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Review

The prevalence of cannabis use disorders in people who use medicinal cannabis: A systematic review and meta-analysis

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ABSTRACT

Background: The prevalence of cannabis use disorders (CUDs) in people who use cannabis recreationally has been estimated at 22%, yet there is a dearth of literature exploring CUDs among people who use medicinal cannabis. We aimed to systematically review the prevalence of CUDs in people who use medicinal cannabis.
Methods: In our systematic review and meta-analysis, we followed PRISMA guidelines and searched three databases (PsychInfo, Embase and PubMed) to identify studies examining the prevalence of CUDs in people who use medicinal cannabis. Meta-analyses were calculated on the prevalence of CUDs. Prevalence estimates were pooled across different prevalence periods using the DSM-IV and DSM-5.
Results: We conducted a systematic review of 14 eligible publications, assessing the prevalence of CUDs, providing data for 3681 participants from five different countries. The systematic review demonstrated that demographic factors, mental health disorders and the management of chronic pain with medicinal cannabis were associated with an elevated risk of CUDs. Meta-analyses were conducted on the prevalence of CUDs. For individuals using medicinal cannabis in the past 6–12 months, the prevalence of CUDs was 29% (95% CI: 21-38%) as per DSM-5 criteria. Similar prevalence was observed using DSM-IV (24%, CI: 14–38%) for the same period. When including all prevalence periods and using the DSM-5, the prevalence of CUDs in people who use medicinal cannabis was estimated at 25% (CI: 18-33%).
Conclusions: The prevalence of CUDs in people who use medicinal cannabis is substantial and comparable to people who use cannabis for recreational reasons, emphasizing the need for ongoing research to monitor the prevalence of CUDs in people who use medicinal cannabis.

1. Introduction

The increase in the use of medicinal cannabis on a global scale has prompted concern about the potential for adverse health effects associated with its medical use (Gliksberg et al., 2023; Potenza et al., 2023; Leung et al., 2022b). Recent literature indicates that over one quarter (27%) of adults in the United States have used cannabis for medicinal reasons (Leung et al., 2022b). More than a dozen nations across the world (e.g., Australia, Canada, United States) have enacted legislation to allow the medical use of cannabis for a variety of medical conditions such as chronic pain, anxiety, sleep difficulties and neurological disorders (European Monitoring Centre for Drugs and Drug Addiction, 2023; Graham et al., 2023). In most countries, only a brief screening process conducted by a physician is typically required to gain access to medical cannabis (Cooke et al., 2023). The monitoring of cannabis use is not usually mandated, and patients are granted the autonomy to select from a diverse range of cannabis products through an administrative entity rather than relying on a traditional prescription-based approach that specifies the doses of cannabinoids that will be used (Graham et al., 2023; Hallinan and Bonomo, 2022). A matter of considerable concern within the realm of public health is that the regular use of medicinal cannabis (e.g. for chronic, life-long conditions) may place patients at a heightened risk of cannabis use disorders, which are prevalent (22% [95% CI: 18–26%]) among individuals who engage in recreational

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cannabis use (Leung et al., 2022a). To date, there is a dearth of literature exploring the prevalence and risk factors for cannabis use disorders among people who use cannabis medicinally.

The diagnostic criteria for cannabis use disorders (CUDs) have evolved over time, as reflected in changes in the Diagnostic and Statistical Manual of Mental Disorders (DSM) editions, and within the International Classification of Diseases (ICD) definitions (Connor et al., 2021). In the DSM-IV, cannabis abuse and dependence were treated as separate entities, with specific criteria for each. Dependence was characterized by a compulsion to use cannabis, loss of control over use and tolerance (American Psychiatric Association, 2022). The DSM-5 removed the distinction between abuse and dependence, introducing a single diagnosis of CUD that varied in severity from mild to moderate and severe. The DSM-5 criteria encompasses symptoms such as the development of tolerance, withdrawal symptoms, unsuccessful efforts to reduce or control use, and continued use despite known adverse consequences (American Psychiatric Association, 2013, 2000). The most recent edition of the ICD system, the ICD-11, describes problematic cannabis use as a pattern of use that leads to significant health, social, or personal problems (WHO, 2019). The broad criteria used in the ICD-11 are less granular than the DSM-5 but captures the essence of problematic cannabis consumption that adversely affects daily life.

Despite medical authorisation, people who use cannabis for medicinal reasons may still develop CUDs (Gendy et al., 2023; Gilman et al., 2023). Over time and increased exposure, these individuals may build a tolerance to the effects of THC, requiring increased doses to achieve the same medicinal effects (Haug et al., 2017). Escalating use can lead to physical and psychological dependence, where consumers experience withdrawal symptoms like irritability, insomnia, or restlessness if they reduce or stop using medicinal cannabis (Bonn-Miller et al., 2014). Moreover, some patients might find themselves dedicating excessive time to obtaining or using medicinal cannabis, or they may persist in its use despite recognizing its adverse effects on their mental health or social, professional, and personal life. It is important to recognize that even within a medical context, the risk of developing CUDs remains, and it is important to track and minimise this risk where possible. In this paper, we aim to conduct the first systematic review of the evidence on the prevalence of CUDs in people who use cannabis for medicinal reasons.

2. Method

2.1. Protocol

The systematic review and meta-analysis was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Supporting Information 1), and the protocol was prospectively registered at the International Prospective Register of Systematic Reviews (PROSPERO) with registration ID: CRD42023396332 (PROSPERO).

