

Psychopharmacology: Examine the Emerging Pharmaceutical Treatments for Mental Health Conditions and their Effectiveness Compared to Traditional Medication

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# Psychopharmacology: Examine the Emerging Pharmaceutical Treatments for Mental Health Conditions and their Effectiveness Compared to Traditional Medication

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# **Abstract**

Study background: Mental health poses health, economic, and social burdens worldwide. The existing pharmaceutical interventions against mental diseases produce undesirable adverse effects, creating the need for the exploration of new treatments for more effective medications that do not yield adverse effects. Methods: The present review involved a literature search from electronic databases, including PubMed, ProQuest, Google Scholar, eb of science, and PsycINFO, and was conducted based on the Patient, Intervention, Comparison, Outcomes, and Studies (PICOS), protocol, and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) checklist. Two independent reviewers were assigned study selection and data collection processes that included 16 studies in the review. Results: A review comparing the effectiveness of emerging pharmaceutical interventions against mental illnesses found that the psychedelic class of medications and cannabinoids are emerging effective medications against mental illnesses, including Major Depressive Disorders (MDD), patients with Treatment-Resistant Depression (TRD), and Post-Traumatic Stress Disorder (PSTD). However, the medications produce mild adverse effects.

**Keywords** - Emerging mental health treatments, Effective medications, traditional medicines, mental health, Psychomarmacology treatment, Psychopharmacology efficacy.

#### 1.0 Introduction

In the last decades, the pharmaceutical sector has experienced burgeoning interests and efforts in exploring different pharmacotherapeutic agents for better clinical outcomes in the management of mental illnesses. The growing research and the pursuit of contemporary medications hail from the increasing health burden posed by mental illnesses, alongside safety and efficacy issues resulting from the traditional conventional interventions [1], [2]. The



multidimensional burden posed by mental diseases includes incapacitating individuals from economic activities, incapacitating and demoralizing a considerable portion of the global workforce, increasing expenditure, and lowering quality of life. With at least 450, 000, 000 individuals suffering from observational and mental illnesses, health burden is felt by individuals and governments from all social classes, including first to third-world countries [3]–[5]. The prevalence of mental health diseases and related mortalities is approximated to increase given the challenging economic times, poor social setup, and psychological issues. The projected increase in prevalence and complications raises the alarm concerning the need for cutting-edge treatment measures.

Despite the multiple pharmaceutical interventions, mental health and its associated burden become a global concern based on the incidence of adverse effects and the efficacy profiles. Literature posits that pharmaceutical interventions against mental illnesses bear a wide array of effects, including cardiovascular effects [6], [7], hepatic functions [8], and reproductive health [9], among other effects on overall well-being. In a bid to develop more effective, and less toxic medications, researchers embarked on studies and investigations for contemporary medications to treat different mental illnesses.

Even though not much has been achieved, the scientific community is proud of newly suggested pharmaceutical agents under study for effectiveness against mental illnesses. Some of the medications include Cariprazine, cannabinoids, psychedelics, ketamine and esketamine, lithium derivatives, and opioid modulators, among other agents [10]–[12]. Some of these pharmaceutical agents have been indicated for different illnesses despite a lack of robust evidence. However, the little evidence from the previous studies points to high effectiveness and fewer adverse effects.

The present review aims at the effectiveness of the contemporary pharmaceutical medications used to treat mental disorders. The review will focus on the reported efficacy outcomes and adverse effects of the newly discovered medications and compare them with the traditional medications. The comparative approach focuses on distinguishing whether the emerging treatments are more effective than the traditional medications.

## 2.0 Methods

## 2.1 Eligibility Criteria

The PICOS protocol was used to determine the eligibility of the individual studies. The PICOS protocol defined the profile of the individual studies eligible for inclusion in the present review [13]–[15]. The inclusion and exclusion criteria were as follows:

#### 2.1.1 Inclusion Criteria

The following inclusion criteria were used in the present review.



# **Table 1: PICOS protocol for inclusion**

#### **PICOS**

P	All patients with mental conditions, including MDD, PSTD, and TRD patients
I	Psychedelics; e. g. 10 mg, 25 mg, and 30 mg Psilocybin,
C	Placebo
0	Safety and efficacy outcomes, including reduced symptomatology and severity, tolerability, improved mood, behaviors, and attitudes
S	All classes of randomized controlled trials, e. g. double-blinded, phase II double-blinded, wait-list controlled clinical trial, and Open-label pilot studies.

