LISBOA
UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA LISBOA

TRABALHO FINAL
MESTRADO INTEGRADO EM MEDICINA

Área Disciplinar Autónoma de Ética e Deontologia Médicas

A review of the ethics of psychedelic use in psychiatry

Nuno Gonçalo Pinto Azevedo

Orientado por:

Professor Miguel Oliveira da Silva

Co-Orientado por:

Doutor Luís Duarte Madeira

Maio 2023

Resumo

Contextualização: Os psicadélicos são conhecidos pelos seus fortes efeitos mentais devido à ativação dos recetores 5HT-2ª no cérebro. Durante os anos 1950 e 1960, estas moléculas foram alvo de vários ensaios clínicos até à sua criminalização com início em 1971. No entanto, o ressurgimento recente da investigação do potencial uso terapêutico dos psicadélicos em perturbações psiquiátricas reemergiu, de igual forma, os problemas deontológicos e éticos nesta temática. Várias questões se levantam à medida que os seus resultados terapêuticos favoráveis se tornam cada vez mais uma realidade. **Objetivo:** Este trabalho tem como finalidade explorar as questões éticas e deontológicas do uso terapêutico de psicadélicos e perceber as suas implicações para o clínico, o paciente e para a sociedade. **Métodos:** Uma pesquisa metodológica sobre estudos com psicadélicos e as suas questões etico-deontológicas no uso clínico, entre 2017 e 2022, foi realizada, no PubMed Central, SCOPUS, EBSCOhost e ScienceDirect. **Resultados:** Um total de 42 artigos que abordam temas éticos e psicadélicos foram usados nesta revisão. **Conclusão:** Os psicadélicos precisam de ser culturalmente contextualizados, o risco de dano epistémico necessita de ser minimizado assim como os reais efeitos psicadélicos e terapêuticos devem ser bem explícitos aquando do consentimento informado. Legalmente, cada país deve-se preparar para o eventual uso terapêutico, tendo em conta o contexto social e as suas limitações. Dados investigacionais acessíveis a todos, assim como a criação de comissões para os avaliar e tomar decisões devem ser criados.

Palavras-chave: ética; terapia assistida com psicadélicos; cultural; legislação; consentimento informado.

Abstract

Background: Psychedelics are known for their powerful mental effects due to their activation of 5HT-2A receptors in the brain. During the 1950s and 1960s, research was conducted on these molecules until their criminalisation, starting in 1971. However, the recent clinical investigation of psychedelics as therapeutic tools for psychiatric disorders has re-emerged the deontological ethical issues surrounding this subject. Questions arise as research on their therapeutic outcomes becomes a reality. **Objective:** This work aims to explore deontological ethics to understand the implications of psychedelics for the clinician, patient, and society. **Methods:** A methodological search of psychedelic studies from 2017 to 2022 was conducted in PubMed Central, SCOPUS, EBSCOhost, and ScienceDirect to address the deontological ethics of clinical psychedelic use. **Results:** A total of 42 articles approaching ethics and psychedelics were considered for this review. **Conclusion:** Psychedelics need to be culturally contextualised, the risk of epistemic harm should be minimised, and the effects of psychedelics accurately represented to ensure informed consent. Open data and commissions are needed to ensure safe and equal distribution.

Keywords: ethics; psychedelic-assisted therapy; cultural; legislation; informed consent.

Index

Abbreviations

AALTD – Anxiety associated with life-threatening diseases

APQ – Attitude on Psychedelics Questionnaire

ARLTC – Anxiety related to life-threatening cancer

DAT – Dopamine transporter

DMT – Dimethyltryptamine

DRLTC – Depression related to life-threatening cancer

EMA – European Medicines Agency

FDA – Food and Drug Administration

IC – Informed consent

IP3 – Inositol triphosphate

LSD – Lysergic acid diethylamide

MAPS – Multidisciplinary Association for Psychedelic Studies

MDD – Major depression disorder

MDMA – 3,4-methylenedioxymethamphetamine

NET – Noradrenaline transporter

PTSD – Post-traumatic stress disorder

SSRIs – Selective serotonin reuptake inhibitors

TRD – Treatment-resistant depression

UNDRIP – United Nations Declaration on the Rights of Indigenous Peoples

USA – United States of America

Substances and Contextualization

In the last decade, there has been an increased interest in the use of psychedelics in clinical practice, which has been accompanied by a large wave of new studies in this field. Yet, this is not a novel interest (Solmi et al., 2022), and studies in the 1950s addressed the potential use of psychedelics in the treatment of psychiatric disorders such as major depression, post-traumatic stress disorder, and anxiety (Solmi et al., 2022). Today, clinical trials in different phases (I, II, and III), taking place in the United States of America, Canada, the United Kingdom, Switzerland, the Netherlands, and Israel, have shown promising results in many psychiatric pathologies (ClinicalTrials.gov, 2022). Current preliminary data on psychedelic use supports physiological safety low risk of dependence or misuse (Johnson et al., 2017). Although clinical trials have yet to demonstrate robust evidence for efficacy, their use is slowly being introduced into clinical practice.

The prevalence of research on alternative molecules with different mechanisms of action such as psychedelics (Schatzberg, 2015) is also partly due to the dearth of new psychiatric interventions in the last decade (D. Health Administration of Veterans Affairs et al., 2017), particularly in trials with conventional drugs, such as SSRIs, that conveyed high failure rates (even against placebo). This research is said to be afflicted by severe faults, including poor diagnostic category clarification, inflated baseline measurements to ensure patients meet eligibility criteria, and inconsistent or unreliable assessments within and across sites (Schatzberg, 2015). Large clinical trials such as STAR*D and I-SPOT have published data on patients who do not respond to selective serotonin reuptake inhibitors or serotonin and norepinephrine reuptake inhibitor monotherapy (Rush et al., 2006; Saveanu et al., 2015). It is important to note that psychedelic treatment requires special care such us psychological support and/or psychotherapy, which separates it from conventional psychopharmacological therapy. This support contributes to the therapeutic effect by shaping the experience during treatment (Carhart-Harris et al., 2017). It is also required for safety reasons during the altered state of consciousness (Johnson et al., 2008), and for being considered relevant for the positive results.

Psychedelics are a class of serotonergic agonists with immediate psychoactive effects (Nichols, 2004) and are divided into typical and atypical, such as ketamine or 3,4-methylenedioxymethamphetamine (MDMA), which have psychedelic-like effects through diverse pharmacological mechanisms, offering qualitatively distinct subjective experiences (Yaden et al., 2022).

Typical psychedelics (see Table 1) are partial agonists of the 5-HT2A serotonin receptors in the pre-frontal cortex, which are coupled to a Gq-type protein. Their binding generates inositol triphosphate (IP3), leading to the release of intracellular calcium and increasing glutamatergic transmission in afferent pyramidal neurons, responsible for the transmission of sensory information, amplifying it (Katzung, 2017).

Table 1. Typical psychedelics, their origins, and the risk of addiction

	Natural Origin	**Addiction/Dependency**
LSD (lysergic acid diethylamide)	Ergot fungi	Non-addictive/No dependency: • Animal studies have not led animals to seek these substances for self-administration. • These molecules do not stimulate the release of dopamine; therefore, they do not activate the mesolimbic dopaminergic system. • Tachyphylaxis phenomena due to downregulation of these receptors have been described.
Psilocybin	*Psilocybe spp.* mushrooms	
Mescaline	Peyote; San Pedro Cactus	
DMT (N,N-dimethyltryptamine)	*Ayahuasca* (mixture of many plants)	

Sources: Lüscher & Ungless, 2006; Nichols, 2004

Atypical psychedelics are often called dissociative and/or empathogenic because they change reality contact and/or increase a person's feelings of connection and empathy. These include ketamine, currently used as an anaesthetic; methylene-

dioxymethamphetamine (MDMA); and 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT), which is present mainly in the venom of the *Bufo alvarius* toad and in some plants (Ermakova et al., 2022). Ketamine's main application is anaesthesia due to its non-competitive antagonism on ionotropic glutamate receptors of the NMDA-type (Katzung, 2017). It is currently also indicated for treatment-resistant depression and is available as a nasal spray in the form of esketamine, already approved by the FDA and EMA, and used in conjunction with a conventional oral antidepressant (McIntyre et al., 2021; Swainson et al., 2019). It is believed that this antidepressant effect may result from stimulating the mTOR pathway by other glutamatergic receptors due to the antagonization of the NMDA receptors (Katzung, 2017). No dependence or addiction by either molecule (ketamine or esketamine) has been described (Lüscher & Ungless, 2006). MDMA is an empathogen that reverses the action of the amine transporters, leading to the release of biogenic amines. It has a greater preference for the serotonin transporter (SERT), but it also binds to the dopamine transporter (DAT) and the noradrenaline transporter (NET) (Morton, 2005). There is not yet consensus on its addiction risk (Lüscher & Ungless, 2006). The role of typical and atypical psychedelics in the treatment of key psychiatric disorders is presented in Table 2. Due to the recent relevance of psychedelic-based treatment strategies for psychiatric disorders, it seems paramount to discuss and detail the ethical issues that could be raised by these new interventions.

