# THE PREVALENCE OF CANNABIS USE DISORDER IN INDIVIDUALS WITH ANXIETY OR RELATED DISORDERS: A SYSTEMATIC REVIEW

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**Abstract**

The self-medication of underlying mental health symptoms is a primary reason for cannabis consumption, driving variation in the prevalence of Cannabis Use Disorder (CUD) in Anxiety and Related Disorders (ARDs). The current study aimed to systematically review predictors of CUD in individuals with a comorbid ARD diagnosis. An online search was conducted in January 2023 with a Boolean search phrase incorporating keywords related to CUD and ARDs in *PubMed, PsycInfo*, and *WoS.* Articles were included if participants/estimates were (a) at least 18 years of age; (b) prospectively assigned a diagnosis of current ARD supported by a clinician interview; c) diagnosed with current or lifetime CUD, cannabis dependence, or abuse via an interview or empirically validated screening tools; and (d) recruited from representative samples. A total of 1057 articles were screened. Five studies for the prevalence of CUD in ARDs ($N$ = 10,896) met the inclusion criteria. Amongst these studies, the proportion of individuals with CUD in any ARD ranged from 3.3% to 19.8%. Amongst veterans with PTSD, four studies met inclusion criteria ($N$ = 1,329), whereby the prevalence ranged from 4.2% to 34%. All results were synthesized narratively. There is a lack of research using clinician-administered interviews to identify accurate prevalence estimates in the literature, resulting in few studies. Studies failed to aggregate estimates of comorbid CUD in specific ARDs, making it difficult to ascertain whether different ARDs are at a higher risk of developing comorbid CUD. Despite methodological variation, this systematic review suggests that individuals with current ARDs may be at risk of developing comorbid CUD in their lifetime. However, future research should incorporate control groups and conduct cross-cultural studies to determine the extent of this relationship accurately.

*Keywords:* Anxiety disorders, Cannabis use, Cannabis use disorder, Comorbidity, Prevalence

## General Summary

This dissertation systematically reviewed research on the prevalence of Cannabis Use Disorder (CUD) in those with Anxiety or Related Disorders (ARDs). A search of research databases found 1616 articles, of which 9 were relevant to the current thesis. Of the 5 papers studying adult general populations, the prevalence of having comorbid CUD alongside an ARD throughout an individual's lifetime ranged from 3.3-19.8%, while current estimates (i.e., CUD diagnosed in the past year) ranged from 4.3-8.7%. Of the 4 papers studying veterans, the prevalence of comorbid CUD alongside Post-Traumatic Stress Disorder (PTSD) throughout an individual's lifetime ranged from 11.3%-12.5%, while current estimates (i.e., CUD at baseline or in the past-year) ranged from 4.1%-34%. Compared to samples without ARDs, those with ARDs were more likely to have comorbid CUD. However, due to the limited number of studies, further research is needed. This is especially true due to substantial variation in the methods reported and the fact that most (8 of 9) studies were from the USA. The present review highlights key gaps and areas for expansion to achieve accurate estimates and improve generalizability. As the legal status of cannabis undergoes transformation worldwide, it is crucial to understand the associated health and social consequences of cannabis use, so healthcare professionals can better screen for underlying CUD in vulnerable populations and inform their treatment approach.

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# The Prevalence of Cannabis Use Disorder in Individuals with Anxiety or Related Disorders: A Systematic Review

Substance Use Disorders (SUDs) are a prevalent and complex illness, with global estimates reaching approximately 2.2% in 2019 (Castaldelli-Maia & Bhugra, 2022). There are variations in these estimates, with higher rates of SUDs impacting higher-income countries, such as North America and Europe. Reportedly, Alcohol Use Disorder (AUD) holds the highest crude prevalence rate globally at 1.45%, followed by Cannabis Use Disorder (CUD) at 0.32% (Castaldelli-Maia & Bhugra, 2022). Cross-cultural, social, and environmental factors likely explain why these two SUDs are the most prevalent (Degenhardt et al., 2016). For example, social norms prominent in Western cultures perceive alcohol as a normalized substance in many social contexts. Along with alcohol, caffeine and tobacco are the three most used substances (World Health Organization [WHO], 2016b). However, cannabis is the most widely used "illegal" substance worldwide, as an estimated 3.9% of the population between the ages of 15-64 consume the substance (Degenhardt et al., 2016).

Despite cannabis being illegal in many countries, some nations are changing their policies to legalize it. For example, in 2013, Uruguay was the first country worldwide to implement cannabis legalization. Similarly, in 2018, Canada legalized cannabis for non-medical cultivation, distribution, and retail, compared to the USA, where the legal status varies in many States yet remains illegal at the Federal level (e.g., Colorado, California, and Virginia; National Cannabis Industry Association, 2016). Decriminalization, tolerance, or coffee shop models are also prominent in many European countries (e.g., Netherlands, Spain, Czech Republic; Gabri et al., 2022), with Germany recently legalizing non-medical cannabis following Malta and Luxembourg (Sabaghi, 2024). It is important to recognize the increasing popularity of cannabis

legalization among policymakers and governments to understand the reasons behind this shift. In Canada, the non-medical use of cannabis has been prohibited since 1923 (Library of Parliament, 2018). Although extensively debated in the early 2000s, it was not until June 2016 that the Canadian government assembled a task force to explore new legislation. Eventually, this led to Bill C-45, which proposed legal access to cannabis and control and regulation of its production, distribution, and sale. The government's rationale for these proposed changes includes safeguarding public health by ensuring access to a secure supply of legal cannabis, promoting low-risk use for adults, protecting youth, enhancing safety for roads, public spaces, and workplaces, alleviating the burden on the criminal justice system, diminishing the demand for illegal cannabis, and fostering new business opportunities. As the legal status of cannabis undergoes gradual transformation and diverse models are implemented worldwide, it is crucial to understand the associated health and social consequences of cannabis use and its legalization.

Comorbidity is the rule rather than the exception when it comes to SUDs, with increased prevalence rates in those with Attention-Deficit/Hyperactivity Disorder (ADHD; Froude et al., 2024; Rohner et al., 2023), Mood Disorders (Hunt et al., 2020; Saha et al., 2021), Posttraumatic Stress Disorder (PTSD; Roberts et al., 2015), Eating Disorders (ED; Bahji et al., 2019), and Anxiety Disorders (Lai et al., 2015). Thus, it is crucial to explore the relationship between problematic substance use behaviours exacerbating certain psychological disorders. Because cannabis use is the most widely used “illegal” substance worldwide, and Anxiety and Related Disorders (ARDs) are among the most prevalent psychological disorders (Kessler et al., 2005a), this makes the current study interesting in the context of various legalization statuses, as rates of CUD may demonstrate similar trends as AUD. There is evidence indicating a rise in frequent, non-medical cannabis use, leading to an elevated risk of developing CUD, which raises global

public health concerns, particularly among youth, adolescents, and young adults (Cerdá et al., 2020; Mennis et al., 2023; O'Grady et al., 2022). Instances of heightened prevalence can be linked to misconceptions, particularly regarding the perceptions of cannabis being harmless and non-addictive (Mennis et al., 2023). Indeed, the implications for cannabis consumption are well documented despite a strong rationale for legalization in many jurisdictions. However, given the misconceptions surrounding cannabis use, it is important to explore what risks persist with cannabis consumption. Therefore, the purpose of this dissertation is to explore the prevalence of CUD in individuals who present with an ARD. This is because cannabis is found to have a bidirectional and transdiagnostic relationship with ARDs, possibly perpetuating or minimizing the extent of any given ARD. With the lack of literature directed toward the complexity involved in this relationship, it is paramount that research efforts aim to understand how cannabis interacts with various ARDs and what the prevalence and predictors are for developing comorbid CUD.

**Cannabis and Cannabis Use Disorder (CUD)**

Cannabis is produced from plants and contains over 100 cannabinoids in various strains (Chandra et al., 2019). The most common two cannabinoids are delta-9-tetrahydrocannabinol (Δ9-THC), the primary psychoactive ingredient that creates an intoxicating effect, and cannabidiol (CBD), a nonintoxicating cannabinoid that has little or no psychoactive effects. To achieve the intoxicating effects of cannabis, it must be heated to activate Δ9-THC. While research on Δ9-THC and CBD is limited due to research constraints regarding various legal statuses, Δ9-THC is believed to cause adverse effects. For example, evidence suggests that Δ9-THC can impair learning, produce psychotic-like effects, and increase anxiety (Chandra et al., 2019; Curran et al., 2016), whereas CBD is believed to offset adverse effects of Δ9-THC and has

analgesic, anti-inflammatory, and anti-anxiety properties (Englund et al., 2013; Morgan et al., 2010; Sharpe et al., 2020).

Indeed, higher concentrations of Δ9-THC lead to more potent cannabis products, which are often desirable (Arterberry et al., 2019; Budney & Borodovsky, 2017). This is particularly relevant for more frequent consumers, who build up a tolerance over time (Davenport, 2021; Ramaekers et al., 2020). The frequency of cannabis consumption is directly correlated with the emergence of adverse consequences (Callaghan et al., 2020; Simpson et al., 2021). This has been well-established in the literature and is related to many of the criteria for CUD in the *Diagnostic and Statistical Manual Fifth Edition* (*DSM-5*; e.g., exceeding intended quantities or durations when using cannabis; American Psychiatric Association [APA], 2013; Choi et al., 2016; Leung et al., 2020). For example, Arterberry et al. (2019) found that those who initiate cannabis and regularly consume products containing 12.3 percent THC are almost five times as likely to develop CUD after one year.

CUD is defined by the *DSM-5* as problematic consumption of cannabis that causes clinically significant impairment or distress (APA, 2013). Specifically, patients must meet at least 2 of the 11 criteria to be diagnosed with the disorder: a) taking cannabis in larger quantities than intended; b) being unable to control cannabis use; c) craving or urges to use cannabis; d) a failure to perform work, school, or home tasks; e) interpersonal problems that are present/persist with continued cannabis use; f) social, occupational, or recreational activities ceasing due to cannabis; g) needing increased amounts of cannabis to become intoxicated or experiencing diminished effects from cannabis; and h) withdrawal symptoms such as sleep difficulty, restlessness, anxiety, or irritability. Prior to the *DSM-5*, the *Diagnostic and Statistical Manual Fourth Edition* (*DSM-IV*) included separate diagnoses of cannabis abuse and cannabis

dependence (APA, 1994) which included criteria that were later used to define CUD in *DSM-5*. Importantly, not everyone who consumes cannabis will go on to develop CUD; among individuals who use cannabis, there is a 1 in 5 risk of developing a CUD (Leung et al., 2020). However, there is an increased risk of developing CUD if cannabis is initiated at a younger age and consumed frequently (i.e., daily/weekly) with higher doses of Δ9-THC.

The age of initiation for cannabis use is a robust factor in predicting many adverse outcomes, including CUD (Fergusson et al., 2006; Hanna et al., 2016; Leung et al., 2020; Lynskey et al., 2003). In an Australian twin study, it was demonstrated that initiating cannabis use at a younger age (< 17 years old) had a 2.3 to 3.9 fold increase in odds of polysubstance use and a 1.6 to 6.0 fold increase in odds of developing a SUD (Lynskey et al., 2003). Furthermore, these findings are relative to their twin, who had not initiated cannabis before the age of 17, demonstrating that it is not solely genetic factors that predict these outcomes. Indeed, those who consume cannabis earlier in life are also at a greater risk of developing CUD (Leung et al., 2020). With the average age of cannabis initiation being reported at 20.4 years old, in younger samples the average age of initiation has been reported as young as 14.3 years old (Health Canada, 2021). Coupled with the variation in legal status and concerns from policymakers, stakeholders, and community members alike, it is important to consider why the legality of cannabis is heavily debated and how cannabis could lead to adverse consequences for vulnerable consumers.

The prevalence of CUD may increase exponentially given the diversification of products and intense increase in Δ9-THC potency (Arterberry et al., 2019; Budney & Borodovsky, 2017; Hammond et al., 2021; Imitaz et al., 2023; Russell et al., 2018). For instance, in the dried flower of regulated cannabis strains, Δ9-THC can range up to 30%, which is considerably higher than

decades ago (Berenson, 2019; Government of Canada, 2018). In 1980, the average Δ9-THC concentration in dried flower forms of cannabis was 3% (Health Canada, 2022b). However, today, the average is around 15%. With additional routes of administration for cannabis (e.g., extracts like edibles and oils; concentrates like wax, butane hash, and shatter), the Δ9-THC potency could be as high as 95% in more concentrated products (Prince & Conner, 2019; Russell et al., 2018). Further, individuals who consume cannabis concentrates (e.g., wax, shatter, budder, butane hash oil) have been found to endorse increased CUD symptom severity, higher psychological dependence, and greater withdrawal symptoms than individuals who consume cannabis in the dried flower form (Bidwell et al., 2018; Freeman & Winstock, 2015; Meier, 2017).

***Gender Differences and Cannabis Use***

There appear to be sex differences in cannabis use, with males twice as likely as females to be diagnosed with CUD (Kozak et al., 2021). Further, women and gender/sexual minorities are more likely to develop cannabis use problems but less likely to acknowledge substance use problems than men (Denisse & Grella, 2017; Dyar, 2022), which may relate to higher prevalence rates of CUD among males (Hall et al., 2020; Kozak et al., 2021). However, there are reports of the gender gap closing concerning the prevalence of cannabis use, which may be related to legalization (e.g., Matheson & Le Foll, 2023).

Coping is a common motive for cannabis use, particularly in women, while other common reasons for consumption include enhancement, social, conformity, and expansion (Green et al., 2003; Simons et al., 1998; Wallis et al., 2022). Indeed, cannabis is often used to relieve symptoms of ARDs, depression, insomnia, ADHD, and chronic pain (Asselin et al., 2022; Sexton et al., 2016; Wallis et al., 2022). However, its effectiveness for mental health treatment is

inconclusive (Pratt et al., 2019). Additionally, women are more likely to experience anxiety, develop a quicker progression to substance use problems, and experience greater social stigma than men (Greenfield et al., 2007; Hernandez-Avila et al., 2004; McLean et al., 2011). Given the relationship between cannabis use, mental health, and gender differences, it is important to examine the potential consequences that can arise with a primary mental health condition and subsequently developing CUD as a result of frequent cannabis use.

**Anxiety and Related Disorders (ARDs)**

In the *DSM-5*, ARDs are characterized by excessive fear, worry, and anxiety toward a perceived or real threat (APA, 2013). These disorders are common, with the global prevalence of ARDs estimated to be roughly 4% in 2019 (Castaldelli-Maia & Bhugra, 2022). Similarly, a meta-regression by Baxter et al. (2012) suggests that past year ARD estimates ranged from 5.3% to 10.4%, depending on geographical and sociocultural differences, which accounted for substantial variation. In the *DSM-5*, there are several types of anxiety disorders listed, including Specific Phobia, Social Anxiety Disorder (SAD), Panic Disorder (PD), Agoraphobia, Generalized Anxiety Disorder (GAD), Separation Anxiety Disorder (SPAD) and Selective Mutism (SM). While the lifetime prevalence for any ARD is estimated to be 41% in China, the prevalence of specific ARDs may vary, with Specific Phobia, Non-Specified Anxiety Disorder, GAD, and SAD being the most common ARDs estimated at 19.6%, 6.9%, 4.7%, and 4.1%, respectively (Guo et al., 2016). Prior to the *DSM-5*, the *DSM-IV* included additional disorders under the classification of *Anxiety Disorders* (e.g., PTSD, Obsessive-Compulsive Disorder). These disorders now feature their own diagnostic section in the *DSM-5*, being *Obsessive-Compulsive and Related Disorders* and *Trauma-and Stressor-Related Disorders* (APA, 2013).

Despite recent changes to the current edition of the *DSM*, there is still substantial overlap in these disorders as they all share overarching similarities.

Given the shared overlap among these disorders, it is unsurprising that the treatment approach is often similar. Gold standard treatments for ARDs are Cognitive Behavioural Therapy (CBT) and Selective Serotonin Reuptake Inhibitors (SSRIs). CBT is not only the most researched form of psychotherapy, but it has the flexibility to treat a wide range of conditions ranging from ARDs, SUDs, EDs, depressive/mood disorders, personality disorders, sleep disorders, psychotic disorders, and many more clinical and non-clinical conditions (David et al., 2018; Hofmann et al., 2012). For this reason, CBT is often thought of as a transdiagnostic treatment, meaning it can be modified to treat a multitude of comorbid conditions simultaneously (Norton et al., 2012). Similarly, SSRIs are commonly prescribed by physicians to alleviate symptoms of anxiety, meaning that it is often prescribed for many ARDs, including OCD and PTSD (Bandelow et al., 2012, 2017).

Finally, the age of onset for ARDs may be variable. In a 2016 meta-analysis of a general population sample, the authors estimate that the average age of onset for ARDs is 21.3 years (de Lijster et al., 2016). However, SPAD is believed to have a significantly earlier onset, around ten years old, whereas GAD was reported around 35 years of age. Importantly, ARDs often face a delay in diagnosis and subsequent treatment (Cheung et al., 2017). Therefore, there are inaccurate estimates of when the condition first presents in individuals.

### *Obsessive Compulsive and Related Disorders*

Obsessive-Compulsive Disorder (OCD) is characterized by the presence of obsessions in the form of intrusive thoughts, images, or urges that are distressing and unwanted (APA, 2013). Individuals with OCD often experience a higher intolerance of uncertainty and, subsequently, a

high intolerance for distress due to the significant anxiety often facilitated by distressing obsessions (Jacoby et al., 2013). As a result, compulsions are performed to mitigate this anxiety and distress. The estimated worldwide lifetime prevalence of OCD is reportedly 1.3% among adults (Fawcett et al., 2020). However, there are gender differences. For example, females are reported to have a higher likelihood of being diagnosed with OCD compared to males, with prevalence rates of 1.5% for females and 1.0% for males, with females being 1.6 times more likely than males to experience OCD in their lifetime (Fawcett et al., 2020).

Advancements in research have led to the discovery of disorders that share a more similar etiology to OCD. For example, Trichotillomania, formally known as an Impulse Control Disorder in the *DSM-IV*, shared more clinical utility and diagnostic validators to OCD (APA, 2013). Now, the *Obsessive-Compulsive and Related Disorders* in the *DSM-5* feature the following disorders: Body Dysmorphic Disorder, Hoarding Disorder, Excoriation (Skin-Picking) Disorder, Trichotillomania (Hair-Pulling), Substance-/Medication-Induced Obsessive-Compulsive and Related Disorder, and Obsessive-Compulsive and Related Disorder due to another medical condition.

The age of onset for OCD may have inaccurate estimates due to misdiagnoses of lesser-known symptom presentations, with symptoms being more likely to go unrecognized by primary care physicians, mental health professionals, and the lay public (Coles et al., 2023; Glazier et al., 2013, 2015). There is a lag between the onset of OCD and receiving adequate treatment, which is estimated to be up to 9 years, with an additional two years for an individual actively seeking help and receiving treatment (Albert et al., 2019). Thus, many individuals may not receive a diagnosis until they are 20-25 years of age (Rasmussen & Eisen, 1992), especially if lesser-known or sub-clinical symptoms present at a much younger age (Anholt et al., 2013).

### *Trauma- and Stressor-Related Disorders*

Formally known under anxiety disorders, *Trauma and Stressor-Related Disorders* in the *DSM-5* feature the following possible diagnoses: Reactive Attachment Disorder, Disinhibited Social Engagement Disorder, PTSD, Acute Stress Disorder, Adjustment Disorders, Other Specified Trauma- and Stressor-Related Disorder, and Unspecified Trauma- and Stressor-Related Disorder (APA, 2013). PTSD is characterized by various symptom clusters such as intrusive thoughts, reoccurring dreams or memories, flashbacks, distress, negative alterations in cognition and mood, avoidance, and psychological reactivity due to previous trauma and exposure to trauma cues (APA, 2013). While the clinical presentation may vary among individuals from dissociative states to fear-based emotional responses, patients must meet at least one criterion for a stressor, intrusion, avoidance, distress and/or functional impairment, and two criteria for negative alterations in cognitions and mood, and for marked alterations in arousal and reactivity within a one-month period. The prevalence of PTSD in the USA is around 6.8%, with females being twice as likely to experience PTSD compared to males (Kessler et al., 2005a). One reason for this gender difference identified in the literature is due to the high rates of sexual assault among women (Cortina & Kubiak, 2006). Consequently, violence is also heavily perpetuated against gender and sexual minorities, putting this population at a higher risk of experiencing trauma and, subsequently, developing PTSD (Roberts et al., 2010). Perceptions of and responses to traumatic events vary among individuals, with research suggesting that only 5% to 10% of people who witness or experience a traumatic event may go on to develop PTSD (Kessler et al., 1995).