2.2. Search strategy and selection criteria

The eligibility criteria were developed based on the framework of the population, exposure, comparison and outcome (PECO) eligibility checklist (Supporting Information 2). Articles that reported human exposure to medicinal cannabis at any level of the population were included. Studies that reported exposure exclusively to recreational cannabis were excluded. If recreational and medicinal cannabis exposure was reported, the study was included. To be included, the study had to report the prevalence (%) of problematic cannabis use, cannabis use disorder, cannabis dependence or cannabis abuse in people who use cannabis for medicinal reasons. We searched PsychInfo, Embase and PubMed for published studies using search terms related to “cannabis use disorder” and “medicinal cannabis” (Supporting Information 3) starting from 2010 to ensure recent literature. The search was performed in March 2023. Google Scholar, hand search, Elicit and other additional searches were performed.

2.3. Selection process

The primary measure was the percentage of those who met the threshold set by the criteria used in each study for problematic cannabis use, CUD, CA or CD (herein ‘Cannabis Use Disorders’), among those who had used cannabis for medicinal reasons.

2.4. Data extraction

Data was extracted by two investigators independently and cross-checked. We extracted data on year of publication, age and gender of participants, how medicinal cannabis exposure was defined (e.g., self-report, possession of medicinal cannabis card), the criteria used for CUDs (e.g., DSM-5), prevalence period, how CUDs were measured (i.e., tool used). We also collected data on the medicinal cannabis products used, route of administration, recreational cannabis use, and other medications used if reported.

2.5. Quality assessment

Two investigators independently assessed the risk of bias for the included studies using the JBI risk-of-bias tool for cross-sectional, cohort and randomised clinical trials (Aromataris and Munn, 2020), with dichotomised scoring for each item. There was a high level of agreement in the assessments between the raters (>90% rating scores across all studies), and consensus was reached for all studies after discussion (Supporting Information 4).

2.6. Data analysis

Random effects meta-analyses were conducted to pool the prevalence estimates extracted. R Studio (version 2023.06.2+561) was used to conduct the meta-analysis. The double arcsine transformation method was used to address variance instability. Cochran’s Q value, as well as I^2 statistics, were used to assess heterogeneity of the study findings. Stratified analyses were conducted by prevalence time frames and diagnostic criteria.

3. Results

The search identified 526 unique records. After title and abstract screening, we included 39 articles for full-text screening. 14 articles were retained for quantitative meta-analyses following full-text screening (see Fig. 1).

3.1. Study design

Ten studies were cross-sectional, two were cohort studies and two were randomized clinical trials. Eight of the samples were located in the United States, two were from Australia, two from Canada, one from Israel and one from Germany (see Table 1).

3.2. Risk of Bias

The quality score for cross-sectional studies was between 6 and 8 out of 10, for cohort studies it was 10 out of 11, and randomised clinical trials were both 11 out of 13. Most of the studies relied on self-report measures for CUDs. Overall, the studies were of good to very good quality and did not have a high risk of bias (see Supporting Information 4; S7, 9, 11.).

