

SYSTEMATIC REVIEW

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# Prevalence of schizophrenia spectrum and bipolar disorder among patients with cannabis induced psychosis: a systematic review and meta-analysis

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## Abstract

**Background** Distinguishing cannabis-induced psychosis from primary psychiatric disorders is difficult and has significant clinical and prognostic implications. Current treatment approaches lack standardized guidelines, potentially leading to the development of schizophrenia spectrum and bipolar disorder. This study systematically reviews the literature and provides a pooled prevalence of later developing these disorders following a cannabis-induced psychosis diagnosis.

**Methods** We systematically reviewed Medline, Embase, Web of Science, Google Scholar, and PsychInfo for studies reporting on a group of patients with cannabis-induced psychosis and subsequent diagnoses of schizophrenia spectrum disorder, bipolar disorder, or both. The search was conducted until January 1, 2025. A modified version of the Newcastle-Ottawa scale was used to assess study quality. Random-effects meta-analyses were conducted to calculate pooled mean prevalence. Random-effects meta-regressions were used to identify predictors of higher prevalence.

**Results** Our strategy identified 13 studies eligible for inclusion with a total population size of 7,515 which reported a total of 16 outcomes of interest. Among cannabis induced psychosis patients, 20% (95% CI:15.8–29.5%) later received a schizophrenia spectrum diagnosis, 5% (95% CI:2.7–6.9%) bipolar and 63% (95% CI:26.8–90.5%) unspecified (both). Compared to individuals receiving a later schizophrenia spectrum disorder diagnosis, patients were 76% less likely to develop bipolar disorder. Later diagnosis of an unspecified disorder showed an approximate 3 folds higher risk with an ARR of 2.52 (95% CI: 1.03–6.15) compared to schizophrenia spectrum disorder alone.

**Conclusions** Approximately one in five patients diagnosed with cannabis-induced psychosis will develop schizophrenia spectrum disorder, while one in twenty will be later diagnosed with bipolar disorder.

**Keywords** Substance induced psychosis, Cannabis induced psychosis, Schizophrenia spectrum, Bipolar disorder

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## Background

Substance-induced psychosis (SIP) is characterized by the occurrence of delusions and/or hallucinations following the consumption or withdrawal of a recently ingested psychoactive substance [1]. It is distinguished from organic psychoses, such as those classified under the schizophrenia spectrum disorder (SSD) umbrella, as symptoms are expected to abate once abstinence is achieved. However, in practice, distinguishing SIP from organic psychosis with concurrent substance use is often challenging [2]. Furthermore, there is ongoing debate regarding the diagnostic validity of SIP, with some advocating for its inclusion under the SSD umbrella [3]. The primary argument for this reclassification is that a significant proportion of SIP patients subsequently develop psychoses independent of substance use. Arendt et al. were the first to illustrate this association, finding that approximately 44.5% of patients with cannabis-induced psychosis (CIP) were later diagnosed with SSD [4]. Subsequent research has shown varying rates of SSD diagnoses among patients with SIP. Among the substances examined, CIP has demonstrated the strongest association with future SSD, therefore exhibiting the most robust support for potential reclassification under the SSD umbrella [5–8]. Reclassification would have significant implications on treatment. Currently, there are no established guidelines for the treatment of CIP, with patients receiving antipsychotics during the symptomatic phase alongside interventions aimed at substance cessation [9]. This approach contrasts with diagnoses under the SSD umbrella, in which patients continue pharmacological treatment after the resolution of acute symptoms and receive long-term psychiatric follow-up [10, 11]. Existing studies on the prevalence of primary psychoses among patients with CIP vary in methodology, reported variables, and rates of subsequent diagnosis. Kendler et al. found that 9.9% of patients diagnosed with CIP later received a schizophrenia diagnosis [7]. Conversely, Komuravelli et al. found that among 23 patients with CIP approximately 78% received a primary psychosis diagnosis at follow-up [12]. To the best of our knowledge, Murrie et al. conducted the only meta-analysis on this association and found that approximately 34% of patients with CIP will be diagnosed with SSD [13]. However, among the six studies included, three utilized the same cohort [4, 6, 14], the Danish Psychiatric Central Register

[15], during overlapping periods, which likely skewed their findings. Since the conclusion of Murrie et al.'s analysis, several large cohort studies have been published exploring the development of SSD following an initial CIP diagnosis, most notably: Myran D.T. et al. ( $n=3,557$ ) [16], and Kendler et al. ( $n=1,000$ ) [7].

Although less extensively researched, several studies have explored the propensity of CIP patients to develop Bipolar Disorder (BD). Starzer et al. found that patients diagnosed with CIP were significantly more likely to develop BD than age- and sex-matched controls [6]. Furthermore, regular cannabis use has been shown to increase the risk of BD, and this association may be attributable to overlapping genetic mechanisms [17, 18]. Given these findings, it is plausible that patients with CIP may carry a greater risk of BD, and exploring this association could clarify the need for the development of treatment guidelines to mitigate both SSD and BD.

