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The Potential Therapeutic Benefits and Safety of Psychedelics in the Treatment of Mental Health Conditions: A Systematic Review

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Abstract

Mental illnesses pose social, economic, and health burdens worldwide. The increasing health burden and mental diseases pose the need for investigating other potential medications. The present review focuses on psychedelic medications. The Patient/Participant, Intervention, Outcomes, and Studies ([PICOS) protocol and the Preferred Reporting Items for Systematic Reviews (PRISMA) checklist guided the establishment of the inclusion criteria. Two reviewers sought eligible studies in electronic databases, including ProQuest, PubMed, Google Scholar, and Web of Science. A total of 17 articles met the inclusion criteria and were reviewed for the potential therapeutic effects of psychedelics, including 3,4-methylenedioxymethamphetamine (MDMA), Lysergic acid diethylamide (LSD), and psilocybin, in the management of psychiatric illnesses. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to assess the level of certainty of evidence. Psychedelics' positive therapeutic effects were reported across the 17 articles. The medications provided relief from psychotic experiences, reduced the severity of depression and anxiety, improved PSTD, improved social cognition, and elevated the mood of the participants. However, adverse effects, including increased irritability, insomnia, rumination, and low mood, were reported and posed the need for patient monitoring. Despite the long-term therapeutic benefits, psychedelics produced adverse effects when used to manage psychiatric illnesses. LSD, MDMA, and psilocybin are emerging as potential medications that could improve the overall quality of life, life satisfaction, and well-being of mentally ill patients.

Keywords: *Psychiatric illness, psychedelics, MDMA, LSD, psilocybin treatment, depressive symptoms, disease severity, and therapeutic outcomes.*

1.0 Introduction

Mental illnesses, also known as psychiatric disorders, refer to health conditions characterized by altered thought processes, emotions, feelings, overall well-being, and behaviors. The disorders vary in clinical presentation and severity and possess overlapping morbidities. The symptomatology of mental disorders varies according to the particular disorders, including depression, obsessive-compulsive disorders, anxiety disorders, PSTD, bipolar disorders, and schizophrenia, among other diseases (Kayiteshonga et al., 2022; Solmi et al., 2022). In 2021, psychiatric disorders were estimated to affect and impose health and economic burdens on 350, 000, 000 people across the world (de Gregorio et al., 2021). The incidence is forecast to increase owing to different factors predisposing the global population to mental disturbance. In the last decade, the mortality rate due to mental illnesses was estimated to be 10% to 14% (Walker et al., 2015). Additionally, the burden of mental illnesses is likely to increase due to a lack of early diagnosis, adequate treatments, and patient follow-up, especially in developing nations. Even though the peak and onset of mental disorders are yet to be defined, the life expectancy of mentally ill persons decreases by 10 to 15 years compared to a healthy population (Solmi et al., 2022).

In the 1950s up until the early 1970s, psychedelic drugs were regarded as "drugs of abuse" and could not be indicated for any disorder due to the adverse effects and lack of documented therapeutic outcomes (Tupper et al., 2015). The increasing prevalence of mental illnesses, alongside comorbid disorders, renewed the investigations on potential medications, including psychedelic drugs. In recent years, psychedelics have been explored as treatments for mental disorders. These scientific studies come after years of fervent debates on psychedelics'' therapeutic benefits and benefits. Historically linked with counterculture movements, the therapeutic benefits of psychedelic drugs, including MDMA, LSD, and psilocybin, are gradually being recognized following clinical applications and results obtained from the scientific or research communities.

In recent studies, psychedelic drugs have been reported to improve the adverse outcomes of mental diseases like symptoms and severe effects like poor quality of life (Magaraggia et al., 2021). However, the evidence has not been convincing due to insufficient evidence, research gaps, and lack of consensus among researchers. By mechanism of action, psychedelic drugs modulate functional brain connectivity and improve mood, thought, perceptions, and consciousness in animals and human beings (de Gregorio et al., 2021), suggesting that they can produce the desired outcomes. The present review focuses on the potential therapeutic and adverse effects of psychedelic medication in the management of psychiatric disorders. The review leans on a risk-benefit analysis, focusing on the beneficial impacts of potential clinical use and indication.

Methods

1.1 Eligibility criteria

The PICOS protocol informed the development of the search strategy to ensure bias-free and comprehensive study search (Amir-Behghadami & Janati, 2020). In this review, the protocol applied in the literature searches for articles relevant to the present topic. The PICOS-based search strategy was as follows:

- (P): Patient/population: The evidence was obtained from mentally ill patients diagnosed with the appropriate diagnostic tools in the respective studies.
- (I): Intervention: Psychedelic drugs, including MDMA, LSD, and Psilocybin.
- (C): Comparison: Placebo

- (O)Outcomes: Positive therapeutic effects, including relief from depressive symptoms, anxiety, mindfulness, improved socio-cognitive performance, better quality sleep, improved global functioning, and self-processing. Also, potential adverse effects, including changes in mood, irritability, hallucinations, and ruminations, were considered.
- (S)Studies: The studies include RCTs.
-

1.2 Information sources

The article search was performed in four electronic databases, including ProQuest, PubMed, Google Scholar, and Web of Science for studies reporting outcomes relevant to the present topic. The study focused on level-one evidence published from January 2010 to October 2023. Majorly, the study search focused on RCTs, including the various designs therein.

1.3 Selection strategy

Two independent reviewers (P.K. and L.F.) independently selected studies from the electronic databases using keywords. The keywords were keyed into the electronic databases to search for potential studies. The following keywords were used during study selection; anxiety disorders, depression, lysergic acid diethylamide, MDMA, depression, PSTD, Psilocybin, mental illness, depressive symptoms, social cognition, mental disorder, psychedelic drugs. Boolean operators “OR” and “AND” were used to combine the keywords. The Boolean operator "OR" was used to combine words with similar meanings, whereas "AND" was used to combine words with dissimilar meanings.

1.4 Selection Process

The two independent reviewers (P.K. and L.F.) independently selected eligible studies and were guided by the PRISMA checklist (Page et al., 2021; Yepes-Nuñez et al., 2021). The reviewers screened the eligible studies against the PICOS protocol and the inclusion criteria to ascertain eligibility. The reviewers discussed any discrepancies and disagreements arising in the individual studies and reached a consensus.

1.5 Data collection process

The two reviewers (P.K. and L.F.) assessed and extracted abstracted data pertaining to the efficacy of psychedelics on the management of mental illnesses from the individual studies into an Excel sheet. Additionally, the reviewers investigated the quality of the eligible studies and reached a consensus on the study quality via dialogue.

1.6 Data Items

The independent reviewers (P.K. and L.F.) extracted the following data from the individual studies: authors' first names, year of article publication, study design, population, intervention, treatment period in months, and the primary outcomes of psychedelic intervention. Risk of bias assessment was performed across the five domains: selection bias, performance, attrition, reporting, and other forms of risk of bias (Igelström et al., 2021; McGuinness & Higgins, 2021). The assessment outcomes of individual studies were used to judge the overall quality of the individual studies.

1.7 Study risk of bias assessment

The Cochrane risk of bias assessment tool was used to assess the risk of bias across the five domains of the individual studies, including selection bias, performance, attrition, reporting, and other forms of risk of bias (Igelström et al., 2021; McGuinness & Higgins, 2021). The overall risk of bias in the included studies was categorized as "Low Risk of Bias," "Unclear

Risk of Bias," and "High Risk of Bias," depending on the assessment outcomes from the above-stated domains. The overall risk of bias assessment ensured the inclusion of studies high-quality studies. The risk of biased outcomes informed the potential impact of the risk of bias and limitations to the review (Frampton et al., 2022). Also, the risk of bias assessment ensured robust and reliable conclusions.

