271.

Fraser, G. A. (2009). The use of a synthetic cannabinoid in the management of treatment-resistant nightmares in posttraumatic stress disorder (PTSD). *CNS neuroscience & therapeutics, 15*(1), 84-88.

Friedman, M. J. (2007). PTSD history and overview. *United States Department of Veterans Affairs.* Online publication https://www.ptsd.va.gov//treat/essentials/history_ptsd.asp

Friedman, M. J., Resick, P. A., Bryant, R. A., & Keane, T. M. (2014). PTSD from dsm-iii to dsm-5. *Handbook of PTSD*, 3-20.

Galatzer-Levy, I. R., Nickerson, A., Litz, B. T., & Marmar, C. R. (2013). Patterns of lifetime PTSD comorbidity: A latent class analysis. *Depression and Anxiety*, *30*(5), 489-496.

Gates, P., & Copeland, J. (2017). Barriers to treatment seeking for cannabis dependence. In *Handbook of cannabis and related pathologies* (pp. 1025-1029). Academic Press.

Gavrilovic, J. J., Schützwohl, M., Fazel, M., & Priebe, S. (2005). Who seeks treatment after a traumatic event and who does not? A review of findings on mental health service utilization. *Journal of Traumatic Stress: Official Publication of The International Society for Traumatic Stress Studies*, *18*(6), 595-605.

Gerger, H., Munder, T., & Barth, J. (2014). Specific and nonspecific psychological interventions for PTSD symptoms: A meta-analysis with problem complexity as a moderator. *Journal of Clinical Psychology*, *70*(7), 601-615.

Gobbi, G., Atkin, T., Zytynski, T., Wang, S., Askari, S., Boruff, J., ... & Mayo, N. (2019). Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: A systematic review and meta-analysis. *JAMA Psychiatry, 76*(4), 426-434.

Gradus, J., P., Lincoln, A. K., Miller, Lawler, E., Sorensen, H. T., & Lash, T. L. (2010). Posttraumatic stress disorder and completed suicide. *American journal of epidemiology, 171*(6), 721-727.

Grant, B. F., Dawson, D. A., & Hasin, D. S. (2001). The alcohol use disorder and associated disabilities interview schedule DSM-IV version. *Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism*.

Grant, B. F., Goldstein, R. B., Chou, S. P., Saha, T. D., Ruan, W. J., Huang, B., & Hasin, D. S. (2011). The alcohol use disorder and associated disabilities interview schedule-diagnostic and statistical manual of mental disorders, version (AUDADIS-5). *Rockville, MD: National Institute on Alcohol Abuse and Alcoholism*.

Grant, B. F., Goldstein, R. B., Saha, T. D., Chou, S. P., Jung, J., Zhang, H., ... & Hasin, D. S. (2015). Epidemiology of DSM-5 alcohol use disorder: results from the National

Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA psychiatry*, *72*(8), 757-766.

Grant, B. F., Goldstein, R. B., Smith, S. M., Jung, J., Zhang, H., Chou, S. P., ... & Hasin, D. S. (2015). The Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5): reliability of substance use and mental health disorder modules in a general population sample. *Drug and alcohol dependence, 148*, 27-33.

Grant, S., Pedersen, E. R., & Neighbors, C. (2016). Associations of posttraumatic stress disorder symptoms with marijuana and synthetic cannabis use among young adult US Veterans: a pilot investigation. *Journal of studies on alcohol and drugs*, *77*(3), 509-514.

Greer, G. R., Grob, C. S., & Halberstadt, A. L. (2014). PTSD symptom reports of patients evaluated for the New Mexico Medical Cannabis Program. *Journal of psychoactive drugs, 46*(1), 73-77.

Grekin, R., Bohnert, K. M., Grau, P. P., Ganoczy, D., & Sripada, R. K. (2021). Rates and predictors of psychotherapy receipt among US veterans with comorbid posttraumatic stress disorder and substance use disorders. *Drug and alcohol dependence reports*, *1*, 100010.

Gros, D. F., Price, M., Magruder, K. M., & Frueh, B. C. (2012). Relations between anxiety symptom severity and psychiatric disorders in veterans with PTSD. *Psychiatry Research, 196*(2-3), 197-201.

Goldenberg, M., IsHak, W. W., & Danovitch, I. (2017). Quality of life and recreational cannabis use. *The American Journal on Addictions*, *26*(1), 8-25.

Goldstein, R. B., Smith, S. M., Chou, S. P., Saha, T. D., Jung, J., Zhang, H., ... & Grant, B. F. (2016). The epidemiology of DSM-5 posttraumatic stress disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions-

III. *Social psychiatry and mental health epidemiology*, *51*(8), 1137-1148.

Gutner, C. A., Pedersen, E. R., & Drummond, S. P. (2018). Going direct to the consumer: Examining treatment preferences for veterans with insomnia, PTSD, and depression. *Psychiatry Research*, *263*, 108-114.

Hall, W., & Degenhardt, L. (2009). Adverse health effects of non-medical cannabis use. *The Lancet*, *374*(9698), 1383-1391.

Hale, A. C., Sripada, R. K., & Bohnert, K. M. (2018). Past-year treatment utilization among individuals meeting DSM-5 PTSD criteria: results from a nationally representative sample. *Psychiatric Services*, *69*(3), 341-344.

Hasin, D. S., Greenstein, E., Aivadyan, C., Stohl, M., Aharonovich, E., Saha, T., ... & Grant, B. F. (2015a). The Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5): procedural validity of substance use disorders modules through clinical re-appraisal in a general population sample. *Drug and alcohol dependence*, *148*, 40-46.

Hasin, D. S., Kerridge, B. T., Saha, T. D., Huang, Pickering, R., Smith, S. M., ... & Grant, B. F. (2016). Prevalence and correlates of DSM-5 cannabis use disorder, 2012-2013: findings from the National Epidemiologic Survey on Alcohol and Related Conditions–III. *American Journal of Psychiatry, 173*(6), 588-599.

Hasin, D. S., Saha, T. D., Kerridge, B. T., Goldstein, R. B., Chou, S. P., Zhang, H., ... & Grant, B. F. (2015b). Prevalence of marijuana use disorders in the United States between 2001-2002 and 2012-2013. *JAMA psychiatry*, *72*(12), 1235-1242.

Hasin, D. S., Sarvet, A. L., Cerdá, 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.

Hasin, D. S., Shmulewitz, D., & Sarvet, A. L. (2019). Time trends in US cannabis use and cannabis use disorders overall and by sociodemographic subgroups: a narrative review and new findings. *The American Journal of Drug and Alcohol Abuse*, *45*(6), 623-643.

Hasin, D., & Walsh, C. (2021). Cannabis Use, Cannabis Use Disorder, and Comorbid Psychiatric Illness: A Narrative Review. *Journal of clinical medicine*, *10*(1), 15.

Hawke, L. D., Wilkins, L., & Henderson, J. (2020). Early cannabis initiation: Substance use and mental health profiles of service-seeking youth. *Journal of Adolescence*, *83*, 112-121.