For PTSD, the age of onset is typically later in life, around 30 years old (Solmi et al., 2021). One reason for this late age of onset may be related to a delay in PTSD symptom onset.

Given the preference to diagnose acute stress disorder succeeding trauma exposure, some individuals may never receive an official PTSD diagnosis despite developing symptoms (APA, 2013). Secondly, if an individual was exposed to previous trauma earlier in life, the expression of symptoms may not be prevalent or distressing until later in life (Bonde et al., 2022). Thus, ongoing stressors may eventually lead to the development of PTSD over time. Overall, many factors contribute to heterogeneity among the age of onset for ARDs, making it difficult to predict and sometimes diagnose an ARD. Conversely, certain populations, such as veterans, are considered vulnerable because the prevalence of PTSD may be as high as 20% (Cypel et al., 2022; Magruder et al., 2015).

**Veterans.**

Veterans are a special population that is at a heightened risk of developing PTSD. This is mainly due to the toll military service has on returning to civilian life after experiencing traumatic events (Sterniczuka & Whelan, 2016). Additionally, veterans are vulnerable to several other comorbidities, such as chronic pain or disabilities (Thompson et al., 2015). Consequently, many veterans, especially those who do not seek immediate treatment, may turn to substances to cope with distress (Back et al., 2014; Sterniczuka & Whelan, 2016). Indeed, cannabis is one of the top three consumed substances among veteran populations (Teeters et al., 2017). A survey conducted among Canadian Armed Forces members who have PTSD found that about half of the participants reported a history of cannabis use, with 23% initiating cannabis use after exposure to trauma (Sterniczuka & Whelan, 2016). The main reasons participants noted for cannabis use related to relaxation, pain reduction, sleep quality, and relief of PTSD and anxiety symptoms.

Back et al. (2014) interviewed veterans from the community with current PTSD and found that 85% of participants' reported that PTSD symptoms were exacerbated with increased

substance use, and 61% reported an improvement in PTSD symptoms once substance use was decreased. Interestingly, about half of the participants presumed the opposite relationship would exist, wherein they initially believed an increase in substance use would decrease their PTSD symptoms. These findings speak to the intricacies of the relationship between substances and mental health. Substance use, such as cannabis, may perpetuate underlying PTSD symptoms and can act to maintain the disorder (Bonn-Miller et al., 2013; Gentes et al., 2016) despite temporary relief of symptoms upon consuming the substance. While the efficacy of medical cannabis as a treatment for PTSD is heavily debated, and randomized clinical trials often consist of small sample sizes, some individuals have reported a benefit or improvement with specific mental health symptoms such as nightmares (e.g., Jetly et al., 2015). A qualitative study by Storey et al. (2023) depicts in greater detail additional reported benefits of cannabis in Veterans with chronic pain, with veterans reporting improvement in their quality of life, sleep, mood, personal life, and pain management. Indeed, many veterans report a number of comorbidities, and cannabis may be a better alternative to pharmacological medication such as opioids. However, more research is needed on the specific dosage, conditions, and form of cannabis that may be most beneficial in this population (Storey et al., 2023). Therefore, for the purpose of the current study, prescribed medical cannabis will not be discussed further. This is because medical cannabis is becoming increasingly prescribed to veterans for physical as well as mental health concerns (e.g., PTSD and Anxiety) despite not being currently approved for these disorders (Health Canada, 2018b; Storey et al., 2023). Further, the *DSM-5* states that an individual cannot be diagnosed with a SUD specifically for a substance that they have been prescribed and taken as directed by a physician (APA, 2013).

As veterans are an at-risk group for several comorbidities associated with combat, injuries, and trauma exposure, non-medical cannabis is often used as a means to relieve associated symptoms (Thompson et al., 2015; Turna & MacKillop, 2021). Indeed, in a systematic review by Turna and MacKillop (2021), they concluded that, generally, cannabis use is higher among veterans than the general population. Strikingly, the types of deployment do not appear to matter, as studies show comparable rates of CUD among veterans deployed in the Vietnam era, post-Vietnam era and Persian Gulf/Mideast (Kline et al., 2009). Further, problematic cannabis use can lead to or exacerbate existing factors among veterans, such as poor marital relations (Bauer et al., 2005), low educational attainment (Grant et al., 2012; Lynskey & Hall, 2000), physical and mental functioning difficulties (Boden & Hoggatt, 2018; Stewart et al., 2018), along with polysubstance use (Feingold et al., 2018). Given the rise of substance use in veteran populations, it is unsurprising that rates of CUD may be heightened. For example, in a study among USA veterans between 2002 and 2009, CUD prevalence increased by more than 50%, while rates of CUD in the general population remained unchanged (Bonn-Miller et al., 2012). Overall, these findings underscore the growing importance of focusing on special populations that are susceptible to developing issues related to cannabis.

**Inpatient and Outpatient Samples.**

The recruitment of different types of ARD samples, such as inpatient, outpatient, or community samples, may affect the reported CUD prevalence. Higher rates of comorbid CUD tend to be observed amongst inpatient ARD samples, whereas, in community samples, the prevalence is often lower (Kedzior & Laeber, 2014). This is because individuals who have an ARD are found to be more likely to consume cannabis (Odds Ratio [*OR*] = 1.24) and, subsequently, are at risk of developing cannabis-related problems (e.g., CUD, *OR* = 1.68).

Similarly, Drakes et al. (2021) found that individuals seeking inpatient or outpatient treatment for EDs are 3.5-3.9 times more likely to experience OCD, demonstrating greater psychopathology that may result in more intensive interventions relative to individuals who have a comorbid ED in the community. Thus, the more intense or severe psychological conditions one presents with, the more likely one may seek professional treatment, such as inpatient care. Conversely, prevalence rates among community samples are expected to be much lower, as they often do not include a large representation of vulnerable populations such as people who are without a home, incarcerated, or seeking psychiatric/rehabilitation through institutions (Carter et al., 2013). Therefore, it is important to consider the specific characteristics of where a population is sampled to interpret the prevalence of two co-occurring conditions.

**ARD Pathology Overlap**

There are close relationships between ARDs, which is reflected in the sequence of *DSM-5* chapters, with *Obsessive-Compulsive and Related Disorders* following anxiety disorders (APA, 2013). Despite their separate chapters, *Trauma- and Stressor-Related Disorders* and *Obsessive-Compulsive and Related Disorders* retain a close relationship with anxiety disorder symptomology. For instance, common underlying constructs that encompass these three *DSM-5* categories are negative affectivity, cognitive thought processes, and coping strategies.

***Negative Affectivity (NA)***

Negative Affectivity (NA) is a trait that includes feelings of disgust, guilt, fear, and nervousness that often influence one's self-concept, cognition, emotional states, and worldview (Watson & Clark, 1984). Accordingly, NA is often present in many disorders, including anxiety, OCD, and PTSD-related disorders, being correlated with a broad range of anxiety symptoms (Watson & Clark, 1984). Moreover, those with PTSD may be misdiagnosed with anxiety or

depressive-related disorder due to NA and physiological responses being related to panic attacks or another specified ARD (Mann & Marwaha, 2023). Similarly, specific OCD subtypes that are lesser known, but highly prevalent are at an elevated risk of being misdiagnosed. For instance, somatic obsessions in OCD were most likely to be misdiagnosed as a specific phobia 40% of the time in a sample of primary-care physicians (Glazier et al., 2015). Similarly, Coles et al. (2023) found that the general population was more likely to select a possible diagnosis of GAD 41% of the time for religious-related obsessions and specific phobia 57% of the time for contamination-related obsessions. This may be due to symptom overlap related to characteristics of fear, guilt, and disgust that can be implicitly implied throughout the vignettes.

### *Cognitive Thought Processes*

Amongst ARDs, while the content of thoughts may differ, difficulty controlling unwanted negative thoughts is a common theme. For example, OCD is characterized by persistent intrusive thoughts (i.e., obsessions) that cause impairment and distress, while a hallmark of PTSD symptomology is intrusive memories, flashbacks, and negative changes in cognition (APA, 2013). While still marked by entirely different criteria, these cognitions may be maintained through shared mechanisms such as Intolerance of Uncertainty (IU). IoC is the desire to find certainty in situations that may be unpredictable, often being driven by heightened distress, such as anxiety, and is present in many ARDs (Bardeen et al., 2012; Gentes & Ruscio, 2011; McKay et al., 2015). Indeed, IoU is a risk factor for GAD and OCD (Fergus & Wu, 2009; Gentes & Ruscio, 2011) and has recently been related to PTSD symptomology (McKay et al., 2015). In GAD, individuals attempt unsuccessfully to control feelings related to worry regarding a variety of future events. Further, IoU is a specifier for worry, which is a core feature of GAD symptomology (APA, 2013; Dugas et al., 2004). When pathological, individuals with ARDs may believe that worrying can

increase control of the situation and prevent negative consequences from occurring (Dugas et al., 2004; Freeston et al., 1994).

### *Coping Strategies*

Akin to all three of these diagnostic categories is how individuals manage distress. One maladaptive coping method may be Experiential Avoidance (EA). EA can occur when an individual is unwilling to engage with internal experiences such as bodily sensations, emotions, thoughts, memories, and behavioural predispositions (Hayes et al., 1996). This is because these experiences are typically unpleasant and anxiety-provoking. While it may seem like a practical desire to avoid unwanted, distressing feelings, it becomes problematic when it is used persistently and can maintain the underlying disorder (Chawla & Ostafin, 2007).

Adverse events can be linked with neutral stimuli, wherein those stimuli can then provoke unwanted memories, thoughts, or emotions, leading to a learned pattern of avoiding that particular trigger (Mowrer, 1956). For example, SAD is characterized as the avoidance of social situations (APA, 2013). Individuals may fear rejection or how others perceive them, resulting in avoiding these events. Similarly, avoidance is a common compulsion for individuals with OCD, akin to how individuals with anxiety want to avoid or escape uncomfortable emotions, sensations, and thoughts (Akbari et al., 2022). Individuals with OCD may attempt to reduce anxiety by avoidance or escape (Foa & McLean, 2016). This is typically in the form of compulsions or rituals that are performed to prevent the feared consequences. Finally, in PTSD, individuals engage in avoidance of thoughts or situations that act as a reminder of their trauma (Foa & McLean, 2016; Sheynin et al., 2017). However, avoidance behaviour often maintains the disorder, contributing to a reinforcing cycle that only further perpetuates the distress and disorder (Hofmann & Hay, 2018).

## Comorbid CUD and ARD

Cannabis use and mental health disorders often have a bidirectional and transdiagnostic relationship. Thus, concurrent disorders, also commonly referred to as dual diagnoses, refer to the co-occurrence of a SUD and mental health problem (The Centre for Addiction and Mental Health, 2018). As previously mentioned, there is a significant lag in diagnosis for many ARDs. Due to these delays and the potential for maladaptive coping with distress, individuals may be prone to develop a secondary disorder, such as a SUD (Kushner et al., 2008; Smith & Book, 2008). In the context of cannabis use and ARD, some individuals may begin using cannabis and later develop a mental health condition (Esmaeelzadeh et al., 2018; Williams et al., 2022). Conversely, individuals may present with anxiety as the primary diagnosis and later develop CUD. However, the directionality of the association between SUD and ARD is broadly inconclusive. Reasons for the variability in findings may relate to a possible confounding variable, such as emotion dysregulation or negative affectivity. Conversely, it may be the conceptualization in the *DSM-IV* criteria differentiating abuse and dependence. For example, data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) demonstrate that anxiety disorders are more strongly associated with drug dependence (*OR* = 6.2) than abuse (*OR* = 1.7; Kushner et al., 2008).

These findings relate to several other conceptual issues noted in the *DSM-IV*, inspiring recent changes to the present *DSM-5* (APA, 1994, 2013). Firstly, while the *DSM* is currently the most consistent and standardized tool for making diagnoses, it is not without its flaws. For example, there may be false positives, wherein the boundary between what is considered "disordered" or "normal" is very small (Wakefield, 2016). It is crucial to recognize that, regardless of whether an adult presents with subclinical symptoms or meets the criteria for a disorder, they should be offered appropriate treatment to prevent the potential escalation of the condition. Additionally, there may be instances of inadvertently causing harm with diagnostic labels or

harming patients with inappropriate treatment. The *DSM-5* initially aimed to minimize these risks by dimensional diagnoses through symptom severity, incorporating biomarkers into diagnoses, reducing within-category heterogeneity, and decreasing high comorbidity rates (Wakefield, 2016). Unfortunately, many of these goals could not be carried out, and there is still room for improvement. Nonetheless, advancements were made from the *DSM-IV* to the *DSM-5*, especially in SUD conceptualization. This resulted in the removal of the legal problems criterion from the substance abuse category in the *DSM-5* due to low endorsement by the general population that disproportionally affected minority groups (Hasin et al., 2013).

Similar issues were evident throughout the abuse/dependence paradigm, prompting the category of *Substance Use Disorders* as a single construct for various substances in the *DSM-5* (Robinson & Adinoff, 2016). For instance, individuals only needed to present with one or more symptoms out of four possible symptoms to meet the criteria for substance abuse. For substance dependence, individuals were required to meet three or more symptoms in a 12-month period, closely resembling current *DSM-5* SUD/CUD criteria. Accordingly, there were circumstances where an individual would meet two substance dependence criteria but no abuse criteria, in which case they would not be given any diagnosis of a SUD (Substance Abuse and Mental Health Services Administration, 2016). Thus, given that substance abuse was perceived as a less severe disorder than substance dependence, in the *DSM-5*, abuse and dependence diagnostic criteria were combined into one disorder. Currently, individuals are required to meet at least 2 out of the 11 criteria in a 12-month period for any given SUD diagnosis (APA, 2013). Despite the recent changes in diagnostic terminology for SUDs, the greater issue that has been persistent remains: why is there a relationship between ARDs and specific SUDs, such as CUD, and how prevalent is this co-occurrence?

## Pathways Explaining Comorbidity

### *Negative Reinforcement*

Individuals with ARDs often look for means to mediate their symptoms. Emotion regulation is the ability to effectively manage, monitor, modify, and evaluate your feelings that arise from an emotional experience (Thompson, 1994). However, when individuals experience the inability to regulate their emotions, they may engage in maladaptive coping behaviours to escape or distract themselves from an aversive emotional state (Baker et al., 2004). Indeed, studies have provided empirical evidence that individuals with anxiety symptomology and SUDs have lower emotion regulation skills (Weidberg et al., 2023; Weiss et al., 2022). Under theories related to maladaptive coping via emotion dysregulation, gender differences may predict poorer outcomes for females. Weidberg et al. (2023) found that female undergraduates who consumed cannabis in the past month not only showed higher levels of stress, anxiety, and depression, but past month cannabis use had an effect on mental health problems when mediated by emotion dysregulation. Although, this was not the case for males. Thus, it appears that past-month cannabis consumers who are women who score higher on psychological distress may be at risk of experiencing poor emotion regulation. These findings are consistent with psychological research demonstrating a high prevalence of anxiety and affective disorders in women relative to men (Altemus et al., 2014). As such, emotion dysregulation may act as a precipitating factor in women, exacerbating the risk of developing cannabis use problems.

### *Self-Medication*

Self-medication or coping with underlying symptoms has been identified as a primary reason for cannabis consumption (Robinson et al., 2011; Simons et al., 1998). Unfortunately, structural adversities often put individuals at risk of not having access to mental health services,

creating an increased sense of responsibility to mitigate symptoms (Asselin et al., 2022; Hughes et al., 2001). Predictors of self-medication include self-pay healthcare costs, inaccessibility to a healthcare practitioner, prior experience with a substance, perceived complexity of the process of obtaining services, a lack of information on medical cannabis benefits, and extended wait times for service (Asselin et al., 2022; Shaghaghi et al., 2014), coupled with limited screening for substance use problems. For instance, a Canadian study found that approximately only 27% of healthcare practitioners frequently assessed for cannabis use problems (Giovanni et al., 2022).

Given that many SUDs go undetected, individuals often learn that substance use can alleviate their anxiety symptoms. This is evident among SAD and AUD, wherein individuals tend to consume alcohol to alleviate interpersonal tension in social situations (Morris et al., 2005). With cannabis, it may be the anxiolytic effects that are desirable to individuals with ARDs. Indeed, Beletsky et al. (2024) suggest in their critical review that the most probable pathway to developing comorbid CUD is self-medication. This is because anxiety acts as a precursor to cannabis use, and the inverse relationship of cannabis use causing anxiety disorders is not well-understood. However, instances have been documented where individuals who consume cannabis and had not previously sought treatment for an ARD may present in a primary care setting due to feeling symptoms consistent with an anxiety diagnosis (Keung et al., 2023; Myran et al., 2024). Yet, it is unclear whether cannabis exacerbated the underlying or sub-clinical anxiety symptoms, was causal to the development of an ARD, or was a symptom of acute cannabis toxicity. Importantly, longitudinal studies are warranted to help better understand the relationship and causality between cannabis and anxiety/ARDs. Nonetheless, cannabis has a dose-dependent relationship with anxiety, wherein low doses are anxiolytic, reducing anxiety, and high doses are anxiogenic,

inducing anxiety (Beletsky et al., 2024). In other words, this means that cannabis use may worsen anxiety-related symptoms among individuals with an underlying ARD.

In a longitudinal study based on waves I and II of the NESARC survey, Robinson et al. (2011) determined that individuals who self-medicated with substances for their ARD (GAD, SAD, PD, and Specific Phobia) were at greater risk of developing substance dependence compared to individuals with an ARD who did not self-medicate. However, the association between cannabis use and ARDs is a complex relationship that likely depends on multiple factors. For example, the Δ9-THC to CBD ratio in that higher concentrations of CBD are believed to be preferable to offset anxiety-related problems (Beletsky et al., 2024; Sharpe et al., 2020). As previously mentioned, the potency of cannabis products is very desirable for frequent non-medical consumers (Davenport, 2021; Ramaekers et al., 2020). This concerns those who consume cannabis to acquire its intoxicating effects, with some individuals willing to pay extra for more potent products (i.e., higher Δ9-THC percentage) as it is perceived as more convenient (Davenport, 2021).

**Meta-Analyses of Comorbid SUDs in ARDs**

Past literature has investigated the co-occurrence of non-clinical cannabis use in ARDs. For instance, a meta-analysis by Twomey (2017) excluded clinical samples and instead examined only associations between cannabis use and anxiety measured by self-reported scales instead of clinician interviews. Twomey (2017) also excluded studies investigating a single anxiety disorder, limiting the scope of their findings. However, they reported a small association between cannabis use and anxiety, $OR = 1.15$, suggesting a minor risk of cannabis use contributing to the escalation of anxiety symptoms.

Another meta-analysis examining epidemiological surveys for comorbid SUDs in anxiety disorders found a strong association between SUDs, mood, and anxiety disorders, with SUDs and

AD having a pooled *OR* of 2.14 to 4.19 depending on the *DSM* classification (i.e., drug dependence, abuse, or SUD; Lai et al., 2015). However, Lai et al. (2015) generalized all substances under SUDs and did not report the specific association between anxiety and CUD, relying on population-based, epidemiological surveys. Additionally, they included studies with participants as young as 15 years old, which may account for heterogeneity in estimates. While 15-year-olds may accurately represent the age of onset for some anxiety disorders, the age of initiation of cannabis in Canada is approximately 18-21 years old (Health Canada, 2021) and may be even higher in other countries. Therefore, comorbid SUDs may be inaccurate as individuals have not yet had the chance to develop and report their occurrence, resulting in potential heterogeneity.