#### 2.1.2 Exclusion Criteria

Studies were excluded in the preview based on the following reasons:

- Irrelevant methodology
- Outcomes irrelevant to the present topic
- Personal opinions

## 2.2 Information on Sources

The initial literature search was performed in electronic databases, including PubMed, ProQuest, Google Scholar, Web of Science, and PsycINFO. The literature search focused on articles reporting emerging pharmaceutical treatments or regimens used to treat various mental health conditions. The literature search was limited to studies published between January 2013 and October 2023.

# 2.3 Search Strategy

During the initial literature search, keywords were used to identify potential articles in the electronic databases. The keywords were used during the literature search: antidepressive agents, therapeutic use\*, Psilocybin, adverse effects \*, administration and dosage, drug therapy, pharmaceutical treatment, pharmacotherapy, mental disease, mental illness, psychiatry, outcome assessment, and combined modality therapy. The Boolean operators "AND" and "OR" combined the keywords during the literature search. The Boolean operator "AND" combined words with dissimilar means, whereas the Boolean operator "OR" combined words with similar meanings.

## 2.4 Selection Process

Two independent reviewers (M.N. and K.L.) were tasked with the study selection process. M.N. and K.L. independently and systematically selected eligible studies for the review. First, the reviewers assessed the titles and abstracts of the potential studies for relevance to the present topic. The abstract and tile screening approved studies for selection concerning the present topic. Secondly, the authors performed a full-text analysis to ascertain the reporting of consistent and relevant outcomes. Lastly, the reviewers compared the eligible studies based on the outcome measures and settled on studies reporting consistent outcomes of interest based on the topic.



#### 2.5 Data Collection Process

The independent reviewers reviewed the outcome measures reported by the individual studies and recorded them in an Excel sheet. The review process involved amicable resolution of any matters arising about the eligibility of the individual studies. M.N. and K.L. independently assessed the matter arising from the studies or any discrepancies and resolved the matters through dialogue.

#### 2.6 Data Items

The present review focuses on the effectiveness of the emerging trends and compares documented outcomes with the existing evidence on the traditional medications used to treat mental illnesses. The study considers the efficacy and safety outcomes, including improved symptomatology, relief of symptoms of various mental diseases, and adverse effects like headache, nausea, and dizziness. Other important variables include the safety of emerging medications like addiction. The intervention of emerging pharmaceutical medications against mental illnesses was assumed to be performed after the patients had been treated with traditional medications. The assumption focused on comparing the clinical outcomes of the emerging therapies against the traditional medications.

# 2.7 Study Risk of Bias Assessments

The Cochrane risk of bias assessment tool was used to examine the risk of bias in the included studies. The tool examined the domains of the risk of bias, including random sequence generation, allocation concealment, blinding of participants, blinding of personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting, alongside other forms of biases [16], [17]. Assessment outcomes of the seven domains informed the overall risk of bias of the included studies, reflecting the quality of the reported evidence.

## 2.8 Synthesis Methods

The PRISMA checklist was used to ensure transparency, quality assurance, and a complete reporting of findings and the review outcomes [18]–[20]. The PRISMA protocol guided a standardized reporting that enhances understanding of the methodology and results, risk of bias assessments, and verification of the review outcomes. Mainly, a qualitative analysis method was used to synthesize the reported outcomes.

## 2.9 Reporting Bias Assessment

The risk of bias assessment was reported by a summary of all the included studies and the assessment outcomes of the individual studies. The summary of the overall risk of bias was reported as "low risk of bias," "moderate risk of bias," and "high risk of bias" depending on the seven domains of study risk of bias: random sequence generation, allocation concealment, blinding of participants, blinding of personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, alongside other forms of biases [21], [22]. The robvis library of R programming language was used to visualize the weighted risk of bias assessment outcomes. The weighted outcomes provided an informative and nuanced summary of the individual domains of risk of bias assessment, rendering the importance of every domain in bias reporting [23], [24]. Also, the Robvis package was used to visualize the risk of bias in the individual studies. The seven domains of risk of bias of the individual studies were assessed to reflect the overall quality of evidence of each study.