Hawn, S. E., Cusack, S. E., & Amstadter, A. B. (2020). A systematic review of the self-medication hypothesis in the context of posttraumatic stress disorder and comorbid problematic alcohol use. *Journal of traumatic stress, 33*(5), 699-708.

Hayley, A. C., Stough, C., & Downey, L. A. (2017). DSM-5 cannabis use disorder, substance use and DSM-5 specific substance-use disorders: Evaluating comorbidity in a population-based sample. European Neuropsychopharmacology, 27(8), 732-743.

Helle, A. C., Trull, T. J., Watts, A. L., McDowell, Y., & Sher, K. J. (2020). Psychiatric Comorbidity as a Function of Severity: DSM-5 Alcohol Use Disorder and HiTOP Classification of Mental Disorders. Alcoholism: Clinical and Experimental Research, 44(3), 632-644.

Hinojosa, C. A., Liew, A., An, X., Stevens, J. S., Basu, A., van Rooij, S. J., ... & Fani, N. (2023). Associations of alcohol and cannabis use with change in posttraumatic stress disorder and depression symptoms over time in recently trauma-exposed individuals. *Psychological medicine*, 1-12.

Hochheimer, M., Sacco, P., & Ware, O. D. (2020). Latent classes of lifetime drug use disorder in national epidemiological survey on alcohol and related conditions–III. *Addictive*

behaviors, *106*, 106379.

Hoskins, M., Pearce, J., Bethell, A., Dankova, L., Barbui, C., Tol, W. A., ... & Bisson, J. I. (2015). Pharmacotherapy for post-traumatic stress disorder: systematic review and meta-analysis. *The British Journal of Psychiatry*, *206*(2), 93-100.

Hyman, S. M., & Sinha, R. (2009). Stress-related factors in cannabis use and misuse: Implications for treatment. *Journal of Substance Abuse Treatment, 36*(4), 400-413.

Ilgen, M. Walton, M. A., Cunningham, R. M., Barry, K. L., Chermack, S. T., De Chavez, P., & Blow, F. C. (2009). Recent suicidal ideation among patients in an inner city emergency department. *Suicide and Life-Threatening Behavior, 39*(5), 508-517.

Jacob, S. N., Dodge, C. P., & Vasterling, J. J. (2019). Posttraumatic stress disorder and neurocognition: A bidirectional relationship?. *Clinical psychology review*, *72*, 101747.

Jacobsen, L. K., Southwick, S. M., & Kosten, T. R. (2001). Substance use disorders in patients with posttraumatic stress disorder: a review of the literature. *American Journal of Psychiatry*, *158*(8), 1184-1190.

Jakupcak, M., Tull, M. T., McDermott, M. J., Kaysen, D., Hunt, S., & Simpson, T. (2010). PTSD symptom clusters in relationship to alcohol misuse among Iraq and Afghanistan war veterans seeking post-deployment VA health care. *Addictive behaviors, 35*(9), 840-843.

Jellestad, L., Vital, N. A., Malamud, J., Taeymans, J., & Mueller-Pfeiffer, C. (2021). Functional impairment in posttraumatic stress disorder: A systematic review and meta-analysis. *Journal of psychiatric research*, *136*, 14-22.

Jetly, R., Heber, A., Fraser, G., & Boisvert, D. (2015). The efficacy of nabilone, a synthetic cannabinoid, in the treatment of PTSD-associated nightmares: a preliminary randomized, double-blind, placebo-controlled cross-over design study. *Psychoneuroendocrinology*, *51*,

585-588.

Johnson, M. J., Pierce, J. D., Mavandadi, S., Klaus, J., Defelice, D., Ingram, E., & Oslin, D. W. (2016). Mental health symptom severity in cannabis using and non-using Veterans with probable PTSD. *Journal of affective disorders*, *190*, 439-442.

Johnson, E. M., & Possemato, K. (2019). Correlates and predictors of mental health care utilization for veterans with PTSD: A systematic review. *Psychological Trauma: Theory, Research, Practice, and Policy*, *11*(8), 851.

Kaltman, S., Krupnick, J., Stockton, P., Hooper, L., & Green, B. L. (2005). Psychological impact of types of sexual trauma among college women. *Journal of Traumatic Stress: Official Publication of The International Society for Traumatic Stress Studies*, *18*(5), 547-555.

Kantor, V., Knefel, M., & Lueger-Schuster, B. (2017). Perceived barriers and facilitators of mental health service utilization in adult trauma survivors: A systematic review. *Clinical psychology review*, *52*, 52-68.

Karila, L., Roux, P., Rolland, B., Benyamina, A., Reynaud, M., Aubin, H. J., & Lancon, C. (2014). Acute and long-term effects of cannabis use: a review. *Current pharmaceutical design*, *20*(25), 4112-4118.

Kazlauskas, E. (2017). Challenges for providing health care in traumatized populations: barriers for PTSD treatments and the need for new developments. *Global health action*, *10*(1), 1322399.

Kearns, N. T., Contractor, A. A., Weiss, N. H., & Blumenthal, H. (2020). Coping Strategy Utilization Among Posttraumatic Stress Disorder Symptom Severity and Substance Use Co-Occurrence Typologies: A Latent Class Analysis. *Psychological Trauma: Theory, Research, Practice, and Policy*. Advance online publication.

Kessler, R. C., Aguilar-Gaxiola, S., Alonso, J., Benjet, C., Bromet, E. J., Cardoso, G., ... & Koenen, K. C. (2017). Trauma and PTSD in the WHO world mental health surveys. *European journal of psychotraumatology*, *8*(sup5), 1353383.

Kessler, R. C., Sonnega, A., Bromet, E., Hughes, M., & Nelson, C. B. (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of general psychiatry*, *52*(12), 1048-1060.

Kevorkian, S., Bonn-Miller, M. O., Belendiuk, K., Carney, D. M., Roberson-Nay, R., & Berenz, E. C. (2015). Associations among trauma, posttraumatic stress disorder, cannabis use, and cannabis use disorder in a nationally representative epidemiologic sample. *Psychology of Addictive Behaviors*, *29*(3), 633.

Khan, S. S., Secades-Villa, R., Okuda, M., Wang, S., Pérez-Fuentes, G., Kerridge, B. T., & Blanco, C. (2013). Gender differences in cannabis use disorders: results from the National Epidemiologic Survey of Alcohol and Related Conditions. *Drug and alcohol dependence*, *130*(1-3), 101-108.

Khantzian, E. J. (1997). The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harvard Review of Psychiatry, 4*(5), 231-244.

Khantzian, E. J. (2003). The self-medication hypothesis revisited: The dually diagnosed patient. *Primary Psychiatry, 10*(9), 47-54.

Khoury, L., Tang, Y. L., Bradley, B., Cubells, J. F., & Ressler, K. J. (2010). Substance use, childhood traumatic experience, and posttraumatic stress disorder in an urban civilian population. *Depression and anxiety*, *27*(12), 1077-1086.