The rationale for the present study is grounded in the methodological limitations of the existing review on CIP and SSD, publication of new large cohort studies, and absence of a review evaluating the development of BD. A systematic review of the literature was conducted to determine the proportion of patients initially diagnosed with CIP who were later diagnosed with SSD or BD. This study aimed to provide an updated pooled rate of SSD among CIP patients, calculate and compare it to the pooled rate of subsequent BD, and identify variables that may influence the development of primary psychosis. In doing so, this study sought to offer insights into the potential reclassification of CIP, the necessity for modifications in its management, and the identification of variables that could affect later psychoses diagnoses among this patient population.

## Methods

### Data sources and study selection

Recommendations were employed based on Bramer et al.'s approach to database selection, found to retrieve 98.3% of all possible results [19]. We used Medline, Embase, Web of Science, Google Scholar and PsychINFO.

### Search strategy

A modified PICO (Population, Intervention, Comparison, Outcome) framework was used to create a search strategy. The population of interest was patients diagnosed with cannabis-induced psychosis, and our outcome was diagnosis at follow-up. Our search strategy did not include an intervention or comparison. MeSH terms, database-specific keywords, and truncation were used, where applicable. There were no limits on the year or language applied. An example of the search terms is presented in Table 1. Medline and Embase were searched using OVID, while PsychINFO was searched using

**Table 1** Search strategy for medline and embase

#### Medline and Embase search strategy

((“substance induced” OR substance-induced OR “cannabis induced” OR cannabis-induced OR “cannabinoid induced” OR cannabinoid-induced OR “marijuana induced” OR marijuana-induced) AND (psycho\* OR schizophren\* OR bipolar) AND (“diagnostic stability” OR diagnostic-stability OR outcome OR “follow up” OR follow-up OR prognosis OR transition OR course OR conversion OR longitudinal)).

EBSCO. Study authors performed database searching up until the 1st of January 2025.

### Study selection and eligibility criteria

Search results were exported from each database and imported to Zotero, where the reference lists were merged and deduplicated. Two reviewers (M. J. and A. T.) screened the titles and abstracts of the potentially relevant studies. Articles were eligible for full-text screening if the abstract contained a cohort of patients with substance-induced psychosis who were followed up longitudinally. The articles which met this criterion had their full text independently reviewed by two reviewers (M.J. and A.T.). Any differences in study inclusion were resolved via consensus or by consulting with a third reviewer (S.R.). Studies were assessed for relevance and assessed against the following inclusion criteria: 1) human participants, 2) case-control study, cohort study, randomized controlled trial, or case series with at least 3 patients, 3) study records data for a set of patients with cannabis-induced psychosis or substance-induced psychosis with cannabis subtype, 4) the same population was reexamined with rates of follow-up diagnosis including either schizophrenia spectrum disorder, bipolar disorder, or both, and 5) diagnosis at index and outcome were made according to DSM or ICD guidelines. Exclusion criteria included [1] meta-analyses, systematic reviews, narrative reviews, or case studies (single patient reports), [2] substance-induced psychosis without cannabis subtype, substance-induced psychosis with alcohol or other substances in addition to cannabis, [3] studies where no outcome data were listed for patients initially diagnosed with cannabis-induced psychosis, and [4] self-reported diagnoses, symptom severity scales, or description of psychotic symptoms without diagnosis.

The reference lists of included studies were searched for additional studies that met the inclusion criteria, which may have been missed. If multiple studies reported on overlapping cohorts, the study with the largest sample was extracted and the others were excluded.

### Data extraction

Data extraction was performed independently by two reviewers (M.J. and A.T.), and the following variables were recorded: year of publication, country, national or subnational, rural/urban, diagnostic method, period of data collection, setting, study type, gender, urine toxicology, mean age of the cohort, mean follow-up duration, and mean time to change. The following outcomes were recorded: number receiving a schizophrenia spectrum disorder diagnosis, and number receiving a bipolar disorder diagnosis. Non-psychotic depression, anxiety,

personality, substance use disorder, and other psychiatric diagnoses were not considered outcomes of interest. Studies that reported more than one outcome of interest had their data extracted, treating each outcome as a separate data point.

### Study quality

The quality of included studies was assessed using a modified version of the Newcastle Ottawa scale for cohort studies. As the aim of our study was to assess the likelihood of later SSD/BD among a cohort initially diagnosed with CIP, comparability and selection of non-exposed cohort domains were omitted. Hence, the maximum quality rating that a study could be given was 6. Further details can be found in the supplementary material.