In Kedzior and Laeber's (2014) meta-analysis, the authors included studies that reported anxiety disorders based on standardized scales in cannabis consumers or non-users with or without CUD. Specifically, they found that cohorts with anxiety experienced 1.24 odds of using cannabis and 1.68 odds of having CUD compared to those without anxiety disorders. However, they did not specify specific anxiety diagnoses as they relied on general population samples and included studies that used clinical interviews and self-reported measures to assess ARDs, while also not separating current and lifetime estimates. Although, a subgroup analysis of 11 studies revealed that individuals with a clinical diagnosis of anxiety are at 1.87 odds of having comorbid CUD relative to two studies, reporting no clinical ARD, who are at 1.14 odds of having comorbid CUD. Kedzior and Laeber (2014) also excluded studies that did not report data from healthy non-users, examining risk ratios (*RR*) between those with and without anxiety. Consequently, many studies were likely excluded if they did not have a healthy control group. Given that this study is a decade old, and cannabis legalization/decriminalization has promoted opportunities for increased access

to cannabis (Budney & Borodovsky, 2017; Imitaz et al., 2023), it is paramount to investigate areas related to CUD comorbidity.

Another meta-analysis of sex differences in CUD amongst people with comorbid mental illness found that males are twice as likely to be diagnosed with CUD, with the odds slightly lowered to 1.6 times if they have a non-specified ARD (Kozak et al., 2021). However, they included only four studies and the corresponding *OR*s instead of aggregate prevalence estimates. Further, some of the included studies were retrospective reports from hospital databases (e.g., Zhu & Wu, 2017), which can be subject to heterogeneity in estimates. Based on the aforementioned theories of emotion dysregulation conflicting with cannabis use research, it is unclear how sex differences persist in anxious clinical samples. Finally, in a systematic review and meta-analysis by Onaemo et al. (2021), they examined the comorbidity of CUD with Major Depressive Disorder (MDD) and GAD, limiting their focus to a single ARD. They did report that individuals are at approximately 3 times greater risk of having GAD along with CUD. Importantly, the directionality of this finding infers that Onaemo et al. (2021) included samples of CUD patients with comorbid GAD, along with nationally representative surveys that utilized self-reported measures (e.g., Kandel et al., 2001). In other words, this does not explore the relationship of presenting with a primary and current diagnosis of ARD and subsequently developing CUD.

While progress has been made in exploring the complex, bidirectional relationship between problematic cannabis use and ARDs, to our knowledge, no previous study has meta-analytically examined the prevalence of CUD in individuals with anxiety and related disorders. Thus, we aimed to be the first to report the aggregate global prevalence of CUD in those with anxiety and related disorders and examine moderators of the variability in estimates.

**The Present Study**

Given the apparent heterogeneity in the prevalence of CUD in ARDs, the present study initially aimed to provide a meta-analytic estimate of lifetime and current CUD comorbidity in ARDs. However, to foreshadow the results, due to the limited pool of eligible studies and profound variation in methods across those identified, a systematic review was performed instead. Although past reviews exist, it is nonetheless necessary to provide an updated systematic review, given the lack of literature reporting prevalence rates among those with an ARD and comorbid CUD. Further, whereas prior groups have attempted meta-analyses on this topic, they do not accurately discern between cannabis use and CUD, ignoring factors driving cannabis use that are not considered problematic. Moreover, different ARDs and special populations may have an especially pronounced relationship with cannabis use, leading to fluctuations in prevalence if not accounted for. Accordingly, an additional narrative review of veteran populations is presented, as we identified an equivalent number of studies pertaining to this special population. The comorbidity of CUD in ARD is multifaceted and may involve a bidirectional relationship or vary depending on the specific ARD/population studied. Therefore, establishing rigorous inclusion criteria is crucial to ensure that the focus is on examining comorbid CUD in the context of a primary ARD rather than an ARD in a primary sample of CUD.

**Hypotheses**

As noted in the preceding section, it had been our intention to conduct a meta-analysis. With that in mind, it had been hypothesized that the prevalence of comorbid CUD would be greater amongst inpatient or outpatient ARD samples than community ARD samples. It was also predicted that more recent studies would have a higher prevalence of comorbid CUD than earlier studies. Further, anxiety samples with a higher percentage of men were predicted to have a greater CUD prevalence. Finally, it was hypothesized that those with ARD would be at greater risk of CUD than

those without ARD. We had also intended to audition a variety of moderator variables (e.g., year of publication, country, population, diagnostic criteria, diagnostic interview, mean age, age of ARD onset, duration of ARD, ARD subtype, and study quality). These hypotheses will still be evaluated from a narrative perspective, although due to our shift toward systematic review rather than meta-analysis, we are no longer able to evaluate them empirically.

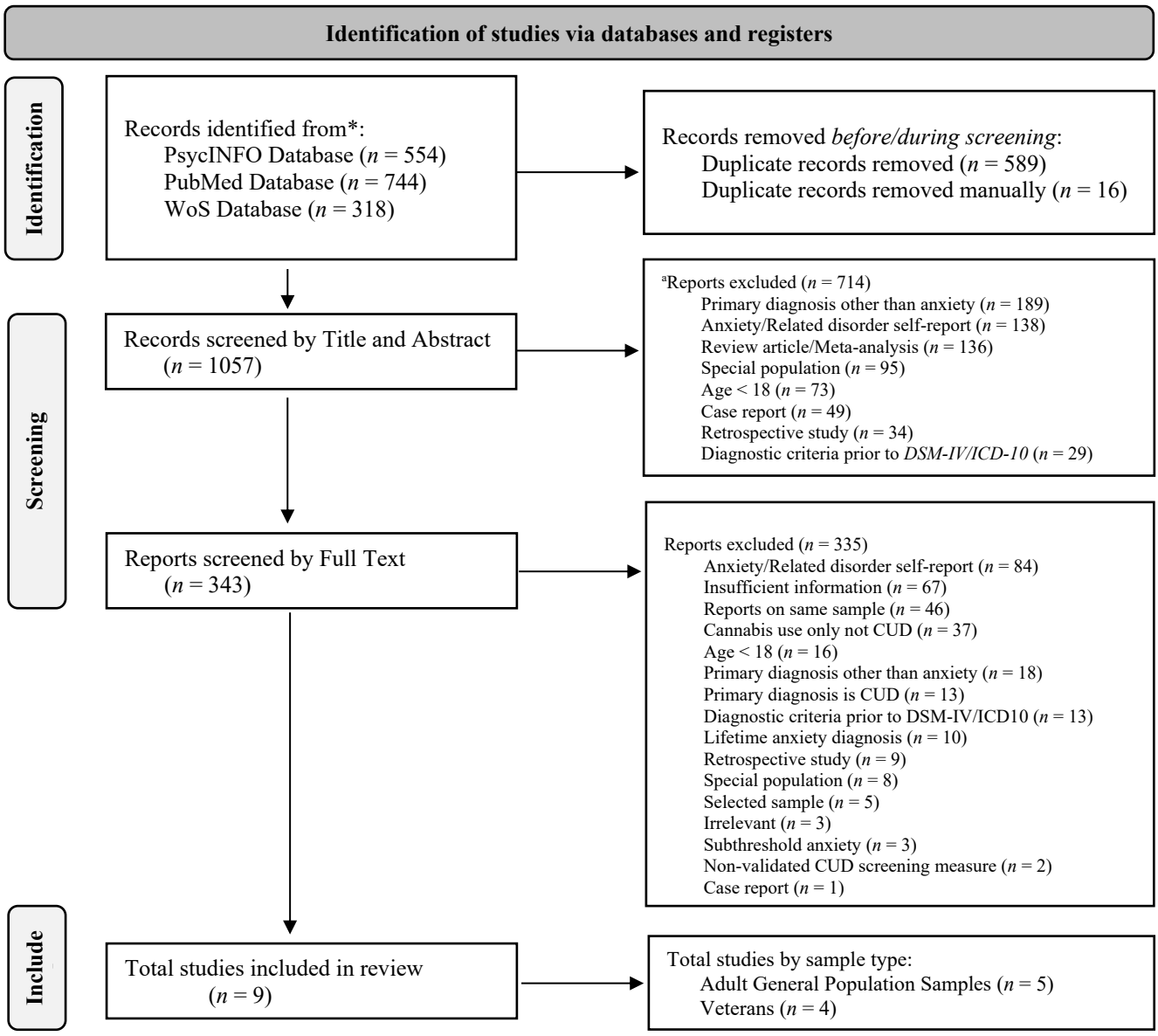
## Method

### Data Sources and Search Strategy

A systematic literature search was conducted online (see Figure 1 and Table 1), consisting of *PubMed*, *PsycINFO*, and *Web of Science* databases, resulting in a total of 1646 articles. The search adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Moher et al., 2009; Page et al., 2021) and Synthesis Without Meta-analysis (SWiM) items (Campbell et al., 2020) outlined in Tables 2 and 3. It is recommended that SWiM guidelines be used as a complement to PRISMA guidelines (Campbell et al., 2020). A research librarian at Memorial University of Newfoundland's Queen Elizabeth II Library was consulted for this study to ensure that the keywords and controlled terms utilized for anxiety and related disorders and CUD accurately reflected the literature of interest (see Table 1 for a description of the search terms). A computer-based search was conducted on January 24, 2023, without date or language restrictions. After removing duplicates, titles and abstracts were screened independently by at least two reviewers in *Covidence* (Covidence Systematic Review Software, 2023) to determine if the articles met the inclusion criteria. Articles deemed relevant underwent full-text review to determine their eligibility and were independently screened by at least two reviewers. All conflicts were resolved through discussion. Finally, this review was not pre-registered with any database, and there were no competing conflicts of interest from the authors.

**Figure 1**

*Prisma Flowchart*




*Note.* [a]Records excluded in the Title and Abstract phase do not add up to the total excluded as there were instances of multiple exclusions.

From: Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., et al. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. https://doi.org/10.1136/bmj.n71

**Table 1**

*Description of Search Terms by Database*

| Database | Search Terms |
|---|---|
| PsycINFO | (("Anxiety disorder" OR "Anxiety Disorders" OR "Panic Disorder" OR "Agoraphobia" OR "Generalized Anxiety Disorder" OR "GAD" OR "Social Phobia" OR "Social Anxiety Disorder" OR "Specific Phobia" OR "Phobic Disorder" OR "Selective Mutism" OR "Mutism" OR "Separation Anxiety Disorder" OR "Obsessive-Compulsive Disorder" OR "OCD" OR "Body Dysmorphic Disorder" OR "Hoarding Disorder" OR "Trichotillomania" OR "Hair-pulling Disorder" OR "Excoriation" OR "Skin picking disorder" OR "Other Specified Obsessive-Compulsive and Related Disorder" OR "Unspecified Obsessive-Compulsive and Related Disorder" OR "Post-traumatic Stress Disorder" OR "PTSD" OR "Reactive Attachment Disorder" OR "Disinhibited Social Engagement Disorder" OR "Acute Stress Disorder" OR "Adjustment Disorder" OR "Other Specified Trauma- and Stressor-Related Disorder" OR "Unspecified Trauma and Stressor-Related Disorder" OR "Anxiety Not Otherwise Specified" OR "Anxiety NOS") AND (“Cannabis Use Disorder” OR “CUD” OR “Marijuana Use Disorder” OR “MUD” OR “Cannabis Dependence” OR “Cannabis Abuse” OR “Cannabis Addiction” OR “Marijuana Addiction” OR “Marijuana Dependence” OR “Marijuana Abuse” OR “Marijuana Use Problems” OR “Cannabis Use Problems” OR “Marijuana-Related Disorder” OR “Cannabis-Related Disorder” OR “Marijuana Related Disorders” OR “Cannabis Related Disorders” OR “Marijuana Use Problem” OR “Cannabis Use Problem”)) |
| PubMed | **S1:** ("Anxiety Disorders"[Mesh] OR "Stress Disorders, Post-Traumatic"[Mesh]) AND ("Marijuana Abuse"[Mesh] OR “Marijuana Smoking”[Mesh])<br>**S2:** (("Anxiety disorder" OR "Anxiety Disorders" OR "Panic Disorder" OR "Agoraphobia" OR "Generalized Anxiety Disorder" OR "GAD" OR "Social Phobia" OR "Social Anxiety Disorder" OR "Specific Phobia" OR "Phobic Disorder" OR "Selective Mutism" OR "Mutism" OR "Separation Anxiety Disorder" OR "Obsessive-Compulsive Disorder" OR "OCD" OR "Body Dysmorphic Disorder" OR "Hoarding Disorder" OR "Trichotillomania" OR "Hair-pulling Disorder" OR "Excoriation" OR "Skin picking disorder" OR "Other Specified Obsessive-Compulsive and Related Disorder" OR "Unspecified Obsessive-Compulsive and Related Disorder" OR "Post-traumatic Stress Disorder" OR "PTSD" OR "Reactive Attachment Disorder" OR "Disinhibited Social Engagement Disorder" OR "Acute Stress Disorder" OR "Adjustment Disorder" OR "Other Specified Trauma- and Stressor-Related Disorder" OR "Unspecified Trauma and Stressor-Related Disorder" OR "Anxiety Not Otherwise Specified" OR "Anxiety NOS") AND (“Cannabis Use Disorder” OR “CUD” OR “Marijuana Use Disorder” OR “MUD” OR “Cannabis Dependence” OR “Cannabis Abuse” OR “Cannabis Addiction” OR “Marijuana Addiction” OR “Marijuana Dependence” OR “Marijuana Abuse” OR “Marijuana Use Problems” OR “Cannabis Use Problems” OR “Marijuana-Related Disorder” OR “Cannabis-Related Disorder” OR “Marijuana Related Disorders” OR “Cannabis Related Disorders” OR “Marijuana Use Problem” OR “Cannabis Use Problem”))<br>**S3:** #1 OR #2 |
| Web of Science | (("Anxiety disorder" OR "Anxiety Disorders" OR "Panic Disorder" OR "Agoraphobia" OR "Generalized Anxiety Disorder" OR "GAD" OR "Social Phobia" OR "Social Anxiety Disorder" OR "Specific Phobia" OR "Phobic Disorder" OR "Selective Mutism" OR "Mutism" OR "Separation Anxiety Disorder" OR "Obsessive-Compulsive Disorder" OR "OCD" OR "Body Dysmorphic Disorder" OR "Hoarding Disorder" OR "Trichotillomania" OR "Hair-pulling Disorder" OR "Excoriation" OR "Skin picking disorder" OR "Other Specified Obsessive-Compulsive and Related Disorder" OR "Unspecified Obsessive-Compulsive and Related Disorder" OR "Post-traumatic Stress Disorder" OR "PTSD" OR "Reactive Attachment Disorder" OR "Disinhibited Social Engagement Disorder" OR "Acute Stress Disorder" OR "Adjustment Disorder" OR "Other Specified Trauma- and Stressor-Related Disorder" OR "Unspecified Trauma and Stressor-Related Disorder" OR "Anxiety Not Otherwise Specified" OR "Anxiety NOS")) AND ((“Cannabis Use Disorder” OR “CUD” OR “Marijuana Use Disorder” OR “MUD” OR “Cannabis Dependence” OR “Cannabis Abuse” OR “Cannabis Addiction” OR “Marijuana Addiction” OR “Marijuana Dependence” OR “Marijuana Abuse” OR “Marijuana Use Problems” OR “Cannabis Use Problems” OR “Marijuana-Related Disorder” OR “Cannabis-Related Disorder” OR “Marijuana Related Disorders” OR “Cannabis Related Disorders” OR “Marijuana Use Problem” OR “Cannabis Use Problem”)) |

**Table 2**

*PRISMA 2020 Item Checklist*

| Section/Topic | Item # | Checklist Item | Location Where Item is Reported |
|---|---|---|---|
| TITLE | | | |
| Title | 1 | Identify the report as a systematic review. | i |
| ABSTRACT | | | |
| Structured summary | 2 | Followed PRISMA abstract guidelines | ii |
| INTRODUCTION | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | 20-23 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | 23 |
| METHODS | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | 33-34 |
| Information sources | 6 | Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | 24-26 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | 24-26 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | 24-25 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming | 34-35, 46-48 |

| | | | |
|---|---|---|---|
| | | data from study investigators, and if applicable, details of automation tools used in the process. | |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | 34-35, 47-49 |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | 34-35, 47-49 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | 35 |
| Effective measures | 12 | Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results. | 36 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5). | 35-36 |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | 35-36 |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | 35-36 |
| | 13d | Describe any methods used to synthesise results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | 35-36 |

| | | | |
|---|---|---|---|
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta regression). | 35-36 |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesised results. | 36 |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | 35 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | 36-37 |
| RESULTS | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram | 26 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | 42-43 |
| Study characteristics | 17 | Cite each included study and present its characteristics. | 46-48 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | 37-38 |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots. | 47-48, 50, 62 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | 40 |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | 50, 62 |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | 60, 67 |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesised results. | 36 |

| | | | |
|---|---|---|---|
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | 39 |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | 42-43 |
| DISCUSSION | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | 68-86 |
| | 23b | Discuss any limitations of the evidence included in the review. | 86-88 |
| | 23c | Discuss any limitations of the review processes used. | 86-88 |
| | 23d | Discuss implications of the results for practice, policy, and future research. | 82-86 |
| OTHER INFORMATION | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | 24 |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | 24 |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | 24 |
| Support | 25 | Describe sources of financial or nonfinancial support for the review, and the role of the funders or sponsors in the review. | iii |
| Competing interests | 26 | Declare any competing interests of review authors. | 24 |
| Availability of data, code, and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | 24-27, 33-42, 47-48 |

**Table 3**

*Synthesis Without Meta-analysis (SWiM) Guidelines*

| SWiM Reporting Item | Item description | Location Where Item is Reported |
|---|---|---|
| METHODS | | |
| 1. Grouping studies for synthesis | 1a. Provide a description of, and rationale for, the groups used in the synthesis (e.g., groupings of populations, interventions, outcomes, study design). | 35 |
| | 1b. Detail and provide rationale for any changes made subsequent to the protocol in the groups used in the synthesis. | 24 |
| 2. Describe the standardized metric and transformation methods used | 2. Describe the standardised metric for each outcome. Explain why the metric(s) was chosen and describe any methods used to transform the intervention effects, as reported in the study, to the standardized metric, citing any methodological guidance consulted. | 36 |
| 3. Describe the synthesis methods | 3. Describe and justify the methods used to synthesise the effects for each outcome when it was not possible to undertake a meta-analysis of effect estimates. | 34-36 |
| 4. Criteria used to prioritize results for summary and synthesis | 4. Where applicable, provide the criteria used, with supporting justification, to select the particular studies, or a particular study, for the main synthesis or to draw conclusions from the synthesis (eg, based on study design, risk of bias assessments, directness in relation to the review question). | 33-37 |
| 5. Investigation of heterogeneity in reported effects | 5. State the method(s) used to examine heterogeneity in reported effects when it was not possible to undertake a meta-analysis of effect estimates and its extensions to investigate heterogeneity. | 36 |
| 6. Certainty of evidence | 6. Describe the methods used to assess the certainty of the synthesis findings. | 36-37 |
| 7. Data presentation methods | 7a. Describe the graphical and tabular methods used to present the effects (eg, tables, forest plots, harvest plots). | 35-46 |
| | 7b. Specify key study characteristics (e.g., study design, risk of bias) used to order the studies, in the text and any tables or graphs, clearly referencing the studies included. | 35-37 |
| RESULTS | | |
| 8. Reporting results | 8. For each comparison and outcome, provide a description of the synthesised findings and the certainty of the findings. Describe the result in language that is consistent with the question the synthesis addresses, and indicate which studies contribute to the synthesis. | 43-68 |
| DISCUSSION | | |
| 9. Limitations of the synthesis | 9. Report the limitations of the synthesis methods used and/or the groupings used in the synthesis and how these affect the conclusions that can be drawn in relation to the original review question. | 86-88 |

**Inclusion Criteria**

Each article was independently screened by at least two reviewers for the title and abstract, with a subset undergoing full-text review to determine its eligibility for inclusion in this systematic review. To be eligible for inclusion: (a) participants had to be at least 18 years of age or older; (b) participants had to be prospectively assigned a diagnosis of a current ARD as defined by either *International Classification of Diseases* (*ICD-10; ICD-11;* WHO, 2016a; 2021) or *Diagnostic and Statistical Manual of Mental Disorders* criteria (*DSM-IV; DSM-5*, APA, 1994; 2013) supported by a clinician interview or a semi-structured/structured interview (e.g., The Structured Clinical Interview for *DSM-5* Disorders; SCID-5, First et al., 2016); c) given the relative scarcity of use of semi-structured/structured diagnostic interviews in the literature for CUD, we allowed studies utilizing both empirically validated screening tools based on *DSM* or *ICD* criteria for CUD diagnoses (all current/lifetime CUD estimates were based on empirically validated screening tools according to the *DSM* or *ICD*; e.g., Cannabis Use Disorders Identification Test-Revised, CUDIT-R; Adamson et al., 2010) or semi-structured/structured diagnostic measures; (d) articles reported the prevalence of current or lifetime CUD in a primary sample of individuals with a current ARD (e.g., anxiety disorders, obsessive-compulsive and related disorders, or trauma-and-stressor-related disorders); (e) all articles reported the lifetime or current prevalence of CUD (e.g., *DSM-5*), cannabis dependence, or abuse (e.g., *DSM-IV*)[1]; and (f) studies were required to recruit representative samples.