1.8 Synthesis Methods

The qualitative synthesis method was used in the present review. The qualitative review drew findings from the individual articles together (Lucas et al., 2007; Thomas & Harden, 2008). Evidence from the individual studies was reviewed for potential positive therapeutic effects of psychedelics alongside the adverse effects. Further, the evidence was critiqued to establish applicability within the structure of PICOS and clinical significance.

1.9 Certainty assessment

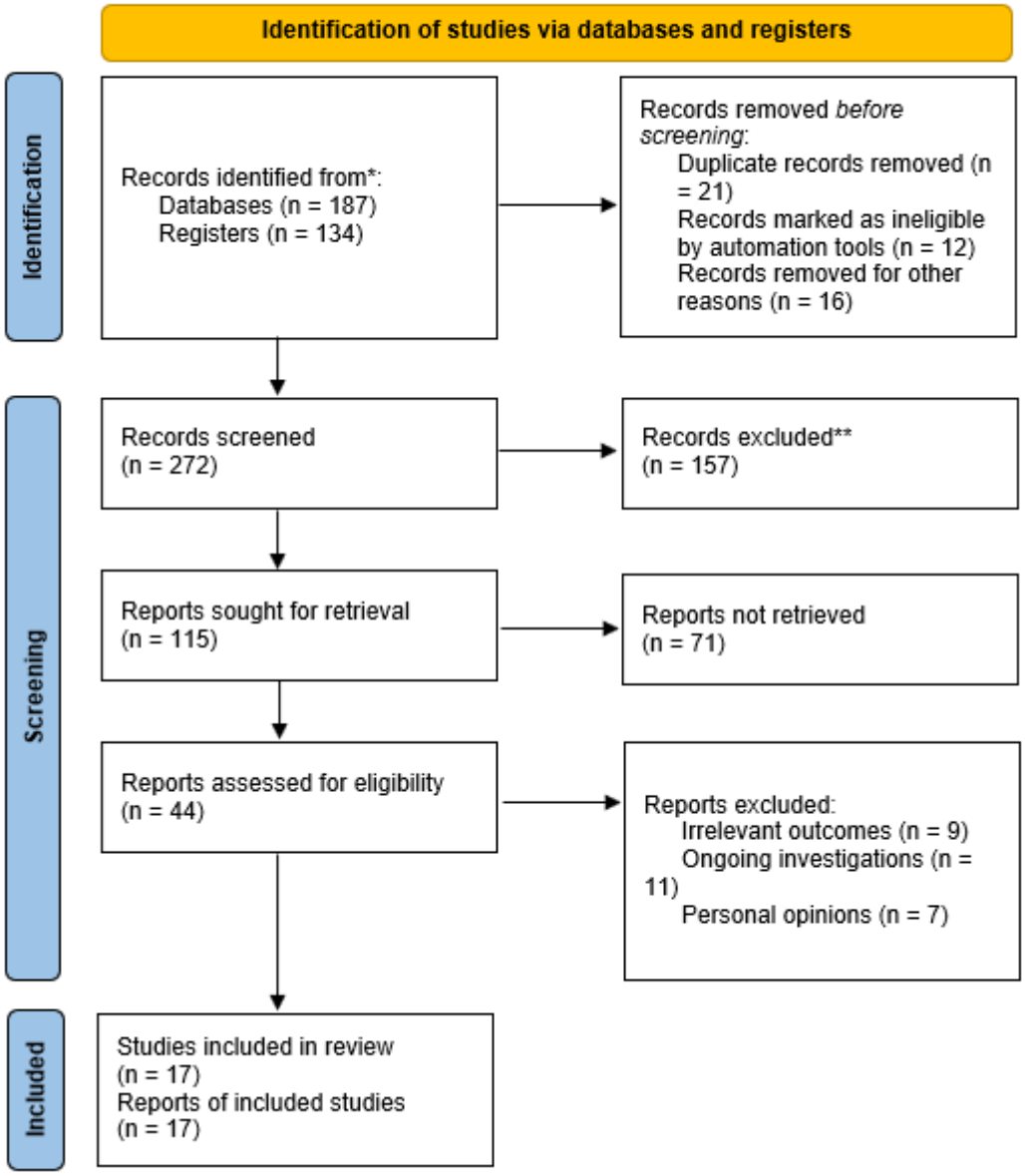
The GRADE approach was used to describe levels of certainty of evidence of the included studies. In this approach, certainty assessment focused on five domains, including risk of bias, inconsistency, indirectness, imprecision, and publication bias (Cuello-Garcia et al., 2022; Granholm et al., 2019). The certainty of the given outcomes was reported as "high," "moderate," "low," and "very low." The certainty of evidence of the outcomes of the present review is crucial for clinical decision-making on the management of mental disorders using psychedelic drugs. Also, the results influence policy formulation regarding clinical practices, support patient-centered care, and inform the overall safety and quality of healthcare.

2.0 Results

2.1 Study selection

The literature search focused on articles reporting the therapeutic benefits and adverse effects of psychedelic medications in the management of psychiatric disorders. The initial search produced 321 potential articles from databases and registers. A total of 49 records were removed before screening, with reasons like duplication, records marked as ineligible by automation tools, and other reasons. The remaining 272 records were screened, excluding 157 records. Only 44 articles remained for abstract and title screening for eligibility. Out of this, 27 articles were excluded with reasons, including irrelevant outcomes to the topic, ongoing investigations, and personal opinions (**Figure 1**). Seventeen articles met the inclusion criteria and were reviewed for psychedelics' therapeutic and adverse effects (Bogenschutz et al., 2015; Danforth et al., 2018; Gasser et al., 2014, 2015; Glazer et al., 2023; Griffiths et al., 2016; Grob et al., 2011; Holze et al., 2023; Malone et al., 2016; Mithoefer et al., 2011, 2019; Oehen et al., 2013; Ot'alora G et al., 2018; Preller et al., 2018; Ross et al., 2016; Wieβner et al., 2023; Wolfson et al., 2020).