# 2.10 Certainty Assessment

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to assess the certainty of the evidence reported by the included studies. The

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assessment focused on the domains of the included studies: selection bias, performance bias, detection bias, attrition bias, and reporting bias to tell the overall quality of evidence [24], [25]. The evidence certainty was rated as "High," "Moderate," "Low," and "Very low."

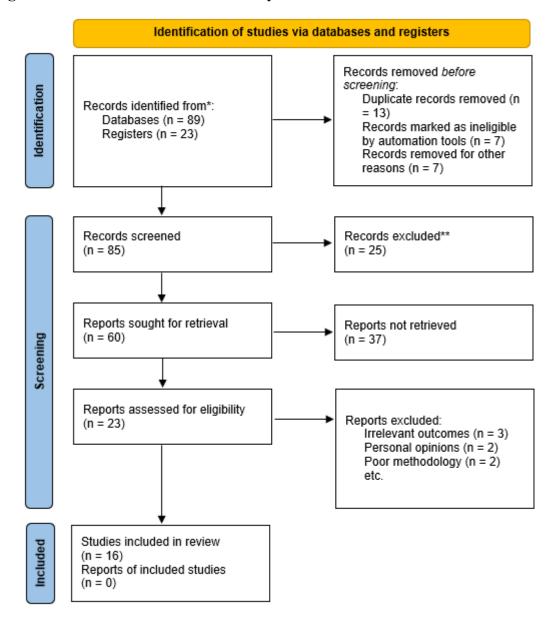
#### 3.0 Results

# 3.1 Study Selection

A total of 112 articles were identified in the databases and registers during the initial search. Out of this, 27 records were removed before the screening process, with reasons like study duplication, articles deemed ineligible by automated tools, and other reasons. The remaining 85 records were screened, removing 25 records. A total of 60 reports remained and were sought for retrieval. Thirty-seven reports still need to be retrieved, leaving 23 for eligibility assessment. Out of this, 7 studies were excluded for poor methodology, personal opinions, and outcomes irrelevant to the present topic (**Figure 1**).



Figure 1: PRISMA Flow Chart for Study Selection



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# 3.2 Study Characteristics

Even though the studies reported emerging pharmaceutical treatments for mental illnesses, the included studies bear unique features. A total of 16 articles were deemed eligible for inclusion based on the above-stated inclusion criteria. By outcome measures, 9 studies reported the efficacy of Psilocybin [26]–[34], representing the class of psychedelics. The studies report the efficacy and clinical outcomes of 10 mg, 25 mg, and 30 mg of Psilocybin among different mental health patients, including Major Depressive Disorders (MDD), patients with Treatment-Resistant Depression (TRD), and Post-Traumatic Stress Disorder (PSTD). The remaining 7 studies reported a comparison of CBD vis-à-vis BZD in the management of mental illnesses [35]–[41]. By origin, 8 studies originated from the United States of America, which was the highest number of studies from a single nation [26]–[29], [31], [36], [37], [39], whereas one study was a multicenter multinational study [32]. The multicenter study was carried out in the Czech Republic, Denmark, Germany, Ireland, the Netherlands, Portugal, Spain & and the United Kingdom. Four studies originated from Canada [30], [35], [38], [40], [41], whereas two studies originated from the United Kingdom [33], [34].

By design, the included studies were clinical trials, open-label pilot studies, and retrospective studies. With a total of 10 studies, RCTs were the majority level of evidence used in the review [26]–[28], [30]–[34], [39], [41]. Further, different RCT classes composing the group include a double-blinded randomized controlled trial, phase II double-blinded trial, phase II randomized, wait-list controlled clinical trial. Additional 5 retrospective studies [29], [35]–[38], [40], and one open-label pilot study were included in the review [29].