**Exclusion Criteria**

[1] Instances of only cannabis dependence were used when cannabis abuse/dependence or cannabis abuse plus dependence categories were not mutually exclusive.

Exclusion criteria for this meta-analysis consisted of the following: (a) failure to use a diagnostic interview or full diagnostic criteria for anxiety and related disorders was not assessed; (b) failure to use a validated screening measure for CUD; (c) studies that reported the prevalence of anxiety and related disorders in CUD samples, or samples with a primary diagnosis of CUD (e.g., studies that recruited participants in treatment for SUDs); (d) retrospective studies or chart reviews; (e) fell below the minimum age requirement; (f) special populations/non-representative samples (e.g., prison sample); (g) review/meta-analysis articles only; (h) insufficient information was presented to compute prevalence estimates; (i) only incidence was reported; (j) sample sizes of less than 20 participants; and (k) studies that used diagnostic criteria prior to *DSM-IV* (e.g., *DSM-III*, *DSM-III-R*, *ICD-9*; APA, 1980, 1987; WHO 1978). In the case of multiple publications that seemed to originate from the same sample (e.g., with an overlap in time of participant recruitment and similar authors), the publication with the largest sample size, or that was most informative, was retained for extraction. Where applicable, authors were contacted for clarification. Finally, veteran samples were included in the review given the near equal representation alongside general population samples in our search, although they will be reviewed separately.

**Data Extraction and Screening**

The following data were extracted from each article: a) author name, b) year of publication, c) sample size, d) sample type (inpatient, outpatient, community, control, or veteran), e) country, f) region, g) mean age and age range, h) gender, i) percent female, j) participation rate, k) diagnostic criteria, l) anxiety diagnostic measure, m) CUD diagnostic measure, n) prevalence window for CUD (lifetime and/or current); o) CUD prevalence; and p) CUD prevalence in cannabis consumers. However, other variables were added during the

extraction phase given their availability (e.g., percent comorbid disorders [in addition to anxiety being the primary presenting concern], the percentage using cannabis, and the percentage who ever used medicinal cannabis). Control samples were operationally defined as individuals without a diagnosis of ARD who were evaluated for CUD. Furthermore, additional data were unable to be extracted for all studies due to the lack of reporting. This included years of education, ethnicity, marital status, age of ARD onset, ARD duration, CUD onset, CUD duration, CUD frequency, and age of initiation for cannabis. All studies were extracted independently by A. R. L. C. with a review by E. J. F.

**Risk of Bias and Quality Assessment**

Risk of bias and study quality ratings were examined using a 10-point assessment adapted from previous studies for clinical epidemiological research and meta-analyses (Agar et al., 2021; Drakes et al., 2021; Fawcett et al., 2019; Fawcett et al., 2020; Froude et al., 2024; Giannakopoulos et al., 2012; Hoy et al., 2012; Russell et al., 2013). Table 4 provides a list of the items along with a scoring guide, where higher scores indicated greater study quality. To assess study quality, each article was scored by A.R.L.C. and can be found in Table 5.

**Approach to Evidence Synthesis**

A narrative synthesis following SWiM guidelines was conducted to report evidence in accordance with these guidelines, as there were insufficient studies to report a meta-analysis. Throughout the study screening phases, sufficient veteran studies were identified to include a synthesis of that literature also. Thus, two separate syntheses were performed. The first dealt with adult general population samples diagnosed with ARDs (general public, community, inpatient, or outpatient samples), while the second dealt with veteran samples. The order of the synthesis is organized via subheadings in accordance with the study's hypotheses. Finally, two

forest plots were generated in *RStudio 4.3.2* and *R 4.3.2* (2023-10-31; R Core Team, 2023) using the *metafor* package (Viechtbauer, 2010) for data visualization of confidence intervals and the raw proportion for each study within the respective synthesis. Because we were interested in the epidemiology of CUD, the most meaningful measure was the untransformed raw prevalence (as percentages) of the total ARD sample that has been diagnosed with CUD. However, Risk Ratios (RR) were extracted or calculated for some studies when applicable, along with the percentage of cannabis consumers with CUD. The studies were arranged from lowest to highest reported prevalence estimates, separated by current (CUD at baseline, past-year, etc.) and lifetime (experienced CUD at any point in their lives) estimates for each sample. This was to accentuate the degree of heterogeneity among included studies. Finally, the adult general population and veteran samples are performed as two separate systematic reviews throughout, including separate tables, forest plots, and syntheses. Each study characteristics table is organized alphabetically, while the study quality ratings in Table 5 are organized from lowest to highest quality. Because a meta-analysis was unable to be conducted, heterogeneity was discussed narratively, while sensitivity analyses were unable to be conducted. Similarly, our methods for assessing the risk of bias are highlighted in Table 4 which include items related to the assessment of risk of bias. Because a narrative review was conducted, there were no issues with missing items, as each study was required to report a prevalence rate to be eligible for inclusion in this review.

**Assessing Certainty in Evidence**

As recommended by Murad et al. (2017), confidence in evidence pertaining to narrative reviews in the absence of a single estimate of effect for observational studies was assessed in accordance with the Grading of Recommendation, Assessment, Development, and Evaluation-Confidence in the Evidence (GRADE; Balshem et al., 2011). Five components were considered

for this approach: 1) methodological limitations of the studies/risk of bias; 2) indirectness of evidence; 3) imprecision of effect estimates; 4) inconsistency/heterogeneity; and 5) risk of publication bias. Confidence ratings started at "serious" (a synonymous "low" rating is recommended for observational studies) and were downgraded by one or more levels if there were concerns regarding individual components or upgraded by one or more levels if applicable (see Table 6 and Table 7 for confidence in evidence ratings for each synthesis). Finally, there is no concern with respect to publication bias, as the underlying assumptions as to how unpublished studies are censored are not generally applicable to the field of epidemiology (Borenstein, 2019).

## Table 4

*Scoring Criteria for Quality Ratings*

| | Item | Scoring Guide | Source |
|---|---|---|---|
| 1. | Was the population clearly defined with demographic characteristics of the study population? (e.g., age, sex, ethnicity, martial status, education, sample type [community, outpatient, inpatient]) | **0** = Not reported in the article/only one or two of the above<br>**1** = Three or more of the above listed | Adapted from Giannakopoulos et al. (2012), variations used in Drakes et al. (2021); Fawcett et al. (2019; 2020); Froude et al. (2024); Russell et al. (2013) |
| 2. | Was the study's sample a close representation of the target population? | **0** = Not a close representation of the target population (90%+ all one gender or ethnicity, strict exclusion criteria, selected sample, or high-risk sample)<br>**1** = Close representation to the target population (e.g., mixed of genders/ethnicities) | Adapted from Hoy et al. (2012); used in Drakes et al. (2021) and Froude et al. (2024) |
| 3. | Was the setting of the study clearly described? (e.g., location and relevant dates or length of recruitment, data collection) | **0** = Not reported directly in the article/only 1 reported<br>**1** = Both reported | Adapted from Fawcett et al. (2019); Froude et al. (2024) |
| 4. | What type of sampling method was employed? | **0** = Not reported, or single restricted non-random sample (e.g., convenience or consecutive sample with patients recruited from a single clinic or region, or a previous research study)<br>**1** = random sample, or multiple restricted non-random sample (e.g., convenience or consecutive sample with patients recruited from more than one clinic or region, or across several previous research studies) | Adapted from Agar et al. (2021) |
| 5. | Was the likelihood of non-response bias minimal? | **0** = The response/participation rate after participants were deemed to meet inclusion/exclusion criteria for the study was < 75%, not reported, or an analysis was performed comparing responders and non-responders showing significant differences in relevant demographic characteristics<br>**1** = The response/participation rate after participants were deemed to meet inclusion/exclusion criteria for the study was 75% or higher or an analysis was performed comparing responders and non-responders which did not show significant difference in relevant demographic characteristics | Adapted from Hoy et al. (2012); variations used in Drakes et al. (2021); Fawcett et al. (2019; 2020); Froude et al. (2024); Russell et al. (2013) |
| 6. | Was the prevalence of CUD broken down according to ARD? | **0** = No report of CUD prevalence by ARD even if ARD subtype data is available<br>**1** = Inclusion of CUD prevalence by ARD reported/ only 1 ARD examined as per study objectives | Adapted from Drakes et al. (2021) |
| 7. | Were the eligibility criteria clearly specified? | **0** = neither specified in the article<br>**1** = Inclusion or exclusion criteria clearly specified in text | Used in Fawcett et al. (2020) |

| | | | |
|---|---|---|---|
| 8. | Who administered the diagnostic interview(s)? | **0** = Not reported, trained lay person, research assistant<br>**1** = Psychiatrist, Psychologist, Physician, Resident, or Mental Health Professional, or supervised trainee | Adapted from Drakes et al. (2021); Fawcett et al. (2019; 2020); Russell et al. (2013) |
| 9. | Was the prevalence window for CUD clearly defined? | **0** = Inference based on the measure used and method<br>**1** = Clearly identified in-text (e.g., 'lifetime'; specifying how 'current' was defined (e.g., 1 month') | Adapted from Fawcett et al. (2019), used in Drakes et al. (2021) and Froude et al. (2024) |
| 10. | Was a control group of individuals without ARD included to measure CUD prevalence? | **0** = No<br>**1** = Yes | Adapted from Froude et al. (2024) |

## Table 5

*Quality Rating Score Breakdown*

| First Author and Year Published | 1. Was the population clearly defined with demographic characteristics? | 2. Was the study's sample a close representation of the target population? | 3. Was the setting of the study clearly described? | 4. What type of sampling method was employed? | 5. Was the likelihood of non-response bias minimal? | 6. Was the prevalence of CUD broken down by ARD? | 7. Were the study inclusion/exclusion criteria clearly specified in-text? | 8. Who administered the diagnostic interview(s)? | 9. Was the prevalence window for CUD clearly defined? | 10. Was there a control group? | Total Score |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Adult General Population Samples** | | | | | | | | | | | |
| Tepe (2012) | ✓ | ✓ | ✗ | ✗ | ✗ | ✓ | ✗ | ✓ | ✗ | ✗ | **4** |
| Martins (2011) | ✗ | ✓ | ✓ | ✓ | ✓ | ✗ | ✗ | ✗ | ✓ | ✗ | **5** |
| Bedard-Gilligan (2018) | ✓ | ✓ | ✗ | ✓ | ✗ | ✓ | ✓ | ✗ | ✓ | ✗ | **6** |
| Degenhardt (2001) | ✓ | ✓ | ✓ | ✓ | ✓ | ✗ | ✓ | ✗ | ✓ | ✗ | **7** |
| Bilevicius (2019) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✗ | ✓ | ✓ | **9** |
| **Veteran Samples** | | | | | | | | | | | ***M* = 6.2** |
| Metrik (2022) | ✓ | ✗ | ✓ | ✗ | ✗ | ✓ | ✓ | ✗ | ✓ | ✗ | **5** |
| Bonn-Miller (2013) | ✓ | ✗ | ✓ | ✗ | ✗ | ✓ | ✓ | ✓ | ✓ | ✗ | **6** |
| Patel (2021) | ✓ | ✓ | ✗ | ✗ | ✗ | ✓ | ✓ | ✓ | ✓ | ✗ | **6** |
| Dillon (2021) | ✓ | ✓ | ✓ | ✓ | ✗ | ✓ | ✓ | ✗ | ✓ | ✗ | **7** |
| | | | | | | | | | | | ***M* = 6** |

*Note*. Low quality = 0-3; Moderate quality = 4-6; High quality = 7-10.

**Table 6**

*Confidence in the Evidence in the Absence of a Single Estimate of Effect for Adult General Population Sample*

| GRADE domain | Guidelines from Murad et al. (2017) | Judgement | Concerns about the certainty of the domain |
|---|---|---|---|
| Methodological limitations of the studies/Risk of Bias | Make a judgement on the risk of bias across studies for an individual outcome. A sensitivity analysis is not possible to determine if the effect changes when studies at high risk of bias are excluded. It is possible to consider the size of a study, its risk of bias and the impact it would have on the summarised effect. | Three out of five studies were from nationally representative samples in their respective regions (USA and Australia). The mean quality ratings across studies was 6.2. Sample sizes ranged from 200 to 7437. | Not serious, borderline |
| Indirectness of evidence | Make a global judgement on how dissimilar the research evidence is to the clinical question at hand (in terms of population, interventions and outcomes across studies). | Research is dissimilar: 3 studies are cross-sectional nationally representative samples; one study examined treatment dropout of inpatient/community sample; one study is an outpatient sample. | Serious |
| Imprecision of effect estimates | Consider the optimal information size (or the total number of events for binary outcomes and the number of participants in continuous outcomes) across all studies. A threshold of 400 or less is concerning for imprecision. Results may also be imprecise when the confidence intervals (CIs) of all the studies or of the largest studies include no effect and clinically meaningful benefits or harms. | The total number of participants included in all samples were 10,896. One study had less than 400 participants ($n$ = 200), all other studies had relatively moderate or large sample sizes for the target population. | Serious |
| Inconsistency/Heterogeneity | Judge inconsistency by evaluating the consistency of the direction and primarily the difference in the magnitude of effects across studies (since statistical measures of heterogeneity are not available). Widely differing estimates of the effects indicate inconsistency | The estimated prevalence varied across the different studies; two studies combined disorders into an overall estimate, two studies provided current estimate, three studies provided lifetime estimates. Mostly White females represented among samples, variation in diagnostic administration. | Serious |
| Risk of publication bias | Publication bias can be suspected when the body of evidence consists of only small positive studies or when studies are reported in trial registries but not published. Statistical evaluation of publication bias is not possible in this case. Publication bias is more likely if the search of the systematic review is not comprehensive. | The search was comprehensive. There is no concern with respect to publication bias as underlying assumptions are not readily applicable to prevalence estimates (Borenstein, 2019). Therefore, risk of publication bias is low. | Not suspected |
| Factors that can raise certainty in evidence: | If one of the three domains that can increase certainty in a body of evidence (typically from non-randomized studies) is noted, consider rating up the grade of certainty, particularly if it is noted in the majority of studies. | More randomization when selecting samples, differentiation of disorders per estimate, recent publications based on *DSM-5* or *ICD-11* criteria, including more males in the primary sample, clinician's administrated diagnostic assessments, identify and perform statistical analyses on non-participant characteristics, adding control groups | - |

*Note*. The outcome of interest is the prevalence of cannabis use disorder in anxiety or related disorders. The table and contents are adapted from Murad et al. (2017) and Balshem et al. (2011). Possible ratings ranged from not suspected, not serious, borderline, serious, very serious.

## Table 7

*Confidence in the Evidence in the Absence of a Single Estimate of Effect for Veteran Sample*

| GRADE domain | Guidelines from Murad et al. (2017) | Judgement | Concerns about the certainty of the domain |
|---|---|---|---|
| Methodological limitations of the studies/Risk of Bias | Make a judgement on the risk of bias across studies for an individual outcome. A sensitivity analysis is not possible to determine if the effect changes when studies at high risk of bias are excluded. It is possible to consider the size of a study, its risk of bias and the impact it would have on the summarised effect. | All studies were from the USA. The mean quality ratings across studies was 6. Sample sizes ranged from 47 to 926. | Very serious |
| Indirectness of evidence | Make a global judgement on how dissimilar the research evidence is to the clinical question at hand (in terms of population, interventions and outcomes across studies). | Females severely underrepresented in half the veteran studies. Samples are a mix of inpatient, outpatient, and community veterans from the USA. | Serious |
| Imprecision of effect estimates | Consider the optimal information size (or the total number of events for binary outcomes and the number of participants in continuous outcomes) across all studies. A threshold of 400 or less is concerning for imprecision. Results may also be imprecise when the CIs of all the studies or of the largest studies include no effect and clinically meaningful benefits or harms. | The total number of participants included in all samples were 1329. Two studies had less than 100 participants, while the other two studies had > 400. Only one study used the CAPS to make PTSD diagnosis, while all other studies used the SCID. | Serious |
| Inconsistency/Heterogeneity | Judge inconsistency by evaluating the consistency of the direction and primarily the difference in the magnitude of effects across studies (since statistical measures of heterogeneity are not available). Widely differing estimates of the effects indicate inconsistency | All studies examined PTSD using similar methods to make the diagnosis. Mostly White males represented among samples. | Serious |
| Risk of publication bias | Publication bias can be suspected when the body of evidence consists of only small positive studies or when studies are reported in trial registries but not published. Statistical evaluation of publication bias is not possible in this case. Publication bias is more likely if the search of the systematic review is not comprehensive. | The search was comprehensive, and no studies included a control group. There is no concern with respect to publication bias as underlying assumptions are not readily applicable to prevalence estimates (Borenstein, 2019). Therefore, risk of publication bias is low. | Not suspected |
| Factors that can raise certainty in evidence | If one of the three domains that can increase certainty in a body of evidence (typically from non-randomized studies) is noted, consider rating up the grade of certainty, particularly if it is noted in the majority of studies. | More randomization, females underrepresented in veteran studies, potential confounds need to be considered (e.g., combat type, sample type). | - |

*Note*. The outcome of interest is the prevalence of cannabis use disorder in anxiety or related disorders. The table and contents are adapted from Murad et al. (2017) and Balshem et al. (2011). Possible ratings ranged from not suspected, not serious, borderline, serious, very serious.

# Results

## Identification of Studies

As shown in Figure 1, of the initial 1646 articles retrieved in the search, after removing duplicates 1057 unique citations were screened by title and abstract review, with 343 articles undergoing full-text review, and a total of 9 total studies ultimately fulfilling inclusion criteria. Five of the studies came from representative samples of the target population (Bedard-Gilligan et al., 2018; Bilevicius et al., 2019; Degenhardt et al., 2001; Martins & Gorelick, 2011; Tepe et al., 2012), whereas a separate four studies were retained relating to veteran samples (Bonn-Miller et al., 2013; Dillon et al., 2021; Metrik et al., 2022; Patel et al., 2021). Importantly, all articles were original reports and identified through the search. While attempts were made to investigate reference lists and included studies from other meta-analyses in the area, none met our inclusion criteria. The percentage agreement between the two reviewers was high for the title and abstract screening, at 92.43%, and the full-text screening, at 98.54%.

The most common reasons for exclusion at the title and abstract stage were due to a primary diagnosis other than an ARD (e.g., Bipolar Disorder, Mood Disorder, Schizophrenia, etc.), self-reported measures being utilized to diagnose the ARD(s), and/or the article reporting a review or meta-analysis rather than primary research. Articles progressed to full-text review unless it was deemed explicitly clear in the abstract that the study would not meet inclusion criteria. The most common reasons for exclusion during the full-text review were self-reported measures used for ARD diagnoses (e.g., Kroon et al., 2023), insufficient information available to determine prevalence estimates (e.g., Hines et al., 2020), and reports originating from the same sample (e.g., Feingold et al., 2016). Notably, wave II of the NESARC, a large cross-sectional study, was intentionally excluded as participants from wave I were resampled; however, wave III

is reported as an independent sample (Hasin & Grant, 2015; Tebeka et al., 2020). Thus, one report was retained from the wave I, while another report was retained from wave III. Finally, authors were contacted in instances where insufficient information was available in-text.