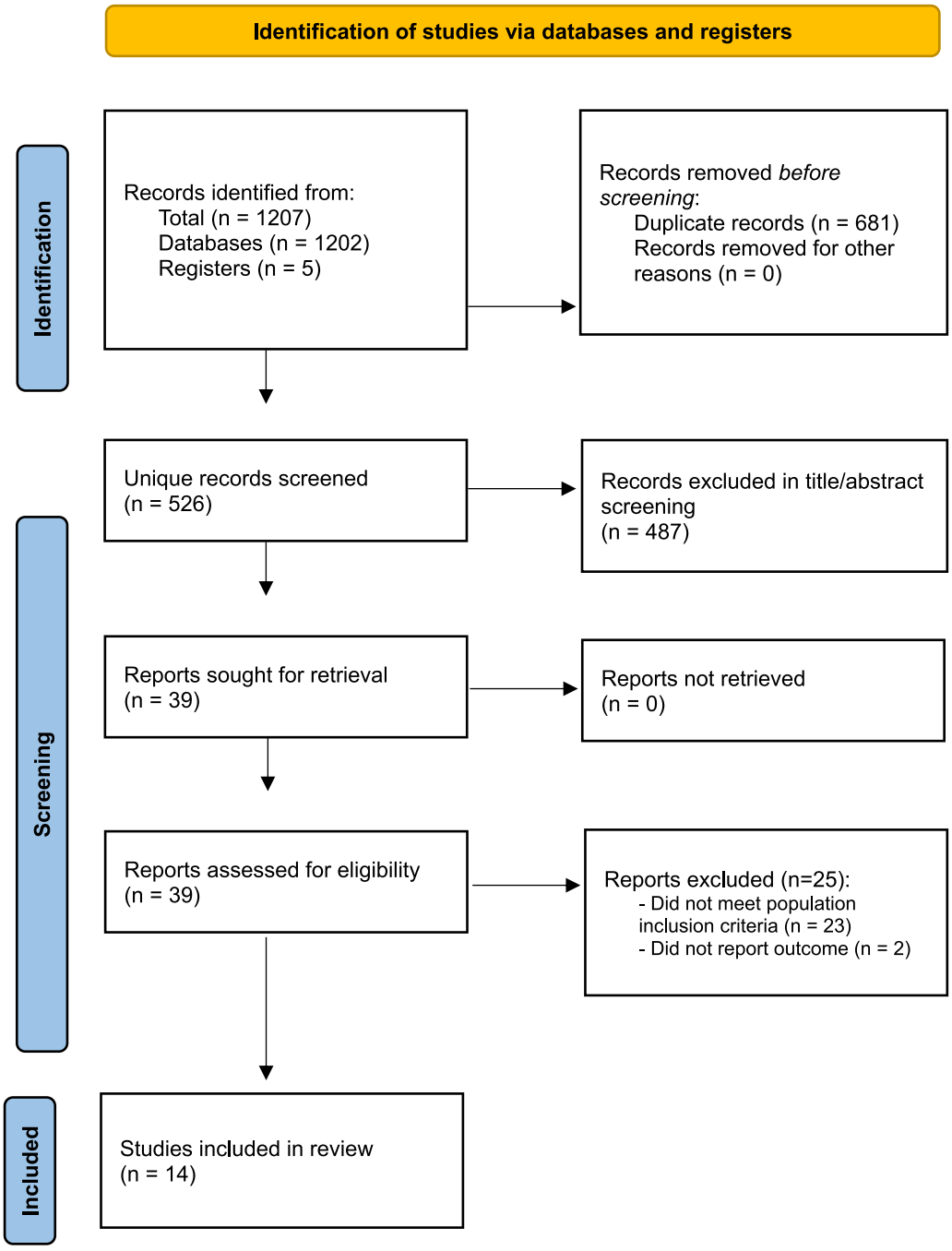

Fig. 1. PRISMA Flowchart.

3.3. Diagnostic criteria

Ten studies used the DSM-5 criteria to diagnose CUDs among people who used medicinal cannabis. Of these, three studies administered novel questionnaires based on the DSM-5 criteria during interviews. Three administered self-report novel questionnaires based on the DSM-5 criteria. One study used the Alcohol Use Disorder and Associated Disabilities Interview 5 (AUDADIS-V, Rubin-Kahana et al., 2022). Finally, three studies used the self-reported Cannabis Use Disorder Identification Test-Revised (CUDIT-R) to screen for CUDs (Adamson et al., 2010). Three studies used the DSM-IV criteria. Of these, one used a novel self-report questionnaire, one used the AUDASIS-IV (Bialas et al., 2023) and another used a structured clinical interview. Degenhardt et al. (2015) used the ICD 10 criteria assessed by the World Health Organization Composite International Diagnostic Interview (WHO CIDI) version 3.0.

3.4. Sample characteristics

Three studies recruited participants with chronic pain; two of which measured past year prevalence of CUDs and one measured lifetime prevalence (Bialas et al., 2023; Degenhardt et al., 2015; Feingold et al., 2016). Two studies recruited participants from medicinal cannabis dispensaries in the US to investigate the past 6-month prevalence of CUDs (Haug et al., 2017; Bonn-Miller et al., 2014). Three studies used national level surveys to assess the past 12-month prevalence of CUDs (Mills et al., 2022; Rubin-Kahana et al., 2022; Lin et al., 2016). One randomised clinical trial assessed numerous time points for CUDs, with 3

Table 1
Study characteristics of the prevalence of cannabis use disorders in people who use medicinal cannabis: a systematic review and meta-analysis.

First Author (year)	Country, setting (sample size)	Female	Mean age (SD)	Design	Criteria (diagnostic tool)	Any CUDs (% [95% CI])		
						Lifetime	6–12 months	3 months
Bialas et al. (2023)	Germany, pain service (*N*=187)	67%	54.4 (–)	Cs	DSM-5 (11 item)	–	29% [23–36%]	–
Bonn-Miller et al. (2014)	USA, medicinal cannabis dispensary (*N*=217)	27%	41.2 (14.9)	Cs	DSM-IV (Structured Clinical Interview; CUDIT-R)	–	38% [31–44%]	–
Cooke et al. (2023)	USA, clinical trial setting (*N*=163)	68%	37.3 (14.4)	RCT	DSM-5 (Structured Clinical Interview; 11 item;)	–	12% [7–17%]	–
Degenhardt et al. (2015)	Australia, pain service (*N*=237)	38%	48.7 (10.1)	Cohort	ICD-10 (WHO CIDI)	33% [27–39%]	–	–
Feingold et al. (2016)	Israel, pain service (*N*=406)	44%	-	Cs	DSM-IV (AUDADIS-IV)	–	21% [17–25%]	–
Gendy et al. (2023)	Canada, substance use inpatient service (*N*=53)	32%	41.3 (10.7)	Cs	DSM-5 (9 item)	–	–	28% [17–41%]
Gilman et al. (2022)	USA, clinical trial setting (*N* = 105)	72%	37.9 (14.3)	RCT	DSM-5 (11 item)	–	–	10% [5–17%]
Gilman et al. (2023)	USA, clinical trial setting (*N*=149)	69%	37.5 (14.6)	Cohort	DSM-5 (11 item)	–	13% [8–19%]	–
Haug et al. (2017)	USA, medicinal cannabis dispensary (*N*=217)	24%	41.2 (14.9)	Cs	DSM-5 (CUDIT-R)	–	35% [29–42%]	–
Lin et al. (2016)	USA, national survey (*N*=336)	46%	-	Cs	DSM-IV (22 item)	–	14% [10–18%]	–
Mills et al. (2022)	Australia, national survey (*N*=905)	43%	44.4 (13.25)	Cs	DSM-5 (11 item)	–	32% [29–35%]	–
Myers et al. (2023)	USA, veterans medical service (*N*=104)	10%	53.0 (14.7)	Cs	DSM-5 (CUDIT-R)	–	47% [38–57%]	–
Rubin-Kahana et al. (2022)	USA, national surveys (*N*=362)	36%	39.9 (0.98)	Cs	DSM-5 (AUDADIS-V)	–	47% [42–52%]	–
Smith et al. (2019)	Canada, university (*N*=240)	57%	23.2 (5.2)	Cs	DSM-5 (CUDIT-R)	14% [10–19%]	–	–