Figure 1: PRISMA flow diagram



2.2 Study Characteristics

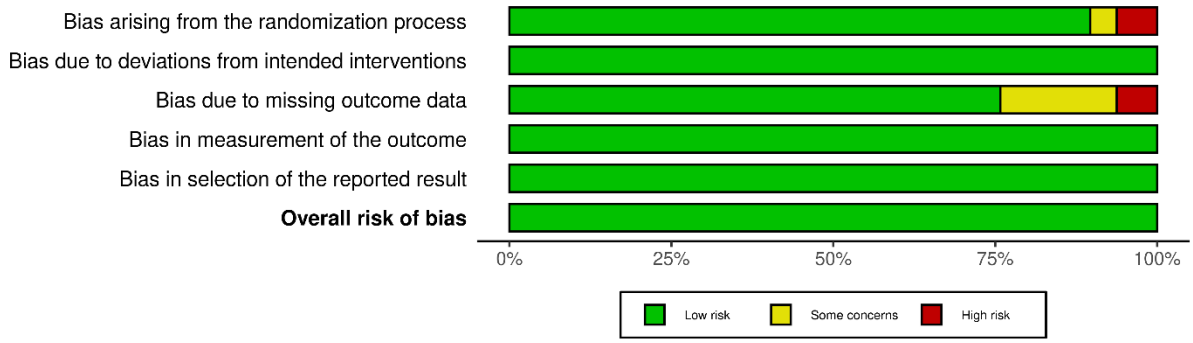
The studies represented different classes of psychedelics used to treat mental illnesses. Six studies reported the therapeutic benefits and adverse effects of MDMA in the management of mental illnesses, including anxiety, depression, and PSTD (Danforth et al., 2018; Mithoefer et al., 2011, 2019; Oehen et al., 2013; Ot'alora G et al., 2018; Wolfson et al., 2020). The therapeutic benefits of varying MDMA doses were reviewed across the six studies to give the overall impression of psychedelic efficacy and safety in the management of mental illnesses. Another six studies reported the therapeutic benefits and adverse effects of LSD in the management of mental illness (Gasser et al., 2014, 2015; Glazer et al., 2023; Holze et al., 2023; Preller et al., 2018; Wieβner et al., 2023). Additionally, six studies reported the potential therapeutic effects of psilocybin in the management of mental disorders (Bogenschutz et al., 2015; Griffiths et al., 2016; Grob et al., 2011; Malone et al., 2016; Ross et al., 2016). Evidence

obtained from the six studies added more evidence on the therapeutic effects of psychedelics in the management of psychiatric disorders (**Supplementary Table 1**).

2.3 Risk of Bias in Studies

The Cochrane risk of bias assessment tool found an overall low risk of bias across the domains (**Figure 2**). The 17 studies were found to have a low risk of bias in 6 domains. However, two domains, the bias arising from the randomization process and bias due to missing outcome data, feature some concerns and a high risk of bias. Even with this, the overall risk of bias does not impugn the quality of evidence in the individual studies.

Figure 2: Summary of risk of bias



Only one study found some concerns due to bias arising from the randomization process (Gasser et al., 2014). Additionally, five studies were found with some concerns regarding bias due to missing outcome data (Danforth et al., 2018; Griffiths et al., 2016; Grob et al., 2011; Mithoefer et al., 2019; Ot'alora G et al., 2018). On the other hand, two studies were found with high concerns regarding bias due to deviations from intended interventions and bias due to missing outcome data (Preller et al., 2018; Wolfson et al., 2020) (**Figure 3**). Nonetheless, the overall risk of biased outcomes of the individual studies was deemed low.

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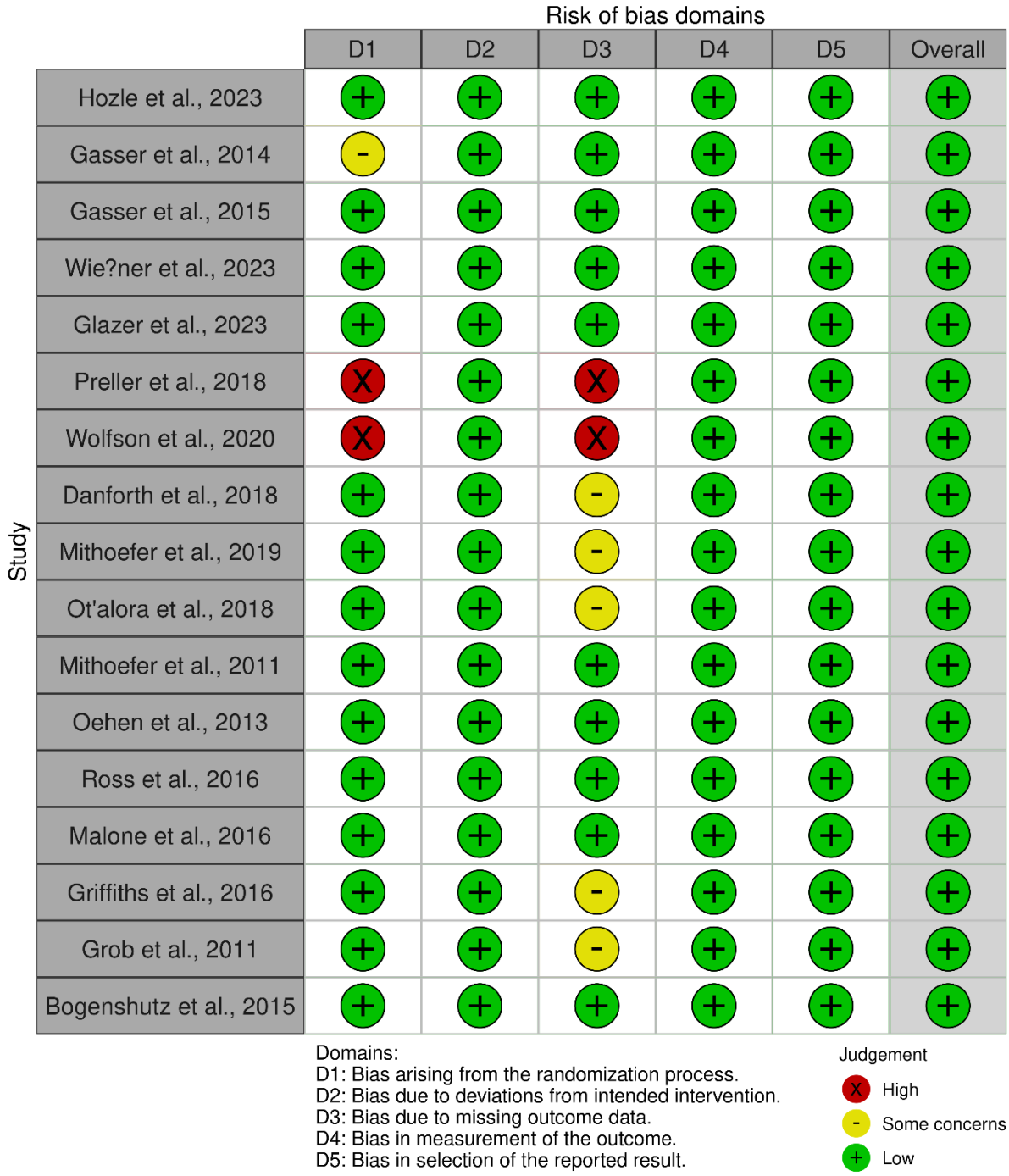
Figure 3: Risk of bias assessment of individual studies



2.4 Results of Individual Studies

Six studies reported psychedelics' potential therapeutic effects in the treatment of mental diseases. A preliminary review of the reported evidence indicates MDMA's therapeutic benefits in mental disorders, including PSTD, depression, and anxiety (Danforth et al., 2018; Mithoefer et al., 2011, 2019; Oehen et al., 2013; Ot'alora G et al., 2018; Wolfson et al., 2020). MDMA's main therapeutic effects reported include reduced anxiety, improved symptoms of PSTD and mindfulness, improved quality of sleep, alleviation of relief, and enhanced global functioning.

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Alleviation of anxiety and depression among autistic adults marked a crucial therapeutic effect of MDMA in mental illnesses. The consistent alleviation of depressive symptoms and the overall improvement of global functioning indicates a significant therapeutic effect of psychedelics in the management of mental illnesses. Additionally, the reported evidence strongly suggested that PSTD patients experienced positive transformations, including mindfulness and growth, following MDMA intervention. The patient's overall well-being and mental health draw from improved sleep quality.