Kiely, J. M., Brasel, K. J., Weidner, K. L., Guse, C. E., & Weigelt, J. A. (2006). Predicting quality of life six months after traumatic injury. *Journal of Trauma and Acute Care*

Surgery, *61*(4), 791-798.

Koenig, L. C. (2021). The Effect of Shame and Trauma on Substance Use Behavior.

Kondev, V., Winters, N., & Patel, S. (2021). Cannabis use and posttraumatic stress disorder comorbidity: Epidemiology, biology and the potential for novel treatment approaches. *International review of neurobiology*, *157*, 143-193.

Krantz, D. S., Shank, L. M., & Goodie, J. L. (2022). Post-traumatic stress disorder (PTSD) as a systemic disorder: Pathways to cardiovascular disease. *Health Psychology*, *41*(10), 651.

Kroon, E., Kuhns, L., & Cousijn, J. (2021). The short-term and long-term effects of cannabis on cognition: recent advances in the field. *Current Opinion in Psychology*, *38*, 49-55.

Kroon, E., Kuhns, L., Hoch, E., & Cousijn, J. (2020). Heavy cannabis use, dependence and the brain: a clinical perspective. *Addiction*, *115*(3), 559-572.

Krysinska, K., & Lester, D. (2010). Post-traumatic stress disorder and suicide risk: A systematic review. *Archives of Suicide Research, 14*(1), 1-23.

Kulesza, M., Pedersen, E. R., Corrigan, P. W., & Marshall, G. N. (2015). Help-seeking stigma and mental health treatment seeking among young adult veterans. *Military behavioral health, 3*(4), 230-239.

Kung, H. C., Pearson, J. L., & Liu, X. (2003). Risk factors for male and female suicide decedents ages 15–64 in the United States. *Social psychiatry and mental health epidemiology*, *38*(8), 419-426.

Kung, H. C., Pearson, J. L., & Wei, R. (2005). Substance use, firearm availability, depressive symptoms, and mental health service utilization among white and African American suicide decedents aged 15 to 64 years. *Annals of epidemiology*, *15*(8), 614-621.

Lake, S., Kerr, T., Buxton, J., Walsh, Z., Marshall, B. D., Wood, E., & Milloy, M. J. (2020).

Does cannabis use modify the effect of post-traumatic stress disorder on severe depression and suicidal ideation? Evidence from a population-based cross-sectional study of Canadians. *Journal of psychopharmacology*, *34*(2), 181-188.

Leadbeater, B. J., Ames, M. E., & Linden-Carmichael, A. N. (2019). Age-varying effects of cannabis use frequency and disorder on symptoms of psychosis, depression and anxiety in adolescents and adults. *Addiction*, *114*(2), 278-293.

LeBouthillier, D. M., McMillan, K. A., Thibodeau, M. A., & Asmundson, G. J. (2015). Types and number of traumas associated with suicidal ideation and suicide attempts in PTSD: Findings from a US nationally representative sample. *Journal of Traumatic Stress*, *28*(3), 183-190.

Leung, J., Chan, G. C., Hides, L., & Hall, W. D. (2020). What is the prevalence and risk of cannabis use disorders among people who use cannabis? A systematic review and meta-analysis. *Addictive behaviors*, *109*, 106479.

Leza, L., Siria, S., López-Goñi, J. J., & Fernandez-Montalvo, J. (2021). Adverse childhood experiences (ACEs) and substance use disorder (SUD): A scoping review. *Drug and alcohol dependence*, *221*, 108563

Litman, J. A. (2006). The COPE inventory: Dimensionality and relationships with approach-and avoidance-motives and positive and negative traits. *Personality and Individual differences*, *41*(2), 273-284.

Livingston, N. A., Farmer, S. L., Mahoney, C. T., Marx, B. P., & Keane, T. M. (2022). Longitudinal course of mental health symptoms among veterans with and without cannabis use disorder. *Psychology of addictive behaviors*, *36*(2), 131.

Livne, O., Razon, L., Rehm, J., Hasin, D. S., & Lev-Ran, S. (2018). The association between

lifetime cannabis use and dysthymia across six birth decades. *Journal of affective disorders*, *234*, 327-334.

Lo, Y., Mendell, N. R., & Rubin, D. B. (2001). Testing the number of components in a normal mixture. *Biometrika*, *88*(3), 767-778.

Loflin, M., Earleywine, M., & Bonn-Miller, M. (2017). Medicinal versus recreational cannabis use: Patterns of cannabis use, alcohol use, and cued-arousal among veterans who screen positive for PTSD. *Addictive Behaviors*, *68*, 18-23.

Looby, A., & Earleywine, M. (2007). Negative consequences associated with dependence in daily cannabis users. *Substance abuse treatment, prevention, and policy*, *2*(1), 1-7.

Luoma, J. B., Chwyl, C., & Kaplan, J. (2019). Substance use and shame: A systematic and meta-analytic review. *Clinical psychology review*, *70*, 1-12.

Magruder, K. M., McLaughlin, K. A., & Elmore Borbon, D. L. (2017). Trauma is a public health issue. *European journal of psychotraumatology*, *8*(1), 1375338.

Manhapra, A., Stefanovics, E., & Rosenheck, R. (2015). Treatment outcomes for veterans with PTSD and substance use: Impact of specific substances and achievement of abstinence. *Drug and alcohol dependence*, *156*, 70-77.

Marel, C., Sunderland, M., Mills, K. L., Slade, T., Teesson, M., & Chapman, C. (2019). Conditional probabilities of substance use disorders and associated risk factors: Progression from first use to use disorder on alcohol, cannabis, stimulants, sedatives and opioids. *Drug and alcohol dependence*, *194*, 136-142.

McCauley, J. L., Killeen, T., Gros, D. F., Brady, K. T., & Back, S. E. (2012). Posttraumatic stress disorder and co-occurring substance use disorders: Advances in assessment and treatment. *Clinical Psychology: Science and Practice, 19*(3), 283-304.

McCutcheon, A. L. (1987). *Latent class analysis* (No. 64). Sage.

McCutcheon, A. L. (2002). Basic concepts and procedures in single-and multiple-group latent class analysis. *Applied latent class analysis*, 56-88.

McGuinness, B., Goel, A., Chen, J., Szalay, D., Ladha, K., Mittleman, M. A., & Harlock, J. (2022). The association of cannabis use disorder with acute limb ischemia and critical limb ischemia. *Vascular and Endovascular Surgery*, *56*(5), 480-494.

Mennis, J., Stahler, G. J., & Mason, M. J. (2023). Cannabis legalization and the decline of cannabis use disorder (CUD) treatment utilization in the US. *Current Addiction Reports*, *10*(1), 38-51.

Merrick, M. T., Ports, K. A., Ford, D. C., Afifi, T. O., Gershoff, E. T., & Grogan-Kaylor, A. (2017). Unpacking the impact of adverse childhood experiences on adult mental health. *Child Abuse & Neglect, 69*, 10-19.

Metrik, J., Bassett, S. S., Aston, E. R., Jackson, K. M., & Borsari, B. (2018). Medical versus recreational cannabis use among returning veterans. *Translational issues in psychological science*, *4*(1), 6.