Abbreviations:
Cs, cross-sectional; RCT, randomised clinical trial.
22 item - 22 item CUD questionnaire in National Survey on Drug Use and Health 2013
11 item – Novel 11 item questionnaire based on DSM-5 CUD criteria
9 item - Novel 9 item questionnaire based on DSM-5 CUD criteria
AUDADIS – IV - Alcohol Use Disorder and Associated Disabilities Interview Schedule 4
AUDADIS-V – Alcohol Use Disorder and Associated Disabilities Interview Schedule 5
CUDIT R – Cannabis Use Disorder Identification Test (Revised)
- not reported, – not measured

Table 2
Meta-analysis results.

	DSM-IV			DSM-5			ICD-10		
	Pooled	(95% CI)	*k*	Pooled	(95%CI)	*k*	Observed	(95% CI)	*k*
Lifetime	-	-	-	0.25**	(0.18,0.33)	10	0.33%	(0.26–0.38)	1*
Recent use (3-month)	-	-	-	0.17	(0.06,0.42)	2	-	-	-
6–12month	0.24	(0.12, 0.37)	3	0.29	(0.21,0.38)	7	-	-	-

Note. – indicates no data for analyses
*meta-analysis not run; **combined lifetime, recent use, 6-12month

months the most protracted (Gilman et al., 2022). A cohort study from the same clinical trial reported a nine month follow up on the rates of CUDs (Gilman et al., 2023). Another clinical trial reported the 12-month prevalence of CUDs (Cooke et al., 2023). One study recruited participants who were incoming into inpatient treatment for substance use disorders (Gendy et al., 2023) and measured CUDs in the following 3 months. Another two studies recruited veterans and a university sample and measured the 6 month prevalence of CUDs (Cooke et al., 2023; Smith et al., 2019). None of the studies excluded participants based on any lifetime cannabis past use but three excluded participants who had used on near-daily (Cooke et al., 2023) or daily use in the past 3 months in an attempt to not confound the sample with participants who may already have or be developing CUDs (Gilman et al., 2023, 2022).

3.5. Symptoms of CUDs

Of the seven studies which described the frequency of endorsed symptoms, over half reported tolerance to cannabis as the most commonly reported symptom of CUDs (Mills et al., 2022; Bialas et al., 2023; Gilman et al., 2022; Cooke et al., 2023). Tolerance was defined by either (Gliksberg et al., 2023) a need for markedly increased amounts of cannabis to achieve desired effect; or a markedly diminished effect with continued use of the same amount of cannabis. Withdrawal, as defined as cannabis taken to relieve or avoid withdrawal symptoms, was also frequently endorsed in numerous studies (Mills et al., 2022; Adamson et al., 2010; Degenhardt et al., 2015). Other common symptoms endorsed were as follows: 1) cannabis was often taken in larger amounts or over a longer period than was intended; 2) a persistent desire or unsuccessful efforts to cut down or control cannabis use; 3) craving; 4) recurrent cannabis use in situations in which it is physically hazardous;

5) continued use despite knowledge of having a persistent or recurrent physical or psychological condition that is likely to have been caused or exacerbated by cannabis use.

3.6. Route of administration and product type

Most studies reported that the majority of participants administered cannabis via inhalation (i.e., through joints, bongs and vaporisers). Only one study reported a majority of oral cannabis administration (74% of the sample used oral dronabinol, see (Bialas et al., 2023)). Mills et al., (2022) found a positive association between inhalation as the route of administration of cannabis and the prevalence of CUDs. Haug et al., (2017) found that inhalation was the most common route of administration and was positively associated with CUDs but noted age differences in the preference of route of administration in which older consumers preferred oral ingestion, while younger and middle-aged consumers preferred inhalation. Information on the specific product type (e.g., cannabis plant matter, vaping liquid, capsules) was not collected by most of the included studies. The nature of medicinal cannabis authorisation to use a range of products rather than prescriptions was noted as a limitation for examining which products were used in multiple studies (Gilman et al., 2023, 2022; Cooke et al., 2023).

3.7. Meta-analysis

We compared the prevalence of CUDs in studies using specific DSM criteria versions and varied prevalence periods. The pooled prevalence of CUDs was 29% (95% CI: 21–38%) as assessed by the DSM-5 criteria in people who had used medicinal cannabis in the past 6–12-month period ($k = 7$; see Table 3; forrest plots are available in Supporting Information 5). Pooled estimates were similar for studies which used the DSM-IV criteria in the 6–12 months prevalence period, estimated at 24% (CI: 14–38%; $k = 3$). CUDs prevalence in the recent use prevalence period (past 3 months) was 17% (CI: 10–28%) when assessed by DSM-5 criteria ($k = 2$). Pooled estimates across all reported prevalence periods using the DSM-5 criteria yielded similar pooled estimates of CUDs at 25% (CI: 18–33%) in people who have used medicinal cannabis (k = 10). Degenhardt et al., (2015) was the only study to use the ICD-10 criteria reporting the lifetime prevalence of CUDs at 33% (CI: 27–39%). Estimates of CUDs between the studies varied largely, ostensibly due to heterogeneity in the populations sampled.