The incidence of adverse effects poses questions regarding the effectiveness and safety of medications in the general management of mental health. The studies reported insomnia, increased irritability and low mood, tolerance issues, and ruminations (Danforth et al., 2018; Mithoefer et al., 2011, 2019; Oehen et al., 2013; Ot'alora G et al., 2018; Wolfson et al., 2020). The adverse effects experienced by a section of patients represent the potential safety issues to be monitored when treating mental illnesses with MDMA. Nonetheless, the reported adverse effects are less severe and are manageable through adequate clinical monitoring and interventions.

LSD's therapeutic effects and safety outcomes in the management of mental disorders emerged through six studies in the present review. The therapeutic outcomes were reported following LSD administration in a supervised and controlled setting. Patients receiving varying doses of LSD had been diagnosed with depression, anxiety, socio-cognitive disorders, and other mental diseases (Gasser et al., 2014, 2015; Glazer et al., 2023; Holze et al., 2023; Preller et al., 2018; Wieβner et al., 2023). The mainstream therapeutic effect of LSD reported by the 6 studies includes improved symptoms of anxiety, depression, social cognition, and overall well-being, suggesting that LSD can produce outstanding clinical benefits for mentally ill patients. The outcomes included long-term and short-term therapeutic benefits with no adverse effects. The alleviation of symptoms of various mental illnesses, improved mindfulness, and psychotic experiences point to the therapeutic benefits of psychedelic medications in the management of mental illnesses.

Lastly, five studies reported psilocybin's therapeutic effects in the management of psychiatric disorders among patients, including cancer patients (Bogenschutz et al., 2015; Griffiths et al., 2016; Grob et al., 2011; Malone et al., 2016; Ross et al., 2016). The overall outcome of the data indicates psilocybin's efficacy against mental illnesses, including depression. After a follow-up period, ranging from 6 to 36 months, participants treated with moderate and single doses of psilocybin reported reduced depression and anxiety, improved quality of life, decreased cravings, improved spirituality, and an overall improved well-being.

2.5 Results Synthesis

Psychedelic drugs are vulnerable to abuse and overdose due to manifestation in the body. Often, psychedelics result in physiological adverse effects like neurotoxicity, hypertension, and cardiovascular complications. On the other hand, psychedelics' psychiatric and psychological effects include hallucination, dependence, self-harm and harm unto others, challenging experiences, and hallucinogen persistent perception complication (Carhart-Harris & Goodwin, 2017; J.J.H. et al., 2018; Rucker et al., 2018; Schlag et al., 2022). The advent of these adverse effects has been the subject when indicating psychedelic drugs like MDMA and LSD in the management of mental illnesses.

Despite the overwhelming evidence regarding the adverse effects of psychedelic drugs, significant knowledge gaps exist regarding the management of mental illnesses. Many of the documented adverse effects of psychedelic drugs result from abuse and dependence where dosing is not considered. Fortunately, recent pharmaceutical and drug discoveries led to the

exploration of the therapeutic effects of psychedelic drugs on mental illnesses. recent studies report that psychedelics, including MDMA, LSD, and psilocybin, have been indicated against mental illnesses like PSTD, anxiety, depression, eating disorders, and substance abuse disorders and have reported positive outcomes (Breeksema et al., 2020; Irizarry et al., 2022). Nonetheless, the incidence and the severity of the therapeutic benefits and potential adverse effects remain unclear due to the grey areas characterizing the use of psychedelics.

The present review investigated the potential therapeutic effects of psychedelics, alongside the adverse effects in the management of mental illnesses, focusing on the clinical risk-benefits of the medications. Six studies reported potential therapeutic and adverse outcomes across different mental illnesses, including PSTD, depression, and social anxiety (Danforth et al., 2018; Mithoefer et al., 2011, 2019; Oehen et al., 2013; Ot'alora G et al., 2018; Wolfson et al., 2020). Alleviation of anxiety arose as a crucial therapeutic effect of MDMA, a psychedelic, in the management of mental illnesses. Psychedelics improve mood and balance emotions, thereby alleviating social anxiety. The outcomes of the present review align with existing literature on MDMA's therapeutic effect of alleviating social anxiety and improving patients' quality of life (Johansen & Krebs, 2009). This evidence suggests that MDMA and other psychedelics can provide mentally ill patients with long-lasting relief from social anxiety, enabling them to face and overcome their fears.

The clinical significance of the reported outcomes points to MDMA's potential benefits in PSTD management. The overwhelming incidence of mindfulness and post-traumatic growth indicates MDMA's therapeutic effects. MDMA administration triggered positive transformations following traumatic events, which is a common objective in PSTD management. Positive transformations and mindfulness are key treatment goals in PSTD (Krystal et al., 2021; Mithoefer et al., 2019; Sottile & Vida, 2022), indicating that the outcomes of the present review imply clinical significance. Literature posits that MDMA helps mentally ill patients face their past traumas and focus on growth. MDMA's empathetic and introspective effects enable patients to forge bonds with their emotions, leading to mindfulness.

In the alleviation of mental illnesses like PSTD and anxiety, the nexus between depression emerges as it is a common comorbidity of many mental illnesses. Also, the severity of depression concurs with the exacerbation of the mental illnesses (Steffen et al., 2020; Thaipisuttikul et al., 2014). The relief of anxiety and PSTD reduces the symptomatology and the severity of depression concurrently. The reduction of the symptomatology and severity of depression informs the clinical therapeutic effect of MDMA in the management of mental illnesses. The review established that MDMA addresses the psychological and emotional underpinnings of depression among patients with mental illnesses, resulting in relief.

Relief against anxiety, PSTD, and depression transitions to improved global functioning following MDMA treatment. Unlike traditional medications, psychedelic drugs yield sustained therapeutic effects in a single administration (Raison et al., 2022; Vargas et al., 2021). The present review found a significant reduction in symptomatology of mental illnesses with a single MDMA administration. However, additional doses were occasionally added to supplement the initial dose. In this perspective, the overall global functioning triggered by MDMA is achieved with the minimum dose. Also, this suggests that a low dose is required to trigger the clinical effects.

Despite MDMA's positive clinical outcomes, the present review found adverse effects posing clinical concerns and questions regarding their overall effectiveness. The main adverse effects found in the review include low mood, irritability, and insomnia. However, these adverse effects were less severe and manageable. The potential adverse effects suggest critical monitoring of patients following MDMA administration. An additional risk-benefit analysis

should be performed before MDMA administration. The incidence of adverse effects is recognized in literature, where the safety concerns of all medications are raised. Based on the severity and manageability of the adverse effects, the theoretical perspectives suggest assessing the risk-benefit outcomes of MDMA in mental illnesses to strike a balance between the overall therapeutic benefits and the adverse effects (Bender & Hellerstein, 2022; Raison et al., 2022). In some studies, MDMA has been reported to be an effective intervention for treatment-resistant PSTD (King & Hammond, 2021). Such theoretical perspectives raise psychedelics' therapeutic profile and present them as potential interventions against mental illnesses.