Firstly, some of these psychedelics are naturally occurring agents that are (or grow in places where they are) ecologically endangered, as well as an important part of Native American and Amazonian cultures. After addressing this theme, we will discuss the changes in cognition, perception, and connection which occur in psychedelic-induced states and how they pose specific challenges to the therapeutic relationship. To conclude our discussion, we will address how several legal restrictions hinder open research on and clinical use of psychedelics, raising legal challenges such as patentability. Our systematic review uses a contemporary one-health approach to ethical issues, exploring their cultural, political, social, and ecological dimensions along

Table 2. Psychedelics and therapies under research

	Depressive Disorders	Anxiety Disorders	Substance Use Disorder	Other Disorders
LSD	_____	Anxiety AALTD	Opioid Use Disorder Alcohol Use Disorder	Cluster Headache
Psilocybin	DRLTC MDD TRD[a]	ARLTC	Nicotine Use Disorder Alcohol Use Disorder	Eating Disorders
DMT	TRD	_____	_____	_____
Ketamine	MDD	_____	Opioid Use Disorder Alcohol Use Disorder[b]	_____
MDMA	_____	_____	Alcohol Use Disorder	PTSD[c]

Abbreviations: AALTD – anxiety associated with life-threatening diseases; **DRLTC –** depression related to life-threatening cancer; **MDD –** major depression disorder; **TRD –** treatment-resistant depression; **ARLTC –** anxiety related to life-threatening cancer; **PTSD –** post-traumatic stress disorder.

[a] Phase IIb concluded.

[b] Phase IIa and Phase IIb concluded. Preparing an Oxford Health NHS Foundation Trust funded Phase III trial.

[c] Phase II and Phase IIIa concluded. Phase IIIb is concluded and under review.

Sources: LSD (Gasser et al., 2014, 2015; Liechti, 2018; Schmid et al., 2021); **Psilocybin** (Bogenschutz et al., 2015, 2022; Carhart-Harris et al., 2017; Goodwin et al., 2022; Griffiths et al., 2016; Grob et al., 2011; Johnson et al., 2014, 2017; Ross et al., 2016; Spriggs et al., 2021); **DMT** (Galvão-Coelho et al., 2020; Palhano-Fontes et al., 2018); **Ketamine** (Grabski et al., 2022; E. Krupitsky et al., 2002; E. M. Krupitsky et al., 2007; López-Díaz et al., 2019; McAndrew et al., 2017; Mollaahmetoglu et al., 2021; Trust, 2022; Wilkinson et al., 2017, 2018); **MDMA** (MAPS Public Benefit Corporation, 2022; Mitchell et al., 2021; Ot'alora G et al., 2018; Sessa et al., 2021)

with classical deontological issues. First, we aim to clarify psychedelics' unique context in some Indigenous cultures and the risk of their intellectual appropriation and

ecological repercussions, as well as the dangers of rapid media portrayal and overenthusiasm towards psychedelics. Second, we aim to explore ethical issues in their applications to a vulnerable population such as mental disorder patients, including the intricacies of written informed consent and questions raised by spiritual or religious occurrences during therapy. Lastly, we intend to discuss the legal framework for psychedelics as well as strategies that countries could implement to improve their use in research and clinical practice.

Methods

Search strategy

This is a systematically constructed integrative review, allowing the inclusion of qualitative and quantitative studies. This review used the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) recommendations as reporting guidelines (M. J. Page et al., 2021).

To identify all potentially eligible studies, an electronic search was conducted using the following databases: PubMed Central, ScienceDirect, EBSCOhost, and SCOPUS. Citation tracking and reference checking of the included studies were used to identify any further relevant studies. The results of this search were then refined by applying inclusion and exclusion criteria. The search and study selection processes were conducted in November 2022. The references were merged and managed using Mendeley. A combination of medical subject headings (MeSH), subject headings, and keywords was developed to conduct the search. Synonyms or abbreviations that were felt to be appropriate were added to the search terms. The search terms were tailored for each database. The search strategy for PubMed Central was the following: "("ethics"[Subheading] OR "ethics"[All Fields] OR "ethics"[MeSH Terms]) AND ("hallucinogens"[All Fields] OR "hallucinogens"[MeSH Terms] OR "hallucinogens"[All Fields] OR "psychedelics"[All Fields])", and the search strategy used for the other databases was: ("ethics AND (hallucinogens OR psychedelics)"). Available databases on

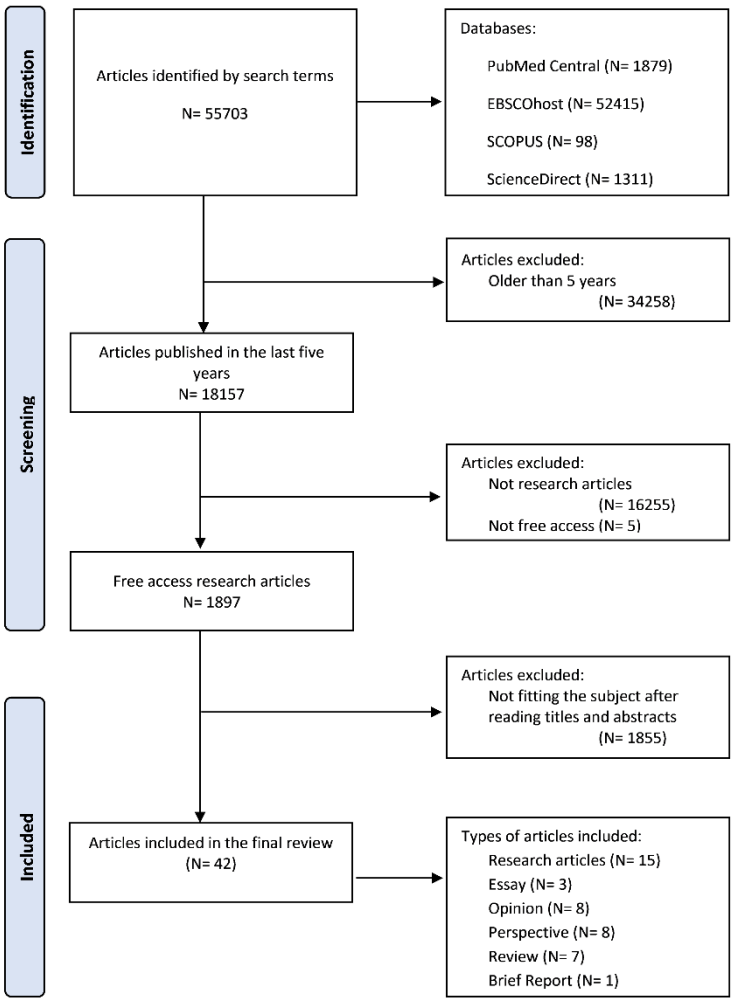

Figure 1. PRISMA flow-diagram explaining the study selection process

science and human health salvaged for this review were the following: "Academic Search Complete", "APA PsycArticles", "APA PsycInfo", "eBook University Press Collection (EBSCOhost)", "eBook Collection (EBSCOhost)", "Library, Information Science & Technology Abstracts", "MEDLINE", and "Psychology and Behavioural Sciences Collection".

The papers were consolidated with a review of five journals of ethics (Nursing Ethics, American Journal of Bioethics, Journal of Medical Ethics, BMC Medical Ethics, and Hasting Center Report) and five journals of psychiatry (World Psychiatry, Lancet Psychiatry, Annual Review of Clinical Psychology, JAMA Psychiatry, and American Journal of Psychiatry), and yet no new paper was found beyond those on the databases.

The search yielded 55703 studies, and their titles and abstracts were reviewed according to the inclusion and exclusion criteria listed below.

Inclusion criteria:

1. Original peer-reviewed studies, theses/dissertations, reviews, follow-up studies, commentaries, opinion pieces, conference abstracts, study protocols of clinical trials
2. Study designs including quantitative, qualitative, mixed-methods, case reports, case series
3. Studies conducted worldwide
4. Eligible psychedelic compounds: psilocybin, LSD, MDMA, ketamine, and ayahuasca
5. Discussion of ethical, legal, and philosophical themes
6. Published in the last five years (2017–2022)
7. English language

Exclusion criteria:

1. Studies in secondary care settings
2. Studies that do not relate their results to ethical, legal, and philosophical issues
3. Duplicated studies

4. Studies that are not free to access
5. All the studies that do not fulfil the inclusion criteria

At the title and abstract screening, 52373 records were excluded based on the above inclusion and exclusion criteria using Mendeley. A total of 42 papers were included for thematic analysis.