### Meta-analyses

We conducted a meta-analysis on the reported total transitions and calculated the pooled mean prevalence using the DerSimonian–Laird random-effects models with inverse variance weighting [20]. This methodology considers sampling variations and heterogeneity in effect sizes. The variance of every prevalence measure was stabilized using the Freeman-Tukey arcsine square-root transformation [21, 22]. Pooled mean prevalence for diagnosis stratified by disease type were calculated [20]. Cochran's Q statistic was used to assess the presence of heterogeneity in effect size.  $I^2$  was used to measure the magnitude of between-study heterogeneity due to true differences in effect size, rather than chance [23]. The 95% confidence interval of the distribution of true prevalence score was used to describe the distribution of true effect sizes [20, 22]. Meta-analyses were conducted in R version 4.0.4 [24], using the meta package [25].

### Meta-regression

Factors associated with higher prevalence and sources of between-study heterogeneity were investigated using random-effects meta-regression analyses. Univariate meta-regression analyses were planned a priori to explore potential sources of heterogeneity and factors associated with higher prevalence estimates. This was conducted by regressing the log-transformed prevalence proportions [26]. At the univariable level, covariates with a  $p$ -value  $\leq 0.2$  were eligible for inclusion into the multivariable analyses. At the multivariable level, covariates with a  $p$ -value  $\leq 0.05$  showed strong evidence for association with the outcome. Studies with missing years of data collection were imputed using the year of publication adjusted for the median difference with the year of data collection. Meta-regressions were conducted in Stata/SE version 16.1 [27] using the metereg package [26].