Evidence reported by six studies provided insight into the therapeutic effects of psychedelics in the management of mental diseases. The six studies overwhelmingly reported long-term therapeutic benefits, including relief from depression and anxiety, alongside improved sociologies functions (Gasser et al., 2014, 2015; Glazer et al., 2023; Holze et al., 2023; Preller et al., 2018; Wieβner et al., 2023). The relief from anxiety and depressive symptomatology bears significant weight in the management of mental diseases, as depression and anxiety stand out as the most debilitating and prevalent mental diseases. Even though the present review established strong evidence regarding the therapeutic effects of LSD in the management of mental illnesses, the existing literature presents the challenges and concerns arising from psychedelic use, including depressive symptoms (King & Hammond, 2021). Further, the improved socio-cognitive functions cut across multiple mental illnesses as it impacts the interpersonal relationships among persons with mental illnesses and overall function. These findings align with the main objectives of the therapeutic goals for mental illnesses. The mainstream pharmaceutic psychotherapy aims at indication of agents that yield positive therapeutic effects, or that can act as adjuncts in the clinical interventions.

The present review found that LSD improves consciousness among persons with mental illnesses and restores mood, cognition, and overall feelings of well-being (Glazer et al., 2023; Wieβner et al., 2023). The treatment modality adopted for mentally ill patients focuses on several outcomes, including increasing mindfulness and alleviation of psychotic experiences. The most common psychotic experiences posing psychiatric concerns include disorganized delusions, hallucinations, speech, and thinking (Staines et al., 2022; Yung & Lin, 2016). The controlled administration of LSD yields positive therapeutic outcomes, suggesting the potential of psychedelic medications in the treatment of mental illnesses. However, the subject of addiction and drug abuse remains paramount regarding psychedelic use. Transient anxiety is a common adverse effect of psychedelic use. Thus, patients should be monitored.

A review of the FIVE studies suggested that psilocybin implicates positive outcomes among persons with psychiatric disorders. The review revealed that psilocybin reduces depression and anxiety, improves quality of life, enhances patients' attitudes towards death and life, and increases spirituality and overall well-being (Bogenschutz et al., 2015; Griffiths et al., 2016; Grob et al., 2011; Malone et al., 2016; Ross et al., 2016). Additionally, psilocybin helps people with a substance use disorder recover and quit addictions. These outcomes suggest that psilocybin implicates a wide array of therapeutic benefits to mentally ill patients, suggesting the importance of the psychedelic class of medications in mental health.

The outcomes of the present review align with the therapeutic benefits and adverse effects reported by previous reviews and other studies. Improved quality of life and overall well-being marks similar outcomes in the present review and previous studies (Breeksema et al., 2020; Gómez-Busto & Ortiz, 2020). Psychedelics improve overall well-being and quality of life by alleviating depressive symptoms, relieving anxiety, improving mood and attitudes, and resulting in life satisfaction. Arguably, psychedelics' therapeutic benefits yield from the clinical outcomes of individual psychiatric disorders.

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2.6 Certainty of Evidence

The GRADE tool was used to assess the overall level of quality of the 17 studies. generally, the studies were found with high level of quality evidence. None of the studies were found with serious concerns across the domains of risk of bias, indirectness, imprecision and risk of bias. The outcomes of quality of evidence does not negatively impugn the conclusions made in the review (**Table 2**).

Table 2: Quality Assessment Table

Quality assessment						**Quality**	**Importance**
No. of studies	Study design	Risk of bias	Indirectness	Imprecision	Other considerations		
Reduced anxiety, improved symptoms of PSTD and mindfulness, improved quality of sleep, alleviation of relief, and enhanced global functioning							
6	RCT	Low	Not serious	Not serious	None	High	Vital
Improved symptoms of anxiety, depression, social cognition, and overall well-being							
6	RCT	Low	Not serious	Not serious	None	High	Vital
Reduced depression and anxiety, improved quality of life, decreased cravings, improved spirituality, and an overall improved well-being							
5	RCT	Low	Not serious	Not serious	None	High	Vital

3.1 Discussion

Mental disorders alter human behavior, mood, and thinking (Galbraith et al., 2021; Gross et al., 2019). The challenging clinical presentation and outcomes of treatment using conventional medications posed the need to explore other medications. Psychedelics are among the pursued medications for the treatment of mental disorders due to their potential therapeutic effects. nonetheless, the safety and the positive outcomes of psychedelic indications for various mental disorders remain unclear due to weak literature and insufficient data from previous studies.

The present review of psychedelic treatment of mental disorders focused on the therapeutic and adverse effects of MDMA, LSD, and Psilocybin in the management of mental disorders, including PSTD, depression, anxiety, eating disorders, and socio-cognitive functioning, among other illnesses. Improved mood, socio-cognitive functioning, thinking, and speech arose as key therapeutic outcomes of psychedelic intervention in mental illnesses (Danforth et al., 2018; Mithoefer et al., 2011, 2019; Oehen et al., 2013; Ot'alora G et al., 2018; Wolfson et al., 2020), whereas transient anxiety, insomnia, increased irritability, and arousal stood out as the critical adverse effects (Gasser et al., 2014, 2015; Glazer et al., 2023; Holze et al., 2023; Preller et al., 2018; Wieβner et al., 2023). The incidence of the adverse effects is slightly low, suggesting that the positive therapeutic effects are more vibrant among mentally ill patients.

Despite the promising therapeutic benefits of psychedelic medications in the management of mental illnesses, patients should be monitored not only against the potential adverse effects but also against addiction or abuse by patients and medical professionals. The present review found that low doses of LSD and MDMA yield positive therapeutic effects among mentally ill patients and can be easily abused when they become easily accessible. Non-clinical abuse or use of psychedelic drugs, including self-intravenous administration, and the liability of

physical dependence among adolescents, medical professionals, drug addicts, and mentally ill patients cannot be overlooked due to a rich history of non-clinical use (Bates & Trujillo, 2021; Heal et al., 2018). Thus, the indication of psychedelics should be subject to rigorous monitoring and patient follow-up to ensure proper use.

Lastly, findings on psilocybin's therapeutic benefits add more weight to the clinical importance of psychedelics in the management of psychiatric illnesses. The present review established that psilocybin improves patients' overall well-being, satisfaction, and quality of life. Arguably, these outcomes are cumulative therapeutic benefits of psilocybin in the treatment of different mental disorders like depression, PSTD, and anxiety, among others (Gómez-Busto & Ortiz, 2020). The multidimensional manifestation of psilocybin's therapeutic effects implicates the advantages of the psychedelic class of medications in the management of mental illnesses. However, patient follow-up and monitoring are necessary due to the incidence of adverse effects and potential abuse.

Limitations of the evidence included in the review

A small number of study participants is a significant limitation of the present review. It is crucial to note the implications of basing clinical practices or conclusions on a small study group. The small study group may need to adequately represent the actual outcomes of psychedelic medications among mentally ill patients in the real-world population. Additionally, data inconsistency merged in the review. Some of the included studies lacked crucial information, including the follow-up period. This impedes decision-making and conclusions on the obtained results.

Limitations of the review processes used

Study selection emerges as a significant limitation in the present review. The study selection identified studies reporting MDMA's potential therapeutic and adverse effects at different follow-up periods and doses. Whereas some studies did not report a follow-up period, others reported varied follow-up periods, ranging from 12 to 72 months. The varied follow-up periods implicate conclusions on the long-term therapeutic or adverse outcomes of MDMA in mental illness management. Likewise, the varied dosing impacts conclusions as the different doses may be hypothesized to cause varying adverse effects. Thus, conclusions cannot be made regarding the therapeutic effects of a particular dose of MDMA within a specific period.