Data extraction, synthesis, and analysis

The studies included were managed using Mendeley. Data extraction was conducted on 11/11/2022. Table 3 presents general information about the studies included, such as bibliographic details, country, design, and purpose.

To make it simpler to comprehend which outcomes were present in each study, a synthesis of findings from chosen publications was done in the next stage by summing earlier findings in another table. The included papers were also subjected to a thematic analysis, which allowed for the identification of themes and subthemes within each of the primary review conclusions. Finding pertinent subjects across the articles was the first part of this procedure. The second step was grouping related topics into bigger groupings in order to organise the final list of subthemes. The themes and subthemes represented in each research study were then summarised in a separate table.

Since this integrative review contains research with a variety of aims, approaches, and results, the findings of all pertinent studies were finally summarised using a qualitative methodology. Because of this, a meta-analysis was not possible.

Quality appraisal

Given the diversity of the studies, the criteria of Hawker's tool (Hawker et al., 2002) were used to evaluate the quality of the research evidence from the chosen publications. There are nine questions in this tool, with answer choices of "good", "fair", "poor", or "very poor". After using the tool, a numerical score was created by grading the responses from 1 (very poor) to 4 (good). As a result, each research project received a score that ranged from 9 to a maximum of 36 points. The following definitions were

used to establish the overall quality grades: high quality (A), 30–36 points; medium quality (B), 24–29 points; and low quality (C), 9-23 points. Appendix 1 presents the tool containing the nine questions.

Results

Study selection and characteristics

From the aforementioned search, 55703 articles resulted. A total of 34258 studies were excluded because they were older than 5 years. An additional 1855 articles were excluded for not fitting the theme of this work, and 16255 were excluded for either being off-topic or not having peer review. Another 5 studies were excluded for not being free to access.

A total of 42 articles were considered through the review process (see Flowchart 1) performed by the authors with joint discussion of divergences. The articles' key characteristics are presented in Table 3. The majority were research articles (15), but there were also reviews (7), perspective articles (8), opinions (8), essays (3), and a brief report (1). A total of 17 countries were represented, with the United States being the most frequent. The studies included were published in the last five years.

Table 3. General characteristics of studies included

References	Country	Study Design	Purpose of study
(Miceli McMillan, 2022)	Australia	Essay	Cultural impact on and injustice towards Indigenous communities due to the scientific use of psychedelics.
(Cusimano, 2022)	USA	Research Article	Discussion with students about problems and solutions related to psychedelic therapy.
(Greif & Šurkala, 2020)	Slovak Republic	Perspective	Initial experiments and reflection about psychedelics' real therapeutic effect.
(Plesa & Petranker, 2022)	Canada	Research Article	Neo-liberalism and the risks of psychedelics in the self-help industry.
(Rucker & Young, 2021)	United Kingdom	Perspective	Discussion of the acceleration of studies on psychedelics and their risks.

(Johnson, 2021)	USA	Opinion	Beliefs and religion during therapy and therapist's own beliefs.
(Bodnár & Kakuk, 2019)	Hungary	Review	Ethics of clinical research with LSD using the 7 dimensions of E. J. Emanuel.
(Miceli McMillan, 2021b)	Australia	Essay	Hedonistic concepts used in psychedelic therapy.
(Langlitz et al., 2021)	USA, Canada, Switzerland, Germany	Perspective	Whether psychedelics can help users connect with their ideals and support moral-political ideas.
(Smith & Appelbaum, 2022)	USA	Review	Recommendations for solutions to novel problems concerning psychedelics.
(Letheby & Mattu, 2021)	Australia, Canada	Review	The establishment of emerging lines of research at the intersection of philosophy and psychedelic science.
(Hauskeller et al., 2022)	United Kingdom	Research Article	The study of psychedelics with dualistic concepts used in colonial and decolonial thought.
(Stauffer et al., 2022)	USA	Research Article	The participation of transgender and gender diverse people in PTSD research and assessment for their openness to MDMA-assisted psychotherapy.
(Miceli McMillan, 2021a)	Australia	Research Article	A bioethical reflection about re-medicalisation of psychedelics.
(Mintz et al., 2022)	USA, United Kingdom	Perspective	Encouragement for further research and debate to make psychedelic research and therapies accessible to members of disability communities.
(Kious et al., 2022)	USA	Perspective	If psychedelics can affect investigators' enthusiasm, raising concerns about bias and scientific integrity.

(Petranker et al., 2020)	Canada	Perspective	The importance of open science on psychedelic research.
(Pilecki et al., 2021)	USA	Opinion	How therapists can mitigate risks and practice within legal and ethical boundaries when incorporating psychedelics into traditional psychotherapy.
(van Amsterdam et al., 2021)	The Netherlands	Research Article	Hypothetical Dutch reform legislation to create a rational MDMA policy.
(Schleim, 2022)	The Netherlands	Opinion	Discussion on context-dependency of placebo effects and moral psychopharmacology.
(Williams et al., 2021)	Australia	Perspective	Discussion of potential psychedelic obstacles to community clinics among a group of clinicians and researchers.
(Page et al., 2021)	United Kingdom	Brief Report	The attitudes and knowledge of NHS psychiatrists on psychedelic-assisted psychotherapy.
(Marcus, 2022)	USA	Research Article	Ethical tensions between curanderos, mental health practitioners, and ayahuasca retreat centres.
(Gerber et al., 2021)	Brazil, Mexico, Switzerland, USA	Opinion	How Indigenous communities are currently unable to claim their rights to traditional medicines, despite international treaties.
(Mocanu et al., 2022)	Canada	Essay	A demonstration that expanding access to psychedelics requires consideration of a range of factors.
(Askew & Williams, 2021)	United Kingdom	Research Article	Critical discourse examining how substances can be used for self-improvement.
(Thal et al., 2021)	Australia, Germany	Review	A description of the current conditions and theoretical knowledge for substance-assisted psychotherapy, including ethics and spiritual

			emphasis, methods, models, and concepts of psychological mechanisms of action.
(Yaden et al., 2022)	USA	Opinion	How psychedelic research should focus on integrating medications into the standard of care, rather than recreating ethical and socio-political problems.
(Campbell & Williams, 2021)	USA, Canada	Perspective	A discussion whether psychiatry should allow patients' preferences to guide policy and law regarding psychedelics.
(Smith & Appelbaum, 2021)	USA	Opinion	A discussion over Oregon and California's different approaches to legalisation, with cautionary precedents.
(Mathai et al., 2022)	USA	Research Article	Informed consent processes for ketamine therapy clinicians to identify potential for growth.
(Žuljević et al., 2022)	Croatia	Research Article	Psychometric properties of the Attitudes on Psychedelics Questionnaire in a sample of the Croatian general population.
(Peterson et al., 2019)	USA, Argentina, Canada	Opinion	Ethical analysis of psychedelic research involving consciousness patients.
(Levin et al., 2022)	USA	Research Article	Examining whether psychiatrists' perceptions of four psychoactive drugs differ from schedules.
(Corrigan et al., 2022)	Ireland	Research Article	Analysing mental health service user attitudes to psychedelics and psilocybin therapy.
(Michaels et al., 2018)	USA	Review	Examining ethnoracial differences in inclusion and recruitment of people of colour in psychedelic clinical trials.
(Phelps, 2017)	USA	Research Article	To review and compile psychedelic therapist competencies derived from the psychedelic literature.

(Smith & Sisti, 2021)	USA	Research Article	To show that psychedelics pose novel risks and require enhanced informed consent, leading to ethical considerations as they move into mainstream clinical psychiatry.
(Brennan et al., 2021)	USA	Research Article	An interview to 23 psychedelic clinicians about nonsexual touch, sexual boundary-setting, and experiences while navigating multiple relationships in their work.
(Dupuis, 2021)	France	Research Article	An argument on how hypersuggestibility is the main factor in making psychedelics powerful for belief transmission, producing doubt, ambivalence, and reflexivity.
(Eleftheriou & Thomas, 2021)	United Kingdom	Review	An explanation of how mindfulness-based interventions and psychedelic therapy have been found to have synergistic effects, but replication is needed to fully understand the effects of set and setting.
(Kuypers et al., 2019)	The Netherlands, United Kingdom, Denmark, USA, Italy	Opinion	To answer questions and provide guidelines for research on microdosing.

Quality appraisal and risk of bias

A quality assessment of the included studies is provided in Appendix 1. All included studies received an A to B grade with a numerical rating of 24–35 (see rating devising on Methods).

Thematic analysis

The themes and subthemes defined after conducting a thematic analysis of each study are presented in the table in Appendix 2. There are three main themes that

correspond to the main findings defined during the protocol phase of this review.