3.8. Narrative review

There were not enough studies reporting estimates of CUD by severity, frequency of use, age, and gender so meta-analyses were not conducted by these subgroups or moderators. Instead, findings were summarised narratively.

3.8.1. Severity of CUDs

Eight studies reported the severity of CUDs, most often within the DSM-5 criteria which categorises CUDs as mild, moderate and severe. There was a higher proportion of mild CUD (55–80%) compared to moderate (11–27%) and severe (0–20%) across studies (see Table 3).

3.8.2. Frequency of use

The frequency of medicinal cannabis use was positively associated with CUDs in some studies. When comparing medicinal to recreational use, one study found that medical cannabis card holders had a higher rate of daily use (64%) than non-card holders (35%; see 27). In another study, people who used cannabis medicinally consumed cannabis more frequently than those who used it recreationally (see Rubin-Kahana et al., 2022). In Lin et al., (2016) frequency of use was positively associated with CUDs, and people who used medical cannabis were 3-times more likely to use cannabis daily (33%) than people who used recreationally (11%).

3.8.3. Age

Rubin-Kahana. et al. (2022) found that people who were younger (*Range*=18–29 years) were more likely to develop CUDs when using medicinal cannabis than older people (*Range*=30–44; $p < .05$). Haug et al., (2017) also found that being younger was a significant predictor of problematic medicinal cannabis use (X^2=15.91, $p < .001$). This was moderated by age of first regular use such that an earlier age of regular use was associated with more problematic use in the younger consumers, but not among older consumers (F=7.62, $p < .001$). One study reported that males were more likely to develop CUDs than females when using medicinal cannabis (Cohen's d=0.12, $p<.05$, see Rubin--Kahana et al., 2022).

3.8.4. Mental health

Of the included studies which investigated medicinal cannabis use among individuals with depression, these concluded that it may place them at a higher risk of developing CUDs (Gilman et al., 2023; Feingold et al., 2016; Smith et al., 2019). Particular symptoms of depression (i.e., heightened dysphoria and lassitude) were associated with a greater risk of CUDs (Bonn-Miller et al., 2014). Rubin-Kahana et al., (2022) found participants with PTSD, mood disorders, psychotic disorders, or personality disorders were more likely to develop CUDs compared to other health conditions. Broad-spectrum measures of psychological health in people using medicinal cannabis were also associated with a greater risk of CUDs, such that poorer psychological health and worsened mental health were associated with higher rates of CUDs (Mills et al., 2022; Degenhardt et al., 2015; Rubin-Kahana et al., 2022). Moreover, individuals experiencing SUDs while using medicinal cannabis were found to be particularly vulnerable to developing CUDs (Gendy et al., 2023).

3.8.5. Chronic pain

The relationship between chronic pain and CUDs in people who used medicinal cannabis was assessed in numerous studies. Adults using medicinal cannabis for chronic pain may be at higher risk of developing CUDs, possibly without a clinically significant reduction in symptoms (Gilman, 2023; Hasin et al., 2023). Individuals using medicinal cannabis for chronic pain who developed CUDs were more likely to have greater symptoms of pain which impact daily functioning in some studies (Degenhardt et al.,2015).

Table 3
The severities of cannabis use disorders among people with cannabis use disorder.

First Author	Year	DSM-5% (n of Total Cannabis Use Disorders) [95% CI]		
		Mild	Moderate	Severe
Bialas et al. (2023)	2023	76% (41) [61–91%]	19% (10)[11–30%]	6% (3) [2–12%]
Cooke et al. (2023)	2023	79% (15)[61–94%]	11% (2) [2–20%]	11% (2) [2–20%]
Gendy et al. (2023)	2023	60% (9) [37–84%]	20% (3) [9–43%]	20% (3) [9–43%]
Gilman et al. (2022)	2022	80% (8) [54–99%]	20% (2) [13–37%]	0% (0) [0–0%]
Gilman et al. (2023)	2023	79% (15) [61–94%]	11% (2) [2–20%]	11% (2) [2–20%]
Mills et al. (2022)	2022	60% (173) [57–63%]	21% (62) [18–24%]	19% (55)[16–23%]
Myers et al. (2023)	2022	73% (40) [64–82%]	24% (13) [14–39%]	7% (4) [1–8%]
Rubin-Kahana et al. (2022)	2022	55% (95) [48–62%]	27% (46) [21–33%]	18% (32)[10–26%]

4. Discussion

The current paper is the first systematic review and meta-analysis to estimate the prevalence and symptoms of cannabis use disorders in people who use medicinal cannabis. In people who use cannabis for medicinal reasons, 25% (95% CI: 18-33%) were estimated to have a CUD when including all prevalence periods using the DSM-5. Our estimate of 25% is marginally higher than the 22% (CI: 18–26%) from a recent meta-analysis on the prevalence of CUDs among people who used cannabis recreationally, which found daily or weekly use and younger age as significant risk factors but with overlapping confidence intervals (Leung et al., 2020).