Implications of the Results for practice, policy, and future research

The current theoretical perspectives do not include several aspects of psychedelic use, including ethical considerations, legal aspects, and potential misuse. Psychedelic medications are gaining popularity in the management of mental illnesses despite few studies reporting the therapeutic profiles and potential adverse effects. Thus, future studies should study the potential adverse effects and therapeutic outcomes of psychedelic drugs in the management of mental disorders.

Currently, clinical practices should be backed by well-defined patient management to monitor potential adverse effects. The preview indicated that transient anxiety is among the most common and severe adverse effects of psychedelic drugs. The high prevalence of transient anxiety indicates the importance of adequate patient monitoring.

The current health protocols and policies do not deliberate solid frameworks for psychedelic use in the management of mental disorders. With the emerging importance and popularity, health policies should include the indication of psychedelic medications in the management of mental disorders. The policies should include a guideline for indication and administration to prevent misuse among patients and medical professionals.

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REFERENCES

Amir-Behghadami, M., & Janati, A. (2020). Population, Intervention, Comparison, Outcomes and Study (PICOS) design as a framework to formulate eligibility criteria in systematic reviews. In *Emergency Medicine Journal* (Vol. 37, Issue 6). https://doi.org/10.1136/emermed-2020-209567

Bates, M. L. S., & Trujillo, K. A. (2021). Use and abuse of dissociative and psychedelic drugs in adolescence. In *Pharmacology Biochemistry and Behavior* (Vol. 203). https://doi.org/10.1016/j.pbb.2021.173129

Bender, D., & Hellerstein, D. J. (2022). Assessing the risk–benefit profile of classical psychedelics: a clinical review of second-wave psychedelic research. In *Psychopharmacology* (Vol. 239, Issue 6). https://doi.org/10.1007/s00213-021-06049-6

Bogenschutz, M. P., Forcehimes, A. A., Pommy, J. A., Wilcox, C. E., Barbosa, P., & Strassman, R. J. (2015). Psilocybin-assisted treatment for alcohol dependence: A proof-of-concept study. *Journal of Psychopharmacology*, *29*(3). https://doi.org/10.1177/0269881114565144

Breeksema, J. J., Niemeijer, A. R., Krediet, E., Vermetten, E., & Schoevers, R. A. (2020). Psychedelic Treatments for Psychiatric Disorders: A Systematic Review and Thematic Synthesis of Patient Experiences in Qualitative Studies. In *CNS Drugs* (Vol. 34, Issue 9). https://doi.org/10.1007/s40263-020-00748-y

Carhart-Harris, R. L., & Goodwin, G. M. (2017). The Therapeutic Potential of Psychedelic Drugs: Past, Present, and Future. *Neuropsychopharmacology*, *42*(11). https://doi.org/10.1038/npp.2017.84

Cuello-Garcia, C. A., Santesso, N., Morgan, R. L., Verbeek, J., Thayer, K., Ansari, M. T., Meerpohl, J., Schwingshackl, L., Katikireddi, S. V., Brozek, J. L., Reeves, B., Murad, M. H., Falavigna, M., Mustafa, R., Regidor, D. L., Alexander, P. E., Garner, P., Akl, E. A., Guyatt, G., & Schünemann, H. J. (2022). GRADE guidance 24 optimizing the integration of randomized and non-randomized studies of interventions in evidence syntheses and health guidelines. *Journal of Clinical Epidemiology*, *142*. https://doi.org/10.1016/j.jclinepi.2021.11.026

Danforth, A. L., Grob, C. S., Struble, C., Feduccia, A. A., Walker, N., Jerome, L., Yazar-Klosinski, B., & Emerson, A. (2018). Reduction in social anxiety after MDMA-assisted psychotherapy with autistic adults: a randomized, double-blind, placebo-controlled pilot study. *Psychopharmacology*, *235*(11). https://doi.org/10.1007/s00213-018-5010-9

de Gregorio, D., Aguilar-Valles, A., Preller, K. H., Heifets, B. D., Hibicke, M., Mitchell, J., & Gobbi, G. (2021). Hallucinogens in mental health: Preclinical and clinical studies on LSD, psilocybin, MDMA, and ketamine. *Journal of Neuroscience*, *41*(5). https://doi.org/10.1523/JNEUROSCI.1659-20.2020

Frampton, G., Whaley, P., Bennett, M., Bilotta, G., Dorne, J. L. C. M., Eales, J., James, K., Kohl, C., Land, M., Livoreil, B., Makowski, D., Muchiri, E., Petrokofsky, G., Randall, N., & Schofield, K. (2022). Principles and framework for assessing the risk of bias for studies included in comparative quantitative environmental systematic reviews. *Environmental Evidence*, *11*(1). https://doi.org/10.1186/s13750-022-00264-0

Galbraith, N., Boyda, D., McFeeters, D., & Hassan, T. (2021). The mental health of doctors during the COVID-19 pandemic. *BJPsych Bulletin*, *45*(2). https://doi.org/10.1192/bjb.2020.44

Gasser, P., Holstein, D., Michel, Y., Doblin, R., Yazar-Klosinski, B., Passie, T., & Brenneisen, R. (2014). Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. *Journal of Nervous and Mental Disease*, *202*(7). https://doi.org/10.1097/NMD.0000000000000113

Gasser, P., Kirchner, K., & Passie, T. (2015). LSD-assisted psychotherapy for anxiety associated with a life-threatening disease: A qualitative study of acute and sustained subjective effects. *Journal of Psychopharmacology*, *29*(1). https://doi.org/10.1177/0269881114555249

Glazer, J., Murray, C. H., Nusslock, R., Lee, R., & de Wit, H. (2023). Low doses of lysergic acid diethylamide (LSD) increase reward-related brain activity. *Neuropsychopharmacology*, *48*(2). https://doi.org/10.1038/s41386-022-01479-y

Gómez-Busto, F. J., & Ortiz, M. I. (2020). Virtual reality and psychedelics for the treatment of psychiatric disease: A systematic literature review. *Clinical Neuropsychiatry*, *17*(6). https://doi.org/10.36131/cnfioritieditore20200606

Granholm, A., Alhazzani, W., & Møller, M. H. (2019). Use of the GRADE approach in systematic reviews and guidelines. In *British Journal of Anaesthesia* (Vol. 123, Issue 5). https://doi.org/10.1016/j.bja.2019.08.015

Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., Cosimano, M. P., & Klinedinst, M. A. (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *Journal of Psychopharmacology*, *30*(12). https://doi.org/10.1177/0269881116675513

Grob, C. S., Danforth, A. L., Chopra, G. S., Hagerty, M., McKay, C. R., Halberstad, A. L., & Greer, G. R. (2011). Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Archives of General Psychiatry*, *68*(1). https://doi.org/10.1001/archgenpsychiatry.2010.116

Gross, J. J., Uusberg, H., & Uusberg, Andero. (2019). Mental illness and well-being: an affect regulation perspective. *World Psychiatry*, *18*(2). https://doi.org/10.1002/wps.20618

Heal, D. J., Gosden, J., & Smith, S. L. (2018). Evaluating the abuse potential of psychedelic drugs as part of the safety pharmacology assessment for medical use in humans. In *Neuropharmacology* (Vol. 142). https://doi.org/10.1016/j.neuropharm.2018.01.049

Holze, F., Gasser, P., Müller, F., Dolder, P. C., & Liechti, M. E. (2023). Lysergic Acid Diethylamide–Assisted Therapy in Patients With Anxiety With and Without a Life-Threatening Illness: A Randomized, Double-Blind, Placebo-Controlled Phase II Study. *Biological Psychiatry*, *93*(3). https://doi.org/10.1016/j.biopsych.2022.08.025

Igelström, E., Campbell, M., Craig, P., & Katikireddi, S. V. (2021). Cochrane's risk of bias tool for non-randomized studies (ROBINS-I) is frequently misapplied: A

methodological systematic review. *Journal of Clinical Epidemiology*, *140*. https://doi.org/10.1016/j.jclinepi.2021.08.022

Irizarry, R., Winczura, A., Dimassi, O., Dhillon, N., Minhas, A., & Larice, J. (2022). Psilocybin as a Treatment for Psychiatric Illness: A Meta-Analysis. *Cureus*. https://doi.org/10.7759/cureus.31796

J.J.H., R., J., I., & D.J., N. (2018). Psychiatry & the psychedelic drugs. Past, present & future. *Neuropharmacology*, *142*.