Theme 1: Cultural, social, and ecological issues

Theme 2: Subjective effects

2.1. Risks, their mitigation, and informed consent

Theme 3: Political, social, and clinical issues

3.1. Changing legal status and possible consequences

3.2. Lack of diversity in the studies

3.3. Risk of biased research

3.4. Clinical application challenges

Discussion

A first primer on cultural, social, and ecological issues

The eventual therapeutic use of psychedelics raises several social issues, including their cultural contextualisation as a colonialist form of appropriation of Indigenous knowledge. The Western approach to psychedelics reframes the ancient practises of diverse and unique cultures that have used psychedelics in the past, risking disturbing their integrity and stability. The paradigmatic case is Maria Sabina, who shared her knowledge of the Mazatec community with one "white man" (Miceli McMillan, 2021a), which led to her arrest, her house being burned down, and the loss of her social role as a healer. Criticisms within Western culture support the idea that it might be wrong to patent this mode of intervention as these are ritualistic approaches whose appropriation was never consented to by Indigenous communities (Gerber et al., 2021).

Therefore, according to Article 11.2 of the United Nations Declaration on the Rights of Indigenous Peoples (UNDRIP), adopted in 2007 and signed on behalf of 144 states, all forms of bioprospecting should include prior consent, and all profits should be shared with the Indigenous community (United Nations, 2002). For that reason, it is suggested that Indigenous people act as key consulting stakeholders to guide therapies, along with scientists, and eventually be included in clinical trials (Gerber et al., 2021).

Besides cultural issues, ecological problems are also at stake. Since most typical psychedelics come from natural organisms, the growing industry around psychedelic science puts their sustainability at risk. Some traditional and Indigenous communities are already experiencing a reduction in the availability of naturally occurring psychedelics for their healing practises (biopiracy) (Miceli McMillan, 2022). The synthesis of active compounds present in natural organisms could help mitigate this ecological issue. However, worries exist that various non-measurable substances that natural forms may have could be important to the hallucinogenic effect, thus posing questions about the therapeutic equivalence of synthetic forms. Additionally, some argue that if we dismiss the ritualistic process, some therapeutic properties would also

be lost and the effect would be lower (Ko et al., 2022). More studies are needed to address these questions.

This same growing industry of psychedelics also risks being linked to contemporary non-medical forms of intervention in mental disorders through the use of self-help ideology. Some of the claims include moral harassment, where the patient could feel shamed or guilty for feeling depressed or anxious and, in such states, feel responsible for recovering alone (Plesa & Petranker, 2022; Rucker & Young, 2021). Most of these non-medical forms of intervention, in private centres with gurus and non-clinical therapists, have almost no evidence in terms of effectiveness and safety. Even today, psychedelics' effectiveness is not fully comprehended as the heterogeneity of their application still offers low fidelity to the models tested in clinical trials (Smith & Appelbaum, 2022). Safety is also an unresolved issue as the immaculate safety results of studies cannot be considered identical to those of clinical settings, where several risks could easily be overlooked, including the concomitant use of antidepressants; personal and family history of mental illness (e.g., schizophrenia or psychosis); as well as the patient's present mindset, which could increase the risk of a "bad trip" and trauma (Pilecki et al., 2021). Therefore, this type of centre should be looked at carefully and may represent harm for the vulnerable psychiatric community.

Another possible issue comes from the media, which may play a role in overcrediting psychedelic interventions by generating unrealistic expectations and non-evidence-based illusions about their actual therapeutic value. Risks and harms appear to be concealed, and pressure is put on mental health services and research to hasten their trials and therapeutic formation due to social need and public hurry (Yaden et al., 2022).

With no safety or effectiveness guarantees, there is a thin line separating present interventions with psychedelics from illegal practises. Indeed, the medical community needs to bear in mind that psychedelics might be offered to patients with mental illness (who are more vulnerable) or to those with no medical conditions (presenting unnecessary risks) and may be offered at unreasonable prices. Therapists must consider that the Helsinki Declaration protects patients against insufficiently researched

therapeutic practises – it is unethical to offer or charge for an intervention that lacks evidence of its therapeutic benefit (World Medical Association, 1964). Moreover, the induced altered state could enable (even healthy) subjects to fail to protect their rights — e.g., be lured into cults, become vulnerable to sexual harassment (Marcus, 2022; Pilecki et al., 2021), and risk other forms of abuse (Langlitz et al., 2021). Considering that psychedelic use is already socially stigmatised in the same way as recreational drug use and abuse, uncareful practises could undermine the future legitimacy of psychedelic research and clinical uses and pose legal problems (Rucker & Young, 2021) similar to those of the 1950s (Yaden et al., 2022).

Another issue that ethicists debate is moral enhancement through use of psychedelics to improve people's moral capacities (Schleim, 2022). Since psychedelics may give subjective experiences to the patients that change their values and beliefs into solid moral ideas (Langlitz et al., 2021), ethicists are concerned about patients' relationship with others. By far, only moral decision-making paradigms have been used in pharmacological experiments, and such experiments were never intended to enhance moral competence (Schleim, 2022). Askew & Williams, 2021, invite us to expand our definition of enhancer to include a substance that exists to complete something that is missing. They classify enhancers into three types based on the discourse of their participants (healing, transformative, and productivity discourses), mentioning that psychedelics are used to improve mental health issues and spirituality and facilitate well-being. The aim of their paper was to rethink the concept of enhancement and to dispel the stigma surrounding it. Since conventional antidepressants can induce a change of self-insight and perspectives, psychedelics are seen as similar, thus not real moral enhancers.

Subjective effects

Hallucinogens are well known for their distortion of reality and for providing unique experiences. However, these same unique experiences may be seen as specious treatment. First and foremost, some ethicists suggest the subjective effects of psychedelic therapy are fundamentally wrong as they lead to the disintegration of reality

perception and hallucinations, which distance patients from reality (Letheby, 2016; Miceli McMillan, 2021b). Yet, several counterarguments could be raised, including questioning the simplistic take that there is “just one true reality”. Letheby and McMillan also support the idea that the metaphysics of psychedelic interventions is akin to that of religious interventions (e.g., religious fervour), arguing that metaphysics is not a theme medicine should rely on in these interventions. Others point to the fact that patients’ reality (from which they escape during interventions) could be traumatic, including for those with major depression with suicidal ideation (Letheby & Mattu, 2021; Miceli McMillan, 2021b). Indeed, after a brief hallucinatory state, the subject can rethink their experience in a natural state, where new elements (that they were previously unaware of) and a new tone to personal problems may emerge (Greif & Šurkala, 2020). This effect supports the need for the presence of well-trained therapists to fairly guide these patients.

Indeed, research shows that psychedelic treatment ranks as one of the most meaningful experiences in some patients’ lives (Garcia-Romeu & Richards, 2018; R R Griffiths et al., 2006, 2008; MacLean et al., 2011; Preller et al., 2017; Schmid & Liechti, 2018), and this should be accounted for by those responsible for these treatments (Thal et al., 2021). During psychedelic intervention, several spiritual (sometimes religious) experiences can take place, and both doctors and therapists might be untrained to deal with these elements. One could imagine that under the supervision of an untrained religious therapist, new meta-religious beliefs could be carelessly initiated (Matthew W. Johnson, 2021), or on the other hand, that an atheist or agnostic therapist could ignore and disrespect patients’ newly formed beliefs (Thal et al., 2021). There is an argument for removing all religious or non-religious iconography from the session room and avoiding suggestion artifices (such as "today we will uncover a «bigger truth»") (Matthew W. Johnson, 2021). Training could be devised to focus on aesthetic aspects and philosophical questions the patient might express, using unspecific spiritual words if necessary and explicit spiritual terms only if they arise primarily from the patient (Thal et al., 2021). In that training, a multidisciplinary team, including anthropologists, philologists, and sociologists (Langlitz et al., 2021), could address the complexity of what could happen in a psychedelic session (Pilecki et al., 2021).

Some issues also arise from the therapists' own subjective experiences, which could draw from their personal use of psychedelics. Many researchers and therapists in the field openly admit to their patients and teams that they have previously experienced psychedelics, which could be both problematic for therapy and a conflict of interest for research (Kious et al., 2022). Indeed, lawyers and regulatory bodies see this as a conflict of interest and bias (McCoy & Emanuel, 2017), and, as the vivid example of Timothy Leary (a researcher of psychotropic drugs that actively promoted their recreational use, leaving aside the scientific method) demonstrates, this field is not different from others, where biased results of clinical research could ensue scientific methodologies are abandoned in favour of personal beliefs. Others consider that previously induced altered states of mind could be essential to empathising with the patient (M. P. Bogenschutz & Forcehimes, 2016; P. M. Bogenschutz, 2013; Metzner, 1998), to the point that some training programmes for therapists include taking psychedelics as a requirement before performing the intervention (Thal et al., 2021), as in the Multidisciplinary Association for Psychedelic Studies (MAPS; MAPS Public Benefit Corporation, 2022a). Yet, there is no evidence for this requirement as therapists who admitted previous psychedelic use were perceived as having less integrity and quality by participants (Forstmann & Sagioglou, 2020). Moreover, this raises concerns about indirect forms of coercion against those who seek to practice therapy in the field. Endorsing disclosure of previous use of psychedelics seems an ethically rational decision for both researchers and therapists (Thal et al., 2021), and naïve researchers should be included on investigational teams and clinical sessions to control bias and reduce conflicts of interest (Kious et al., 2022).