Mills, K. L., Teesson, M., Ross, J., & Peters, L. (2006). Trauma, PTSD, and substance use disorders: findings from the Australian National Survey of Mental Health and Well-Being. *American Journal of Psychiatry*, *163*(4), 652-658.

Mittal, D., Drummond, K. L., Blevins, D., Curran, G., Corrigan, P., & Sullivan, G. (2013). Stigma associated with PTSD: perceptions of treatment seeking combat veterans. *Psychiatric rehabilitation journal*, *36*(2), 86.

Mueller, J., Moergeli, H., & Maercker, A. (2008). Disclosure and social acknowledgement as predictors of recovery from posttraumatic stress: A longitudinal study in crime

victims. *The Canadian Journal of Psychiatry*, *53*(3), 160-168.

Morgan, G. B. (2015). Mixed mode latent class analysis: An examination of fit index performance for classification. *Structural Equation Modeling: A Multidisciplinary Journal*, *22*(1), 76-86.

Mota, N. P., Turner, S., Taillieu, T., Garcés, I., Magid, K., Sethi, J., ... & Afifi, T. O. (2019). Trauma exposure, DSM-5 post-traumatic stress disorder, and sexual risk outcomes. American journal of preventive medicine, 56(2), 215-223.

Najavits, L. M., & Anderson, M. L. (2015). *Psychosocial treatments for posttraumatic stress disorder.* In P. E. Nathan & J. M. Gorman (Eds.), *A guide to treatments that work* (p. 571–592). Oxford University Press.

Najt, P., Fusar-Poli, P., & Brambilla, P. (2011). Co-occurring mental and substance abuse disorders: a review on the potential predictors and clinical outcomes. *Psychiatry research*, *186*(2-3), 159-164.

National Academies of Sciences, Engineering, and Medicine. (2017). The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research.

National Institute on Alcohol Abuse and Alcoholism. (2015). *National epidemiologic survey on alcohol and related conditions III (NESARC-III)*. Rockville, MD: Author.

Newman, D. L., Moffitt, T. E., Caspi, A., & Silva, P. A. (1998). Comorbid mental disorders: implications for treatment and sample selection. *Journal of Abnormal Psychology, 107*(2), 305.

Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2007). Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation

study. *Structural equation modeling: A multidisciplinary Journal*, *14*(4), 535-569.

Ohayon, M., Shapiro, C. (2000). Sleep disturbances and mental health disorders associated with posttraumatic stress disorder in the general population. *Comprehensive Psychiatry*, *41*(6), 469–478.

O'Neil, M. E., Nugent, S. M., Morasco, B. J., Freeman, M., Low, A., Kondo, K., ... & Kansagara, D. (2017). Benefits and harms of plant-based cannabis for posttraumatic stress disorder: A systematic review. *Annals of internal medicine*, *167*(5), 332-340.

Orsolini, L., Chiappini, S., Volpe, U., De Berardis, D., Latini, R., Papanti, G. D., & Corkery, J. M. (2019). Use of medicinal cannabis and synthetic cannabinoids in post-traumatic stress disorder (PTSD): a systematic review. *Medicina*, *55*(9), 525.

Ouellette, M. J., Puccinelli, C., Rowa, K., Elcock, A., & McCabe, R. E. (2019). Cannabis Use in Patients Seeking Therapy for Anxiety and Related Disorders: A Descriptive Study. *Canadian Journal of Addiction*, *10*(3), 30-37.

Pacella, M. L., Hruska, B., & Delahanty, D. L. (2013). The physical health consequences of PTSD and PTSD symptoms: A meta-analytic review. *Journal of Anxiety Disorders, 27*(1), 33–46. https://doi.org/10.1016/j.janxdis.2012.08.004

Padgett, R. N., & Tipton, R. J. (2020). Identifying latent classes with ordered categorical indicators. *arXiv preprint arXiv:2009.07345*.

Pagura, J., Stein, M. B., Bolton, J. M., Cox, B. J., Grant, B., & Sareen, J. (2010). Comorbidity of borderline personality disorder and posttraumatic stress disorder in the US population. *Journal of mental health research*, *44*(16), 1190-1198.

Palm, K. M., Strong, D. R., & MacPherson, L. (2009). Evaluating symptom expression as a function of a posttraumatic stress disorder severity. *Journal of Anxiety Disorders*, *23*(1),

27-37.

Panagioti, M., Gooding, P. A., & Tarrier, N. (2009). Post-traumatic stress disorder and suicidal behavior: A narrative review. *Clinical Psychology Review, 29*(6), 471-482.

Papastavrou, E., Farmakas, A., Karayiannis, G., & Kotrotsiou, E. (2011). Co morbidity of post-traumatic-stress disorders and substance use disorder. *Health Science Journal*, *5*(2), 107.

Patton, D. V. (2020). A history of United States cannabis law. *JL & Health*, *34*, 1.

Patton, G. C., Coffey, C., Carlin, J. B., Sawyer, S. M., & Lynskey, M. (2005). Reverse gateways? Frequent cannabis use as a predictor of tobacco initiation and nicotine dependence. *Addiction*, *100*(10), 1518-1525.

Pietrzak, R. H., Goldstein, R. B., Southwick, S. M., & Grant, B. F. (2011). Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of anxiety disorders, 25*(3), 456-465.

Piper, A., & Berle, D. (2019). The association between trauma experienced during incarceration and PTSD outcomes: A systematic review and meta-analysis. *The Journal of Forensic Psychiatry & Psychology*, *30*(5), 854-875.

Possemato, K., Wray, L. O., Johnson, E., Webster, B., & Beehler, G. P. (2018). Facilitators and barriers to seeking mental health care among primary care veterans with posttraumatic stress disorder. *Journal of Traumatic Stress*, *31*(5), 742-752.

Ranganathan, M., & D'Souza, D. C. (2006). The acute effects of cannabinoids on memory in humans: a review. *Psychopharmacology*, *188*, 425-444

Ranney, R. M., Maguen, S., Bernhard, P. A., Holder, N., Vogt, D., Blosnich, J. R., & Schneiderman, A. I. (2023). Treatment utilization for posttraumatic stress disorder in a

national sample of veterans and nonveterans. *Medical Care*, *61*(2), 87-94

Ravindran, L. N., & Stein, M. B. (2009). Pharmacotherapy of PTSD: premises, principles, and priorities. *Brain research*, *1293*, 24-39.

Rehder, K., & Bowen, S. (2019). PTSD symptom severity, cannabis, and gender: a zero-inflated negative binomial regression model. *Substance use & misuse*, *54*(8), 1309-1318.

Resick, P. A., Monson, C. M., & Chard, K. M. (2008). *Cognitive processing therapy: Veteran/military version*. Washington, DC: Department of Veterans' Affairs.

Reynolds, K., Pietrzak, R. H., El-Gabalawy, R., Mackenzie, C. S., & Sareen, J. Prevalence of mental health disorders in US older adults: findings from a nationally representative survey. *World Psychiatry, 14*(1), 74-81.