## Study Characteristics

### *Adult General Population Samples*

Table 8 outlines the characteristics of the articles included and their corresponding sample characteristics. In total, 10,896 participants were included in the adult general population sample, with sample sizes ranging from 200 to 7437. The age of the samples ranged from 18-65+, with an overall mean age of 38.8 (*SD* = 6.1). Further, 60% of the studies were recruited from the community, 20% from outpatient clinics, and 20% from a mix of inpatient and outpatient sources. Eighty percent of the studies were from the USA, with the remaining study (20%) taking place in Australia (Degenhardt et al., 2001). The average percentage of females was 69.8%, with 72% of the total sample identifying as White. Regarding ARD and CUD diagnostic criteria, 80% of the studies reported using *DSM-IV* criteria, while one study (20%) used *DSM-5* criteria to make diagnoses. However, the ARD diagnostic measures varied, with 40% using the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS), a fully structured diagnostic interview designed for trained lay interviewers (Grant et al., 2001). The remainder of the samples used either the PTSD Symptom Scale Interview (PSSI; Foa et al., 2016; 20%), the Composite International Diagnostic Interview (CIDI; WHO, 1993; 20%), or the Structured Clinical Interview for *DSM* Disorders (SCID; First et al., 2016; 20%) to make diagnoses. In terms of CUD diagnostic measures, 40% used the SCID, 40% used the AUDADIS, and one study (20%) used the CIDI. Three of the studies (60%) only provided lifetime estimates of comorbid CUD in an ARD (Bedard-Gilligan et al., 2018; Martins &

Gorelick, 2011; Tepe et al., 2012), while the other two studies (40%) provided current estimates (Bilevicius et al., 2019; Degenhardt et al., 2001).

Two studies exclusively reported comorbid CUD prevalence in PTSD (Bedard-Gilligan et al., 2018; Bilevicius et al., 2019); one study examined comorbid CUD prevalence in SAD (Tepe et al., 2012); and the other two studies reported the prevalence of comorbid CUD in any anxiety disorder (e.g., PD, agoraphobia, specific phobia, SAD, and GAD among comorbid CUD, Martins & Gorelick, 2011; SAD, agoraphobia, PD, GAD, OCD, and PTSD with comorbid CUD, Degenhardt et al., 2001). Of these five studies, only Bilevicius et al. (2019) included a control sample (i.e., a sample evaluated for CUD which did not have a diagnosed ARD). Importantly, none of these studies required prior cannabis use as an inclusion criterion.

Studies conducted by Martins and Gorelick (2011) and Bilevicius et al. (2019) were based on data from the NESARC, waves I and III, respectively. This large-scale nationally representative study was based on noninstitutionalized general population samples (Grant et al., 2015). Similarly, Degenhardt et al. (2001) included data from the Australian National Survey of Mental Health and Well-Being (NSMHWB). This is a nationally representative cross-sectional survey of Australians aged 18 years and over. The other two studies included convenience sampling techniques from clinical treatment-seeking samples at outpatient clinics (Tepe et al., 2012) or a combination of inpatient and community samples (Bedard-Gilligan et al., 2018).

### *Veteran Samples*

In the veteran samples, 1329 participants were included, with sample sizes ranging from 47 to 926 (see Table 9 for a summary of study characteristics). All four of these studies examined veterans who had a diagnosis of PTSD via clinician interviews and were based in the USA. Of the studies, two provided lifetime prevalence estimates of comorbid CUD among

veterans with PTSD (Dillon et al., 2021; Patel et al., 2021), and three studies provided current estimates of comorbid CUD among veterans with PTSD (Bonn-Miller et al., 2013; Metrik et al., 2022; Patel et al., 2021). Similar to the adult general population samples, none of the veteran samples required their participants to consume cannabis to be eligible for participation, with the exception of Metrik et al. (2022), who required veterans to have consumed cannabis at least once in their lifetime. One study reported the age range of the sample, which was from 23-77 (Patel et al., 2021). Overall, the studies had a mean overall age of 44.9 (*SD* = 9.6). The average percentage of females was 10.9%, with 57.2% of the total sample identifying as White. Regarding ARD and CUD diagnostic criteria, 75% of the studies reported using *DSM-IV* criteria, while one study (25%) used *DSM-5* criteria to make diagnoses. For the diagnostic measures for PTSD diagnoses, 75% of the studies used the SCID, with one study using the Clinician-Administered PTSD Scale for *DSM-5* (CAPS-5; Weathers et al., 2013). In terms of CUD diagnostic measures, all studies used a variation of the SCID. Finally, samples were primarily recruited from inpatient (25%) or outpatient (50%) residential treatment programs, apart from Metrik et al. (2022) who recruited veterans from the community (25%).

## Table 8

*Study Characteristics for Adult General Population Samples*

| First Author (Year) | Sample Size | Sample Type | Country | *Age M(SD)* | Percent Female | Percent White | ARD Diagnostic Measure | CUD Diagnostic Measure | Prev. Window (CUD) | Anxiety Disorder(s) Assessed | % Ever Used Cannabis | Prev. Comorbid CUD | Prev. Comorbid CUD in Cannabis Users | Quality Rating |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bedard-Gilligan (2018)[a] | 200 | I, COM | USA | 37.41 | 75.5 | 65.5 | PSSI (DSM-IV) | SCID-IV (DSM-IV AD) | LT | PTSD | - | 18.6 | | 6 |
| Bilevicius (2019)[b] | 1779 | GP | USA | 42.19 (14.8) | 70.5 | 62.0 | AUDADIS (DSM-5) | AUDADIS (DSM-5 CUD) | CUR (PY) | PTSD | 51.2 | 8.7 | 17.0 | 9 |
| Bilevicius (2019)[b] | 34530 | CG | USA | 45.81 (16.7) | 55.6 | 52.7 | AUDADIS (DSM-5) | AUDADIS (DSM-5 CUD) | CUR (PY) | No PTSD | 30.0 | 2.4 | 0.08 | 9 |
| Degenhardt (2001)[c] | 607 | GP | Australia | - | - | - | CIDI (DSM-IV/ICD-10) | CIDI (DSM IV/ICD-10 AD) | CUR (PY) | SAD, Agoraphobia, PD, GAD, OCD, PTSD | 6.8 | 4.3 | 63.2 | 7 |
| Martins (2011)[d] | 7437 | GP | USA | - | - | - | AUDADIS (DSM-IV) | AUDADIS (DSM-IV AD) | LT | PD, Agoraphobia, Specific Phobia, SAD, GAD | 29.4 | 3.3 | 10.6 | 5 |
| Martins (2011)[e] | 30614 | CG | USA | | | | AUDADIS (DSM-IV) | AUDADIS (DSM-IV AD) | LT | PD, Agoraphobia, Specific Phobia, SAD, GAD | 14.7 | .4 | 2.7 | 5 |
| Tepe (2012) | 873 | O | USA | 39.6 (11.9) | 63.3 | 88.5 | SCID-IV (DSM-IV) | SCID-IV (DSM-IV AD) | LT | SAD | - | 19.8 | | 4 |

*Note.*

[a] Excluded current diagnosis of *DSM-IV* substance dependence within the previous three months (treatment study). Lifetime substance dependence or abuse was allowed.

[b] Prevalence values are reflective of calculated values based on the number of participants; not the weighted prevalence values reported in text.

[c] Prevalence values are based on weighted values reported in text; sample size was obtained from a different published paper by the same author, wherein they report on the same sample.

[d] Percentage of ever using cannabis is defined as lifetime users in text; prevalence values are based on weighted proportions.

[e] The control group is defined as having no psychiatric disorder assessed via the AUDADIS (includes Mood Disorder: [Major Depression, Dysthymia, Mania, and Hypomania], Anxiety Disorder [panic with Agoraphobia, panic without Agoraphobia, Social Phobia, Specific Phobia, and Generalized Anxiety Disorder], and Schizophrenia).

*Abbreviations*: AD = Cannabis Abuse and Dependence; AUDADIS = The Alcohol Use Disorder and Associated Disabilities Interview Schedule; CIDI = The Composite International Diagnostic Interview; CG = Control group; COM = Community sample; CUD = Cannabis Use Disorder; CUR = Current prevalence window; I = Inpatient; ICD = International Classification of Diseases; DSM = Diagnostic and Statistical Manual of Mental Disorders; GP = General population; GAD = Generalized Anxiety Disorder; LT = Lifetime prevalence window; O = Outpatient; OCD = Obsessive-Compulsive Disorder; PY = Past year; PD = Panic Disorder; PSS-I = Posttraumatic Stress Disorder Symptoms Scale Interview; PTSD = Posttraumatic Stress Disorder; SAD = Social Anxiety Disorder; SCID = The Structured Clinical Interview for *DSM* Disorders; "-" = not reported.

**Table 9**

*Study Characteristics for Veteran Samples*

| First Author (Year) | Sample Size | Sample Type | Country | *M*(*SD*) age | Percent Female | Percent White | ARD Screening Measure | CUD Diagnostic Measure | Prev. Window (CUD) | Anxiety Disorder(s) Assessed | % Ever Used Cannabis | Prev. Comorbid CUD | Prev. Comorbid CUD in Cannabis Users | Quality Rating |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bonn-Miller (2013) | 260 | IP | USA | 52.57 (5.47) | 0 | 59.1 | SCID-IV (DSM-IV) | SCID-IV (DMS-IV AD) | CUR (TI) | PTSD | - | 31.2 | - | 6 |
| Dillon (2021)[a] | 926 | COM, OP | USA | 37.45 (10.26) | 20.5 | 47.8 | SCID-IV (DSM-IV) | SCID-IV (DMS-IV AD) | LT | PTSD | - | 11.3 | - | 7 |
| Metrik (2022) | 47 | COM | USA | 33.56 (9.44) | 7 | 80.0 | CAPS (DSM-IV) | SCID NP (DSM-IV AD) | CUR (TI) | PTSD | 100 | 34.0 | 34.0 | 5 |
| Patel (2021)[b] | 96 | OP | USA | 48.7 (13.0) | 25.8 | 41.9 | SCID-5 (DSM-5) | SCID-5 (DSM-5 CUD) | CUR | PTSD | - | 4.1 | - | 6 |
| Patel (2021) | 96 | OP | USA | 48.7 (13.0) | 25.8 | 41.9 | SCID-5 (DSM-5) | SCID-5 (DSM-5 CUD) | LT | PTSD | - | 12.5 | - | 6 |

*Note*.

[a] Demographic variables are based on entire sample of veterans ($N = 3028$), as reported, rather than those with PTSD ($n = 926$).

[b] Authors were emailed for data clarification, specifically, the current prevalence window for comorbid CUD in PTSD (of the 96 with PTSD, 4 had current CUD and 12 had lifetime CUD). Demographic variables are based on the entire sample of veterans ($N = 124$), as reported, and not those with PTSD ($n = 96$).

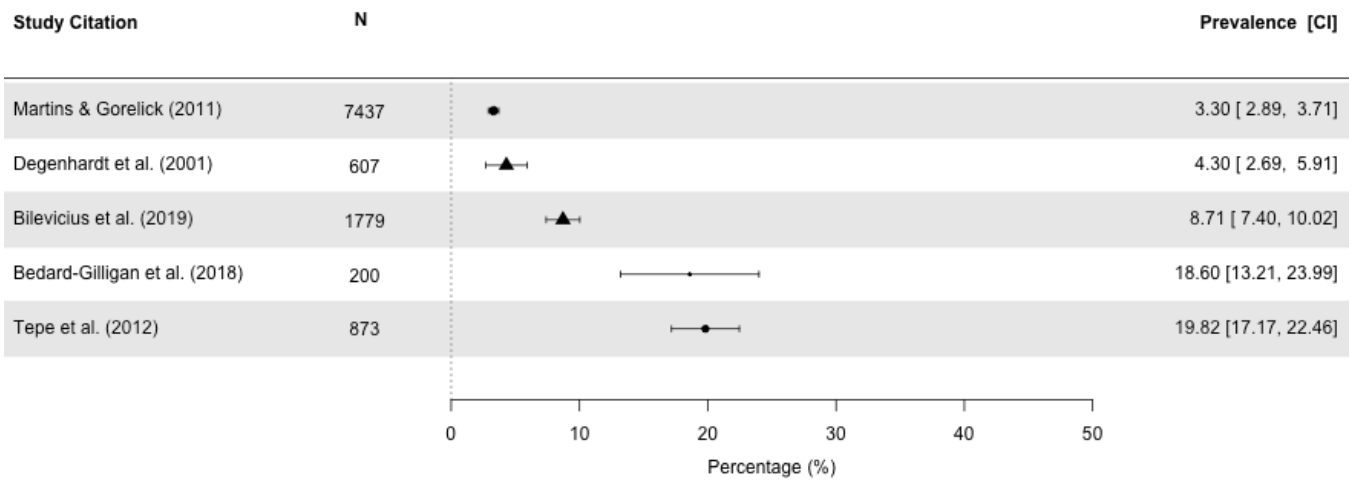
*Abbreviations*: AD = Cannabis Abuse or Dependence; CAPS = Clinician Administered PTSD Scale; CUD = Cannabis Use Disorder; CUR = Current prevalence window; I = Inpatient; ICD = International Classification of Diseases; DSM = Diagnostic and Statistical Manual; G = General population; GAD = Generalized Anxiety Disorder; LT = Lifetime prevalence window; O = Outpatient; OCD = Obsessive-Compulsive Disorder; PY = Past year; PD = Panic Disorder; PSS-I = Posttraumatic Stress Disorder Symptoms Scale Interview; PTSD = Post Traumatic Stress Disorder; SAD = Social Anxiety Disorder; SCID = The Structured Clinical Interview for *DSM* Disorders; SCID-NP = The Structured Clinical Interview for *DSM* Disorders (non-patient edition); TI = Treatment intake; "-" = not reported.

**Adult General Population Sample of Clinically Diagnosed ARDs**

Three studies reported lifetime estimates for comorbid CUD. The lifetime estimates range from 3.3% to 19.8%, while current (past year) CUD in ARD estimates ranged from 4.3% (cannabis dependence only) to 8.7% (see Figure 2). The next section will synthesize studies based on the specific ARD examined, however, we will be avoiding direct comparisons across different ARDs as too little data are available for any given disorder.

**Figure 2**

*Forest Plot of Adult General Population Samples*




*Note*. Forest plot representing CUD prevalence (%) for the lifetime and current measurement windows. Points and error bars reflect raw estimates (percentage) with the corresponding 95% confidence intervals. The prevalence reported in each publication is represented by the black square or triangle (● = lifetime prevalence window for CUD; ▲= current prevalence window for CUD).

### *Prevalence of Comorbid CUD among Individuals with PTSD*

Two samples yielded prevalence estimates examining comorbid CUD among individuals with PTSD (Bedard-Gilligan et al., 2018; Bilevicius et al., 2019). Specifically, Bedard-Gilligan et al. (2018) found that of the 200 participants diagnosed with PTSD, 18.6% also experienced comorbid lifetime CUD. Bedard-Gilligan et al. (2018) aimed to examine the relationship between PTSD and substance use by exploring treatment outcomes for patients with PTSD who participated in prolonged exposure or drug therapy (i.e., sertraline). Interestingly, approximately 75% of this sample were females, reporting diverse trauma experiences of adult sexual assault, child physical or sexual assault, non-sexual assault, accident/natural disaster, witnessing death or violence, and combat or war. Conversely, Bilevicius et al.'s (2019) sample is more representative of the general population in North America, wherein the risk of developing current comorbid CUD with PTSD is estimated to be almost 4 times greater compared to individuals who have CUD without PTSD (*RR* = 3.6). Bilevicius et al. (2019) aimed to examine PTSD and chronic pain in relation to comorbid CUD. They found that 8.7% of individuals in this NESARC wave III survey with PTSD reported current, past year CUD.

Because Bedard-Gilligan et al. (2018) recruited from a treatment-seeking sample and examined lifetime CUD rates, it is unsurprising that they found a higher prevalence rate than Bilevicius et al. (2019). However, unlike Bedard-Gilligan et al. (2018), they fail to explore possible trauma exposure that may inform estimates. In summary, it appears that PTSD alone may increase the risk of CUD in these populations, although this is only based on one study with a control group.

### *Prevalence of Comorbid CUD among Individuals with SAD*

Only one study, Tepe et al. (2012), examined the comorbidity between CUD and SAD, finding that 19.8% of individuals clinically diagnosed with SAD also were diagnosed with lifetime comorbid CUD. In a sample of 3200 outpatients in the USA, 873 (27.3%) met the criteria for SAD and were included in this study. However, patients with SAD and CUD did report fewer problems with physical functioning compared to those with SAD and no CUD, which may be due to a lower mean age or perceived benefits of self-medicating with cannabis. Given that this is the only study examining the prevalence of CUD in individuals with SAD exclusively, it is challenging to confidently say whether this prevalence estimate is representative of the broader population.

***Prevalence of Comorbid CUD among Individuals with any ARDs***

Two studies examined the prevalence of comorbid CUD among individuals with any ARD. These two studies used large, nationally representative cross-sectional surveys from the USA NESARC wave I survey (Martins & Gorelick, 2011) and the Australian NSMHWB (Degenhardt et al., 2001) to determine the relationship between substance use and mood and anxiety disorders. While neither study reported comorbidity rates broken down by individual ARDs, Martins and Gorelick (2011) found that lifetime SUDs were higher in participants with a psychiatric disorder than those without any psychiatric disorder. For ARDs (i.e., PD, Agoraphobia, Specific Phobia, SAD, or GAD), participants were eight times at greater risk for developing cannabis abuse and dependence (*RR* = 8.3) relative to those who did not have any disorder. For cannabis dependence only, the prevalence was lower, at 0.5% (*RR* = 12.5), and cannabis abuse at 1.6% (*RR* = 2.3).[2] In Degenhardt et al.'s (2001) study, they found that the

[2] Although it would be preferable to use the raw (unweighted) data, they were unavailable; for that reason, risk ratios were calculated for these results using the weighted prevalence values in each respective group.

prevalence of current CUD in ARDs (SAD, Agoraphobia, PD, GAD, OCD, or PTSD) was 4.3% for cannabis dependence and 0.9% for cannabis abuse.

***Sample Type and Year of Study***

Addressing our hypothesis that proposed CUD prevalence would be greater among inpatient or outpatient ARD samples relative to community ARD samples, followed by the hypothesis that more recent studies would yield higher prevalence rates, we provide a narrative review examining the sample types. Overall, a variety of sample types were reported, such as national surveys in the country's respective regions, treatment-seeking samples (i.e., inpatient), or a combination of outpatient and community samples, creating challenges to compare across studies. Nonetheless, comparing the prevalence rates across studies is important when determining the representativeness of estimates.

Three studies used data that were obtained from nationally representative samples. First, Martins and Gorelick's (2011) study consisted of data from wave I of the NESARC study (2001-2002). They found the lowest overall prevalence estimate for lifetime CUD (cannabis abuse and dependence) in any ARD (PD, Agoraphobia, Specific Phobia, SAD, or GAD) of 3.3%. Importantly, data from this survey took place in 2001-2002 in the USA, and they still found high prevalence rates for ARDs and comorbid SUDs, particularly for Tobacco Use Disorder (31.7%) and AUD (20.3%). In contrast, Bilevicius et al. (2019) reported data from a subset of participants with PTSD in wave III of the NESARC study (2012-2013). The prevalence rate in this study among a subsample of participants with PTSD was 8.7%, relative to a control sample with CUD and without PTSD (2.4%). These two findings may underscore the legality of cannabis, corresponding to a societal shift in favour of the legalization of non-medical cannabis. Given the large gap in years from which each wave took place, it is possible the higher prevalence rates

reflected in the Bilevicius et al. (2019) study indicate an attitude shift, with non-medical cannabis becoming not only more accessible in some states but more socially acceptable as well. Another possibility may be reflected in the different versions of the *DSM* that were used, specifically related to CUD criteria (*DSM-5*) relative to cannabis abuse and dependence (*DSM-IV*).