Risks, their mitigation, and informed consent

There are several risks when using psychedelics, including physical and mental side effects and the increased vulnerability of an altered state of consciousness.

Psychedelics' mechanisms of action encompass physical (ranging from cardiovascular to systemic effects) and mental (e.g., hallucinations/reality, contact/rebound, symptoms/trauma) risks (Williams et al., 2021). There are several reports of (1) rebound depressive and anxious symptoms as well as acute stress

reactions occurring in psychedelic sessions, both of which require mitigation in a safe setting with medical and psychological assistance (Bodnár & Kakuk, 2019; Dupuis, 2021; Gasser et al., 2015; Roland R. Griffiths et al., 2016; Kaelen et al., 2016; Williams et al., 2021); (2) interaction with other drugs, particularly MAO inhibitors (dos Santos et al., 2018; M. W. Johnson et al., 2008); (3) prolonged psychosis, which is expected in 5 out of 5000 general patients, 37 out of 4300 psychiatric patients and 4 out of 1000 patients with personal or family history of psychotic disorder when taking psilocybin (Greif & Šurkala, 2020) and has also been observed in those using other classic psychedelics (Bodnár & Kakuk, 2019; Williams et al., 2021). The latter risk has determined that psychosis be an exclusion criterion in most clinical trials (Bodnár & Kakuk, 2019). Another exclusion criterion being used (e.g., exclusion of transgender, people of colour) can also undermine fair and equal access to treatment with psychedelics (see below).

Patients in altered states of consciousness are more vulnerable as they seem not to be able to protect their own interests (therefore, they are at greater risk of abuse from their therapists/doctors/practitioners). Here a series of large concerns are raised regarding the particularities of informed consent (IC) in psychedelic research (see Table 4): (1) altered consciousness states are always radically different each time (Bodnár & Kakuk, 2019), and thus IC should be given by every patient undertaking this therapeutic intervention (both first-timers and those who have tried psychedelics previously). (2) The extent of the exploration of the effects relating to this intervention also needs to be clarified in the IC, and it must reveal which expectations are unrealistic (created by the media; Smith & Appelbaum, 2022) and which of the evidence-based effects that exist for each type of medical situation (Pilecki et al., 2021). (3) IC must include all types of decision-making following psychedelic intake, such as the physical limits between patient and therapist (including physical touch and sexual acts) and the risk of self-lesions, violent events against therapists, and property destruction (Greif & Šurkala, 2020; Matthew W. Johnson, 2021; Letheby & Mattu, 2021; Smith & Appelbaum, 2022; Thal et al., 2021). Indeed, psychedelics are empathogens and increase suggestibility/susceptibility (Langlitz et al., 2021), resulting in a vulnerable state of mind (Letheby & Mattu, 2021) that makes patients liable to abuse from their treatment providers (nurses, psychiatrist, therapists) as after intake they might be less likely to

refuse physical touch and sexual abuse and decide into sexual behaviours they will later (in a clearheaded state) consider forms of abuse (Marcus, 2022; Pilecki et al., 2021; Smith & Appelbaum, 2022). (4) IC might need to include existential long-term side effects (Letheby & Mattu, 2021), which might comprise conversion of moral, philosophical, political, and religious beliefs (Matthew W. Johnson, 2021; Langlitz et al., 2021; Thal et al., 2021). Many important features of psychedelic use have been discovered, including long-standing trait personality changes such as neuroticism turning into openness/impulsivity (Erritzoe et al., 2018; Roland R. Griffiths et al., 2018; Lebedev et al., 2015; MacLean et al., 2011) and non-spiritual, atheist, or agnostic patients becoming religious believers (Langlitz et al., 2021; Letheby & Mattu, 2021; Smith & Sisti, 2021), a change that could have a systemic impact in life. (5) The IC procedure should also account for potential cultural mismatches between patient and therapist (Langlitz et al., 2021, Smith & Appelbaum, 2022), as well as referring to the fact that the patient will be guided during the therapy session to avoid misunderstandings while in the state of catharsis and resolution. (6) IC should also include an advance directive regarding the decision to leave the session during the altered hallucinogenic state. This would allow researchers/clinicians to circumvent involuntary coercive measures (physical or chemical) against free will during an altered state of mind; however, paternalistic action may be required (or deciding on a person of trust/family member/caregiver who makes decisions about the subject during such states), including, for instance, a no driving rule until the next day (Bodnár & Kakuk, 2019). (7) IC should be personalised for patients with physical and mental impairment (Mintz et al., 2022), particularly those with dementia or cognitive deficits, to determine whether caregivers could take on the decision-maker role considering the complex changes this intervention involves (Peterson et al., 2019). IC in these situations must consider the vulnerability of those who choose these interventions (e.g., mentally impaired patients who bring desperation to their caregivers).

IC in the field of psychedelic treatment is an area for development as evidenced by the fact that even 23 clinics approved by the American Society of Ketamine Physicians, Psychotherapists, & Practitioners (ASKP3), have concluded that most IC processes need improvement (Mathai et al., 2022).

Table 4. Psychedelic Informed Consent

Areas under research for psychedelic informed consent
Access to information and consent for every person, regardless of whether they have taken psychedelics previously.
Discussion about psychedelics' effects, patient's expectations, and existing evidence-based practises.
Therapeutic boundaries and attitudes in case of sexual acts, self-lesions, violence against therapists, and property destruction.
Consent for existential long-term side effects such as moral, philosophical, political, and religious belief conversion.
Consideration of potential belief mismatch between patient and therapist as well as avoiding misunderstandings during catharsis and resolution.
Suspension of patient's decision to leave the session under psychedelic effects and consideration of nominating a caregiver to decide for the patient.
Ability of caregivers to consent for physically and mentally impaired patients.

Political, social, and clinical issues

Changing legal status and possible consequences

From a legal point of view, psychedelics are today perceived as substances with no medical use, with a risk of addiction and abuse, and are considered illegal across the world (INCB, 2022), which seems to ignore recent evidence of their benefits. However, (1) many psychiatrists express additional concerns about other drug classes, such as benzodiazepines, which are legal but subject to questionable regulation (Levin et al., 2022), and (2) some studies indicate openness towards psilocybin therapy (Corrigan et al., 2022), with 72% of people with mental disorders considering therapeutic psilocybin research important to continue and 54% willing to try the therapy if prescribed.

Because of the eventual therapeutic use, procedures to change the legal status of psychedelics should take place. Changing their legal status could involve two

possibilities: (1) legalisation, which opens up psychedelics to a regulated market and changes their overall social cosmology (Plesa & Petranker, 2022), or (2) decriminalisation, which involves reducing penalties, encouraging treatment for abuse, and harm reduction support (Plesa & Petranker, 2022). Legalisation of psychedelics could send the wrong message to vulnerable populations, such as those with personal and family histories of psychotic disorders (Smith & Appelbaum, 2021), and paradoxically put research and medical use at risk due to psychedelics' availability and the risk of abuse (Yaden et al., 2022). Decriminalisation could reduce stigma but still offer restricted access to substances under specific circumstances, such as medical and psychological supervision (Plesa & Petranker, 2022; Smith & Appelbaum, 2022).

Examples of the two legal approaches include two states in the USA: (1) Oregon, which decriminalised psilocybin for clinical interventions through the Oregon Psilocybin Services Act and nominated the Oregon Health Authority, a multidisciplinary en-tity that regulates investigation, clinical practice, and guidelines, to oversee the process (Smith & Appelbaum, 2021) and (2) California, which legalised possession, personal use, and non-profit sharing of psychedelics for adults (Smith & Appelbaum, 2021). A conservative approach could be necessary since these substances are still under research with no formal approval for any disorder (Smith & Appelbaum, 2021; Yaden et al., 2022). Portugal, which decriminalised drugs of abuse in 2001, is also a good example of both the pros and cons of decriminalisation. After 5 years, heroin and other similar drug-related casualties were reduced by more than half, the rate of HIV infections among drug users decreased, and the number of people seeking treatment for drug addiction more than doubled (Greenwald, 2009). However, the number of hospitalisations for psychotic disorders rose from 24 to 588, and the proportion of individuals with associated cannabis-use disorder increased from 0.87% to 10.60% (Gonçalves-Pinho et al., 2020).