**Table 2: Study Characteristics Table** 

Study ID, Year of Publication	Design	Country of Origin	Participants	Intervention	Comparison	Follow-up (Weeks)	<b>Primary Outcomes</b>
Carhart- Harris et al., 2018	A double- blinded randomized controlled trial	United Kingdom	n=26; 6 females with moderate to severe treatment-resistant depression	P.O. 10 mg & 25 mg of Psilocybin 7 days apart, assessed from 1 week to 6 months	Placebo	72	Good tolerability, rapid symptom improvements
Carhart- Harris et al., 2016	A double- blinded randomized controlled trial	United Kingdom n=12; 6 males & 6 P.O. 10 mg & 25 mg Placebo females, with Psilocybin, 7 days apart, moderate-to-severe and assessed after 1 unipolar, treatment- resistant major depression			Psilocybin was well tolerated, reduced symptoms of depression and anxiety		
Goodwin et al., 2022	Phase II double- blind trial	Czech Republic, Denmark, Germany, Ireland, the Netherlands, Portugal, Spain & United Kingdom	n=428; 242 females TRD	PO 10 mg & 25 mg Psilocybin.	Placebo		Psilocybin 25 mg single dose reduced depression more than the 10 mg within 3 weeks. However, adverse effects, including nausea, dizziness & and headache, were reported.
Goodwin et al., 2023	Phase II double- blind trial	United States of America	n=233 TRD patients	PO 10 mg & 25 mg Psilocybin.	Placebo		At 3 weeks, Psilocybin improved depression symptoms, anxiety, depression severity & functioning
Rosenblat et al., 2022	Phase II randomized , wait-list	Canada	n=377 MDD, TRD, & Bipolar 2 disorder females patients aged 18 to 70 years	PO 25 mg & 10 mg for 6 months	Placebo	216	Positive tolerability and improved symptoms of depression.



	controlled						
	clinical trial						
Arronson et al., 2022	Open-label pilot study	United States of America	n=100 MDD & PSTD patients averaged 40.5 years	PO 25 mg & 10 mg for 6 months	Placebo	12	Psilocybin demonstrated broad- spectrum efficacy across depression treatment resistance
Griffiths et al., 2011	RCT	United States of America	n=18 adults	PO 25 mg & 30 mg Psilocybin	Placebo	14	Improved mood, behavior & attitudes
Davis et al., 2021	RCT	United States of America	n=870 MDD patients aged 21 to 75 years	PO 25 mg & 30 mg Psilocybin	Placebo		Decreased symptoms of depression within 4 weeks of treatment.
Gukasyan et al., 2022	RCT	United States of America	n=24 MDD patients, 67% females, 92% Caucasian	Psilocybin	Placebo	12	Decreased GRID-HAMD scores at 1, 3, 6, & 12 months of follow-up
Purcell et al., 2019	Retrospecti ve study	Canada	n=147, average age; 47.7 years, 61% females, 54% with a history of cannabis use	CBD	BZD	24	More than half of patients treated with cannabinoids discontinued BZD therapy. further studies on risk-benefit recommended
Francisco et al., 2019	Retrospecti ve study	United States of America	n=165	CBD	BZD	40	Compared to BZD, cannabis was found to be less harmful and healthier
Oliva et al., 2017	Retrospecti ve study	United States of America	n=1135601	CBD	BZD	27	adverse incidences like overdose suicidal- related outcomes in the BZD group than CBD
Drost et al., 2017	Retrospecti ve study	Canada	n=303	CBD	BZD	4 to 10	improved PSTD symptoms
Wan et al., 2017	RCT	United States of America	n=837	CBD	BZD	10	Improved concentration,

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							appetite, sleep, and relief from depression and anxiety.
Cahill et al., 2022	RCT	Canada	n=214, 57% older than 50 years, 58% males	CBD	BZD	6	Improvement in sleep and relief from recurrent pain
Gitau et al., 2022	Retrospecti ve study	Canada	n=723	CBD	BZD		55.5% of participants did not report adverse outcomes of cannabis use

HIIT: High-intensity interval training.

RCT: Randomized controlled trial.

TRD: Treatment-resistant depression.

MDD: Major depressive disorder.

PSTD: Post-traumatic stress disorder.

CBD: Cannabinoids.

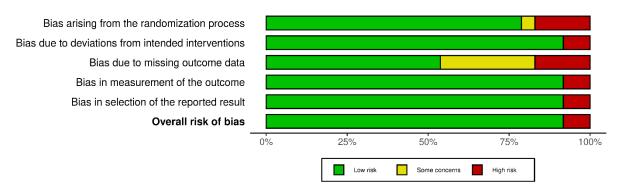
BZD: Benzodiazepines.