Similar to Martins and Gorelick (2011), a nationally representative cross-sectional Australian study conducted in 1997 by Degenhardt et al. (2001) found that the past-year prevalence of CUD in any ARDs was 4.3% for cannabis dependence and 0.9% for cannabis abuse. Finally, because only two samples included either outpatient samples (Tepe et al., 2012), or a combination of inpatients and community samples (Bedard-Gilligan et al., 2018), it is difficult to compare these two studies. However, both studies found the highest overall lifetime estimates, 19.8% and 18.6%, respectively, relative to the large, nationally representative, cross-sectional samples. Overall, studies primarily sampling from treatment-seeking populations (inpatient/outpatients) appeared to have the highest prevalence rates relative to general, nationally representative samples. This makes sense as the sample size for Tepe et al. (2012) and Bedard-Gilligan et al. (2018) was smaller, consisting of convenience sampling for individuals with an ARD who were seeking treatment, as opposed to the other three large-scale, nationally representative samples that employed random sampling among the lay public.

### *Gender Differences*

To evaluate our hypothesis concerning gender differences and CUD prevalence, only three of the studies reported the demographic gender/sex distribution, comprising approximately 69.8% of females among all studies included. Therefore, it is difficult to determine overall if males or females are more likely to develop comorbid CUD if they have a primary ARD. However, Tepe et al. (2012) reported the gender breakdown of those with or without comorbid CUD who had also

been diagnosed with SAD. Among the total sample of individuals with SAD, there were 873 participants, of which 553 (63.3%) were female and 320 (36.7%) were male. Among the 553 females with SAD, 85 (15.4%) had comorbid CUD, relative to the 320 males with SAD, of which 88 (27.5%) had comorbid CUD. Thus, patients with SAD and comorbid CUD had higher odds of being male than female compared to SAD patients without CUD (*RR* = 1.8).

Bilevicius et al. (2019) do not report any gender demographic characteristics regarding what proportion of males or females who have PTSD also have comorbid CUD. However, they report that 49 participants presented with chronic pain, CUD, and PTSD, while a control group of 125 individuals had chronic pain, CUD, but no PTSD, broken down by gender. Specifically, they found a significant difference between males and females in these groups, where females are more likely to be diagnosed with CUD if they have PTSD compared to males (59.2% vs. 40.8%), whereas males without PTSD are more likely to have CUD compared to females without PTSD (57.6% vs. 42%). However, these findings should be interpreted cautiously as the sample size for chronic pain, PTSD, and CUD is much smaller than just the PTSD only sample.

Bedard-Gilligan et al. (2018) only reported that 151 women and 49 men comprised their sample of chronic PTSD (75.5% female), wherein they found an overall prevalence of 18.6% for comorbid CUD in PTSD, the second highest prevalence estimate among all included studies. Thus, these findings appear to align with Bilevicius et al. (2019), given that both samples examined CUD associations in PTSD samples and found the two highest prevalence estimates out of all studies included in a predominantly female sample. However, Bedard-Gilligan et al. (2018) do not report the gender breakdown for PTSD and CUD.

While Degenhardt et al. (2001) failed to report the number of female or male participants in the article's text, the authors found that males were at two times greater odds of being heavily

involved with cannabis than females (*OR* = 2.4). However, females were more likely to meet the criteria for ARDs and affective disorders relative to males (*OR* = 0.6).

### *ARD Samples Compared to Non-ARD Samples*

Bilevicius et al. (2019) and Martins and Gorelick (2011) were the only studies that reported a control group. However, the control groups are not comparable, with Bilevicius et al.'s (2019) operationally defined as individuals without the target ARD and Martins and Gorelick's (2011) defined as having no current or past psychiatric disorder. Thus, we cannot make strong conclusions about our fourth hypothesis. Nonetheless, both studies comprised a large, representative sample of adults across the USA. Given that the risk of developing comorbid CUD in PTSD is almost four times higher than those without PTSD, there may be an association wherein individuals with PTSD are at greater risk of developing comorbid CUD (Bilevicius et al., 2019). Similarly, Martins and Gorelick (2011) determined that individuals with any ARD were eight times more likely to experience comorbid CUD relative to individuals with no disorder. However, we cannot generalize these claims as only one other study examined PTSD and did not include a control group, and relatedly, other studies examining other ARDs did not include control groups.

## Exploratory Synthesizes for Adult General Population Samples

### *Cannabis and ARD-Related Variables*

Three studies assessed the age of onset for CUD or ARDs, the age of first cannabis use, the number of joints smoked, or the percentage of individuals who reported cannabis consumption in the sample. Martins and Gorelick (2011) mention that the AUDADIS measured the quantity and frequency, age of onset, duration, and persistence of use of alcohol and tobacco, illegal drugs including marijuana, cocaine, and heroin, and prescription medications including analgesics,

sedatives, tranquillizers, and stimulants, but do not further describe these characteristics in text. Thus, the next sections will synthesize exploratory variables that studies reported on.

**Age of Onset.**

Among individuals who met the criteria for past-year CUD in their sample, Bilevicius et al. (2019) found that an older age of cannabis initiation was associated with chronic pain, proposing that individuals may have waited and exhausted other options prior to trying cannabis to alleviate their pain. Moreover, Tepe et al. (2012) reported that the outpatient sample of SAD patients had a mean age of onset of around 12 years old (*SD* = 8.3), and for CUD, the mean age of onset was 16 years (*SD* = 6.7). Overall, this would suggest that SAD emerges earlier in life than CUD, implying that SAD develops first, underscoring an important directionality in the relationship between ARDs and CUD. However, longitudinal research is necessary to verify this pattern, and further, it could be that SAD tends only to be diagnosed or identified first, rather than appearing in that order.

**Cannabis Frequency-Related Variables.**

Other reported study characteristics include the percentage of the sample who reported ever using cannabis and to what extent. This is an important statistic to consider because it reflects both a necessary precondition for the development of CUD, as well as an upper limit on the prevalence of CUD in a given sample. For instance, among individuals with ARD in Degenhardt et al.'s (2001) study, only 6.8% of the sample reported ever using cannabis. In other words, the prevalence of those with an ARD and comorbid CUD who have ever consumed cannabis in their lifetime is much higher, at 63.2%, compared to 4.3% of their entire sample. Similarly, Martins and Gorelick (2011) reported that of the 7437 individuals with an ARD, 29.4% were lifetime cannabis consumers. Of those who have consumed cannabis, the prevalence of individuals with an ARD and comorbid

CUD is now at 10.6% compared to 3.3%. Martins and Gorelick (2011) were the only study to account for these conditional estimates because unconditional rates cluster together abstainers and consumers of a substance, of which only the latter group is at risk of SUDs. Finally, Bilevicius et al. (2019) reported that 51.2% ($n$ = 910) of individuals with PTSD in their sample reported ever using cannabis, relative to the control group without PTSD, where 30% reported ever using cannabis ($n$ = 10,362). Again, when considering this detail, the prevalence rate of comorbid CUD in individuals with ARDs increases to 17% instead of 8.7%.

Further, across various types of chronic pain, Bilevicius et al. (2019) reported cannabis-related severity variables that correlate with PTSD. Across all three categories of chronic pain, the number of joints smoked a day was highest for individuals with PTSD only. Similarly, PTSD only or PTSD with chronic pain appeared to have a lower age of onset relative to individuals who only reported chronic pain. Among those with CUD, severe CUD was most commonly classified in the sample, and PTSD was associated with a more severe CUD diagnosis.

Similarly, in another PTSD sample, Bedard-Gilligan et al. (2018) reported that there is a greater risk of treatment dropout among patients with PTSD who have consumed cannabis in the past month or have lifetime CUD. Approximately 13.5% of the sample reported past month cannabis consumption, and that cannabis use in the last 30 days relative to more than 30 days since cannabis use (55.6% vs. 27%), or lifetime CUD relative to no CUD (48.6% vs. 28.4%) predicted treatment dropout.

While these estimates are not entirely comparable, they do provide a possible explanation for the range in estimates. For instance, reporting of these variables may provide an explanation for the low prevalence rates of CUD in ARDs, particularly among Degenhardt et al.'s (2001) sample, as a very low percentage of individuals reported ever consuming cannabis (6.8%),

eliminating the possibility of CUD comorbidity in an ARD diagnosis. However, when only looking at those having tried cannabis, the prevalence of comorbid CUD in any ARD increased by 14 times, changing the prevalence from 4.3% to 63.2%. It is also noteworthy that Tepe et al. (2012) reported the highest prevalence estimate. However, the proportion of cannabis consumers within their sample is unclear, raising questions about the true significance of their 19.8% estimate

***Common Psychiatric Comorbidities among Individuals with ARDs***

One study reported psychiatric comorbidities such as other SUDs, ARDs, mood disorders, impulse control disorders, somatoform disorders, and EDs alongside a primary SAD diagnosis (with or without CUD; Tepe et al., 2012), while Bilevicius et al. (2019) examined depressive disorders, other ARDs, and SUDs among those with PTSD and no PTSD. Tepe et al. (2012) found that individuals with comorbid SAD and CUD were 4 times more likely to experience an additional SUD in their lifetime, 1.7 times more likely to experience PTSD, and 1.8 times more likely to experience Specific Phobia relative to those with SAD who did not have CUD ($p < .001$). The current estimates were not significant. Furthermore, regarding lifetime comorbidity estimates for individuals with a current SAD diagnosis, 40.1% had another drug use disorder, 37.3% had a comorbid AUD, 73.3% had comorbid MDD, 13.9% had comorbid Dysthymic, 11.7% had comorbid Bipolar Disorder, and 70% had another comorbid Anxiety Disorder. The most common comorbid Anxiety Disorders reported in current SAD individuals were GAD (28%), PTSD (26.4%), Specific Phobia (18.7%), and Anxiety Not Otherwise Specified (16.5%).

Similarly, Bilevicius et al. (2019) found that individuals with PTSD were more likely to have a comorbid depressive, other anxiety, or SUD condition relative to those without PTSD ($p < .001$). Among those with chronic pain, PTSD, and CUD, participants were also more likely to have

a secondary depressive or anxiety disorder but not another SUD, compared to those with CUD, chronic pain, but no PTSD.

Finally, Martins and Gorelick (2011) reported associations among other SUDs such as AUD, cocaine, amphetamines, opioids, sedatives, tobacco, heroin, tranquillizers, hallucinogens, inhalants, and others. Overall, they found that 31.7% of individuals with an ARD had a comorbid tobacco dependence, and 20.3% had a comorbid AUD. All other substance comorbidities were less than 3% in prevalence.

***Heterogeneity among Adult General Population Samples***

Many of the studies included in this synthesis are heterogeneous and not comparable. Regarding sampling issues, three studies utilized random sampling, while the other two used convenience sampling, primarily from treatment-seeking individuals. This results in heterogeneity among the samples, as convenience sampling from clinics tends to recruit individuals with severe symptoms, possibly inflating the true prevalence rate in the general population. However, this population is quite common in epidemiological research and is representative of the target population (i.e., individuals with an ARD). Nonetheless, it is imperative to consider this when interpreting the results. Furthermore, regarding sampling, 80% of the included studies were all conducted in the USA, which is likely not generalizable to the true estimate of the global population. Finally, much of the heterogeneity in prevalence estimates is likely attributable to the percentage of individuals who have consumed or initiated cannabis in their lifetime. Only three studies reported these participant characteristics, changing the prevalence rate ranges for lifetime estimates from 3.3%-19.8% to 11.2%-19.8% and current estimates from 4.3%-8.7% to 17.0%-63.2%. This is because if individuals with an ARD have never consumed cannabis, there is no possibility they would ever develop CUD, showing a significantly lower prevalence range than

studies where there are higher percentages of cannabis consumers. Only one study addressed this issue, where they reported unconditional rates of CUD in ARDs at 3.3% and conditional rates increased to 10.6% (Martins & Gorelick, 2011).

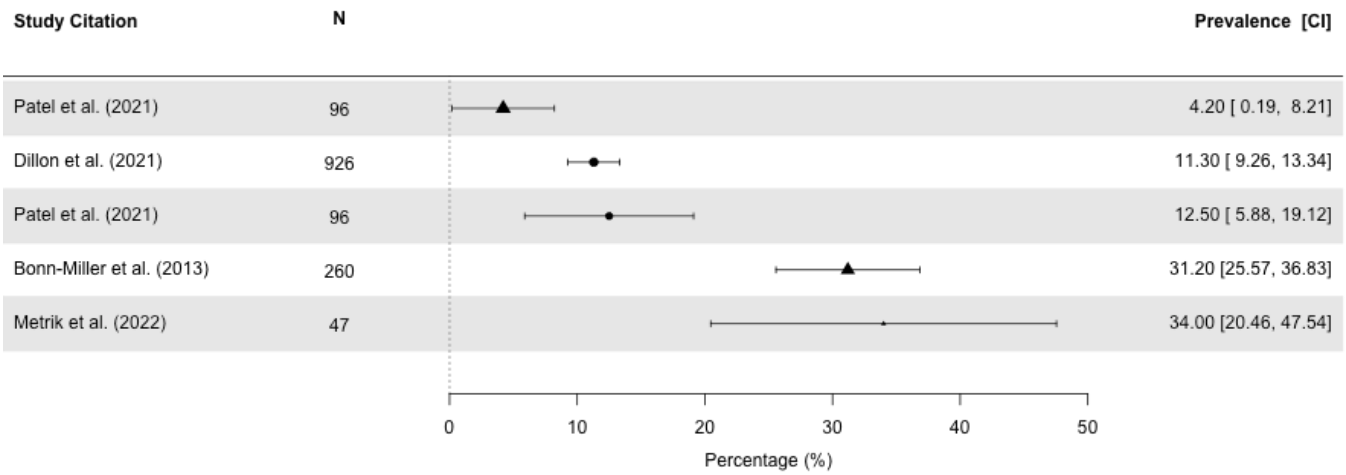
Secondly, we were unable to compare prevalence rates across studies for many individual ARDs as two studies provided "prevalence any" estimates (i.e., the prevalence of having at least one of a possible five or six ARDs), creating many challenges in our initially proposed meta-analyses. Finally, only one study was conducted recently enough to utilize *DSM-5* criteria. This may impact prevalence rates as there were instances where we were unable to discern whether studies that used the *DSM-IV* cannabis abuse and dependence criteria were mutually exclusive (i.e., participants were not overlapping amongst the two diagnoses; Degenhardt et al., 2001). This also created challenges in conducting our meta-analysis as we already would have had to separate studies by lifetime or current CUD windows and the type of diagnostic measure used for CUD.

**Veteran Populations of Clinically Diagnosed PTSD**

Because we decided to conduct an additional narrative synthesis specific to veterans, given their level of nearly equal representation in our search, there are no specific hypotheses pertaining to this population. Thus, this synthesis will be largely exploratory, highlighting trends and patterns in the literature, but will be organized similarly to how the adult general population synthesis was conducted. Among the veteran samples, the prevalence estimates included for the four veteran studies all had individuals with a primary diagnosis of PTSD and comorbid CUD. The prevalence estimates ranged from 4.1% to 34%, current estimates ranged from 4.1% to 34%, while lifetime estimates included 11.3% and 12.5% (see Figure 3).

**Figure 3**

*Forest Plot of Veteran Samples*




*Note*. Forest plot representing CUD prevalence (%) for the lifetime and current measurement windows. Points and error bars reflect raw estimates (percentage) with the corresponding 95% confidence intervals. The prevalence reported in each publication is represented by the black square or triangle (● = lifetime prevalence window for CUD, ▲= current prevalence window for CUD).

### *Prevalence of Comorbid CUD among Veterans with PTSD*

For current estimates, Bonn-Miller et al. (2013) conducted a longitudinal study assessing combat-exposed military veterans at two-time points. At treatment intake, 31.2% of veterans with PTSD ($n$ = 260) had comorbid CUD. Importantly, this sample consisted of all male veterans who were at a Veteran Affairs residential rehabilitation program for PTSD between 2000-2008. Similarly, Metrik et al. (2022) conducted a longitudinal study of 361 veterans who have used cannabis at least once in their lifetime and were deployed after September 11, 2001. At treatment intake (baseline), there were 47 veterans with PTSD, of which 16 had comorbid CUD (34%). Finally, Patel et al. (2021)[3] included a sample of 124 veterans to investigate Non-Suicidal Self-Injury Disorder (NSSID), as that is particularly high among veterans seeking treatment for PTSD (Kimbrel et al., 2017). Accordingly, of the 96 veterans diagnosed with PTSD, 4.1% met the criteria for a current CUD.

In terms of lifetime CUD diagnoses being comorbid alongside PTSD, Dillon et al. (2021) conducted a study on veterans who were deployed in the Iraq/Afghanistan era after September 11, 2001 ($N$ = 3028) to determine associations between CUD, anger, and aggression. Out of these veterans, 926 were diagnosed with PTSD, and 105 (11.3%) presented with lifetime CUD. Finally, Patel et al. (2021) provided a second estimate for their sample of 96 veterans with PTSD, and 12.5% met the criteria for CUD in their lifetime. Overall, both lifetime estimates are comparable, while current estimates appear to be more heterogeneous, ranging from the lowest and highest reported prevalence rates in all the samples. Thus, other factors within the studies likely impact the prevalence estimate reported. However, the studies all used similar diagnostic

[3] Current estimates for CUD prevalence in PTSD were provided through contact with the authors.

tools to make PTSD and CUD diagnoses. Below, we examine possible factors that influence heterogeneity and may contribute to the overall prevalence estimates among the included studies.

### *Sample Type and Study Year*

Among the veteran studies, there were diverse methods of recruitment. For example, Bonn-Miller et al. (2013) recruited participants from a men's only Veteran Affairs (VA) residential rehabilitation program between 2000 and 2008, making this the only inpatient sample out of all included studies. Similarly, Patel et al. (2021) study was sponsored by the VA and sought participants from the Durham VA Health Care System. However, the recruitment type is described as resembling outpatient. Further, Metrik et al. (2022) recruited community samples of veterans who had consumed cannabis at least once in their lifetime and were returning from Iraq and Afghanistan between 2013 and 2016. Finally, Dillon et al. (2021) recruited an outpatient/community sample of Veterans who participated in previous related VA studies between 2005 and 2015.

Only one study recruited inpatient samples, resulting in the second-highest overall prevalence estimate. For the highest overall estimate, Metrik et al. (2022) not only had the smallest sample size but was the only veteran study to report the number of participants who had ever initiated cannabis (100%), which was part of their eligibility criteria. Thus, Metrik's community sample and current CUD estimate are difficult to compare, given how they only included 47 veterans with PTSD, all of whom had consumed cannabis before. Finally, because many of the veteran studies were either longitudinal or recruited participants for over a decade, it is challenging to evaluate if the year of study influenced the prevalence rates.

### *Gender Differences*

Among the included studies, it is evident that females are severely underrepresented in veteran populations. For example, Bonn-Miller et al.'s (2013) sample is entirely male. Similarly, Metrik et al.'s (2022) sample only included 7% females. Importantly, these two studies reported the highest prevalence estimates. In the other two studies, while significantly lower than males, Patel et al. (2021) made efforts to oversample female veterans, which comprised 25.8% of the overall sample, which was comparable to Dillon et al. (2021), including a sample of 20.5% of females. Although, these were the only two samples also to report lifetime estimates, introducing a potential confound. Considering these findings, it is noted that this synthesis cannot be generalized to female veterans, as they only comprise 10.9% of the total veteran sample. Therefore, it is difficult to determine gender differences in veterans with PTSD and comorbid CUD. While it cannot be said with certainty whether the prevalence rates are attributed to the CUD prevalence window or gender differences, it should be noted that, typically, lifetime prevalence windows are much larger than current prevalence windows throughout epidemiological works. Thus, it is possible that gender can explain this discrepancy, and the lifetime prevalence rates among these studies may be underestimated, or the current rates may be overestimated.

### *Types of Combat*

Based on the four included studies, veterans varied in terms of deployment type. For instance, Bonn-Miller et al. (2013) reported that their sample of veterans had been exposed to combat via the military and were currently residing in a residential rehabilitation treatment program for PTSD. Similarly, Dillon et al. (2021) took the initiative to include self-report scales that assessed the frequency, duration, severity, and percentage of combat and trauma exposure ($M$ = 11.05, $SD$ = 10.54) via the Combat Exposure Scale (Keane et al., 1989), controlling for

these variables in their analyses. Accordingly, veterans with CUD reported significantly higher depression scores and PTSD severity ratings ($p < .01$) relative to those without CUD (Dillon et al., 2021).