Reilly, D., Didcott, P., Swift, W., & Hall, W. (1998). Long-term cannabis use: characteristics of users in an Australian rural area. *Addiction*, *93*(6), 837-846.

Reisman, M. (2016). PTSD treatment for veterans: What's working, what's new, and what's next. *Pharmacy and Therapeutics*, *41*(10), 623.

Robinson, T., Ali, M. U., Easterbrook, B., Coronado-Montoya, S., Daldegan-Bueno, D., Hall, W., ... & Fischer, B. (2022). Establishing risk-thresholds for the association between frequency of cannabis use and development of cannabis use disorder: A systematic review and meta-analysis. *Drug and Alcohol Dependence*, 109582.

Roos, L. E., Mota, N., Afifi, T. O., Katz, L. Y., Distasio, J., & Sareen, J. (2013). Relationship between adverse childhood experiences and homelessness and the impact of axis I and II disorders. *American Journal of Public Health*, *103*(S2), S275-S281.

Roth, S., & Cohen, L. J. (1986). Approach, avoidance, and coping with stress. *American Psychologist, 41*(7), 813-819.

Ruglass, L. M., Lopez-Castro, T., Cheref, S., Papini, S., & Hien, D. A. (2014). At the crossroads: The intersection of substance use disorders, anxiety disorders, and posttraumatic stress disorder. *Current Psychiatry Reports, 16*(505), 1–9.

Rumalla, K., Reddy, A. Y., & Mittal, M. K. (2016). Recreational marijuana use and acute ischemic stroke: a population-based analysis of hospitalized patients in the United States. *Journal of the neurological sciences*, *364*, 191-196.

Salas, J., Norman, S. B., Tuerk, P. W., van den Berk-Clark, C., Cohen, B. E., Schneider, F. D., ... & Scherrer, J. F. (2021). PTSD improvement and substance use disorder treatment utilization in veterans: Evidence from medical record data. *Drug and alcohol dependence*, *218*, 108365.

Salyers, M. P., Bosworth, H. B., Swanson, J. W., Lamb-Pagone, J., & Osher, F. C. (2000). Reliability and validity of the SF-12 health survey among people with severe mental illness. *Medical care*, 1141-1150.

Sareen, J. (2014). Posttraumatic stress disorder in adults: impact, comorbidity, risk factors, and treatment. *The Canadian Journal of Psychiatry*, *59*(9), 460-467.

Sareen, J. (2018). Posttraumatic stress disorder in adults: Epidemiology, pathophysiology, clinical manifestations, course, assessment, and diagnosis. Retrieved from https://www.uptodate.com/contents/posttraumatic-stress-disorder-in-adultsepidemiology-pathophysiology-clinical-manifestations-course-assessment-anddiagnosis.

Sareen, J., Cox, B. J., Afifi, T. O., Stein, M. B., Belik, S. L., Meadows, G., & Asmundson, G. J. G. (2007). Combat and peacekeeping operations in relation to prevalence of mental disorders and perceived need for mental health care: Findings from a large representative sample of military personnel. *Archives of General Psychiatry, 64*(7), 843-

852. https://doi.org/10.1001/archpsyc.64.7.843

Sareen, J., Cox, B. J., Clara, I., & Asmundson, G. J. (2005). The relationship between anxiety disorders and physical disorders in the US National Comorbidity Survey. *Depression and Anxiety, 21*(4), 193-202.

Schafer, I., & Najavits, L. M. (2007). Clinical challenges in the treatment of patients with posttraumatic stress disorder and substance abuse. *Current opinion in psychiatry*, *20*(6), 614-618.

Scherrer, J. F., Salas, J., Cohen, B. E., Schnurr, P. P., Schneider, F. D., Chard, K. M., ... & Lustman, P. J. (2019). Comorbid conditions explain the association between posttraumatic stress disorder and incident cardiovascular disease. *Journal of the American Heart Association*, *8*(4), e011133.

Schnyder, N., Panczak, R., Groth, N., & Schultze-Lutter, F. (2017). Association between mental health-related stigma and active help-seeking: systematic review and meta-analysis. *The British Journal of Psychiatry*, *210*(4), 261-268.

Schnurr, P. P., & Lunney, C. A. (2019). Residual symptoms following prolonged exposure and present-centered therapy for PTSD in female veterans and soldiers. *Depression and Anxiety*, *36*(2), 162-169.

Schuster, R. M., Hareli, M., Moser, A. D., Lowman, K., Gilman, J., Ulysse, C., ... & Evins, A. E. (2019). Cross-domain correlates of cannabis use disorder severity among young adults. Addictive behaviors, 93, 212-218.

Schwartz, G. (1978). Estimating the dimension of a model. *The Annals of Statistics, 6*, 461–464.

Scott, K. M., Lim, C., Al-Hamzawi, A., Alonso, J., Bruffaerts, R., Caldas-de-Almeida, J. M., Florescu, S., et al. (2016). Association of mental disorders with subsequent chronic

physical conditions: World Mental Health Surveys from 17 countries. *JAMA Psychiatry, 73*(2), 150-158.

Secades-Villa, R., & Fernández-Artamendi, S. (2017). Gender differences in cannabis use disorders. In *Handbook of Cannabis and Related Pathologies* (pp. 131-137). Academic Press.

Shalev, A. (2009). Posttraumatic stress disorder and stress-related disorders. *Psychiatric Clinics, 32*(3), 687-704.

Shalev, A., Liberzon, I., & Marmar, C. (2017). Post-traumatic stress disorder. *New England journal of medicine*, *376*(25), 2459-2469.

Shapiro, F. (2001). *Eye movement desensitization and reprocessing (EMDR): Basic principles, protocols, and procedures*. Guilford Press.

Shen, Y., Hendricks, A., Zhang, S., & Kazis, L. E. (2003). VHA enrollees' health care coverage and use of care. *Medical Care Research and Review*, *60*(2), 253-267.

Shishko, I., Oliveira, R., Moore, T. A., & Almeida, K. (2018). A review of medical marijuana for the treatment of posttraumatic stress disorder: Real symptom re-leaf or just high hopes?. *Mental Health Clinician, 8*(2), 86-94.

Smith, D. C., Garthe, R. C., Lee, A., Kim, S., Thebaud, M., & Kovacevic, L. (2023). Expanded Adverse Childhood Experiences (ACEs) and Adult Cannabis Use: A Latent Class Analysis. *Cannabis*, *6*(1), 1.

Smith, K. E., & Graham, B. M. (2020). The long-term psychological impact of childhood trauma: Effects on emotion regulation, coping, and stress response in adulthood. *Journal of Behavioral and Brain Science, 10*(4), 19-35.

Smith, S. M., Goldstein, R. B., & Grant, B. F. (2016a). The association between post-traumatic

stress disorder and lifetime DSM-5 mental health disorders among veterans: Data from the National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III). *Journal of mental health research*, *82*, 16-22.

Smith, H. L., Summers, B. J., Dillon, K. H., & Cougle, J. R. (2016b). Is worst-event trauma type related to PTSD symptom presentation and associated features?. *Journal of Anxiety Disorders*, *38*, 55-61.