#### 3.3 Risk of Bias In Studies

The Cochrane Risk of bias assessment tool revealed an overall low risk of bias in the included studies (**Figure 2**). A general trend of low risk of bias was found across the 6 domains of risk of bias assessment, including bias arising from the randomization process, bias due to deviation from intended interventions, bias due to missing outcome data, bias in the measurement of outcomes, bias in the selection of the reported result, and the overall risk of bias across the studies.

Figure 2: A Summary of the Risk of Bias Assessment



The Cochrane risk of bias tool assessed the domains of risk of bias assessment of the 16 studies. Three out of the 16 studies were found to have an overall high risk of bias [30]–[32], whereas the rest of the studies were found to have an overall low risk of bias across the five domains (**Figure 3**). This suggests that the overall quality of evidence reported by the studies was high across a majority of the included articles.



Figure 3: Risk of bias assessment outcomes of individual studies.

		Risk of bias domains							
		D1	D2	D3	D4	D5	Overall		
	Carhart-Harris et al., 2018	+	+	+	+	+	+		
	Carhart-Harris et al., 2016	-	+	+	+	+	+		
	Goodwin et al., 2022	X	X	X	X	X	X		
	Goodwin et al., 2023	X	X	X	X	X	X		
	Rosenblat et al., 2022	X	X	X	X	X	X		
	Arronson et al., 2022	X	+	X	+	+	+		
	Griffiths et al., 2011	X	+	X	+	+	+		
Study	Davis et al., 2021	+	+	-	+	+	+		
ξŢ	Gukasyan et al., 2022	+	+	-	+	+	+		
	Purcell et al., 2019	+	+	-	+	+	+		
	Francisco et al., 2019	+	+	+	+	+	+		
	Oliva et al., 2017	+	+	+	+	+	+		
	Drost et al., 2017	+	+	+	+	+	+		
	Wan et al., 2017	+	+	+	+	+	+		
	Cahill et al., 2022	+	+	-	+	+	+		
	Gitau et al., 2022	+	+	-	+	+	+		

D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.

D3: Bias due to missing outcome data.

D4: Bias in measurement of the outcome. D5: Bias in selection of the reported result. Judgement

High

Some concerns



#### 3.4 Results of Individual Studies

Generally, the 9 studies reported that Psilocybin improved various symptoms of mental illnesses, including anxiety and depression. Psilocybin 10 mg and 25 mg reduced the symptoms of depression among European patients, mainly adults, within 3 weeks of treatment [26]–[34]. A notable relief of the symptoms of depression and improved outcomes among the patients were reported after 3 weeks of treatment. Also, Psilocybin treatment impacted long-term effects, lasting up to 12 months. A review of the results from the studies indicates that a single dose of Psilocybin may not be efficacious. The reported evidence shows that a stat dose of 10 mg of Psilocybin, followed by a 15 mg dose, or a stat dose of 25 mg, followed by a dose of 30 mg, was more efficacious than a single dose. Reduced severity of depression stood out as a consistent efficacy outcome of the Psilocybin treatment. The consistent reporting of reduced severity of depression indicates that clinical application of Psilocybin is likely to lower depression or depressive symptoms of mental diseases. This outcome suggests that Psilocybin can be indicated for reducing the severity of depression among mentally ill patients. Additionally, Psilocybin proved efficacy against a wide array of mental diseases, including PSTD, MDD, and TRD among culturally diverse patients. The present review revealed that male and female patients of European, Caucasian, and American patients benefited from Psilocybin treatment.

A review of 7 studies reported the CBD as an emerging pharmaceutical agent used to manage mental illnesses. The investigation compared CBD's effectiveness against BZDs to inform the overall clinical outcomes of the contemporary intervention. Generally, the 7 studies reported that CBD is an effective treatment for mental illnesses as it improves overall well-being and mental health among patients [35]–[41]. Of note, the review found that patients discontinued BZD use following CBD intervention. This suggests CBD's effectiveness and efficacy. CBD's reported efficacy outcomes, like improved sleep, mood modulation, and relief from anxiety, chronic pain, and depression, suggest the overall effectiveness over BZDs. Additionally, CBD was reported to be less harmful than BZDs, suggesting the safety of the emerging treatments.