Metrik et al. (2022) took it a step further and reported that the majority of veterans in their sample had combat experience (88.6%) and, of those who endorsed a traumatic event via the CAPS ($n = 184$), 80% reported trauma-related to combat. A further 61% reported directly experiencing a traumatic event, 61% reported witnessing a traumatic event occur to someone else, and 17% reported learning that a traumatic event happened to a family member or friend. Only one study, Patel et al. (2021), did not report any specific details pertaining to veterans' deployment experiences within their study. Based on these findings, it appears that combat type may impact prevalence rates.

***Comorbid Disorders***

In Bonn-Miller et al.'s (2013) study, among all veterans with a primary diagnosis of PTSD, 80% also met criteria for a mood disorder and 18.1% met criteria for another ARD other than PTSD. Similarly, cannabis was not the only substance that was used among veterans in this sample: 79.6% met criteria for AUD, 33.1% met criteria for a cocaine use disorder, 19.2% met criteria for an amphetamine use disorder, 12.7% met criteria for an opioid use disorder, and 6.5% met criteria for a sedative use disorder. In Patel et al.'s (2021) study, approximately half of their sample met the criteria for a lifetime diagnosis of NSSID, with other prevalent lifetime diagnoses of Borderline Personality Disorder (66.1%), MDD (94.9%), OCD (50.8%), PD (27.1%), SAD (16.9%), GAD (27.1%), and AUD (71.2%) being comorbid in this sample. In Dillon et al.'s (2021) study, the authors found that current CUD was significantly associated with increased

odds of problems with managing anger, aggressive impulses/urges, and problems controlling violence, supporting early interventions and treatment initiatives.

Finally, in Metrik et al.'s (2022) study, they reported the percentage of cannabis use and other drugs (e.g., alcohol, tobacco, and other drugs) used per day, indicating that other SUDs could be examined as a potential comorbid condition alongside PTSD. Veterans are a vulnerable population, where PTSD is not only extremely prevalent, but other comorbid disorders/conditions also coincide with these diagnoses. It appears that MDD and AUD are the most common comorbid conditions among the included veteran studies, although this conclusion is based on limited data. Nonetheless, it is imperative to report these variables and, if possible, measure them using validated clinician interviews to discern accurate prevalence rates in the population and determine potential causes of heterogeneity among the samples.

### *Heterogeneity among Veteran Samples*

Akin to the aforementioned issues of heterogeneity addressed in the adult general population samples, there are additional items to mention for the veteran samples. However, all the veteran samples examined PTSD, making it easier to compare across studies, and utilized similar diagnostic tools based on clinician interviews to make the diagnosis. Nonetheless, only one study considered elaborating on the combat types in sufficient detail (Metrik et al., 2022). Given that veterans are a vulnerable population, there are concerns that sample variation in combat experience could contribute to variation in prevalence estimates. For instance, CUD may be directly related to the number or types of traumatic events experienced or witnessed. Another primary source of heterogeneity among the veteran studies are the samples, which are primarily comprised of White male veterans. While it is unclear if these samples represent veteran

populations, two studies had little to no female veteran representation, which cannot be ignored nor generalized to all veterans' experiences.

## Discussion

This systematic review provides a narrative synthesis for the prevalence of CUD among individuals who have an ARD, along with a separate synthesis for veterans with PTSD and comorbid CUD. Overall, we found that in the adult general population samples ($n$ = 5), lifetime estimates for CUD in individuals with an ARD ranged from 3.3% to 8.7%, while current estimates ranged from 4.3% to 19.8%. Based only on two studies that implemented control groups, there is preliminary evidence to suggest higher prevalence rates of CUD in individuals with ARDs compared to those without. Specifically, one study reported that the risk of developing CUD in PTSD is four times greater than those without PTSD (Bilevicius et al., 2019). Similarly, another study estimated the risk of CUD in any ARDs to be eight times greater relative to individuals with no psychiatric disorder (Martins & Gorelick, 2011). Among the veteran samples ($n$ = 4), lifetime estimates of comorbid CUD in veterans with PTSD ranged from 11.3% to 12.5%, with a wider range of current estimates, from 4.1% to 34%. While distinct trends and themes were noted separately in each synthesis, veterans appear to have a higher range of current estimates relative to the adult general population samples. Despite these findings, it was also evident throughout this review that there are sources of heterogeneity that must not be overlooked among the included studies in each separate synthesis.

### Sample Type

Regarding sample type, much of the heterogeneity among included studies may be attributed to sampling techniques. Indeed, this source of error may also extend to the sample size, diagnostic approach, classification system (i.e., *DSM-IV* vs. *DSM-5*), and related demographic

differences. Most strikingly, the adult general population samples were recruited from variable sources, consisting of either inpatient, outpatient, and community groups representative of clinical, treatment-seeking populations or large-scale national surveys representative of the general population. Conversely, the veteran sample included mostly inpatient and outpatient residential treatment groups, apart from one study that recruited veterans who had consumed cannabis at least once in their lifetime, primarily from the community. Given that a single psychiatric condition (depending on the severity) can increase the risk of SUDs, the general trend often observed in the frequency of having a comorbid SUD in ARD populations increases from community/population samples to outpatient samples to inpatient samples, respectively (Hakobyan et al., 2020).

### *Adult General Population Samples*

Various sampling techniques were employed among the adult general population samples. As a result, we were unable to confidently say that increased prevalence estimates were attributed to inpatient/outpatient samples relative to community samples because only one study included inpatient samples mixed with community sampling (Bedard-Gilligan et al., 2018), and another sample relied solely on outpatient recruitment (Tepe et al., 2012). However, it may be that convenience sampling explained the heightened prevalence rate. Indeed, three of the included studies employed random sampling techniques from nationally representative samples in the USA and Australia, while the other two studies were primarily convenience samples of treatment-seeking patients from clinic referrals in the USA, a common type of non-probability sampling in clinical research (Acharya et al., 2013; Stratton, 2021). Thus, recruitment of treatment-seeking populations may involve more complex and severe mental health symptoms and comorbidity than community samples. Indeed, it is common practice for meta-analyses to

separate community samples and epidemiological studies from clinical, treatment-seeking studies (inpatient/outpatient studies; Ioannidis et al., 2008). Thus, the results are not generalizable beyond the study populations, and the true prevalence rate may be lower and closer to the rates reflected in the general population samples.

### *Veteran Samples*

Similarly, various sampling techniques were employed among the veteran samples. For the highest overall estimate, Metrik et al. (2022) not only had the smallest sample size but was the only veteran study to report the number of participants who had ever consumed cannabis (100%) from the community. While objectively, this may seem like the opposite of what was observed in the adult general population sample (i.e., inpatient/outpatient prevalence rates were higher than general population samples), it may be because 100% of Metrik et al.'s (2022) sample have consumed cannabis at least once in their lifetime, as previous cannabis consumption was a part of their study's inclusion criteria. Because the other veteran studies did not report the percentage of individuals who have consumed cannabis in their lifetime, it is difficult to be certain whether this characteristic can explain how Metrik et al. (2022) observed the highest prevalence rate. Alternatively, it may be related to their underpowered study, with only 47 veterans, resulting in an artificially high estimate.

Dillon et al. (2021) reported a relatively high lifetime estimate for community/outpatient samples with PTSD, whereby this estimate may be more reflective of the true rate given that they also had the largest sample size of veterans with PTSD ($n$ = 925). Finally, Patel et al.'s (2021) lifetime and current estimates in a sample of outpatient veterans with PTSD demonstrate patterns that are typically observable in epidemiological research, where lifetime estimates are higher and current estimates are much lower (e.g., Kessler et al., 2005a, 2005b). Further, the lifetime

estimates appear to be the most reliable, as Patel et al. (2021) and Dillon et al. (2021) both recruited their samples from either outpatients or a mix of outpatient/community samples. Given that Dillon et al. (2021) had the highest quality rating and the largest sample size, it complements Patel et al. (2021) study, suggesting that the lifetime estimate among veterans with PTSD and comorbid CUD may be between 11.3% and 12.5%. Given that these two studies included the most diverse samples, considering a relatively fair representation of ethnicities and genders, there may be less heterogeneity in lifetime estimates for outpatient samples relative to other studies that provide current estimates for either inpatient, outpatient, or community samples that consist of mostly White male veterans. Importantly, caution is needed due to the dearth of research in this area.

**Year of Study**

It was proposed that there would be a relationship between more recent studies and higher prevalence rates. While much of the rationale was grounded on the increase of Δ9-THC and more concentrated products rising in popularity in recent years (Prince & Conner, 2019; Russell et al., 2018), it is also possible that accessibility and social acceptability play a role. Even though cannabis is not legalized worldwide, it is gaining traction, with proponents of legalization promoting social acceptability (Simkins & Allen, 2020). Further, many countries are adopting diverse policy models to minimize the associated harms with the illegalization and criminalization of cannabis consumption (e.g., Kavousi et al., 2021). Simultaneously, there are concerns about competition from unregulated sources. For example, many individuals may be keen to purchase from unregulated markets due to the lower prices, quality/potency of products, selection of products, loyalty to previous distributors, access to information, and greater convenience (Donnan et al., 2022; Goodman et al., 2022). Thus, given the globalization and

diversification of cannabis products in more recent years, it would not be surprising to see a rise in cannabis use and CUD. Indeed, studies have reported that regular (i.e., weekly/daily) cannabis consumption has escalated across all demographics (Health Canada, 2022a; Imitaz et al., 2023; Zuckermann et al., 2020). It has also been argued that legalization will increase rates, with early survey data from Canada and the USA suggesting that cannabis potency and consumption rates are increasing (Hammond et al., 2021; Health Canada, 2018a, 2019, 2021, 2022a).

### *Adult General Population Samples*

It appears that PTSD is not the only ARD that is at risk for CUD, and the difference in prevalence rates among these three studies could partially represent the year in which the study was conducted. For instance, Degenhardt et al. (2001) and Martins and Gorelick's (2011) studies took place in 1997 and 2001, respectively, whereas Bilevicius et al.'s (2019) study was conducted from 2012-2013. Moreover, considering that Bilevicius et al. (2019) solely examined PTSD, whereas Degenhardt et al. (2001) included PTSD as one of the potential ARD diagnoses, this suggests that the variance in the years during which the studies were conducted might explain prevalence disparities rather than specific ARDs having a particularly heightened association with CUD, in this instance. Overall, Degenhardt et al.'s (2001) prevalence estimates are comparable to the first wave of the NESARC study (3.3% for abuse and dependence; Martins & Gorelick, 2011), aligning with the possibility that legalization or social acceptability may influence prevalence rates due to sampling biases or social desirability. However, without two studies to compare pre-and post-legalization, coupled with the fact that Australia has not legalized non-medical cannabis use as of 2024, it is difficult to make any conclusions.

In the adult general population samples, studies from Martins and Gorelick (2011) and Bilevicius et al. (2019) were both from NESARC samples at wave I (2001-2002) and wave III

(2012-2013), respectively. Although these samples are mutually exclusive, and the sampling techniques are comparable, we cannot cross-compare the rise in prevalence rates from 3.3% to 8.6% because both estimates are from two different CUD windows (lifetime vs. current), examining different ARDs, and two different *DSM* classifications (*DSM-IV* vs. *DSM-5*). Nonetheless, there is a trend where studies conducted from the late 90s to the early 2000s demonstrate the lowest prevalence rates, relative to those conducted in 2012 and later.

Initially, we proposed that the rise in CUD may be attributed to the year the studies were conducted. Further evidence of this hypothesis may be supported by Degenhardt et al.'s (2001) study, where they used a nationally representative sample of Australians conducted in 1997, finding the prevalence of cannabis dependence to be 4.3%. Degenhardt et al. (2001) and Martins and Gorelick's (2011) studies were the two lowest overall prevalence rates reported and the earliest studies to be conducted, both combining any ARDs rather than differentiating between specific ARD diagnoses. Interestingly, Degenhardt et al.'s (2001) study measures current CUD while Martins and Gorelick's (2011) study measures lifetime CUD, yet their estimates are also lower than other studies examining the respective prevalence windows for CUD. Therefore, this leaves only a few other plausible explanations for these low prevalence estimates.

Heterogeneity between studies could be attributed to the *DSM* classification of CUD, where Degenhardt et al. (2001) did not combine prevalence rates of cannabis abuse and dependence like Martins and Gorelick (2011). Interestingly, Martins and Gorelick (2011) report a high prevalence of other SUDs from 2001-2002, such as tobacco and alcohol, also supporting theories of cannabis use and CUD having the potential to become more prevalent in more recent years (Asbridge et al., 2016; Kourgiantakis et al., 2023), and therefore, resembling higher prevalence rates such as that observed in Bilevicius et al. (2019). However, it is important to note

that Martins and Gorelick (2011) and Bilevicius et al. (2019) examine any ARD or only PTSD, respectively, making these two estimates difficult to compare or say with certainty that the year of study influenced prevalence rates.

Another possible explanation as to why these studies achieved the lowest overall prevalence estimates relates to the percentage of the sample that has ever consumed cannabis. Akin to Metrik et al.'s (2022) study, when a large percentage of a sample has initiated cannabis at least once in their lifetime, this means that there is a substantially increased risk of developing CUD (Leung et al., 2020) and observing a higher overall prevalence estimate. For example, Bilevicius et al. (2019) reported that of 1779 individuals with PTSD, only ~51% had ever consumed cannabis in their lifetime. Therefore, the prevalence of comorbid CUD in individuals with PTSD is higher when only calculating the prevalence in individuals who had consumed cannabis. Conversely, Degenhardt et al.'s (2001) sample only reported that ~7% of individuals with any ARD had ever consumed cannabis, and ~29% in Martins and Gorelick's (2011) study identified as lifetime cannabis consumers. Thus, it is not shocking that these studies reported such a low prevalence rate, as not many people in the sample had ever even tried cannabis, and may have been relying on other substances, such as those mentioned in Martins and Gorelick's (2011) study, to help alleviate symptoms and distress associated with ARD diagnoses. Ultimately, there are likely many factors that contribute to how and why people choose to consume cannabis and earlier studies with only a limited number of participants ever having access to cannabis likely influence heterogeneity among estimates.

### *Veterans*

While it is challenging to evaluate if the year of study influenced the prevalence rates for veterans, the theoretical and political implications of cannabis legalization and accessibility

discussed above may also pertain to other sub-populations, such as veterans. For instance, Bonn-Miller et al. (2013) reported the earliest recruitment from 2000-2008, followed by Dillon et al. (2021), which took place between 2005-2015, and finally, Metrik et al.'s (2022) study was conducted between 2013 and 2016. Because these estimates contain a mix of lifetime and current CUD estimates, coupled with samples being inpatient, community, or outpatient samples, and samples being underpowered, we cannot claim that year of study has an impact on prevalence rates, despite Metrik et al.'s (2022) sample being the most recent study and coincidentally having the highest prevalence rate. However, it is also the smallest sample size, where 100% of veterans with PTSD were cannabis consumers.

**Gender Differences**

Among the adult general population samples, females were often oversampled, whereas the opposite was true for the veteran samples. This appears to be a systemic problem in the literature, where females are more likely to be diagnosed with an ARD than males (Farhane-Medina et al., 2022), and conversely, in veteran samples, females are underrepresented (Poole, 2021). Given that many of the samples could not distinctly differentiate the breakdown of CUD by ARD diagnosis and gender, we cannot make any definite conclusions. Further, there is the question of whether veterans are at greater risk of comorbid CUD compared to the general population or, in contrast, if it may be partially driven by a gender reversal from predominantly females with ARDs studied in general population samples relative to veteran samples representing more males with PTSD and comorbid CUD. For instance, Lev-Ran et al. (2012) analyzed NESARC I data and reported that females who consume cannabis or have CUD report greater impairments in mental health and quality of life relative to males. Based on our results from the synthesis, we can compare our findings to trends already noted in the literature.

### *Adult General Population Sample*

Overall, the evidence is inconclusive regarding gender differences and ARDs with comorbid CUD, with Tepe et al.'s (2012) study providing the most compelling evidence that men are more likely to be diagnosed with CUD relative to females. Because the primary ARD in Tepe et al.'s (2012) sample was SAD, these findings cannot be generalized to other ARDs. In contrast to our expectations, there is only slight evidence from Bilevicius et al.'s (2019) subsample of individuals with PTSD, CUD, and chronic pain suggesting that females with PTSD and chronic pain are more likely to develop CUD. However, this should be interpreted with caution as the total sample size of this subsample only included 174 participants. Further, these results would likely not generalize to the public or special populations, especially those without chronic pain. For example, many individuals often consume cannabis as a means to manage symptoms associated with chronic pain which could potentially inflate estimates of CUD in certain populations (Romero-Sandoval et al., 2018).

Finally, because Bedard-Gilligan et al. (2018) only provided the number of women and men in their sample (~75% women), coupled with their study representing the second-highest prevalence estimate, it is consistent with the other included adult general population studies where females are more likely to be recruited in ARD samples. Indeed, the literature does support that females are twice as likely to be diagnosed with PTSD relative to their male counterparts (Christiansen & Hansen, 2015; Perrin et al., 2013). However, how this relationship transfers to the comorbidity of CUD is less clear. We are also unable to evaluate how this relationship may appear across various ARDs.

In an online Dutch survey, a network analysis was performed among participants reporting weekly cannabis use, wherein men over reported 6 out of the 11 criteria for CUD in the

*DSM-5* (Kroon et al., 2023). However, while women were more likely to self-report anxiety and mood disorders, in men, anxiety disorders were linked to CUD primarily through the criteria relating to unsuccessful attempts to reduce/quit cannabis, and mood disorders were only associated with CUD through anxiety disorders. In contrast, for women, depression was associated with CUD through withdrawal and craving symptoms, while anxiety was linked through mood disorders in the network model. Overall, these findings are indicative of gender differences not only among the mechanisms and interaction of cannabis use and comorbidities but also demonstrate the implications of how CUD is conceptualized in the *DSM* and the potential impact on prevalence rates among genders.

While the literature suggests that females are more likely to develop an ARD based on psychosocial and biological factors, it is unclear whether males are going undetected and underreported (Farhane-Medina et al., 2022). Conversely, it is suggested that men are more likely to develop externalizing disorders, such as SUDs (Kozak et al., 2021; Kroon et al., 2023; Farhane-Medina et al., 2022). In a study by Dugas et al. (2019), they identified several factors associated with an increased likelihood of problematic (i.e., daily) cannabis use, including older age, male gender, elevated family and general stress levels, alcohol, cigarettes, and other tobacco product use, as well as the presence of smoking habits among parents, siblings, and friends. Higher body mass index, increased impulsivity and novelty-seeking tendencies, along with lower self-esteem, were also identified as contributors to the heightened odds of engaging in problematic cannabis use.

There is evidence that young adult men of racial/ethnic minorities, as well as those of lower socioeconomic/educational status, tend to engage in more frequent (e.g., daily) use of cannabis products (Jeffers et al., 2021). This is alarming as men, influenced by societal norms,

may be less inclined to seek help for mental health or substance use issues due to perceived expectations of strength and self-reliance (Lindinger-Sternart, 2015; Oliver et al., 2005). Additionally, individuals with lower socioeconomic/educational status may face financial barriers to accessing healthcare services (Asselin et al., 2022; Shaghaghi et al., 2014). Accessing treatment and support for cannabis use problems typically involves financial resources. Individuals without sufficient coverage may be discouraged from seeking assistance due to affordability concerns, resulting in restricted access to high-quality healthcare services, including programs for mental health and substance use treatment.

### *Veteran Sample*

For the veteran studies, again, we are unable to draw any conclusions regarding gender differences as the samples were largely composed primarily of male veterans. However, two studies included about 20-25% of females in their samples, yet it is unclear if this is representative of the ratio of male to female veterans. Previous research suggests that females would represent 10% of the veteran population in 2018, with this number estimated to grow to 14% by 2033 (Yano et al., 2010). However, the Department of VA reports that 44.2% of females are enrolled in their healthcare system (Yano et al., 2010), and in Canada, female veterans represent approximately 13% of the population as of 2022 (Veteran Affairs Canada, 2021).