Some (Government of Canada, 2022; Mocanu et al., 2022; Smith & Appelbaum, 2022) argue that, rather than changing the law, it is possible to regulate these sub-stances specifically for research and treatment, creating institutions ("trip houses") that could develop programmes for patients under medical supervision (Cusimano, 2022). A Dutch multidisciplinary policymaking group suggested optimal MDMA policies (van

Amsterdam et al., 2021) that comprise (1) regulation issues, including sales of MDMA to users, environmental protection, quality control, licencing departments, a fixed minimum value, export, and import, and creating MDMA-related risk management (inc. reducing crimes) and (2) measuring/monitoring prevalence, users' health including adverse and side effects, criminality, and financial costs and benefits. National or regional governments should be responsible for prevention policy, harm reduction, and health education. For this last matter, the Attitude on Psychedelics Questionnaire (APQ) has been shown to be a good tool to evaluate the general population's knowledge about psychedelics and opinions on their legal status and policies (Žuljević et al., 2022).

In addition to legal status, commercialisation is an important matter to discuss. Patenting psychedelics is an ethical concern as future marketing would reduce availability to specific communities (e.g., ayahuasca in Indigenous cultures) due to costs and other restrictions (Gerber et al., 2021; Hauskeller et al., 2022). The issue of patenting also introduces a risk of bias and conflicts of interest with the participation of pro-profit companies in clinical trials (Plesa & Petranker, 2022). Patenting therapeutic procedures and protocols that were not created but rather copied from Indigenous rituals is also seen as problematic (Feinberg, 2018; Lutkajtis, 2019; Smith & Appelbaum, 2022). This patenting procedure may come from neoliberal ideologies behind "liberty" to use psychedelics (Lyons & Carhart-Harris, 2018; Nour et al., 2017) and may be contradictory to the communitarian social values of native ceremonies (Askew & Williams, 2021; Plesa & Petranker, 2022). A full-sized use of psychedelics in such a way has been coined "McPsychedelics" (Noorani, 2020; Plesa & Petranker, 2022), referring to the risk of trivialising their use in Western society.

Thus, governments must be fully informed before addressing psychedelic use in their politics and legal actions.

Lack of diversity in studies

Another social issue is that research is being conducted on selected samples that may not be representative of those who will benefit from the intervention. For instance, it seems problematic that transgender and gender diverse individuals are seldomly included (Stauffer et al., 2022). Additionally, Indigenous people, who correspond to 4.6% of participants (Michaels et al., 2018), and people with physical disabilities are rarely included (Mintz et al., 2022), in contrast with White people, who make up 82.3% of participants (Michaels et al., 2018); these misrepresented groups would benefit from clinical research in this field. They not only share possible contexts for trauma (e.g., through discrimination) but also experience to a greater extent all the nosologies for which psychedelic research is devised (Michaels et al., 2018). Therefore, a Phase IIIb clinical trial on MDMA for PTSD treatment implicitly included non-White individuals (MAPS Public Benefit Corporation, 2022b). Future clinical trials should take this as an example for their samples.

Risk of biased research

Over the last few years, many articles regarding psychedelic therapy have been published, increasing the amount of information about this topic.

Authors suggest the need for enhanced research that would be able to address bias and ultimately tackle non-evidence-based media coverage (Plesa & Petranker, 2022). In this field of research, considering all possible biases and confounding factors, they suggest pre-registration, double- and triple-blind protocols, open materials and open data, constraints on generality, replication, and adversarial collaboration that would reduce conflicts of interest (Muthukumaraswamy et al., 2021; Petranker et al., 2020; Plesa & Petranker, 2022; Tetlock & Mitchell, 2009; Yaden et al., 2022). These study protocols would finally allow practitioners to understand the mechanisms of action, to adjust the ideal dosage, to select the most efficient compounds and ultimately to guide clinical practice (Yaden et al., 2022). This guidance should then be clustered into official nationwide multidisciplinary norms for therapists and physicians, researchers, and regulators (Bodnár & Kakuk, 2019; Smith & Appelbaum, 2022; Thal et al., 2021; Williams

et al., 2021). Ethical codes like the MAPS Code of Ethics and the Code of Ethics for Spiritual Guides from the Council on Spiritual Practices might be seen as examples of guidelines to use during sessions (Council on Spiritual Practices, 2001; MAPS, 2021; Thal et al., 2021).

Clinical application challenges

Psychedelics are being devised to address clinical situations as an alternative to ineffective contemporary interventions (see Table 5). However, the need for new interventions should not take precedence over evidence of efficacy and effectivity and training of mental health professionals. Any hasty preparation of therapists may result in harm and unsafe settings (Carroll, 2014; Plesa & Petranker, 2022; Williams et al., 2021). To illustrate this, a recent report from the United Kingdom suggests that many psychiatrists were unsure of how to administer psychedelics and their role in psychiatric therapy (L. A. Page et al., 2021). It is recommended that diverse training be given to therapists and prescribers and that it be accredited by national and official regulated entities (Phelps, 2017; Williams et al., 2021).

In addition to therapist training, a calm, natural-like and personalised setting is also important because it appears to reduce adverse events and increase the therapeutic effects of psychedelics. This setting should be infrastructurally inclusive, allowing physically disabled people to enrol (Mintz et al., 2022; Williams et al., 2021).

Once evidence-based clinical practice becomes possible, accessibility, overall price, and co-payment are important questions for a treatment that aims to address trauma and resistant forms of mental illness, keeping in mind that patients could have limited resources due to the impact of their symptoms on their functioning (George et al., 2020; Williams et al., 2021). For instance, if this becomes a pro-profit industry (as it is in the USA; Aday et al., 2020; Williams et al., 2021), then governing bodies will have to tackle how to offer long-term interventions for those who suffer from chronic and intractable psychiatric disorders (the estimated cost of MDMA in the USA is $15,000; Hausfeld, 2019), in order to give equitable access to treatment for all those who need it (Pilecki et al., 2021).

The last clinical problem that may arise is that research in an artificial setting differs from real-life practice, where clinicians might fail to correctly select patients (misdiagnosis), exclude those at risk, or use psychedelics in off-label situations (Williams et al., 2021). This off-label usage may put the patient's safety at risk and undermine treatment benefits (Noorani, 2020). We suggest a controlled and wider overview of the diagnosis by clinicians before undertaking this kind of intervention.

Table 5. Ethical challenges to introducing psychedelics

1.	Haste to prepare therapists, leading to harm and unsafe settings
2.	Accredited training by national and official regulated entities should be required
3.	Personalised setting concerning each patient
4.	Accessibility, overall price, and co-payment
5.	Governing entities and their regulation over potential psychedelic pro-profit industry
6.	Difficulty of following up on these patients
7.	Possible misdiagnosis, underdiagnosis, and off-label usage

Conclusions

This review studied the complexity and multi-perspective issues surrounding psychedelic therapy, affording some practical conclusions for research, regulation, socio-cultural, and clinical matters. Psychedelics need to be culturally contextualised due to their traditional use by Indigenous people, the risk of a pro-profit industry colonising these traditions, and their previous status and fame during the 1960s. Because of the unique mental effects of psychedelics, epistemic harm must be minimised by separating metaphysical and religious questions without denying the patient's psychedelic experience. Professional therapists must be present to mitigate the physical and mental effects of sessions. In terms of representativity, misrepresented groups must be included throughout the studies to reduce bias and because these social groups are more likely to experience socially associated trauma. Once undertaken, fully informed consent should be assured, and more research should be done to better concretise this consent. In order to avoid potential conflicts of interest, these studies or clinical sessions should integrate naïve-to-psychedelics professionals. In this kind of therapy, population risks and preparation should be evaluated by each country's legal and clinical entities. Open data research and multidisciplinary commissions are required to better adjust clinical guidelines and create a more precise system. Many ethical challenges on a practical and logistical level call for more regulation to ensure safe and equal distribution for those needing therapy.

More research is needed on these themes to further evaluate psychedelics and their use as therapy.