**Results**

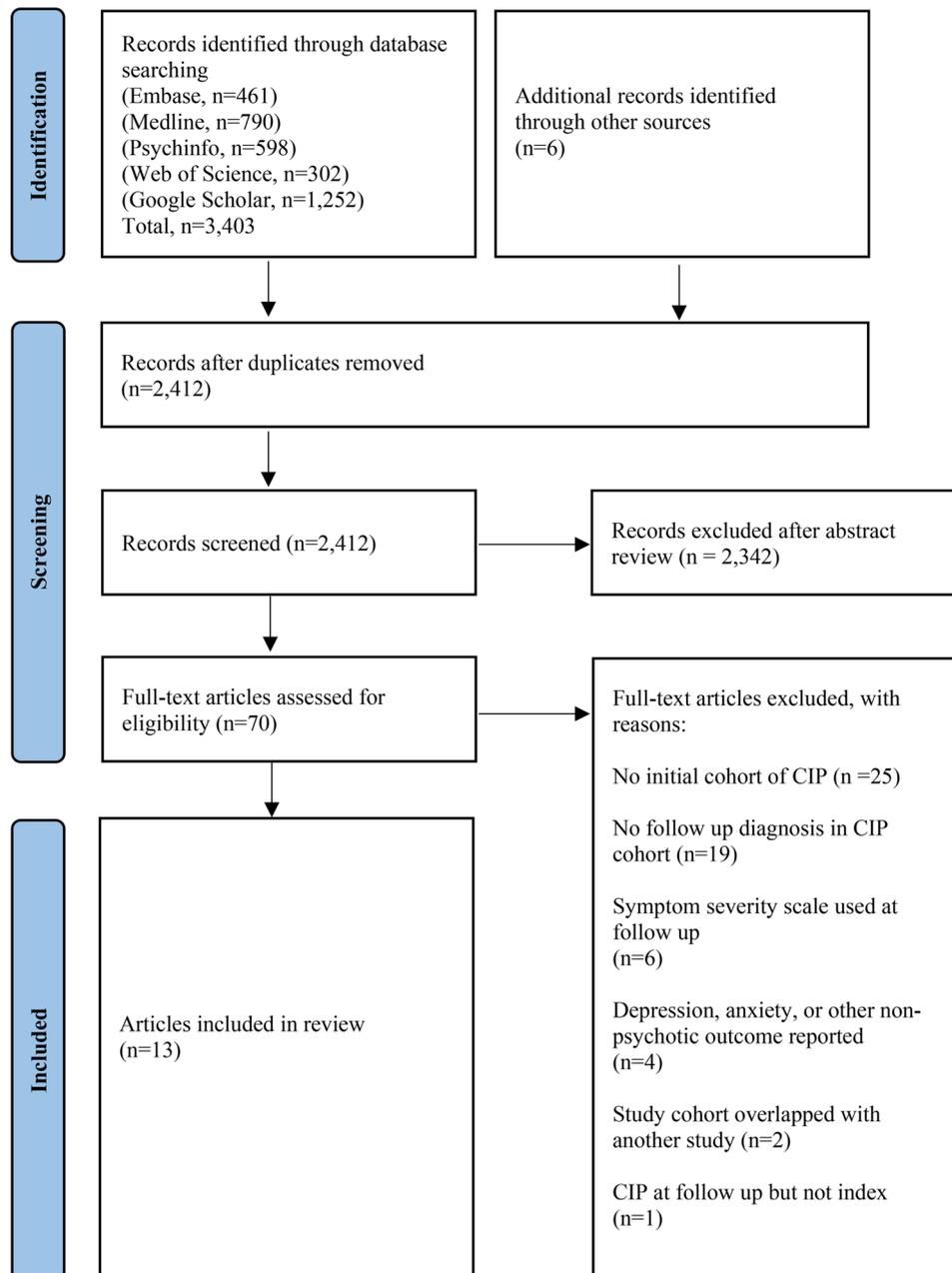
**Search results**

Screening and study selection are described in Fig. 1. The search strategy identified a total of 3,403 records. After duplicate removal and article screening, 13 studies met inclusion criteria, reporting on a total of 16 outcomes of interest.

The 13 studies extracted were all cohort studies, with the majority utilizing population registers, providing a total population size of 7,515 individuals (Table 2).

The 13 studies reported on a total of 16 outcomes of interest, i.e. 3 studies independently reported rates of

later diagnosis for both schizophrenia spectrum disorder and bipolar disorder among their cohorts. We identified three main groups based on the outcomes reported: outcome diagnosis of schizophrenia spectrum (10 studies with 7,326 patients), outcome diagnosis of bipolar (3 studies with 2,089 patients), and unspecified (3 studies with 189 patients). The unspecified category represents studies reporting the cumulative rates of later SSD or BD. More than half of the included studies were from Europe (62%), followed by Asia (31%), and one study was from North America. From the eight studies with available data on the age of patients, the weighted average age



**Fig. 1** Prisma flowchart of study screening and selection

**Table 2** Variables and characteristics of extracted studies

Study	Pub- lica- tion Year	Country	Study quality	Setting	Study type	Sam- ple size	SSD	BD	Un- spec- ified
[28] (Alderson et al., 2017)	2017	Scotland	2	Inpatient	Retrospective Cohort	276	✓		
[29] (Chuenchom et al., 2024)	2024	Thailand	4	Inpatient	Retrospective Cohort	214	✓		
[30] (Ghosh et al., 2024)	2024	India	6	Inpatient and outpatient	Retrospective Cohort	134			✓
[31] (Inchausti L. et al., 2022)	2022	Spain	4	Inpatient	Retrospective cohort	32			✓
[7] (Kendler K.S. et al., 2019)	2019	Sweden	6	Inpatient and outpatient	Prospective cohort	1,000	✓		
[12] (Komuravelli et al., 2011)	2011	England	2	Inpatient	Retrospective cohort	23			✓
[16] (Myran D.T. et al., 2023)	2023	Canada	3	Inpatient and outpatient	Retrospective cohort	3,557	✓		
[5] (Niemi-Pynttari J.A. et al., 2013)	2013	Finland	5	Inpatient	Retrospective cohort	125	✓		
[8] (Rognli E.B. et al., 2023)	2023	Norway	2	Inpatient and outpatient	Retrospective Cohort	562	✓	✓	
[32] (Shah et al., 2017)	2017	India	5	Inpatient	Retrospective cohort	35	✓	✓	
[33] (Singal A. et al., 2015)	2015	India	5	Inpatient	Prospective cohort	5	✓		
[34] (Skryabin V.Y. & Vinnikova M.A., 2019)	2019	Russia	4	Inpatient	Prospective cohort	60	✓		
[6] (Starzer et al., 2018)	2018	Denmark	2	Inpatient and outpatient	Retrospective cohort	1,492	✓	✓	

SSD Schizophrenia Spectrum Disorder, BD Bipolar disorder

**Table 3** Risk of bias assessment scored via an adapted Newcastle Ottawa scale

Study	Representa- tiveness of the exposed cohort	Ascertain- ment of exposure	Demonstration that outcome of interest was not present at start of study	Assess- ment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	Total
[28] (Alderson et al., 2017)	-	-	*	-	*	-	2
[29] (Chuenchom et al., 2024)	-	*	*	*	*	-	4
[30] (Ghosh et al., 2024)	*	*	*	*	*	*	6
[31] (Inchausti L. et al., 2022)	-	*	*	-	*	*	4
[7] (Kendler K.S. et al., 2019)	*	*	*	*	*	*	6
[12] (Komuravelli et al., 2011)	-	-	*	-	*	-	2
[16] (Myran D.T. et al., 2023)	*	-	*	-	-	*	3
[5] (Niemi-Pynttari J.A. et al., 2013)	-	*	*	*	*	*	5
[8] (Rognli E.B. et al., 2023)	*	-	*	-	-	-	2
[32] (Shah et al., 2017)	-	*	*	*	*	*	5
[33] (Singal A. et al., 2015)	-	*	*	*	*	*	5
[34] (Skryabin V.Y. & Vinnikova M.A., 2019)	-	*	*	*	-	*	4
[6] (Starzer et al., 2018)	*	-	*	-	-	-	2

Legend: \* is awarded when the study fulfills criteria listed under the column heading, - represents study not fulfilling criteria under column heading, Total represents the sum of \* awarded to each study representing the number of domains each study has satisfied

among the 2,304 patients was 25.4 years. Most, 82.3%, of patients were males among the 10 studies which reported this outcome.