As in Leung et al., (2020), our narrative review suggests that the risk of CUDs may be higher in people who use medicinal cannabis frequently, use greater quantities of medicinal cannabis daily and are more likely to use medicinal cannabis via inhalation. Demographic predictors of CUDs when using medicinal cannabis may include being younger in age and male. Physical and mental health conditions as associated risk factors were also identified (e.g., chronic pain and mental health disorders). Cooke et al., (2023) posited that increased symptoms of pain, which impact daily functioning, led to more frequent medicinal cannabis use and consequently the development of CUDs. They noted that it is unlikely that cannabis use directly worsened pain. Instead, it is proposed that individuals experiencing higher levels of pain turn to medicinal cannabis more frequently as a pain management strategy. The link between greater cannabis use and greater pain might indicate that cannabis is not effectively addressing pain symptoms but may increase the risk of CUDs for those using cannabis for chronic pain (Cooke et al., 2023). The development of a CUD may, in turn, impair their ability to manage their pain and the demands of everyday life.

The present review found withdrawal and tolerance to be two of the most frequently reported criteria across the included studies. Two included studies examined the effect of removing the tolerance and withdrawal criteria and recalculating the prevalence of CUDs in the sample. For Mills et al., (2022) and Bialas et al., (2022), this resulted in a reduction in the number of CUDs identified in the study (25% versus 32%; 14% versus 29%, respectively). The validity, specificity and sensitivity of the adjusted criteria were not tested. The rationale for removing these criteria stems from the medicinal authorisation of cannabis, with some researchers claiming withdrawal and tolerance should be removed when assessing medicinal use (as in Opiate Use Disorder; OUD) (Bialas et al., 2023) and others suggesting the criteria should be changed to CUD-Cannabis for Therapeutic Purposes (CTP) to adjust for medicinal use (Chung et al.,2023). The DSM-5 OUD criteria states that tolerance and withdrawal symptoms are not considered applicable for individuals utilising opioids under appropriate medical oversight. Conversely, no such exemption is provided in the DSM-5 diagnostic criteria for CUD and does not incorporate provisions for appropriate medical supervision.

Recent research has highlighted that while tolerance and withdrawal may be removed for prescription medications within appropriate medical treatment, medicinal cannabis differs in being acquired through a recommendation rather than a standard prescription. The unique regulatory system means physicians recommending cannabis lack control over the dosages, potencies, frequencies and even products that their patients use in some jurisdictions, often without specific clinical guidelines (Cooke et al.,2023). Other researchers have questioned the rationale for removing withdrawal and tolerance from the criteria because these are symptoms that are important to track. Some have also highlighted that it was the argument that tolerance and withdrawal were ‘expected’ in people who used opioid medications long-term that led to the severe underestimation of the harms and prevalence of opioid use disorder in patients using opioids for medical purposes (Hasin et al., 2023).

Dual use motives of cannabis (i.e., medicinal and recreational) complicate the estimation of the prevalence of CUDs in people who use medicinal cannabis. The definition of ‘medicinal’ or ‘recreational’ use is often obscured by the flexible cannabis authorisation processes, which do not adhere to the traditional approach of prescribing specific drugs and dosages. Previous studies have shown that many people who used cannabis self-reported dual use motives (Leung et al., 2022b). Within the reviewed literature, there were various strategies employed to measure the recreational use of medicinal cannabis products or the use of recreational cannabis alongside medicinal cannabis. Bonn-Miller et al., (2014) and Haug et al., (2017) used a comprehensive cannabis motives questionnaire to delineate medicinal from recreational motives (Lee et al., 2009). In their sample taken from a medicinal cannabis dispensary, Bonn-Miller et al., (2014) found that using medicinal cannabis for coping, boredom, enjoyment, celebration, to alter perception, availability and experimentation was associated with disordered cannabis use; all motives which may reflect recreational cannabis use. In a similar population, Haug et al. (2017) found that coping motives significantly predicted problematic cannabis use. However, all the participants in this study were classified as medicinal cannabis patients because they had a medicinal cannabis authorisation. Another study by Bialas et al., (2022) reported recreational use of cannabis by 16% of the sample, with one in five of those participants reporting the use of recreational cannabis up until the initiation of medicinal cannabis. Other included studies utilised self-report questions to disentangle medicinal use from recreational use, and others such as Mills et al., (2022), allowed participants to respond to the study regardless of whether they were prescribed medicinal cannabis but simply if they self-identified as using cannabis medicinally. Motives for use may be an essential factor to consider in the context of CUDs. Still, many of the included studies did not examine these comprehensively which warrants greater attention in future research (Hasin et al., 2023).

There is a serious question here of how researchers, clinicians and public health agencies are to distinguish medicinal cannabis patients when varied proportions also use cannabis recreationally whilst authorised for medicinal use and others claim to be using cannabis medicinally without authorisation. There is no simple biological approach for separating potential ‘recreational use misuse’ whilst an individual is approved and using medicinal cannabis. There arises a further concern regarding potential research participants who might not genuinely represent medicinal patients, leading to what can be termed “trojan horse” participation. Such participants might not provide meaningful data, especially if their reasons for cannabis use diverge from their claim to be using medically (Graham et al., 2023). The current review highlights the complexity in delineating recreational and medicinal cannabis consumers and emphasises both the need for a valid methodology to separate use motives, or the consistent use of reliable tools in research to monitor motives of cannabis use when prescribed medicinally.