Appendices

Appendix 1: Quality assessment of the studies using the Hawker et al. tool

References	Abstract/ title	Introduction/ aims	Data collection	Sampling	Analysis	Ethics/bias	Results	Generability	Implications	Total	Grade
(Miceli McMillan, 2022)	4	4	1	1	3	4	3	2	3	25	B
(Cusimano, 2022)	4	4	4	3	3	4	3	3	4	32	A
(Greif & Šurkala, 2020)	3	4	1	1	3	4	4	2	3	25	B
(Plesa & Petranker, 2022)	4	4	2	2	3	4	3	3	4	29	B
(Rucker & Young, 2021)	3	3	1	1	3	4	3	2	4	24	B
(Matthew W. Johnson, 2021)	2	3	1	1	3	4	3	3	4	24	B
(Bodnár & Kakuk, 2019)	4	4	3	2	4	4	4	3	4	32	A
(Miceli McMillan, 2021b)	4	4	1	1	3	4	3	2	3	25	B
(Langlitz et al., 2021)	4	3	1	1	3	4	3	3	4	26	B
(Smith & Appelbaum, 2022)	3	4	1	1	4	4	4	3	4	28	B
(Letheby & Mattu, 2021)	4	4	1	1	3	4	4	3	4	28	B

(Hauskeller et al., 2022)	4	4	1	1	3	4	2	3	3	25	B
(Stauffer et al., 2022)	3	4	3	4	4	4	3	3	4	32	A
(Miceli McMillan, 2021a)	4	4	2	1	2	4	3	3	4	27	B
(Mintz et al., 2022)	4	4	2	1	3	4	3	3	4	28	B
(Kious et al., 2022)	4	4	1	1	4	4	3	3	4	28	B
(Petranker et al., 2020)	4	4	2	1	3	4	3	3	4	28	B
(Pilecki et al., 2021)	4	4	2	1	3	4	3	3	4	28	B
(van Amsterdam et al., 2021)	4	4	4	3	4	4	4	4	4	35	A
(Schleim, 2022)	3	3	2	1	3	4	3	3	3	25	B
(Williams et al., 2021)	4	4	2	1	4	4	4	3	4	30	A
(L. A. Page et al., 2021)	4	4	3	2	3	4	3	3	4	30	A
(Marcus, 2022)	3	4	2	1	3	4	3	3	3	26	B
(Gerber et al., 2021)	3	4	2	1	3	4	2	3	4	26	B
(Mocanu et al., 2022)	4	4	2	1	3	4	3	3	4	28	B
(Askew & Williams, 2021)	4	4	4	3	4	4	4	3	4	34	A
(Thal et al., 2021)	4	4	2	1	4	4	3	3	4	29	B

(Yaden et al., 2022)	3	3	1	1	4	4	3	2	3	24	B
(Campbell & Williams, 2021)	4	3	1	1	3	4	3	2	3	24	B
(Smith & Appelbaum, 2021)	4	4	2	1	3	4	3	2	3	26	B
(Mathai et al., 2022)	4	4	4	4	4	4	3	4	4	35	A
(Žuljević et al., 2022)	4	4	4	3	4	4	4	3	4	34	A
(Peterson et al., 2019)	4	4	3	2	3	4	3	3	4	34	A
(Levin et al., 2022)	4	4	4	4	4	4	4	3	4	30	A
(Corrigan et al., 2022)	4	4	3	3	4	4	3	3	4	35	A
(Michaels et al., 2018)	4	4	3	3	4	4	3	3	4	32	A
(Phelps, 2017)	4	4	2	1	4	4	3	3	4	32	A
(Smith & Sisti, 2021)	4	4	2	1	4	4	3	3	4	29	B
(Brennan et al., 2021)	4	4	4	3	3	4	4	3	4	29	B
(Dupuis, 2021)	4	4	3	1	3	4	3	3	4	33	A
(Eleftheriou & Thomas, 2021)	4	4	2	2	3	4	3	3	4	29	B
(Kuypers et al., 2019)	4	4	3	2	3	4	3	3	4	30	A

Appendix 2: Themes and subthemes represented in the studies included

References	Themes/ Subthemes						
	Theme 1.	Theme 2.	Subtheme 2.1.	Subtheme 3.1.	Subtheme 3.2.	Subtheme 3.3.	Subtheme 3.4.
(Miceli McMillan, 2022)	Cultural use of psychedelics; Ecological impact						
(Cusimano, 2022)				The creation of trip houses for clinical intervention			
(Greif & Šurkala, 2020)		Risk/ Benefit of psychedelics					
(Plesa & Petranker, 2022)	Self-hep industry			Decriminalisation		Funding of studies	Risk of not well-trained therapists
(Rucker & Young, 2021)	Private centres and risk for patients						
(Matthew W. Johnson, 2021)		Meta-religion-beliefs during sessions	Risk of sexual assault				
(Bodnár & Kakuk, 2019)		Risk/ Benefit of psychedelics	Informed consent		Small clinical trials	Need for peer-review	
(Miceli McMillan, 2021b)		Meta-religion-beliefs during sessions					
(Langlitz et al., 2021)	Private centres and risk for patients	Meta-religion-beliefs during sessions	Informed consent				

(Smith & Appelbaum, 2022)	Private centres and risk for patients		Informed consent	Commercialisation; Decriminalisation		Need for peer-review	
(Letheby & Mattu, 2021)		Meta-religion-beliefs during sessions	Informed consent				
(Hauskeller et al., 2022)	Cultural use of psychedelics						
(Stauffer et al., 2022)					Inclusion of gender diverse people on trials		
(Miceli McMillan, 2021a)	Cultural use of psychedelics; Ecological impact						
(Mintz et al., 2022)			Informed consent		Inclusion of patients with physical disability on trials		
(Kious et al., 2022)		Use of psychedelics on therapists;				Risk of conflicts of interest by researchers	
(Petranker et al., 2020)						Need for open data trials	
(Pilecki et al., 2021)	Private centres and risk for patients; Cultural use of psychedelics		Informed consent				Inaccessibility for some patients

(van Amsterdam et al., 2021)				MDMA policy in the Netherlands			
(Schleim, 2022)	Moral enhancement with psychedelics		Informed consent				
(Williams et al., 2021)			Effects of psychedelics			Need for peer-review	Risk of not well-trained therapists; Lack of infrastructures
(L. A. Page et al., 2021)							Risk of not well-trained therapists;
(Marcus, 2022)	Cultural use of psychedelics		Risk of sexual assault				
(Gerber et al., 2021)	Cultural use of psychedelics						
(Mocanu et al., 2022)				Legal status in Canada			
(Askew & Williams, 2021)	Moral enhancement with psychedelics						
(Thal et al., 2021)		Meta-religion-beliefs during sessions; Use of psychedelics on therapists;	Informed consent			Need for peer-review	
(Yaden et al., 2022)	Self-hep industry					Need for peer-review	Risk of not well-trained therapists

(Campbell & Williams, 2021)					Inclusion of patients on trials		
(Smith & Appelbaum, 2021)	Self-hep industry			Risks of legalisation			
(Mathai et al., 2022)			Informed consent				
(Žuljević et al., 2022)							Instrument for assessing attitudes in general population
(Peterson et al., 2019)			Informed consent				
(Levin et al., 2022)				Drug policy and therapists' beliefs on psychedelics			
(Corrigan et al., 2022)							Survey on psychiatry patients about psychedelics
(Michaels et al., 2018)					Inclusion of people of colour on trials		
(Phelps, 2017)				Drug policy and therapists' beliefs on psychedelics			Competencies of therapists
(Smith & Sisti, 2021)		Meta-religion-beliefs during sessions	Informed consent; Effects of psychedelics				

(Brennan et al., 2021)			Risk of sexual assault				
(Dupuis, 2021)	Cultural use of psychedelics	Meta-religion-beliefs during sessions					
(Eleftheriou & Thomas, 2021)			Effects of psychedelics				
(Kuypers et al., 2019)			Effects of psychedelics			Need for peer-review	

Annexes

Annex 1: Hawker´s tool for studies quality appraisal

The nine questions in the tool are as follows:

1. Abstract and title: Did they provide a clear description of the study?	Good: structured abstract with full information and clear title
	Fair: abstract with most of the information.
	Poor: inadequate abstract.
	Very poor: no abstract.
2. Introduction and aims: Was there a good background section and clear statement of the aims of the research?	Good: full but concise background to discussion/study containing up-to-date literature review and highlighting gaps in knowledge; clear statement of aim AND objectives including research questions.
	Fair: some background and literature review; research questions outlined.
	Poor: some background but no aim/objectives/questions OR aims/objectives but inadequate background.
	Very poor: no mention of aims/objectives; no background or literature review.
3. Method and data: Are the methods appropriate and clearly explained?	Good: method is appropriate and described clearly (e.g. questionnaires included); clear details of the data collection and recording.
	Fair: method appropriate, description could be better; data described.
	Poor: questionable whether the method is appropriate; method described inadequately; little description of data.
	Very poor: no mention of method AND/OR method inappropriate AND/OR no details of data.
4. Sampling: Was the sampling strategy appropriate to address the aims?	Good: details (age/gender/race/context) of who was studied and how they were recruited and why this group was targeted; the sample size was justified for the study; response rates shown and explained.
	Fair: sample size justified; most information given but some missing.
	Poor: sampling mentioned but few descriptive details.
	Very poor: no details of the sample.
5. Data analysis: Was the description of the data analysis sufficiently rigorous?	Good: clear description of how the analysis was carried out. Qualitative studies: Description of how themes derived/respondent validation or triangulation. Quantitative studies: Reasons for tests selected hypothesis driven/numbers add up/statistical significance discussed.
	Fair: descriptive discussion of the analysis.