**Risk of bias assessment**

The studies included ranged in quality, with the lowest scoring 2/6 and the highest scoring 6/6. The median study quality was 4, further details of the methodology used to determine study quality can be found in the supplementary material (Modified quality assessment scale). Scoring and quality of each study are shown in Table 3.

**Meta-analysis**

Forest plots of the meta-analyses stratified by disorder type are presented in Figure 2. Among the SSD subgroup, the pooled mean prevalence of patients who transitioned was 20% (95% CI:14-28%). Within the BD subgroup, the pooled mean prevalence was 5% (95% CI:3-7%). Within the unspecified schizophrenia or bipolar disorder subgroup, the pooled mean prevalence was 63% (95% CI:44-81%). The meta-analysis among patients with schizophrenia spectrum disorder showed evidence of heterogeneity (p <0.5), with wide prediction intervals and I<sup>2</sup>>50%. This indicates that most of the variation is true variation in prevalence rather than sampling variation

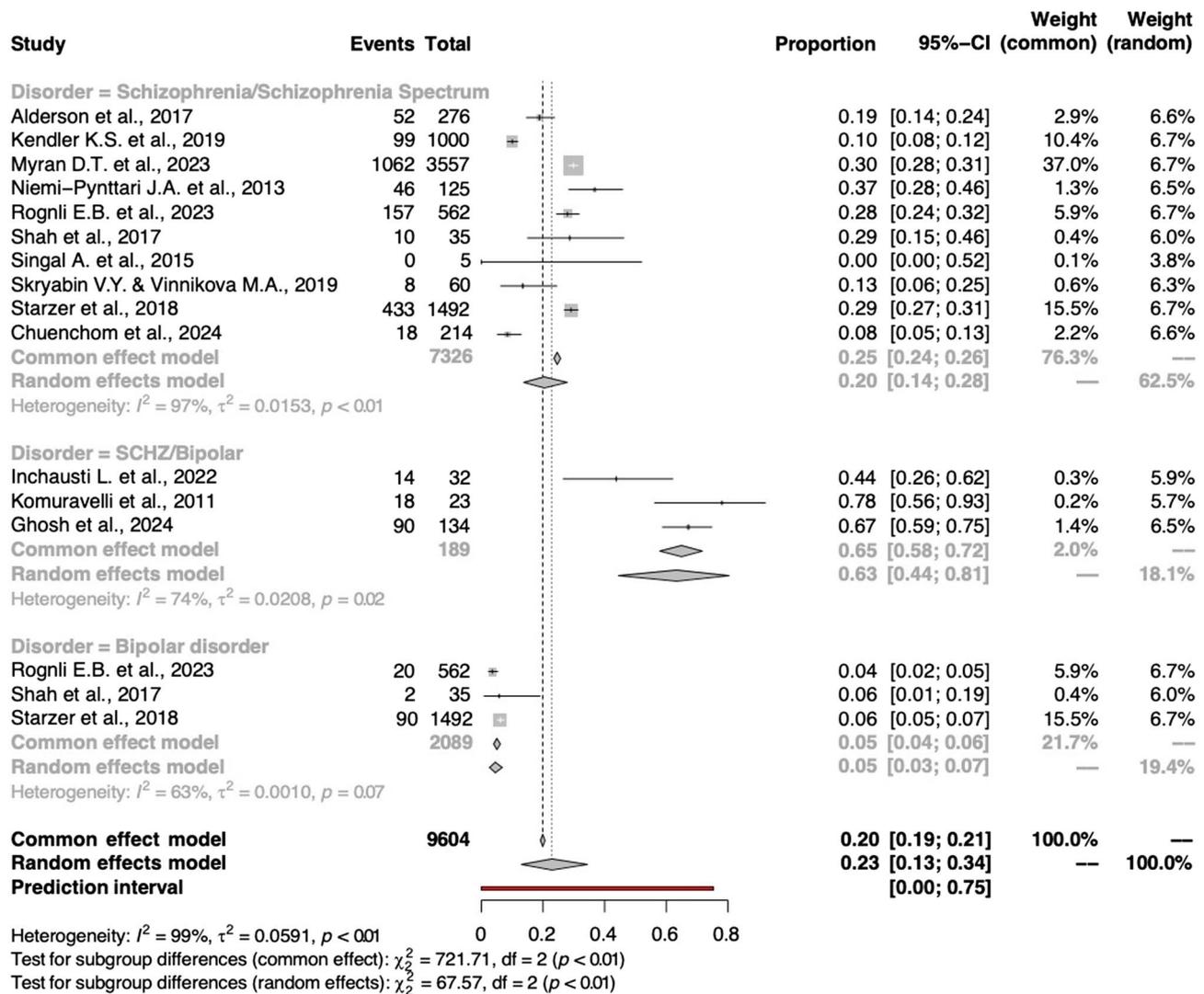


Fig. 2 Forest plot of included studies

or chance. Similar heterogeneity between studies was observed for the unspecified disorder subgroup while the bipolar disorder group demonstrated moderate heterogeneity. (Tab. 4)