The variance in the methodologies and design of the studies is a major limitation within this review. Estimates using different measures of different diagnostic criteria may be too disparate to pool. We possessed restricted statistical capability to discern the impacts of additional potential moderators. Further, the preponderance of our estimates originated from predominantly cross-sectional studies employing self-reported measures which are susceptible to recall bias and social desirability. Optimally, our inclusion criteria would have been limited to longitudinal cohort studies that began before the initiation of both recreational and medicinal cannabis use and tracked the emergence of CUDs over time. However, to the best of our knowledge, only one study on medicinal cannabis use has partially utilised this approach to date (see Gilman et al., 2022). Given that this review is the first of its kind, further research should be aimed at monitoring the population-level prevalence of CUDs in people who use medicinal cannabis, particularly in the face of growing liberalisation and accessibility. The review also highlights the need for public health messaging on the adverse effects of using cannabis for medicinal reasons, irrespective of whether its self-prescribed or authorised by a medical professional, as these effects

may be largely unknown to consumers. Additionally, this review underscores the significance for researchers and clinicians to measure recreational use in people who use medical cannabis, highlighting the necessity for enhanced measures to systematically monitor motives associated with medicinal and recreational cannabis use.

5. Conclusion

The current meta-analysis estimates that the prevalence of CUDs in people who use medicinal cannabis is 25% (95% CI: 18-33%). Frequency of cannabis use, and certain demographics such as younger age and male gender appear to increase risk, as they do in recreational cannabis consumers. Individuals with mental health disorders, especially those using cannabis for depression and SUDs, may be at elevated risk. Chronic pain management with medicinal cannabis may increase the risk of CUDs. The study highlights challenges in distinguishing between recreational and medicinal use and the complexity this poses for cannabis research in both contexts given the growing liberalisation of cannabis policies. As medicinal cannabis popularity grows, there is a need for ongoing research to monitor CUDs prevalence in people who use medicinal cannabis.

CRediT authorship contribution statement

Janni Leung: Supervision, Resources, Project administration, Methodology, Formal analysis, Conceptualization. **Daniel Stjepanovic:** Supervision, Resources, Project administration, Methodology, Conceptualization. **Valentina Lorenzetti:** Writing – review & editing, Supervision, Resources. **Christy Cheung:** Writing – review & editing, Visualization, Validation, Data curation. **Wayne Hall:** Supervision, Resources, Methodology, Conceptualization. **Danielle Dawson:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors report no conflicts of interest.

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There are no additional relationships to disclose

Patents and Intellectual Property

There no are patents to disclose

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There are no additional activities to disclose

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.drugalcdep.2024.111263.

References

Adamson, S.J., Kay-Lambkin, F.J., Baker, A.L., Lewin, T.J., Thornton, L., Kelly, B.J., et al., 2010. An improved brief measure of cannabis misuse: the cannabis use disorders identification test-revised (CUDIT-R)*. Drug Alcohol Depend. 110 (1–2), 137–143.

American Psychiatric Association, American Psychiatric Association, editors. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. 4th ed., text revision. Washington, DC: American Psychiatric Association; 2000. 943 p.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders [Internet]. Fifth Edition. American Psychiatric Association; 2013 [cited 2023 Oct 23]. Available from: ⟨https://psychiatryonline.org/doi/book/10.1176/appi.books.9780890425596⟩

American Psychiatric Association, editor. Diagnostic and statistical manual of mental disorders: DSM-5-TR. Fifth edition, text revision. Washington, DC: American Psychiatric Association Publishing; 2022. 1 p.

Aromataris, E., Munn, Z., 2020. Chapter 7: Systematic reviews of etiology and risk. JBI Manual for Evidence Synthesis [Internet]. JBI, In. Available from: ⟨https://synthesismanual.jbi.global⟩.

Bialas, P., Böttge-Wolpers, C., Fitzcharles, M.A., Gottschling, S., Konietzke, D., Juckenhöfel, S., et al., 2023. Cannabis use disorder in patients with chronic pain: overestimation and underestimation in a cross-sectional observational study in 3 German pain management centres. Pain 164 (6), 1303–1311.

Bonn-Miller, M.O., Boden, M.T., Bucossi, M.M., Babson, K.A., 2014. Self-reported cannabis use characteristics, patterns and helpfulness among medical cannabis users. Am. J. Drug Alcohol Abus. 40 (1), 23–30.

Chung, T., Steinberg, M.L., Bridgeman, M.B., 2023. Recommendation for cannabis use disorder diagnosis in a context of cannabis for therapeutic purposes. JAMA Psychiatry 80 (5), 409.

Connor, J.P., Stjepanović, D., Le Foll, B., Hoch, E., Budney, A.J., Hall, W.D., 2021. Cannabis use and cannabis use disorder. Nat. Rev. Dis. Prim. 7 (1), 16.

Cooke, M.E., Potter, K.W., Jashinski, J., Pascale, M., Schuster, R.M., Tervo-Clemmens, B., et al., 2023. Development of cannabis use disorder in medical cannabis users: a 9-month follow-up of a randomized clinical trial testing effects of medical cannabis card ownership. Front. Psychiatry 14, 1083334.

Degenhardt, L., Lintzeris, N., Campbell, G., Bruno, R., Cohen, M., Farrell, M., et al., 2015. Experience of adjunctive cannabis use for chronic non-cancer pain: findings from the pain and opioids in treatment (POINT) study. Drug Alcohol Depend. 147, 144–150.