## 3.5 Results Syntheses

A review of evidence on the effectiveness of Psilocybin reveals effectiveness comparable to traditional medications used to treat mental illnesses. Psilocybin treatment, including 10 mg, 25 mg, and 30 mg, produced acute short-term and long-term effectiveness among PSTD, MDD, and TRD patients. The present findings align with previous reviews where Psilocybin has been found to have tremendous efficacy against mental illnesses, including depression, treatment-resistant depression, MDD, and PSTD [42]–[44]. According to the literature, Psilocybin is emerging as a pharmacotherapy due to its effectiveness and efficacy compared to traditional pharmaceutical interventions. The present review established that the positive effects of Psilocybin interventions were felt quickly at low doses.

Psilocybin's effectiveness was attributed to the clinical outcomes. The present review found a wide array of positive clinical outcomes, including relief of depressive symptoms, reduced severity of depression, high tolerability, relief from symptoms like anxiety depression, and improved cognitive functions. The preference of Psilocybin regards the high tolerance, low resistance among patients, and the relief from the main symptoms of mental illnesses [45]. The clinical outcomes reported from 3 weeks of the assessment to the 12<sup>th</sup> month indicate rapid onset of action and the long-term outcomes of the psychedelic class of medications.

The present review featured consistent small doses of Psilocybin, 10 mg, 25 mg, and 30 mg, and considerable tolerability [26]–[34]. High tolerance at low doses is a critical factor in the effectiveness of any pharmaceutical agent. The high tolerability at low doses points to

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Psilocybin's effectiveness and the potential of other psychedelic drugs with efficacy against mental illnesses. These findings align with the previous trials where antidepressants were well-tolerated at low doses [46], [47]. With a maximum dose of 30 mg, Psilocybin proves to be an effective contemporary pharmaceutical medication used to treat mental illnesses. The high efficacy at low doses outdoes the traditional medications used to manage mental conditions, whose doses are as high as 50 mg, 100 mg, et cetera.

The clinical relevance and future rationale for psilocybin regards reduced severity of depression among mentally ill patients. The present review established that low doses of Psilocybin reduced the severity of depression in mental health treatment, suggesting the potential efficacy and safety therein. Psilocybin's advantage over traditional pharmacotherapy for mental illnesses regards the reduction of severity of depression among participants at low doses. Previous studies report that Psilocybin significantly reduces the severity of depression among mentally ill patients, affirming the relevance and clinical importance of the present review [48], [49]. Despite its clinical effectiveness, Psilocybin poses a challenge to the management of mental illnesses through the incidence of adverse effects, including headache, nausea, and dizziness. The review found a mild but considerable incidence of adverse effects among the study participants. The considerable headache cannot be ignored, considering the importance of the importance of high quality of life in mental health treatment. However, literature and previous studies suggest that Psilocybin-related headache is dose-dependent, suggesting that higher doses result in more severe headaches than low doses [50]. These perspectives influence the clinical indication and use of Psilocybin in mental health management. Low doses of Psilocybin gain more importance and clinical effects than high doses.

The preview proceeded with a comparison of CBD against BZDs in the management of mental illnesses. A review of evidence collected from 7 studies indicated improved overall well-being and mental health among participants receiving CBD than BZDs [35]–[41]. These findings concur with results obtained from the previous investigations. Small studies investigating CBD's effectiveness reported that CBD yields outstanding results in mental illnesses, including overall well-being and improved mental status. All doses of CBD have been associated with improved mental health progress and general well-being [51]–[53]. The present results indicate a clinically significant perspective regarding the treatment of mental illnesses. The traditional medications, including BZDs, focused on improving the patient's well-being and mental status. With the advantage of CBD, traditional medications are becoming effective, and their indication is likely to decrease.

Additional evidence on the effectiveness of CBD over BZD regarded the latter's discontinuation when co-administered. Evidence from the review overwhelmingly indicated that a majority of the patients discontinued BZD as soon as they started consuming CBD. BZD's discontinuation points to CBD's effectiveness. BZD discontinuation could result from CBD's effects, like improved sleep relief from depression, chronic pain, and anxiety [54], [55]. However, CBD's indication and use have been contentious due to the adverse effects of misuse and potential abuse. The sudden legalization of marijuana in many states across the world could result in extensive misuse, leading to addiction. Nevertheless, addiction and misuse among mentally ill patients have not been reported.