**Associations between prevalence and population characteristics**

The results of the univariable meta-regression analyses are presented in Table 2. As the only variable significant at the univariable level was “disorder”, we were unable to proceed with the planned multi-variable analysis. The “disorder” variable explained 75.23% of the variation in prevalence. Compared to individuals receiving a later SSD diagnosis, patients were 76% less likely to develop BD, statistically significant at the univariable level with a p-value of 0.001. Later diagnosis of unspecified (cumulative schizophrenia spectrum and bipolar disorder) is significant when compared to SSD alone and shows an

approximate 3 folds higher risk with a p-value of 0.004. Due to the limited number of significant variables in univariable analyses, the planned multivariable meta-regression was not feasible. A post hoc exploratory meta-regression within the SSD subgroup (10 studies) was conducted to investigate heterogeneity. No additional significant covariates were identified, and substantial heterogeneity ( $I^2 > 50\%$ ) persisted, likely due to unmeasured or unreported factors across studies.

**Discussion**

Our study identified a total of 13 studies which reported on patients diagnosed with CIP receiving a later diagnosis of SSD and/or BD. We stratified and analyzed our meta-analysis into three distinct outcomes of schizophrenia spectrum, bipolar and unspecified. Several studies recorded rates of later diagnosis for both SSD and BD which gave us a total of 16 prevalence measures.

**Table 4** Univariable meta-regression analyses for prevalence of transition

Cannabis induced conversions			Outcome measures	Sample size	Univariable analysis		
			<i>n</i>	Total <i>N</i>	RR (95% CI)	<i>p</i> -value	Adjusted R <sup>2</sup>
Population characteristics	Location	National	8	9,066	1.00		3.02
		Subnational	8	538	1.64 (0.60-4.52)	0.311	
	Site	Urban and Rural (Mixed)	9	9,200	1.00		0.00
		Urban	7	404	1.16 (0.39-3.44)	0.773	
	Year of Data collection	Before 2006	6	4,408	1.00		0.00
		After 2006	10	5,196	0.87 (0.30-2.54)	0.782	
	Year of data collection continuous		16	9,604	0.99 (0.90-1.07)	0.724	0.00
	Disorder	Schizophrenia	10	7,326	1.00		75.23
		Bipolar	3	2,089	0.24 (0.11-0.50)	0.001	
		Mixed or Unspecified	3	189	3.02 (1.54-5.92)	0.004	
	Clinical setting	Inpatient and outpatient	7	8,799	1.00		0.00
		Inpatient	9	805	1.36 (0.48-3.84)	0.541	
Urine Toxicology done	No	10	9,223	1.00		0.00	
	Yes	6	381	0.75 (0.24-2.35)	0.600		

CI Confidence interval, RR Risk Ratio

Approximately 20% of the patients within our pooled CIP cohort received an SSD diagnosis, which is lower than the 34% reported in the 2020 meta-analysis by Murrie et al. [13]. Several factors likely contribute to this finding, most notably, 71.8% of the pooled cohort was drawn from studies published following the completion of Murrie et al.'s review (Figure 2) [7, 8, 16, 29, 34]. Moreover, as previously discussed, the inclusion of three studies utilizing the same population register likely skewed Murrie et al.'s findings and resulted in patient duplication [13]. Among the studies included in our analysis, the rate of later diagnosis varied substantially from 0% to 37%. High heterogeneity was observed in the SSD subgroup meta-analysis, which was not explained by the variables examined in the meta-regression. Even after a post hoc exploratory analysis within this subgroup, the sources of heterogeneity remained unclear. This is likely due to unmeasured study-level factors such as differences in diagnostic criteria, follow-up duration, or population characteristics. Methodological variations between studies may also have contributed. For example, studies that drew their cohort from national or provincial population registers reported higher rates of SSD, with a range (10%-37%) and higher median (29.5%), compared with studies that sourced their data from a single hospital, range (0%-29%) and median (10.5). The use of nationwide and province-wide population registers likely enabled the capture of patients who had attended multiple hospitals over the course of the follow-up period, likely contributing to the higher rates of SSD. Future research should adopt standardized reporting to better identify and understand these sources of heterogeneity.