Sommer, J. L., Mota, N., & El-Gabalawy, R. (2018). Maladaptive eating in posttraumatic stress disorder: A population-based examination of typologies and medical condition correlates. *Journal of traumatic stress, 31*(5), 708-718.

Sommer, J. L., Reynolds, K., El-Gabalawy, R., Pietrzak, R. H., Mackenzie, C. S., Ceccarelli, L., ... & Sareen, J. (2021). Associations between physical health conditions and posttraumatic stress disorder according to age. *Aging & mental health*, *25*(2), 234-242.

Spinazzola, J., Blaustein, M., & Van Der Kolk, B. A. (2005). Posttraumatic stress disorder treatment outcome research: The study of unrepresentative samples?. *Journal of Traumatic Stress: Official Publication of The International Society for Traumatic Stress Studies*, *18*(5), 425-436.

Stander, V. A., Thomsen, C. J., & Highfill-McRoy, R. M. (2014). Etiology of depression comorbidity in combat-related PTSD: a review of the literature. *Clinical psychology review*, *34*(2), 87-98.

StataCorp. (2017). *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC.

Stecker, T., Fortney, J. C., Hamilton, F., & Ajzen, I. (2007). An assessment of beliefs about mental health care among veterans who served in Iraq. *Psychiatric Services*, *58*(10), 1358-1361.

Stein, M. B. (2021). Psychotherapy and psychosocial interventions for posttraumatic stress disorder in adults. Retrieved from https://www.uptodate.com/contents/psychotherapy-and-psychosocial-interventions-for-posttraumatic-stress-disorder-in-adults.

Stein, D. J., Ipser, J. C., & Seedat, S. (2015). Pharmacotherapy for post-traumatic stress disorder (PTSD). *The British Journal of Psychiatry, 206*(2), 93-100. https://doi.org/10.1192/bjp.bp.114.145078

Steinert, C., Hofmann, M., Leichsenring, F., & Kruse, J. (2015). The course of PTSD in naturalistic long-term studies: high variability of outcomes. A systematic review. *Nordic journal of psychiatry*, *69*(7), 483-496.

Stinson, F. S., Ruan, W. J., Pickering, R., & Grant, B. F. (2006). Cannabis use disorders in the USA: prevalence, correlates and co-morbidity. *Psychological medicine*, *36*(10), 1447-1460.

Tang, S., Ports, K. A., Zhang, K., & Lin, H. C. Adverse childhood experiences, internalizing/externalizing symptoms, and associated prescription opioid misuse: A mediation analysis. *Preventive medicine, 134*, 106034.

Teicher, M. H., & Samson, J. A. (2016). Childhood maltreatment and psychopathology: A case for ecophenotypic variants as clinically and neurobiologically distinct subtypes. *American Journal of Psychiatry, 173*(11), 1117-1133.

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. *Archives of internal medicine*, *167*(3), 221-228.

Tomczyk S., Isensee B., & Hanewinkel R. (2016). Latent classes of polysubstance use among

adolescents—a systematic review. *Drug and Alcohol Dependence, 160*, 12–29.

Tripp, J. C., Jones, J. L., Back, S. E., & Norman, S. B. (2019). Dealing with complexity and comorbidity: Comorbid PTSD and substance use disorders. *Current Treatment Options in Psychiatry*, *6*(3), 188-197.

Tripp, J. C., Worley, M. J., Straus, E., Angkaw, A. C., Trim, R. S., & Norman, S. B. (2020). Bidirectional relationship of posttraumatic stress disorder (PTSD) symptom severity and alcohol use over the course of integrated treatment. *Psychology of addictive behaviors*, *34*(4), 506.

Tull, M. T., McDermott, M. J., & Gratz, K. L. (2016). Marijuana dependence moderates the effect of posttraumatic stress disorder on trauma cue reactivity in substance dependent patients. *Drug and alcohol dependence*, *159*, 219-226.

Tull, M. T., & Roemer, L. (2003). Alternative explanations of emotional numbing of posttraumatic stress disorder: An examination of hyperarousal and experiential avoidance. *Journal of Psychopathology and Behavioral Assessment*, *25*, 147-154

Turna, J., & MacKillop, J. (2021). Cannabis use among military veterans: A great deal to gain or lose?. *Clinical psychology review*, 101958.

Turner, S., Taillieu, T., Cheung, K., & Afifi, T. O. (2017). The relationship between childhood sexual abuse and mental health outcomes among males: Results from a nationally representative United States sample. *Child Abuse & Neglect, 66*, 64–72.

Van Ameringen, M., Mancini, C., Patterson, B., & Boyle, M. H. (2008). Post-traumatic stress disorder in Canada. *CNS neuroscience & therapeutics, 14*(3), 171-181.

Volkow, N. D., Hampson, A. J., & Baler, R. D. (2017). Don't worry, be happy: Endocannabinoids and cannabis at the intersection of stress and reward. *Annual Review of*

Pharmacology and Toxicology, 57, 285-308.

Vujanovic, A.A., Bonn-Miller, M.O., Petry, N.M. (2016). Co-occurring posttraumatic stress and substance use: Emerging research on correlates, mechanisms, and treatments—Introduction to the special issue. *Psychology of Addictive Behaviors. 30(*7):713–719. [PubMed: 27786510]

Wagner, F. A., & Anthony, J. C. (2002). From first drug use to drug dependence: developmental periods of risk for dependence upon marijuana, cocaine, and alcohol. *Neuropsychopharmacology, 26*(4), 479-488.

Walker, E. R., McGee, R. E., & Druss, B. G. (2015). Mortality in mental disorders and global disease burden implications: A systematic review and meta-analysis. *JAMA Psychiatry, 72*(4), 334-341.

Wall, M. M., Liu, J., Hasin, D. S., Blanco, C., & Olfson, M. (2019). Use of marijuana exclusively for medical purposes. *Drug and alcohol dependence*, *195*, 13-15.

Ware, J. E., Kosinski, M., & Keller, S. D. (1996). A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical care*, 220-233.

Ware, M. A., Wang, T., Shapiro, S., Collet, J. P., & COMPASS Study Team. (2010). Cannabis for the management of pain: Assessment of safety study (COMPASS). *Journal of Pain, 11*(12), 1232–1238. https://doi.org/10.1016/j.jpain.2010.08.002

Watson, P. (2019). PTSD as a public mental health priority. *Current Psychiatry Reports*, *21*, 1-12.

Wills, T. A. (1990). Stress and coping in early adolescence: Relationships to substance use in urban school samples. *Health Psychology, 9*(6), 766-777. https://doi.org/10.1037/0278-

6133.9.6.766

Wills, T. A., & Hirky, A. E. (1996). *Coping and substance abuse: A theoretical model and review of the evidence.* In M. Zeidner & N. S. Endler (Eds.), *Handbook of coping: Theory, research, applications* (p. 279–302). John Wiley & Sons.

Wilkinson, S. T., van Schalkwyk, G. I., Davidson, L., & D'Souza, D. C. (2016). The formation of marijuana risk perception in a population of substance abusing patients. *Psychiatric quarterly*, *87*(1), 177-187.