Similarly, one study conducted with the NESERC wave III data suggests that female veterans with past-year PTSD represent 11.4% of the population whereas male veterans represent 5.2% of the population (Lehavot et al., 2018). Not only is the prevalence of current PTSD higher in women veterans than men, but both show elevated rates of PTSD relative to the civilian population (6.0% and 2.7%, respectively). Potential reasons for the heightened estimates of PTSD in female veterans include being more likely to experience sexual harassment and

assault prior to their services, and even during deployment (Brunet et al., 2015; Hourani et al., 2015). In contrast, males may be more likely to experience combat or different trauma exposures (Brunet et al., 2015). Thus, without these details being reported in research or with samples that are unrepresentative of the female veteran population, it is difficult to ascertain the true estimate of PTSD among male and female veterans. However, is also possible that the two veteran studies that employed more females relative to the other studies had a proportion of females who never consumed cannabis. Indeed, the literature does suggest that males are more likely to initiate and consume cannabis more frequently than females (Hall et al., 2020; Kozak et al., 2021).

## Exploratory Narrative Synthesis

### *Cannabis-Related Variables*

Several exploratory syntheses were explored, whereby we identified important variables often overlooked in many studies. Firstly, as mentioned above, the prevalence rate for comorbid CUD in ARDs is much higher when only considering the percentage of the sample who have ever consumed cannabis. Some studies neglected to report this information, which is an important, limiting factor as to the highest CUD prevalence possible in that sample; individuals not exposed to cannabis cannot develop CUD. Further, there was insufficient information among the included studies to assess other potential influences. For example, studies often neglected important variables that are cited throughout the literature as having an influence on problematic cannabis consumption, such as the frequency participants consumed cannabis, the types of cannabis products consumed, Δ9-THC and CBD concentration/potency, and age of cannabis initiation (Arterberry et al., 2019; Hall et al., 2020; Hines et al., 2020; Leung et al., 2020; Russell et al., 2018). While smoking dried cannabis flower, either in the form of a joint, pipe, or bong, is the most common route of administration (Health Canada, 2022a; Jeffers et al., 2021), this mode

of use is concerning when coupled with higher-potency products, as it could lead to a reinforcing pathway due to the intense dopaminergic and anxiolytic effects (Kubilius et al., 2018). Further, individuals who consume cannabis concentrates tend to endorse increased CUD symptom severity, psychological dependence, and withdrawal symptoms than individuals who consume cannabis in the dried flower form (Bidwell et al., 2018; Freeman & Winstock, 2015; Meier, 2017), marking this as an important participant characteristic for studies to account for.

***Comorbid Conditions and External Factors***

Overall, it appears that individuals with a primary diagnosis of any ARD may be at risk for not only CUD, but other SUDs, psychiatric conditions, physical disabilities, and increased severity/extent of combat in veteran samples. These variables can provide context to the complexity of the relationship, explaining possible pathways and heterogeneity among estimates. For instance, a diagnosis of an ARD may lead to not only SUDs, but mood disorders or other psychiatric conditions simultaneously. Similarly, physical disabilities/injuries may contribute to the development of an ARD or mood disorder, which then leads to the development of a SUD. While the purpose of this review was narrowed down to examine CUD comorbidity in individuals with ARDs, it is important to consider how or why this relationship persists. In fact, it may be much more complex than just a relationship between two variables and measuring other variables in various models can provide a glimpse into possible pathways and risk factors.

It may be the case that an additional factor affecting prevalence rates across studies is the percentage of those with an ARD who have a comorbid depressive disorder. For example, across many of the included studies, MDD was a highly reported comorbid disorder with ARDs and CUD. Research does provide evidence of a high co-occurrence between anxiety and depressive disorders, anxiety (e.g., GAD) and CUD, and depressive disorders and CUD (Belzer & Schneier,

2004; Kessler et al., 2005a; Onaemo et al., 2021). Thus, it is possible that depressive disorders/symptomology could mediate the relationship between anxiety and CUD (Frojd et al., 2011). If research is conducted among types of SUD that are comorbid alongside specific ARDs, healthcare professionals can prioritize early interventions and treatment plans for at-risk groups.

For the veteran samples, Metrik et al. (2022) described the most detailed combat experience, with the highest percentage of veterans reporting intensive trauma/combat experience, which may correspond to why they also reported the highest prevalence rate among all the included studies. Importantly, whether veterans are deployed in combat arms or support trades does not dictate if they were exposed to traumatic events (Storey et al., 2023). Indeed, veterans in support trades may report undergoing enemy fire while undergoing a supply run.

Further, due to various deployment experiences, many veterans may be at risk of developing physical or mental impairments, or comorbidities. For instance, anecdotes from veterans detail instances where prescription medication for chronic pain associated with combat was associated with an influx of symptoms related to suicidality, an increase in PTSD severity, and cognitive impairments (Storey et al., 2023). Unsurprisingly, undergoing these related challenges can lead to the co-occurrence of a depressive disorder (Liu et al., 2019). Consequently, cannabis may be perceived as a safer alternative with less severe side effects to help cope with associated negative affect and distress. Similarly, one study found that among veterans with comorbid PTSD and MDD, motivation to use cannabis to aid with sleep mediated the relationship between PTSD and MDD (Metrik et al., 2016). When accounting for coping motives, such as alleviating negative affect/distress in their model, sleep mediated the effects of PTSD and MDD on CUD. Importantly, many veterans may either self-medicate with cannabis or are prescribed cannabis by a healthcare professional. In Canada, from 2023 to 2024, the federal

government provided $191 million in reimbursement for medical cannabis to over 24,000 veteran patients (Veteran Affairs Canada, 2024). While the use of medical cannabis is heavily debated, and healthcare professionals may be hesitant to prescribe or screen for cannabis-related problems (Christensen et al., 2021; Giovanni et al., 2022), there are consequences for neglecting cannabis as a line of treatment for mental health among veterans. For example, when there is a disconnect between healthcare professionals and patients, there is a lack of education and support on cannabis consumption, which can increase problems with cannabis (Bujarski et al., 2016). However, there are also valid concerns about prescribing cannabis, such as whether the patient will have the ability to stay active in military service and doubts about whether providers themselves are educated and experienced enough to prescribe cannabis as a treatment. Nonetheless, cannabis as a sleep aid for veterans can help explain to providers why their patients may have ambivalence about quitting cannabis (Metrik et al., 2016) and neglecting valid patient concerns about cannabis use can result in a lack of understanding and disconnect between providers and patients.

**Clinical Implications**

The results obtained from this systematic review are relevant because they highlight the importance of explaining the complexity involved in ARD-related comorbidities such as CUD. Indeed, knowing the prevalence of CUD among individuals with ARDs allows healthcare professionals to assess and manage co-occurring conditions, informing their treatment approach. Further, if future research can support that there is an increased risk of CUD in ARD populations, targeted interventions that are transdiagnostic in nature may not only help treat patients but inform clinicians to better probe for underlying SUDs. Finally, while considering the societal implications of SUDs and how much stigma the public and professionals tend to endorse

(e.g., Corrigan et al., 2009; Lloyd, 2013; Schomerus et al., 2010; van Boekel et al., 2013), increasing awareness and recognition of CUD among individuals with ARDs can help reduce the stigma surrounding both conditions, improving help-seeking, disclosure, and access to treatment. Recognizing that these disorders commonly co-occur can promote more empathetic and supportive attitudes towards individuals seeking help for mental health and substance use challenges. Therefore, it is essential to enhance screening and psychoeducation for SUDs among primary care and allied health professionals (Hawk & D'Onofrio, 2018). Healthcare professionals, stakeholders, and policymakers play a significant role in providing psychoeducation on cannabis use risk factors, such as potency and frequency of consumption. A lack of oversight and guidance from healthcare professionals on safer cannabis use guidelines could lead to cannabis-related harms if patients try to manage consumption on their own, relying on peers and the internet for information (Kruger et al., 2020). For starters, disseminating a resource such as the lower-risk cannabis use guidelines (LRCUG; Fischer et al., 2022) more broadly in clinics, non-profit organizations, and regulated cannabis distributors could be an effective strategy to reduce cannabis-related harms and comorbidities.

Health promotion is an essential strategy for many policymakers and healthcare professionals. However, current regulations prohibit retailers from promoting anything cannabis-related, which includes disseminating promotions from online publishers, such as research (Health Canada, 2022). Currently, this may be having a drastic impact on the way consumers are informed about cannabis products, as retailers may be the first point of contact for cannabis initiation. One study found that many provincial online licensed retailers violated the Cannabis Act guidelines for the promotion of cannabis (Sheikhan et al., 2021). This was especially prominent across social media platforms such as Facebook, Instagram, and Twitter, often lacking

age restrictions, glamorizing the brand, and neglecting to include risk information. While these findings can suggest a need to enforce current laws for cannabis promotions since social media is a hub for youth to gain misinformation on cannabis, they also may suggest revisions to the current regulations. If standards were developed, it could alleviate misconceptions and promote harm reduction, lower-risk use, and early intervention/prevention. Given the recency of cannabis legalization, there are expected to be delays in how regulations are implemented for research to inform best practices. However, the LRCUG cautions against using non-medical cannabis when an individual has pre-existing mental health issues, including ARDs (Fischer et al., 2022), which could be particularly beneficial for consumer knowledge prior to purchasing or initiating cannabis.

The distinction between the use of prescription medications (e.g., SSRIs) or cannabis in alleviating anxiety-related symptoms is a subject of ongoing debate. Although SSRIs and CBT are widely regarded as the gold standard treatments, the empirical support for cannabis in the treatment of ARDs remains limited (Pratt et al., 2019). For instance, although some studies suggest that certain cannabis properties (e.g., CBD) may be effective in treating conditions like PTSD, SAD, and GAD, a meta-analysis revealed that these associations were no longer significant when adjusting for publication bias (Bahji et al., 2020). Additionally, OCD and PD were not included in this analysis due to the absence of qualifying studies. This highlights a gap in understanding how cannabis interacts with specific ARDs, psychotropic drugs, and underlying family histories, such as a predisposition to psychosis (Bahji et al., 2020; Carvalho & Vieira-Coelho, 2022). Moreover, SSRIs are prescribed and administered under the supervision of a healthcare professional, ensuring that their use is carefully monitored. In contrast, cannabis is becoming frequently used as self-medication for anxiety symptoms (Leung et al., 2022), often

without the same level of medical oversight. However, the scarcity of evidence does not necessarily indicate that cannabis is ineffective; rather, it underscores the need for further research to validate its therapeutic potential.

Proponents of medical cannabis often cite the perceived benefits, with individuals reporting symptomatic relief or enhancements in quality of life (Back et al., 2014; Das et al., 2024; Green et al., 2003; Sterniczuka & Whelan, 2016). Yet, much of the extant literature and mass media frequently overemphasize the adverse effects of cannabis, sometimes contributing to increased stigmatization, particularly among non-medical consumers (Coles et al., 2024; Mortensen et al., 2020). Similarly, there is a risk of over-pathologizing individuals who consume cannabis and have an ARD. Indeed, cannabis does have anxiolytics and analgesic properties, producing relaxing effects akin to the consumption of an alcoholic beverage on occasion. In instances of non-problematic cannabis use, a diagnosis of CUD would not be applicable as there is no distress or impairment to the individual's life. Nonetheless, it is important for healthcare professionals to screen for signs of problematic use when patients present with an ARD. This can be achieved by adopting a balanced approach where occasional cannabis consumption is deemed acceptable while also promoting awareness of potential risks and encouraging safer consumption practices, such as using a higher CBD-to-THC ratio or avoiding inhalation methods (Fischer et al., 2022). This strategy ensures that individuals are both informed about the potential consequences of cannabis use and empowered to make safer choices. Ultimately, reducing rates of non-disclosure or avoidance of healthcare professionals due to their ambivalence toward prescribing medical cannabis would also decrease risks associated with self-medication, such as inappropriate dosage, CUD, misperceptions of efficacy, and non-supervision from healthcare professionals (Asselin et al., 2022; Kedzior et al., 2014; Volkow et al., 2014; Wallis et al., 2022).

As a final caveat, although we do not have an overall meta-analytic estimate of the prevalence of comorbid CUD in a typical ARD sample, we have identified individual studies showing a 1 in 5 rate of ARDs with comorbid CUD. Research demonstrates that 10-25% of individuals may have an ARD at some point in their lives, whereby 24% will also have a co-occurring SUD (Skinner et al., 2004). This leads to important implications for clinicians concerning the identification and treatment of comorbid SUDs in ARD populations. For individuals with concurrent disorders, it is less important whether ARDs caused SUD onset or vice versa; rather, they are mental health issues that interact with each other (Canadian Centre on Substance Abuse, 2009). However, having a single, more severe psychiatric disorder increases the risk of developing concurrent SUDs (Hakobyan et al., 2020).

Patients with concurrent disorders are more likely to receive less care than needed and do not have access to formal healthcare, such as physicians/clinicians (Urbanoski et al., 2007; Wiktorowicz et al., 2019). Further, individuals with concurrent disorders are also three to four times more likely to be hospitalized and experience higher rates of morbidity, mortality, unemployment, poverty, homelessness, social isolation, and incarceration than those with only one disorder (Abram & Teplin, 1991; Compton et al., 2005; Dilonardo et al., 2008; Ruglass et al., 2014; Rush et al., 2011; Todd et al., 2004). This is partly because traditional treatment approaches involve unparalleled care, with separate providers, organizations, and funding within the healthcare system (Hakobyan et al., 2020; Ruglass et al., 2014). Consequently, SUDs may be neglected in treatment, resulting in patients having their needs unmet. Accordingly, research proposes that integrated treatment is the gold standard for concurrent disorders (Rugless et al., 2014; Rush, 2011). For example, in Newfoundland and Labrador, service-level integration guidelines for concurrent disorders involve mental health and addiction treatment by the same

clinician in the same setting or through a collaborative approach where two or more healthcare professionals ensure the patient is receiving access to services/supports and continuity of care (Health Canada, 2015). Similarly, integrated approaches can involve psychosocial/behavioural therapy (e.g., exposure-based therapy, CBT) and pharmacotherapy (e.g., sertraline; Rugless et al., 2014). While this recommendation sounds promising in theory, unfortunately, many provinces such as Newfoundland and Labrador are unable to implement this treatment approach as there is an over-reliance on facility-based care, resulting in a fragmented system that requires change to better represent and meet patient needs (Government of Newfoundland and Labrador, n.d.). Recognizing these issues has led to efforts to initiate system-level changes, prioritizing support for individuals with complex and interacting challenges.

Because an individual's pathway to concurrent disorders is unique and likely a result of interacting risk, precipitating, and perpetuating factors, it is important to identify markers of concurrent disorders and begin treatment as early as possible to establish optimal outcomes. Indeed, the reciprocal relationship between ARDs and SUDs can be complex, imitating symptoms from either disorder (Rugless et al., 2014; Skinner et al., 2004). Therefore, identifying the efficacy of various treatments and tailored interventions that match patient symptom presentations are needed to help understand and establish personalized care, patient engagement, improved outcomes (i.e., reduction in treatment dropout/symptoms/SUD reoccurrence), and optimal resource allocation.

**Strengths, Limitations, and Future Directions**

While we were unable to conduct a meta-analysis to obtain an aggregate estimate for the prevalence of CUD in individuals with ARDs, this systematic review provides a detailed account of ongoing issues in the literature. However, it is not without limitations. Although our search

was comprehensive and we met with a research librarian to reduce the likelihood of missing key articles, it is possible that some articles were missed in the search. Thus, there are steps that can be taken to re-identify articles that may have been missed in the initial search, such as including more databases and conducting an updated search. Indeed, the sample size from each synthesis was small, limiting our ability to draw conclusions pertaining to our hypotheses.

Another limitation was the general lack of available literature. Specifically, there was a limited number of studies that included representative control groups in research investigating ARD-CUD comorbidity. Further, many of the samples were not comparable due to methodological heterogeneity. For instance, there was variability in sampling techniques, including differences in sample sources (inpatient, outpatient, community), diagnostic classifications (*DSM-IV* and *DSM-5*), sample sizes, and recruitment methods (random vs. non-random sampling). Ultimately, this variability limited our ability to make any direct comparisons across studies, hindering our confidence in estimates and preventing aggregation.

A major bias identified in this review pertained to regional variability. Almost all the included studies in both reviews, with the exception of one, were conducted in the USA, limiting the overall global generalizability of our findings. Considering recent policy developments globally around cannabis legalization, it was disappointing that we were unable to discuss any potential implications further. The legal status of cannabis, availability of treatment options, and healthcare system structures can differ between countries and may influence patterns of cannabis use, access to treatment, and prevalence of CUD. By limiting the analysis to studies conducted in the USA, the review may overlook important nuances related to policy and healthcare system influences on ARD and CUD comorbidity prevalence. Finally, there may be temporal factors that influence estimates, but unfortunately, because of heterogeneity among studies, it may be

merely a coincidence that we observed this trend, and this finding should be interpreted with caution.

Future research should aim to report current or lifetime estimates for CUD, carefully distinguishing between different ARDs as it is possible that some ARDs are at greater risk of CUD than others. Indeed, both current and lifetime rates are informative. However, current estimates are limited to only providing a snapshot of a specific time window. Thus, when examining current estimates, it is possible to miss someone who has struggled with CUD for decades. Similarly, retrospective prevalence rates (i.e., lifetime estimates) have issues with recall errors. Nonetheless, we were unable to evaluate any estimates for disorders such as OCD, GAD, and specific phobia, for example, and this may be a gap in the literature that is worth investigating. In addition to reporting specific ARDs, it is also paramount that studies include cannabis-related variables, such as the number or percentage of participants in the sample that have consumed cannabis in their lifetime. Neglecting these characteristics contributes to heterogeneity within the prevalence estimates.

Further, more recent studies using the *DSM-5* or *ICD-11* criteria would benefit the field of study, as cannabis abuse and dependence diagnoses have been criticized on the grounds of creating diagnostic orphans, hierarchical diagnoses, and incorrect assumptions (Hasin et al., 2013). Additionally, studies would benefit from greater representation concerning not only geographical regions but also the inclusion of more females in veteran studies and more ethnic diversity throughout. Finally, many studies were excluded in the screening phase due to individual estimates being reported in text (i.e., only the prevalence of CUD in the entire sample) instead of the prevalence of CUD in ARDs. However, we also observed the opposite, where the prevalence of ARDs in CUD samples was reported. Providing these estimates and being clear

about the directionality of the outcome is crucial for interpreting the prevalence estimates with validity. While it may be arbitrary to say that ARD is the primary disorder (rather than CUD), often, the primary diagnosis is defined by the treatment setting. For instance, we excluded samples where participants were attending residential drug treatment centres as all subjects would, by definition, have a SUD diagnosis, and would demonstrate a ceiling effect on prevalence estimates.

Through exploratory syntheses, we observed a potential for complex interactions between variables such as gender, trauma exposure, substance use patterns, and various mental health diagnoses/comorbidities. Acknowledging these interactions requires careful consideration of multiple factors and may pose challenges in drawing definitive conclusions. However, to better understand the relationship between ARDs and CUD, longitudinal studies are warranted to determine potential pathways of this relationship. Further, network models may be quite informative in elucidating the relationships among variables or symptoms within a system, such as symptoms of mental disorders or risk factors for certain outcomes. When more data permits, a future meta-analysis will be able to examine the moderators we initially proposed (age of initiation, gender, sample/setting, etc.). However, studies must carefully consider how they measure these factors, especially concerning cannabis-related variables such as potency, which are challenging to standardize and measure consistently across studies.

## Conclusion

Our attempts to conduct a meta-analytic estimate for the comorbidity of CUD in individuals with ARDs resulted in a systematic review of two study populations: adult general population samples and veteran samples. While our conclusions are tempered, given the limited number of studies currently available, preliminary evidence suggests that individuals with ARDs

are at an increased risk of experiencing comorbid CUD. However, insufficient studies also hindered our ability to draw conclusions from this systematic review. Nonetheless, the contents of this review are informative as we draw on critical issues in the literature to hopefully inform future studies as we approach transformative policies worldwide concerning cannabis legalization. Understanding the potential health and social consequences of cannabis use and what specific populations are at risk of heightened comorbidity is imperative to inform healthcare professionals on the importance of screening ARD populations for CUD comorbidities and, subsequently, investigating viable treatment options.

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