Regarding variables that may have impacted the development of SSD, age and sex have been shown to be risk factors, with younger patients and males being more likely to develop an organic psychosis following CIP [4, 7, 8]. Although we were unable to verify this association in our analysis, studies that reported these variables skewed heavily towards male patients and young adults. However, it is important to note that among the general population, male patients are more likely to be diagnosed with SSD at a younger age compared to females [35, 36]. Hence, the association observed across the studies that reported this trend may be a feature of SSD generally and not specific to CIP. Lastly, repeated emergency admissions for CIP have also been associated with an increased risk of developing SSD [8]. This may be indicative of an underlying diagnosis of organic psychoses being repeatedly misattributed to cannabis use, reflective of patients who struggle to remain abstinent, or a combination of the two.

To our knowledge, this is the first meta-analysis to examine the rate of BD among patients initially diagnosed with CIP. All three studies that examined this outcome also reported on the rates of later SSD within the same cohort [6, 8, 32]. The proportion of patients who received a BD diagnosis was significantly lower than that of patients who received a later SSD diagnosis across all three studies. This is consistent with our finding that patients were 76% less likely to receive a BD diagnosis compared to SSD. The limited number of studies examining BD among the CIP cohort prevented the identification of variables that may affect the risk of BD in this population. Rognli et al. found that women with SIP were

approximately twice as likely as men to be later diagnosed with BD, but Starzer et al.'s analyses failed to demonstrate this trend [6, 8]. Neither study found a difference in the rates of BD diagnoses between patients with CIP and those with other substance-induced psychoses. We found that the pooled mean prevalence of BD following CIP was 5%. This was comparable to the reported lifetime prevalence of bipolar disorder in the national comorbidity survey (4.4 %) [37]. Starzer et al. previously reported that patients diagnosed with CIP are significantly more likely to subsequently receive a diagnosis of BD than sex- and age-matched controls [6]. However, their analysis did not account for the presence of regular cannabis use, which has been demonstrated to significantly increase the risk of developing BD compared with non-users [18]. This omission complicates the ability to draw definitive conclusions regarding whether individuals diagnosed with CIP exhibit a higher incidence of subsequent BD than the general population or those who regularly use cannabis.

Among the studies that reported an unidentified cumulative later diagnosis of SSD/BD, the pooled mean prevalence was 63%. This figure is substantially higher than the pooled rates of SSD and BD reported by Starzer et al. (35.1 %) [6] and Rognli E.B. et al. (31.5 %) [8]. The discrepancy between our findings and those documented in the literature can likely be attributed to several factors. Notably, the pooled population in this study was considerably smaller than the cohort size of the previously mentioned studies, which may have contributed to the reduced reliability, as evidenced by the wide confidence interval (44–81%). Furthermore, there may have been variability in the outcomes under investigation. For instance, Rognli et al. included persistent delusional disorder and acute and transient psychotic disorders within the SSD outcome [8]. In contrast, Komuravelli et al. additionally incorporated schizoaffective disorder and psychosis not otherwise specified [12]. The broader SSD umbrella likely contributed to the higher rates of subsequent SSD/BD diagnoses observed in the unspecified group. Additionally, the cohort studied by Ghosh et al. was sourced from patients attending a dual-diagnosis clinic who exhibited high rates of cannabis use disorder [30]. Hence, this cohort and its prognoses may not be comparable to those of the broader CIP patient population.

### Biological pathways

While the precise biological mechanism underlying the development of cannabis-induced psychosis (CIP) remains unclear, several pathways have been proposed. McGuire et al. found that individuals who developed psychosis following cannabis consumption were more likely to have a first-degree relative with schizophrenia than those with cannabis-negative psychosis, suggesting

a genetic association with the development of CIP [38]. Additionally, the tetrahydrocannabinol (THC) component of cannabis is known to bind to and activate endocannabinoid receptors, which subsequently modulate the release of gamma-aminobutyric acid (GABA), influencing the functioning of dopamine pathways within the central nervous system [39, 40]. A 2022 systematic review examining the role of genetic polymorphisms in CIP found that genes involved in dopamine pathway function were associated with CIP development [41]. Additionally, a 2018 murine study demonstrated that subjects exposed to high levels of THC during adolescence exhibited life-long alterations in serotonin 2A receptor signaling, which has also been implicated in schizophrenia [42].

Given a definitive association between CIP and BD has not been established, there is a scarcity of research investigating potential biological mechanisms. Nevertheless, several pathways and mechanisms have been proposed that may elucidate a causal relationship between cannabis use and the onset of bipolar disorder. These pathways could potentially explain an underlying connection between CIP and BD, should one exist. Analogous to the pathway linking cannabis and psychosis, alteration of dopamine signaling by THC, particularly within the mesolimbic system, is hypothesized to contribute to manic symptoms [43]. Additionally, several common molecular findings have been identified among cannabis users and individuals with bipolar disorder. Notable examples include alterations and deficiencies in the cytoskeleton of the olfactory neuroepithelium and a reduction in the neuropeptide orexin-A, a critical regulator of the sleep-wake cycle [44, 45].