Johansen, P., & Krebs, T. S. (2009). How could MDMA (ecstasy) help anxiety disorders? A neurobiological rationale. *Journal of Psychopharmacology*, *23*(4). https://doi.org/10.1177/0269881109102787

Kayiteshonga, Y., Sezibera, V., Mugabo, L., & Iyamuremye, J. D. (2022). Prevalence of mental disorders, associated co-morbidities, health care knowledge and service utilization in Rwanda – towards a blueprint for promoting mental health care services in low- and middle-income countries? *BMC Public Health*, *22*(1). https://doi.org/10.1186/s12889-022-14165-x

King, F., & Hammond, R. (2021). Psychedelics as Reemerging Treatments for Anxiety Disorders: Possibilities and Challenges in a Nascent Field. *FOCUS*, *19*(2). https://doi.org/10.1176/appi.focus.20200047

Krystal, J. H., Kelmendi, B., & Petrakis, I. L. (2021). Psychotherapy-supported MDMA treatment for PTSD. *Cell Reports Medicine*, *2*(8). https://doi.org/10.1016/j.xcrm.2021.100378

Lucas, P. J., Baird, J., Arai, L., Law, C., & Roberts, H. M. (2007). Worked examples of alternative methods for the synthesis of qualitative and quantitative research in systematic reviews. *BMC Medical Research Methodology*, *7*. https://doi.org/10.1186/1471-2288-7-4

Magaraggia, I., Kuiperes, Z., & Schreiber, R. (2021). Improving cognitive functioning in major depressive disorder with psychedelics: A dimensional approach. *Neurobiology of Learning and Memory*, *183*. https://doi.org/10.1016/j.nlm.2021.107467

Malone, T., Mennenga, S. E., Ross, S., Bossis, A., Guss, J., Babb, J., Kalliontzi, K., Corby, P., Schmidt, B. L., Su, Z., Agin-Liebes, G., Cohen, B., & Belser, A. (2016). Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. *Journal of Psychopharmacology*, *30*(12).

McGuinness, L. A., & Higgins, J. P. T. (2021). Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. *Research Synthesis Methods*, *12*(1). https://doi.org/10.1002/jrsm.1411

Mithoefer, M. C., Feduccia, A. A., Jerome, L., Mithoefer, A., Wagner, M., Walsh, Z., Hamilton, S., Yazar-Klosinski, B., Emerson, A., & Doblin, R. (2019). MDMA-assisted psychotherapy for treatment of PTSD: study design and rationale for phase 3 trials based on pooled analysis of six phase 2 randomized controlled trials. *Psychopharmacology*, *236*(9). https://doi.org/10.1007/s00213-019-05249-5

Mithoefer, M. C., Wagner, M. T., Mithoefer, A. T., Jerome, L., & Doblin, R. (2011). The safety and efficacy of ±3,4-methylenedioxymethamphetamine- assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress

disorder: The first randomized controlled pilot study. *Journal of Psychopharmacology*, *25*(4). https://doi.org/10.1177/0269881110378371

Oehen, P., Traber, R., Widmer, V., & Schnyder, U. (2013). A randomized, controlled pilot study of MDMA (±3,4- Methylenedioxymethamphetamine)-assisted psychotherapy for treatment of resistant, chronic Post-Traumatic Stress Disorder (PTSD). *Journal of Psychopharmacology*, *27*(1). https://doi.org/10.1177/0269881112464827

Ot'alora G, M., Grigsby, J., Poulter, B., Van Derveer, J. W., Giron, S. G., Jerome, L., Feduccia, A. A., Hamilton, S., Yazar-Klosinski, B., Emerson, A., Mithoefer, M. C., & Doblin, R. (2018). 3,4-Methylenedioxymethamphetamine-assisted psychotherapy for treatment of chronic posttraumatic stress disorder: A randomized phase 2 controlled trial. *Journal of Psychopharmacology*, *32*(12). https://doi.org/10.1177/0269881118806297

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. In *The BMJ* (Vol. 372). https://doi.org/10.1136/bmj.n71

Preller, K. H., Schilbach, L., Pokorny, T., Flemming, J., Seifritz, E., & Vollenweider, F. X. (2018). Role of the 5-HT2A receptor in self- and other-initiated social interaction in lysergic acid diethylamide-induced states: A pharmacological fMRI study. *Journal of Neuroscience*, *38*(14). https://doi.org/10.1523/JNEUROSCI.1939-17.2018

Raison, C. L., Jain, R., Penn, A. D., Cole, S. P., & Jain, S. (2022). Effects of Naturalistic Psychedelic Use on Depression, Anxiety, and Well-Being: Associations With Patterns of Use, Reported Harms, and Transformative Mental States. *Frontiers in Psychiatry*, *13*. https://doi.org/10.3389/fpsyt.2022.831092

Ross, S., Bossis, A., Guss, J., Agin-Liebes, G., Malone, T., Cohen, B., Mennenga, S. E., Belser, A., Kalliontzi, K., Babb, J., Su, Z., Corby, P., & Schmidt, B. L. (2016). Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: A randomized controlled trial. *Journal of Psychopharmacology*, *30*(12). https://doi.org/10.1177/0269881116675512

Rucker, J. J. H., Iliff, J., & Nutt, D. J. (2018). Psychiatry & the psychedelic drugs. Past, present & future. In *Neuropharmacology* (Vol. 142). https://doi.org/10.1016/j.neuropharm.2017.12.040

Schlag, A. K., Aday, J., Salam, I., Neill, J. C., & Nutt, D. J. (2022). Adverse effects of psychedelics: From anecdotes and misinformation to systematic science. In *Journal of Psychopharmacology* (Vol. 36, Issue 3). https://doi.org/10.1177/02698811211069100

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., Il Shin, J., Kirkbride, J. B., Jones, P., Kim, J. H., Kim, J. Y., Carvalho, A. F., Seeman, M. V., Correll, C. U., & Fusar-Poli, P. (2022). Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. In

Molecular Psychiatry (Vol. 27, Issue 1). https://doi.org/10.1038/s41380-021-01161-7

Sottile, R. J., & Vida, T. (2022). A proposed mechanism for the MDMA-mediated extinction of traumatic memories in PTSD patients treated with MDMA-assisted therapy. In *Frontiers in Psychiatry* (Vol. 13). https://doi.org/10.3389/fpsyt.2022.991753

