INPLASY

Overview Of Review (OoR) on PSILOCYBIN in Psychiatric Disorders

INPLASY202480022

doi: 10.37766/inplasy2024.8.0022

Received: 04 August 2024

Published: 04 August 2024

Cutrufelli, P; Di Francesco, A; Rodolico, A; Concerto, C; Furnari, R; Marano, L; Mineo, L; Moncada, A; Rampello, M; Petralia, A; Signorelli MS.

Corresponding author:
Pierfelice Cutrufelli

pierfelicecutrufelli@yahoo.it

Author Affiliation:
Psychiatry Unit, Department of Clinical and Experimental Medicine, University of Catania.

ADMINISTRATIVE INFORMATION

Support - No funding.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202480022

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 August 2024 and was last updated on 04 August 2024.

INTRODUCTION

Review question / Objective This protocol outlines the methodology for an "Overview of Review" (OoR) study which aims to conduct a comprehensive analysis of systematic reviews with meta-analyses of psilocybin randomized clinical trials. The primary objective is to provide an evaluation of the therapeutic effects, safety profiles, and adverse effects of psilocybin as documented in the best evidence available. :
P (Population): Patients included in systematic reviews who have undergone psilocybin therapy for various clinical indications (DSM-5-TR or ICD-10 Disorders)
I (Intervention): Psilocybin therapy.
C (Comparison): placebo, no treatment, or other standard drug or no drug therapies
O (Outcomes):
1. Therapeutic effects of psilocybin (efficacy).
2. Acceptability and tolerability of psilocybin therapy
3. Prevalence and severity of adverse effects associated with psilocybin therapy (safety profile).

Rationale The motivation for this study arises from the recent surge in interest in psilocybin therapy and the need to consolidate the growing body of findings, which at the moment constitute scattered evidence. Psilocybin, a naturally occurring psychedelic compound found in certain species of mushrooms, has garnered significant scientific and therapeutic interest in recent years. Given the potential significance of psilocybin in revolutionizing mental health treatment and our understanding of consciousness, along with the rapidly evolving research landscape, this overview of reviews is timely and crucial. It aims to provide a comprehensive, evidence-based assessment of the current state of psilocybin research, which could inform future clinical applications, research directions, and policy decisions.

Condition being studied Psilocybin therapy in subjects diagnosed with psychiatric disorders according to international diagnostic criteria such as the ICD-10 and DSM-5-TR.

METHODS

Search strategy A search strategy utilizing a single word search and wildcard symbols ("psilo*") will be employed to maximize search sensitivity. Search fields will include title, abstract, and keywords. An initial search will be executed at the commencement of the review process, while a concluding search will be performed prior to finalizing the manuscript. Only databases recognized by recognized governmental bodies or credible associations have been considered. Five databases - PubMed, PsycINFO, Cochrane Database of Systematic Reviews (CDSR), Epistemonikos and Web of Science - have been then selected based on their wide recognition, rigorous standards, and the breadth and quality of their content. To ensure linguistic feasibility for the team and to incorporate high-quality literature, only English and Italian literature will be considered.

Participant or population Individuals with psychiatric conditions identified in accordance with global diagnostic guidelines, including the ICD and DSM.Subjects diagnosed with psychiatric disorders according to international diagnostic criteria such as the ICD and DSM.Subjects with psychiatric disorders as diagnosed by international standards like ICD and DSM.

Intervention Psilocybin therapy (with or without psychotherapy), alone or as an add-on.

Comparator Any, exception made for other psychedelic intervention.

Study designs to be included Systematic reviews with meta-analysis. The reviews should include and analyze Randomized Controlled Trials (RCTs). Meta-analytic data incorporating non-RCT studies will be omitted from our report.

Eligibility criteria The inclusion criteria for systematic reviews to be considered in this overview are as follows: 1) The systematic reviews must present meta-analytic evidence or provide additional analysis of aggregated data from primary studies. 2)The reviews should include and analyze Randomized Controlled Trials (RCTs) involving psychiatric patients undergoing psilocybin therapy (with or without psychotherapy), alone or as an add-on, and compare it with an appropriate alternative intervention or control group. 3) The reviews should report at least one outcome derived from a meta-analysis of RCTs and measure relevant clinical outcomes using validated methods. 4) Network meta-analyses that meet the above criteria will also be included. Reviews involving co-administration of psilocybin therapy with other psychedelics or ketamine, or studies where control groups also receive a psychedelic, will be excluded.

Information sources Electronic Databases for Biomedical and Psychological Research: PubMed, PsycINFO, Web of Science.
Systematic Reviews databases: Cochrane Database of Systematic Reviews (CDSR), Epistemonikos.
We will try to contact original authors where feasible. Additionally, we will examine the bibliographies of included studies to identify further references.