Wilkinson, S. T., Stefanovics, E., & Rosenheck, R. A. (2015). Marijuana use is associated with worse outcomes in symptom severity and violent behavior in patients with posttraumatic stress disorder. *The Journal of clinical psychiatry, 76*(9), 1174-1180.

Wittchen, H. U., Fröhlich, C., Behrendt, S., Günther, A., Rehm, J., Zimmermann, P., ... & Perkonigg, A. (2007). Cannabis use and cannabis use disorders and their relationship to mental disorders: a 10-year prospective-longitudinal community study in adolescents. *Drug and alcohol dependence*, *88*, S60-S70

Wolf, E. J., Miller, M. W., Krueger, R. F., Lyons, M. J., Tsuang, M. T., & Koenen, K. C. (2010). Posttraumatic stress disorder and the genetic structure of comorbidity. *Journal of abnormal psychology, 119*(2), 320.

Wyatt, G. E., Guthrie, D., & Notgrass, C. M. (1992). Differential effects of women's child sexual abuse and subsequent sexual revictimization. *Journal of Consulting and Clinical Psychology, 60*, 167–173.

Zeisser, C., Thompson, K., Stockwell, T., Duff, C., Chow, C., Vallance, K., ... & Lucas, P. (2012). A 'standard joint'? The role of quantity in predicting cannabis-related problems. *Addiction Research & Theory*, *20*(1), 82-92.

Zlotnick, C., Rodriguez, B. F., Weisberg, R. B., Bruce, S. E., Spencer, M. A., Culpepper, L., & Keller, M. B. (2004). Chronicity in posttraumatic stress disorder and predictors of the course of posttraumatic stress disorder among primary care patients. *The Journal of nervous and mental disease*, *192*(2), 153-159.

Zlotnick, C., Warshaw, M., Shea, M. T., Allsworth, J., Pearlstein, T., & Keller, M. B. (1999). Chronicity in posttraumatic stress disorder (PTSD) and predictors of course of comorbid PTSD in patients with anxiety disorders. *Journal of Traumatic Stress: Official Publication of The International Society for Traumatic Stress Studies*, *12*(1), 89-100.

Appendix A

DSM-5 Diagnostic Criteria for Posttraumatic Stress Disorder

A. Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways:

   1. Directly experiencing the traumatic event(s).
   2. Witnessing, in person, the event(s) as it occurred to others.
   3. Learning that the traumatic event(s) occurred to a close family member or close friend.
   4. Experiencing repeated or extreme exposure to aversive details of the traumatic event(s).

B. Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the traumatic event(s) occurred:

   1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).
   2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s).
   3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring.
   4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
   5. Marked physiological reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).

C. Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:

   1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).

2. Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).

D. Negative alterations in cognitions and mood associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:

1. Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol, or drugs).
2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world.
3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame himself/herself or others.
4. Persistent negative emotional state (e.g., fear, horror, anger, guilt, or shame).
5. Markedly diminished interest or participation in significant activities.
6. Feelings of detachment or estrangement from others.
7. Persistent inability to experience positive emotions.

E. Marked alterations in arousal and reactivity associated with the traumatic event(s), beginning or worsening after the traumatic event(s) occurred, as evidenced by two (or more) of the following:

1. Irritable behavior and angry outbursts (with little or no provocation) typically ex pressed as verbal or physical aggression toward people or objects.
2. Reckless or self-destructive behavior.
3. Hypervigilance.

4. Exaggerated startle response.
5. Problems with concentration.
6. Sleep disturbance (e.g., difficulty falling or staying asleep or restless sleep).

F. Duration of the disturbance (Criteria B, C, D, and E) is more than 1 month.

G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

H. The disturbance is not attributable to the physiological effects of a substance (e.g., medication, alcohol) or another medical condition.

Note: In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental. Criterion A4 does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work related.

Appendix B

DSM-5 Diagnostic Criteria for Cannabis Use Disorder

A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

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

a. The characteristic withdrawal syndrome for cannabis (refer to Criteria A and B of the criteria set for cannabis withdrawal, pp. 517-518).

A. Cessation of cannabis use that has been heavy and prolonged (i.e., usually daily or almost daily use over a period of at least a few months).

B. Three (or more) of the following signs and symptoms develop within approximately 1 week after Criterion A:

1. Irritability, anger, or aggression.
2. Nervousness or anxiety.
3. Sleep difficulty (e.g., insomnia, disturbing dreams).
4. Decreased appetite or weight loss.
5. Restlessness.
6. Depressed mood.
7. At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache.

b. Cannabis (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.

Specify current severity:

305.20 (F12.10) Mild: Presence of 2-3 symptoms.

304.30 (F12.20) Moderate: Presence of 4-5 symptoms.

304.30 (F12.20) Severe: Presence of 6 or more symptoms.

Appendix C

ACE Items Included in NESARC-III

Before you were 18 years old…

Item	Content	ACE category
1	How often did a parent/other adult living in your home swear at or insult you or say hurtful things?	Emotional abuse
2	How often did a parent/other adult living in your home act in any other way that made you afraid you would be physically hurt?	Emotional abuse
3	How often did a parent/other adult living in your home push, grab, shove, slap or hit you?	Physical abuse
4	How often did a parent/other adult living in your home hit you so hard that you had marks or bruises or were injured?	Physical abuse
5	How often did an adult/other person touch or fondle you in a sexual way when you didn't want them to or were too young to know what was happening?	Sexual abuse
6	How often did an adult/other person have you touch their body in a sexual way when you didn’t want to or were too young to know what was happening?	Sexual abuse
7	How often did an adult/other person attempt to have sexual intercourse with you when you didn’t want them to or were too young to know what was happening?	Sexual abuse
8	How often did an adult/other person actually have sexual intercourse with you when you didn’t want them to or were too	Sexual abuse

	young to know what was happening?	
9	How often did a parent/other adult living in your home make you go hungry or not prepare regular meals?	Physical neglect
10	How often did you go without things you needed like clothes, shoes or school supplies because a parent/other adult living in your home spent the money on themselves?	Physical neglect
11	How often did a parent/other adult living in your home ignore or fail to get you medical treatment when you were sick or hurt?	Physical neglect
12	How often were you made to do chores that were too difficult or dangerous for someone your age?	Physical neglect
13	How often were you left alone or unsupervised when you were too young to be alone, that is, before you were 10 years old?	Physical neglect
14	Felt there was someone in family who wanted me to be a success?	Emotional neglect
15	Felt there was someone in family who helped me feel I was important or special?	Emotional neglect
16	My family was a source of strength and support?	Emotional neglect
17	Felt I was part of a close knit family?	Emotional neglect
18	Someone in my family believed in me?	Emotional neglect
19	How often did your father/other adult male push, grab, slap or throw something at your mother/other adult female?	Household physical violence
20	How often did your father/other adult male kick, bite, hit your mother/other adult female with a fist or something hard?	Household physical violence
21	How often did your father/other adult male repeatedly hit your	Household

	mother/other adult female for at least a few minutes?	physical violence
22	How often did your father/other adult male threaten your mother/other adult female with a knife/gun or use a knife/ gun to hurt her?	Household physical violence
23	Parent/other adult living in home was a problem drinker/ alcoholic?	Household substance abuse
24	Parent/other adult living in home had similar problems with drugs?	Household substance abuse
25	Parent/other adult living in home went to jail or prison?	Incarcerated household member
26	Parent/other adult living in home was treated/ hospitalized for a mental illness?	Household mental illness
27	Parent/other adult living in home attempted suicide?	Household mental illness
28	Parent/other adult living in home actually committed suicide?	Household mental illness
29	Did biological or adoptive parents get divorced or permanently stop living together before respondent was 18?	Parental separation/divorce