### Limitations

This study has several limitations. Despite an extensive review of the literature, we were able to identify a relatively low number of studies for inclusion. Much of the literature that appeared to be relevant to our topic failed to adequately describe a CIP cohort within their study and hence were not included. Due to the relatively low number of included studies, the effect of variables that may have had an impact on later SSD/BD diagnoses (e.g. inpatient versus outpatient, use of urine toxicology) may have been masked. Of the studies included, many did not report on variables and characteristics that are known to influence risk of later diagnosis. This can partly be attributed to the CIP cohort and their later diagnoses being a secondary outcome of interest in much of the literature. For example, a number of studies described a broader SIP cohort and their later diagnoses without describing outcomes for a CIP cohort. This limited our ability to determine the impact of several variables which have previously been associated with risk of developing SSD/BD namely: age, gender and mean follow up time [4, 8,

28]. Thereby preventing us from including these variables in the meta-regression and analyzing the effect they likely had on later diagnosis.

Within the schizophrenia spectrum subgroup, there was heterogeneity in the outcome being examined. Six studies reported results for patients transitioning to schizophrenia exclusively, while the remaining projects reported on transition to a broader schizophrenia spectrum umbrella with some including schizoaffective disorder and/or delusional disorder and brief psychotic disorder. It should be noted that the studies which reported on later diagnosis of a broader schizophrenia spectrum diagnosis also included some of the larger cohorts [5, 8, 16]. We were unable to determine the proportion of patients diagnosed with schizophrenia versus other diagnoses. This limited our ability to directly compare all studies included within this subgroup and likely contributed to the high degree of heterogeneity observed in our results.

### Conclusion and clinical implications

The findings of this study contribute to the expanding body of research on this subject. Several scholars have questioned the classification of SIP as a distinct diagnostic entity. Bramness et al., in a 2024 review, advocated for the reclassification of SIP under the SSD umbrella [3]. The authors asserted that SIP exhibits several features that more closely resemble a primary psychosis rather than one solely attributable to substance effects. Of note, the authors highlighted that CIP carries a risk of schizophrenia similar to that of SSD diagnoses, such as brief and atypical psychoses, as reported by Murrie et al. [13]. The results of this study indicate that approximately one in five patients with CIP will develop primary psychoses, which, although significant, are not comparable to the rate of schizophrenia among the aforementioned SSD diagnoses. Despite this, as Bramness et al. asserts, it may serve greater clinical utility to treat SIP and particularly CIP patients in a manner more similar to a primary psychotic disorder [3]. With the relaxation of legal restrictions on the sale and/or possession of cannabis and the development of highly concentrated strains, there may be an increase in CIP presentations [46, 47]. Therefore, it is crucial to develop comprehensive, evidence-based guidelines for treatment of CIP. Starzer et al. previously recommended that patients diagnosed with CIP should be monitored for a minimum of two years [6]. Shah et al. found that all CIP patients who remained abstinent from cannabis failed to develop schizophrenia [32]. Several studies have reported lower relapse rates when patients diagnosed with first-episode psychosis continue anti-psychotic medication after symptom remission [48, 49]. Ongoing research seeks to explore the benefits and drawbacks of long-term antipsychotic use in patients with SIP

[50]. Collectively, these findings and developments are promising for the creation of a comprehensive long-term approach to CIP. However, further attention and research into this growing topic are necessary.

In the present study, it was found that approximately one in twenty patients diagnosed with CIP will develop BD. The rate of subsequent BD is significantly lower than that of SSD, and it remains unclear whether patients with a CIP diagnosis are at an elevated risk compared to the general population and regular cannabis users. More research is needed on this topic, particularly to identify variables that may help distinguish between patients at risk for BD versus SSD. Currently, however, there is a much stronger link between SSD and CIP.

### Abbreviations

SIP	substance induced psychosis
CIP	cannabis induced psychosis
SSD	schizophrenia spectrum disorder
BD	bipolar disorder
THC	tetrahydrocannabinol

### Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12888-025-07382-2>.

Supplementary Material 1.

Supplementary Material 2.

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### Authors' contributions

M.J. and S.R. conceived of the presented idea. M.J. and A.T. developed a framework for and carried out study selection. M.J. and A.T. performed data extraction, REK performed analysis. M.J., REK and S.R. wrote the manuscript. All authors have reviewed and agree to the submission and publication of the submitted manuscript.

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### Data availability

All data generated or analyzed during this study are included in this published article and its supplementary information files.

### Declarations

#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

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