In the last decades, the risk-benefit analysis on CBDs has been conducted in multiple studies. The risk-benefit analysis focused on the harm posed by CBD and compared it against the traditional medications used to treat mental illnesses to tell the overall effectiveness, efficacy, and safety. Some of the studies consistently reported that CBD is less harmful than traditional medications used to treat mental illnesses. These findings align with the evidence reported by



the present study, suggesting the effectiveness of CBD over the traditional medications used to manage mental illnesses [56], [57]. The safety and harm of the emerging medications regard the overall clinical outcomes reported by the patients. The traditional medications used to treat mental illnesses are characterized by adverse effects associated with their interactions with the body receptors' pharmacokinetic and pharmacodynamic properties. However, the emerging medications have been modified to ensure fewer long and short-term effects.

# 3.6 Reporting Bias

The risk of bias assessment revealed a general trend of low risk of bias across the domains of risk of bias. The consistently low risk of bias across the studies suggests solid evidence regarding the effectiveness of emerging treatments for mental illnesses. Only 3 studies were found with a high risk of bias, which cannot impugn the overall conclusion regarding the evidence reported. Additionally, a risk of bias summary across the domains revealed a low risk of bias across the domains.

# 3.7 Certainty Of Evidence

The GRADE tool found that the studies reported high-quality evidence. Generally, the assessment revealed a general trend of high-quality evidence in the assessed domains. The consistent quality of evidence suggests the robustness of reported evidence. This implies that the evidence was solid and can be backed by previous studies and literature.

## 4.0 Discussion

# 4.1 General Interpretation

Psilocybin's indication has risen in the last decades owing to the beneficial effects among patients with mental health conditions. Indication and use of low doses of Psilocybin, 10 mg, 25 mg, and 30 mg, produced positive clinical outcomes, including relief of depressive symptoms, reduced severity of depression, high tolerability, relief from symptoms like anxiety depression, and improved cognitive functions. Even though mental health conditions feature unique clinical manifestations, the above-mentioned clinical effects, alongside decreased severity of depression, feature in the present review.

## 4.2 Limitations of the Evidence

The review found that psychedelics tremendously improve symptoms of various mental illnesses and alleviate mood, anxiety, and the severity of depression among adults. However, not much is reported regarding the effectiveness of psychedelics among children. The lack of evidence on psychedelics' effectiveness among children aligns with the efficacy profile of traditional medications indicated for various mental illnesses. In the last decades, concerns have been raised regarding the increasing incidence of mental illnesses among children implies that the outstanding evidence limited to adult participants is a significant limitation to the indication or importance of psychedelics for children with mental illnesses.

## 4.3 Limitations of the Review Processes

The present review should have considered studies from other parts of the world, including Africa, South America, and Asia. However, the emerging treatments are not genetically related, suggesting that ethnicity could not significantly affect the study outcomes. However, future studies should consider cross-cultural populations for inclusivity.



# 4.4 Implications of Study Results on Practice, Policy and Future Research

The present outcomes impact future research due to the insufficient evidence pointing to the effectiveness of Psilocybin among adolescents. Even though the evidence reported on Psilocybin's effectiveness is not entirely convincing, a lack of evidence regarding Psilocybin's efficacy among adolescents and children is needed to ascertain safety and efficacy. Thus, future research should focus on children and adolescent participants to gain insights into whether Psilocybin and other psychedelics are effective among adolescents and young children.

The results of the present review impact clinical practice and policy for psychedelics, especially regarding the safety and efficacy of Psilocybin in the treatment of mental conditions. The study findings point to efficacy outcomes and adverse effects that raise questions about the overall clinical outcomes of the pharmaceutical interventions. Thus, clinical practice should consider Psilocybin indications for MDD, RTD, and PSTD cautiously to cushion the adverse effects.

Policy regards the clinical practice and future studies on Psilocybin and other psychedelics in the treatment of various mental disorders. A policy guiding and safeguarding further studies and the examination of Psilocybin's efficacy is necessary to explore all possible outcomes that could drive forward the treatment of mental illnesses. The existing evidence indicates Psilocybin's efficacy against MDD, RTD, and PSTD, alongside safety concerns, suggesting potential clinical importance. The policy should ensure extensive research and investigation on the clinical effectiveness of the pharmaceutical intervention, including potential mechanisms for enhancing the safety and efficacy of mental illness treatments.

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