Appendix D

Cannabis Use Latent Class Analysis Variable Breakdown

1. Quantity
    a. On the days that you used marijuana in the last 12 months, about how many joints did you usually smoke in a single day? (Quantity past year)
    b. At the time you were using marijuana the MOST, about how many joints did you usually smoke in a single day? (Quantity peak use)
2. Frequency
    a. During the last 12 months, about how often did you use marijuana? (Frequency average)
    b. Think about the time when you were using marijuana the MOST. At that time about how often did you use it? (Frequency peak use)
3. Duration
    a. About how long did that period last when you were using marijuana that frequently?
4. Age of First Use
    a. How old were you when you first used marijuana? (Age of onset)
5. Medicinal Cannabis Use
    a. Did you use medical marijuana in the last 12 months? (Medicinal use past year)
6. Cannabis Use Disorder (Composite score lifetime)

Appendix E

NESARC *DSM-5* CUD Criteria

A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Larger/Longer (1 question)
    a. Had times when you ended up using more, or for longer, than you intended
2. Quit or Cut Down (2 questions)
    a. Often used medicine/drugs in larger amounts or for a longer period of time than intended
    b. More than once wanted to stop or cut down on using
3. Time Spent (2 questions)
    a. Had a period when you spent a lot of time using medicine/drugs or getting over its bad aftereffects.
    b. Had a period when you spent a lot of time ensuring drug availability.
4. Craving (2 questions)
    a. Felt a very strong urge or desire to use a medicine/drug.
    b. Wanted it so badly that you couldn't think of anything else.
5. Role Interference (3 questions)
    a. Had job or school problems due to medicine/drug use.
    b. Continued to use medicine/drugs even though it was causing problems at school or work.
    c. Had a period when medicine/drug use interfered with taking care of your family.
6. Social Problems (3 questions)

a. Had arguments with family or friends as a result of medicine/drug use.
b. Continued to use medicine/drugs even though it was causing problems with family or friends.
c. Got into physical fights while under the influence of medicine/drugs.

7. Given Up (2 questions)
    a. Gave up or cut down on important activities in order to use drugs.
    b. Gave up or cut down on interesting activities in order to use drugs.
8. Hazardous Use (2 questions)
    a. More than once drove a vehicle while under the influence of medicine or drugs.
    b. Found yourself under the influence of medicine/drugs in dangerous situations.
9. Continued use Despite Problems (2 questions)
    a. Continued to use medicine/drugs even though you knew it was making you feel depressed, uninterested in things, or suspicious of other people.
    b. Continued using even though you knew it was causing another health problem.
10. Tolerance (2 questions)
    a. Ever found that you had to use much more of the medicine/drug to get the desired effect?
    b. Ever found that the usual amount of medicine/drug had less effect?
11. Withdrawal (2 questions with subdivisions)
    a. The characteristic withdrawal syndrome for cannabis
        1. Irritability, anger or aggression
            i. Irritability
            ii. anger or aggression.

2. Nervousness or anxiety
3. Sleep difficulty
    i. insomnia
    ii. disturbing dreams
4. Decreased appetite or weight loss
5. Restlessness
6. Depressed mood
7. At least one of the following physical symptoms causing significant discomfort:
    i. abdominal pain
    ii. shakiness/tremors
    iii. sweating
    iv. fever
    v. chills
    vi. headache

b. Cannabis (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.
    1. Took more of the same or similar drug to get over any of these bad aftereffects.

Appendix F

NESARC Coding for *DSM-5* PTSD Symptom Severity

A. Criterion A

1. n12q1A = PTSD_A1.
2. n12q1B = PTSD_A2.
3. n12q2A = PTSD_A3_1.
4. n12q2B = PTSD_A3_2.
5. n12q1c = PTSD_A4_1.
6. n12q1d = PTSD_A4_2.

B. Criterion B

1. n12q5A = PTSD_B1_1.
2. n12q5B = PTSD_B1_2.
3. n12q5C = PTSD_B2.
4. n12q5D = PTSD_B3_1.
5. n12q5E = PTSD_B3_2.
6. n12q5F = PTSD_B4.
7. n12q5G = PTSD_B5.

C. Criterion C

1. n12q5I = PTSD_C1.
2. n12q5J = PTSD_C2_1.
3. n12q5K = PTSD_C2_2.

D. Criterion D

1. n12q5L = PTSD_D1.
2. n12q5N = PTSD_D2_1.
3. n12q5O = PTSD_D2_2.
4. n12q5P = PTSD_D2_3.
5. n12q5Q = PTSD_D3_1.
6. n12q5R = PTSD_D3_2.
7. n12q5S = PTSD_D4_1.
8. n12q5T = PTSD_D4_2.
9. n12q5U = PTSD_D4_3.
10. n12q5V = PTSD_D4_4.
11. n12q5W = PTSD_D5.
12. n12q5X = PTSD_D6.
13. n12q5Y = PTSD_D7_1.
14. n12q5Z = PTSD_D7_2.

E. Criterion E

1. n12q5AA = PTSD_E1.
2. n12q5BB = PTSD_E2.
3. n12q5CC = PTSD_E3.
4. n12q5DD = PTSD_E4.
5. n12q5EE = PTSD_E5.
6. n12q5FF = PTSD_E6.

F. Criterion F

1. n12q6c = PTSD_F.

G. Criterion G

1. n12q8A = PTSD_G_1.
2. n12q8B = PTSD_G_2.
3. n12q8C = PTSD_G_3.
4. n12q8D = PTSD_G_4.
5. n12q8E = PTSD_G_5.
6. n12q8F = PTSD_G_6.

Appendix G

Types of Traumatic Exposure

1. Sexual assaultive trauma (sexually abused before age 18, sexually assaulted as an adult)
2. Physical assaultive trauma (physically abused before age 18, beaten up by spouse/ romantic partner, beaten up by someone else)
3. Life-threatening illness (serious or life-threatening illness)
4. Life-threatening injury (serious or life-threatening injury, injured in a terrorist attack)
5. Psychological trauma (saw a dead body or body parts, kidnapped/held hostage, stalked, mugged/held up/threatened with a weapon)
6. Witnessed trauma
7. Other trauma (natural disaster, active military combat, peacekeeper/relief worker, civilian in a war zone, refugee, prisoner of war, juvenile detention/jail, other)