European Monitoring Centre for Drugs and Drug Addiction. Cannabis laws in Europe: questions and answers for policymaking. [Internet]. LU: Publications Office; 2023 [cited 2023 Oct 20]. Available from: ⟨https://data.europa.eu/doi/10.2810/151113⟩

Feingold, D., Goor-Aryeh, I., Bril, S., Delayahu, Y., Lev-Ran, S., 2016. Problematic use of prescription opioids and medicinal cannabis among patients suffering from chronic pain. Pain. Med., pnw134

Gendy, M., Taisir, R., Sousa, S., Costello, J., Rush, B., Busse, J.W., et al., 2023. Prevalence of cannabis use disorder among individuals using medical cannabis at admission to inpatient treatment for substance use disorders. Addict. Behav. 142, 107667.

Gilman, J., 2023. A potential downside of cannabis legalisation for older adults with pain. Lancet Psychiatry 10 (11), 823–824.

Gilman, J.M., Schuster, R.M., Potter, K.W., Schmitt, W., Wheeler, G., Pachas, G.N., et al., 2022. Effect of medical marijuana card ownership on pain, insomnia, and affective disorder symptoms in adults: a randomized clinical trial. JAMA Netw. Open 5 (3), e222106.

Gilman, J.M., Potter, K., Schuster, R.M., Hoeppner, B.B., Eden Evins, A., 2023. Cannabis use for medical symptoms: patterns over the first year of use. Addict. Behav. 144, 107719.

Gliksberg, O., Kushnir, T., Sznitman, S.R., Lev-Ran, S., Brill, S., Amit, B.H., et al., 2023. Negative experiences of patients using medicinal cannabis: a systematic review of qualitative studies. J. Clin. Nurs. 32 (17–18), 5607–5618.

Graham, M., Chiu, V., Stjepanović, D., Hall, W., 2023. A provisional evaluation of Australia's medical cannabis program. Int. J. Drug Policy 122, 104210.

Hallinan, C.M., Bonomo, Y.A., 2022. The rise and rise of medicinal cannabis, what now? medicinal cannabis prescribing in Australia 2017–2022. IJERPH 19 (16), 9853.

Hasin, D.S., Wall, M.M., Alschuler, D.M., Mannes, Z.L., Malte, C., Olfson, M., et al., 2023. Chronic pain, cannabis legalisation, and cannabis use disorder among patients in the US Veterans Health Administration system, 2005 to 2019: a repeated, cross-sectional study. Lancet Psychiatry 10 (11), 877–886.

Haug, N.A., Padula, C.B., Sottile, J.E., Vandrey, R., Heinz, A.J., Bonn-Miller, M.O., 2017. Cannabis use patterns and motives: a comparison of younger, middle-aged, and older medical cannabis dispensary patients. Addict. Behav. 72, 14–20.

Lee, C.M., Neighbors, C., Hendershot, C.S., Grossbard, J.R., 2009. Development and preliminary validation of a comprehensive marijuana motives questionnaire. J. Stud. Alcohol Drugs 70 (2), 279–287.

Leung, J., Chan, G.C.K., Hides, L., Hall, W.D., 2020. What is the prevalence and risk of cannabis use disorders among people who use cannabis? a systematic review and meta-analysis. Addict. Behav. 109, 106479.
Leung, J., Lim, C.C.W., Chiu, V., Chung, J., Mekonen, T., Dawson, D., et al., 2022b. Prevalence and correlates of cannabis use for medicinal reasons – An Australian cross-sectional study. Addict. Behav. Rep. 15, 100436.
Leung, J., Chan, G., Stjepanović, D., Chung, J.Y.C., Hall, W., Hammond, D., 2022a. Prevalence and self-reported reasons of cannabis use for medical purposes in USA and Canada. Psychopharmacology 239 (5), 1509–1519.
Lin, L.A., Ilgen, M.A., Jannausch, M., Bohnert, K.M., 2016. Comparing adults who use cannabis medically with those who use recreationally: results from a national sample. Addict. Behav. 61, 99–103.
Mills, L., Lintzeris, N., O'Malley, M., Arnold, J.C., McGregor, I.S., 2022. Prevalence and correlates of cannabis use disorder among Australians using cannabis products to treat a medical condition. Drug Alcohol Rev. 41 (5), 1095–1108.
Myers, M.G., Ganoczy, D., Walters, H.M., Pfeiffer, P.N., Ilgen, M.A., Bohnert, K.M., 2023. Assessing the diagnostic utility of the Cannabis Use Disorder Identification Test – Revised (CUDIT-R) among veterans with medical and non-medical cannabis use. Drug Alcohol Depend. 247, 109876.
Potenza, M.N., Bunt, G., Khalsa, J.H., 2023. Addiction medicine physicians and medicinal cannabinoids. JAMA Psychiatry 80 (7), 659.
PROSPERO [Internet]. Available from: ⟨https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023396332⟩
Rubin-Kahana, D.S., Hassan, A.N., Sanches, M., Le Foll, B., 2022. Medical Cannabis and Past-Year Cannabis Use Disorder Among Adult Recreational Users in the United States: results from a Nationally Representative Sample. Front Psychiatry 13, 836908.
Smith, J.M., Mader, J., Szeto, A.C.H., Arria, A.M., Winters, K.C., Wilkes, T.C.R., 2019. Cannabis use for medicinal purposes among Canadian University Students. Can. J. Psychiatry 64 (5), 351–355.
WHO). International Classification of Diseases, Eleventh Revision (ICD-11) [Internet]. 2019. Available from: ⟨http://id.who.int/icd/entity/1913137404⟩