Main outcome(s) 1) Therapeutic efficacy: This domain will report the effectiveness of psilocybin therapy, such as symptom reduction, remission and response rates, improvements in the quality of life and/or disability reduction.
2) Acceptability and Tolerability: Patient's ability to endure the treatment, measured through dropout rates due to side effect (tolerability) or due to any other reason (acceptability).

Additional outcome(s) Safety: Incidence of severe adverse events, physical or mental health complications, or any reported fatalities.

Data management Pairs of authors will independently scrutinize search results from each database, adhering to the predetermined inclusion and exclusion criteria. Any conflicts will initially be addressed through comprehensive discussion and consensus between authors. In cases of persistent disagreements, we will involve a third pre-designated reviewer to provide a resolution.
Two researchers, working independently, will extract data from the selected studies, focusing particularly on clinical indications, therapeutic effects, adverse reactions, safety profiles, and other outcomes relevant to psilocybin therapy. Calculated meta-analytic data and effect sizes from individual studies, as presented in the included meta-analyses, will be extracted. Crucial plausible determinants of therapeutic efficacy, including dosage regimens and follow-up intervals, will be utilized to further categorize and aggregate meta-analyses. A cross-verification process will ensure data consistency, with any discrepancies resolved through in-depth discussion and consensus.

Quality assessment / Risk of bias analysis The AMSTAR-2 framework (Shea et al. 2017), a comprehensive tool designed to assess the methodological quality of systematic reviews, will

be used to evaluate the quality of the selected reviews. This process will be conducted independently by two authors and any disagreements will be resolved as described previously.

Strategy of data synthesis A qualitative data representation of relevant outcomes will be made thought charts and tables, reporting all relevant found data.
We will also conduct an overlapping analysis to assess the degree of similarity among the selected studies, with a focus on the intersectionality of participant populations, interventions, outcomes, and methodologies. Key metrics will include the Corrected Covered Area (CCA) and excess of significance bias (ESB). To analyze the quality of the evidence base, we will stratify the studies using Ioannidis criteria, which consider factors such as the number of studies, total participants, cases, p-values of pooled effect sizes, I^2 values for heterogeneity/inconsistency, imprecision (statistical power), risk of bias, methodological quality (AMSTAR rating), and specific p-values for Egger's test, Ioannidis' test for ESB, and jackknife meta-analysis. During stratification, results will be verified by replication if the original reported effects from each included study in the meta-analysis are presented by the authors. We will utilize the Meta-umbrella tool for data synthesis and replication (Gosling et al. 2023). Meta-umbrella is a tool designed to automate the calculations required for umbrella reviews. It automatically performs tasks such as assessment of heterogeneity (I^2), tests for small-study effects, and tests for excess statistical significance. By utilizing meta-umbrella, we aim to enhance the rigor and efficiency of our umbrella review process, providing a robust and easily replicable synthesis of the available evidence while maintaining high standards of statistical analysis.

Subgroup analysis Evidence will be divided contingent upon the availability of adequate data.
By population:
Analyses will differentiate among reviews encompassing diverse psychiatric diagnoses. These diagnoses will be categorized according to the definitions provided in the studies and grouped based on the criteria utilized by the authors, as well as the psychopathological domains examined.
By intervention:
- Reviews examining psilocybin therapy as a standalone treatment in psychiatric patients.
- Reviews assessing psilocybin therapy as an adjunctive treatment in psychiatric patients.
- Reviews considering different dosages or routes of psilocybin
- Reviews evaluating the combination of psychotherapy and psilocybin therapy in psychiatric patients.
By comparator:-Reviews evaluating different control conditions
By outcome:
-Different measures for psychopathological metrics and symptomatological status
-Different timepoints and follow up assessments.

Sensitivity analysis Not Applicable (Overview of Review design).

Language restriction English; Italian.

Country(ies) involved Italy.

Keywords Psilocybin; Psilocybin therapy; Overview of Review; Umbrella analysis; Psychedelics; Psychiatric Therapy; Emerging Psychopharmacology.

Dissemination plans Findings will be reported following the PRIOR guidelines (Pollock et al. 2019); a comprehensive manuscript will be developed, which will undergo an internal review by all authors to ensure accuracy and clarity. The finalized manuscript will be submitted to a peer-reviewed journal, and findings will also be disseminated via conference presentations, workshops, and other scientific forums, targeting both the scientific community and the general public. The team will explore open access publication options to maximize the study's reach and impact.

Contributions of each author
Author 1 - Pierfelice Cutrufelli.
Email: pierfelicecutrufelli@yahoo.it
Author 2 - Antonio Di Francesco.
Author 3 - Alessandro Rodolico.
Author 4 - Carmen Concerto.
Author 5 - Rosaria Furnari.
Author 6 - Leonardo Marano.
Author 7 - Ludovico Mineo.
Author 8 - Alessandro Moncada.
Author 9 - Martina Rampello.
Author 10 - Martina Rampello
Author 11 - Maria Salvina Signorelli.