Staines, L., Healy, C., Coughlan, H., Clarke, M., Kelleher, I., Cotter, D., & Cannon, M. (2022). Psychotic experiences in the general population, a review; Definition, risk factors, outcomes and interventions. In *Psychological Medicine* (Vol. 52, Issue 15). https://doi.org/10.1017/S0033291722002550

Steffen, A., Nübel, J., Jacobi, F., Bätzing, J., & Holstiege, J. (2020). Mental and somatic comorbidity of depression: A comprehensive cross-sectional analysis of 202 diagnosis groups using German nationwide ambulatory claims data. *BMC Psychiatry*, *20*(1). https://doi.org/10.1186/s12888-020-02546-8

Thaipisuttikul, P., Ittasakul, P., Waleeprakhon, P., Wisajun, P., & Jullagate, S. (2014). Psychiatric comorbidities in patients with major depressive disorder. *Neuropsychiatric Disease and Treatment*, *10*. https://doi.org/10.2147/NDT.S72026

Thomas, J., & Harden, A. (2008). Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Medical Research Methodology*, *8*. https://doi.org/10.1186/1471-2288-8-45

Tupper, K. W., Wood, E., Yensen, R., & Johnson, M. W. (2015). Psychedelic medicine: A re-emerging therapeutic paradigm. *CMAJ*, *187*(14). https://doi.org/10.1503/cmaj.141124

Vargas, M. V., Meyer, R., Avanes, A. A., Rus, M., & Olson, D. E. (2021). Psychedelics and Other Psychoplastogens for Treating Mental Illness. In *Frontiers in Psychiatry* (Vol. 12). https://doi.org/10.3389/fpsyt.2021.727117

Walker, E. R., McGee, R. E., & Druss, B. G. (2015). Mortality in Mental Disorders and Global Disease Burden Implications. *JAMA Psychiatry*, *72*(4). https://doi.org/10.1001/jamapsychiatry.2014.2502

Wießner, I., Falchi, M., Palhano-Fontes, F., Feilding, A., Ribeiro, S., & Tófoli, L. F. (2023). LSD, madness and healing: Mystical experiences as possible link between psychosis model and therapy model. *Psychological Medicine*, *53*(4). https://doi.org/10.1017/S0033291721002531

Wolfson, P. E., Andries, J., Feduccia, A. A., Jerome, L., Wang, J. B., Williams, E., Carlin, S. C., Sola, E., Hamilton, S., Yazar-Klosinski, B., Emerson, A., Mithoefer, M. C., & Doblin, R. (2020). MDMA-assisted psychotherapy for treatment of anxiety and other psychological distress related to life-threatening illnesses: a randomized pilot study. *Scientific Reports*, *10*(1). https://doi.org/10.1038/s41598-020-75706-1

Yepes-Nuñez, J. J., Urrútia, G., Romero-García, M., & Alonso-Fernández, S. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Revista Espanola de Cardiologia*, *74*(9). https://doi.org/10.1016/j.recesp.2021.06.016

Yung, A. R., & Lin, A. (2016). Psychotic experiences and their significance. In *World Psychiatry* (Vol. 15, Issue 2). https://doi.org/10.1002/wps.20328

1. Appendix

Supplementary Table 1: Study characteristics table

STUDY	STUDY DESIGN	Population	INTERVENTION	CONTROL	TREATMENT PERIOD (WEEKS)	OUTCOME MEASURES
Hozle et al., 2023	2-center, double-blind, placebo-controlled trial	n=44	PO 200 µg LSD	Placebo	16	Long-term relief from anxiety
						Long-term relief from depression
						Acute transient anxiety was reported as an adverse effect
Gasser et al., 2014	A double-blinded, randomized, active, placebo-controlled pilot study.	n=12	PO 200 µg LSD	Placebo	12	Reduced anxiety
						No adverse effects were reported.
Gasser et al., 2015	A double-blinded, randomized, active, placebo-controlled pilot study.	n=10	PO 200 µg LSD	Placebo	12	Medically administered LSD yielded psychotherapeutic effects.
						The medication was safe and beneficial to mentally ill patients
Wießner et al., 2023	A randomized, double-blind, placebo-controlled, crossover study	n=25	PO 50 µg LSD	Placebo	NA	LSD emerged as a healing tool for mental illnesses
						Increased mindfulness and relief from psychotic experience.
Glazer et al., 2023	A randomized, double-blind, placebo-controlled study	n=42	PO 13 & 26 µg LSD	Placebo	NA	Low LSD doses improved cognition, mood, and feelings of well-being
						Significant relief from depressive symptoms
Preller et al., 2018	Double-blind, randomized, counterbalanced, crossover study	n=24	PO 100 µg LSD	Placebo		Improved sociocognitive deficits, overall well-being, and self-processing
Wolfson et al., 2020	Randomized pilot study	n=18	MDMA	Placebo	NA	Reduced anxiety
						Improved post-traumatic growth mindfulness
						Improved sleep quality, reduced depression, improved global functioning
Danforth et al., 2018	Randomized, double-masked, placebo-controlled pilot study	n=12	70 to 125 mg MDMA	Placebo	72	Improved social anxiety among autistic adults
Mithoefer et al., 2019	Six randomized, double-blind, controlled clinical trials	n=103	75 mg, 10 mg & 125 mg MDMA	Placebo	3 to 5	MDMA was well tolerated among adults with PSTD
						PSTD symptoms improved; re-experiencing, negative mood or cognition, avoidance, and increased arousal
						Symptoms of depression improved.
Ot'alora et al., 2018	Randomized phase II-controlled trial	n=28	100 mg and 125 mg	Placebo	12	Reported safety includes insomnia, increased irritability, low mood, and ruminations.
						Notable relief for anxiety, psychosis, depression, and ADHD

Mithoefer et al., 2011	Randomized, double-blind, controlled pilot study	n= 20	MDMA	Placebo		Improved PSTD symptoms and cognition
Oehen et al., 2013	A randomized, controlled pilot study	n= 20	23 mg + 12.5 mg MDMA	Placebo	12	No severe adverse effects were reported. Improved PSTD symptoms and cognition
Ross et al., 2016	Double-blind, placebo-controlled, crossover trial	n= 29	single-dose psilocybin (0.3 mg/kg)	Placebo	6.5	Reduced anxiety and depression Improved quality of life, relief from distress, and improved attitudes towards death
Malone et al., 2016	Double-blind, placebo-controlled, crossover trial	n= 29	single-dose psilocybin (0.3 mg/kg)	Placebo	6.5	Reduced anxiety and depression Improved quality of life, relief from distress, and improved attitudes towards death
Griffiths et al., 2016	Double-blind, placebo-controlled, crossover trial	n= 51	high psilocybin dose of 22 or 30 mg/70 kg	Placebo	6	Decreased anxiety, depressed mood, improved attitudes and self-belief in life Improved spirituality, overall well-being, and life satisfaction, and enhanced interpersonal relationships
Grob et al., 2011	Double-blind, placebo-controlled study	n= 12	Moderate psilocybin dose of 0.2 mg/kg	Placebo	6	Reduced anxiety and mood elevation A positive trend regarding the therapeutic benefits was reported.
Bogenshutz et al., 2015	RCT	n= 10		Placebo	36	Decreased cravings and abstinence self-efficacy

2.

3. ***LSD: Lysergic acid diethylamide***
4. ***MDMA: 3,4-Methylenedioxymethamphetamine***
5. ***PSTD: Post-traumatic stress disorder***

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