	Poor: minimal details about analysis.
	Very poor: no discussion of the analysis.
6. Ethics and bias: Have ethical issues been addressed and has necessary ethical approval been gained? Has the relationship between researchers and participants been adequately considered?	Good: ethics: when necessary, issues of confidentiality, sensitivity, and consent were addressed; bias: researcher was reflexive and/or aware of own bias.
	Fair: lip service was paid to the above (i.e. these issues were acknowledged).
	Poor: brief mention of issues.
	Very poor: no mention of issues.
7. Results: Is there a clear statement of the findings?	Good: findings are explicit, easy to understand, and in a logical progression; tables, if present, are explained in text; results relate directly to aims; sufficient data are presented to support findings.
	Fair: findings mentioned but more explanation could be given; data presented relate directly to results.
	Poor: findings presented haphazardly, not explained, and do not progress logically from results.
	Very poor: findings not mentioned or do not relate to aims.
8. Transferability or generalisability: Are the findings of this study transferable (generalisable) to a wider population?	Good: context and setting of the study are described sufficiently to allow comparison with other contexts and settings, plus a high score in Q4 (sampling).
	Fair: some context and setting described but more needed to replicate or compare the study with others, plus a fair score or higher in Q4.
	Fair: some context and setting described but more needed to replicate or compare the study with others, plus a fair score or higher in Q4.
	Very poor: no description of context/setting.
9. Implications and usefulness. How important are these findings to policy and practice?	Good: contributes something new and/or different in terms of understanding/insight or perspective; suggests ideas for further research; suggests implications for policy and/or practice.
	Fair: two of the above.
	Poor: only one of the above.
	Very poor: none of the above.

References

Aday, J. S., Bloesch, E. K., & Davoli, C. C. (2020). 2019: A year of expansion in psychedelic research, industry, and deregulation. Https://Doi.Org/10.1177/2050324520974484, 6, 205032452097448. https://doi.org/10.1177/2050324520974484

Askew, R., & Williams, L. (2021). Rethinking enhancement substance use: A critical discourse studies approach. International Journal of Drug Policy, 95, 102994. https://doi.org/10.1016/j.drugpo.2020.102994

Bodnár, K. J., & Kakuk, P. (2019). Research ethics aspects of experimentation with LSD on human subjects: a historical and ethical review. Medicine, Health Care and Philosophy, 22(2), 327–337. https://doi.org/10.1007/s11019-018-9871-9

Bogenschutz, M. P., & Forcehimes, A. A. (2016). Development of a Psychotherapeutic Model for Psilocybin-Assisted Treatment of Alcoholism. Journal of Humanistic Psychology, 57(4), 389–414. https://doi.org/10.1177/0022167816673493

Bogenschutz, P. M. (2013). Studying the Effects of Classic Hallucinogens in the Treatment of Alcoholism: Rationale, Methodology, and Current Research with Psilocybin. In Current Drug Abuse Reviews (Vol. 6, Issue 1, pp. 17–29). https://doi.org/http://dx.doi.org/10.2174/15733998113099990002

Brennan, W., Jackson, M. A., MacLean, K., & Ponterotto, J. G. (2021). A Qualitative Exploration of Relational Ethical Challenges and Practices in Psychedelic Healing. Journal of Humanistic Psychology. https://doi.org/10.1177/00221678211045265

Campbell, M., & Williams, M. T. (2021). The Ethic of Access: An AIDS Activist Won Public Access to Experimental Therapies, and This Must Now Extend to Psychedelics for Mental Illness. Frontiers in Psychiatry, 12(July), 1–5. https://doi.org/10.3389/fpsyt.2021.680626

Carhart-Harris, R. L., Roseman, L., Bolstridge, M., Demetriou, L., Pannekoek, J. N., Wall, M. B., Tanner, M., Kaelen, M., Mcgonigle, J., Murphy, K., Leech, R., Curran, H. V., & Nutt, D. J. (2017). Psilocybin for treatment-resistant depression : fMRI-measured brain

mechanisms. Scientific Reports, June, 1–11. https://doi.org/10.1038/s41598-017-13282-7

Carroll, K. M. (2014). Lost in translation? Moving contingency management and cognitive behavioral therapy into clinical practice. Annals of the New York Academy of Sciences, 1327(1), 94–111. https://doi.org/10.1111/NYAS.12501

ClinicalTrials.gov. (2022). Search of psychedelic; hallucinogen | Phase 1, 2, 3 - Results on Map. https://clinicaltrials.gov/ct2/results/map?term=psychedelic%3B+hallucinogen&phase=012&map=

Corrigan, K., Haran, M., McCandliss, C., McManus, R., Cleary, S., Trant, R., Kelly, Y., Ledden, K., Rush, G., O'Keane, V., & Kelly, J. R. (2022). Psychedelic perceptions: mental health service user attitudes to psilocybin therapy. Irish Journal of Medical Science, 191(3), 1385–1397. https://doi.org/10.1007/s11845-021-02668-2

Council on Spiritual Practices. (2001). Code of Ethics for Spiritual Guides. https://csp.org/docs/code-of-ethics-for-spiritual-guides

Cusimano, J. (2022). A pilot psychedelic psychopharmacology elective. Currents in Pharmacy Teaching and Learning, 14(5), 680–685. https://doi.org/10.1016/j.cptl.2022.04.019

dos Santos, R. G., Bouso, J. C., Alcázar-Córcoles, M. Á., & Hallak, J. E. C. (2018). Efficacy, tolerability, and safety of serotonergic psychedelics for the management of mood, anxiety, and substance-use disorders: a systematic review of systematic reviews. Expert Review of Clinical Pharmacology, 11(9), 889–902. https://doi.org/10.1080/17512433.2018.1511424

Dupuis, D. (2021). Psychedelics as Tools for Belief Transmission. Set, Setting, Suggestibility, and Persuasion in the Ritual Use of Hallucinogens. Frontiers in Psychology, 12(November), 1–16. https://doi.org/10.3389/fpsyg.2021.730031

Eleftheriou, M. E., & Thomas, E. (2021). Examining the Potential Synergistic Effects Between Mindfulness Training and Psy-chedelic-Assisted Therapy. Frontiers in Psychiatry, 12(August). https://doi.org/10.3389/fpsyt.2021.707057

Ermakova, A. O., Dunbar, F., Rucker, J., & Johnson, M. W. (2022). A narrative synthesis of research with 5-MeO-DMT. Journal of Psychopharmacology (Oxford, England), 36(3), 273–294. https://doi.org/10.1177/02698811211050543

Erritzoe, D., Roseman, L., Nour, M. M., MacLean, K., Kaelen, M., Nutt, D. J., & Carhart-Harris, R. L. (2018). Effects of psilocybin therapy on personality structure. Acta Psychiatrica Scandinavica, 138(5), 368–378. https://doi.org/10.1111/ACPS.12904

Feinberg, B. (2018). Undiscovering the pueblo magico: Lessons from huautla for the psychedelic renaissance. Plant Medicines, Healing and Psychedelic Science: Cultural Perspectives, 37–54. https://doi.org/10.1007/978-3-319-76720-8_3/COVER

Forstmann, M., & Sagioglou, C. (2020). How psychedelic researchers' self-admitted substance use and their association with psychedelic culture affect people's perceptions of their scientific integrity and the quality of their research. Public Understanding of Science, 30(3), 302–318. https://doi.org/10.1177/0963662520981728

Garcia-Romeu, A., & Richards, W. A. (2018). Current perspectives on psychedelic therapy: use of serotonergic hallucinogens in clinical interventions. International Review of Psychiatry, 30(4), 291–316. https://doi.org/10.1080/09540261.2018.1486289

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), 57–68. https://doi.org/10.1177/0269881114555249

George, J. R., Michaels, T. I., Sevelius, J., & Williams, M. T. (2020). The psychedelic renaissance and the limitations of a White-dominant medical framework: A call for Indigenous and ethnic minority inclusion. Journal of Psychedelic Studies, 4(1), 4–15. https://doi.org/10.1556/2054.2019.015

Gerber, K., Flores, I. G., Ruiz, A. C., Ali, I., Ginsberg, N. L., & Schenberg, E. E. (2021). Ethical Concerns about Psilocybin Intel-lectual Property. ACS Pharmacology and Translational Science, 4(2), 573–577. https://doi.org/10.1021/acsptsci.0c00171

Gonçalves-Pinho, M., Bragança, M., & Freitas, A. (2020). Psychotic disorders hospitalizations associated with cannabis abuse or dependence: A nationwide big data analysis. International Journal of Methods in Psychiatric Research, 29(1). https://doi.org/10.1002/MPR.1813

Government of Canada. (2022). Special Access Programme - Drugs. https://www.canada.ca/en/health-canada/services/drugs-health-products/special-access/drugs/special-access-programme-drugs.html

Greenwald, G. (2009). Drug Decriminalization in Portugal: Lessons for Creating Fair and Successful Drug Policies. SSRN Elec-tronic Journal. https://doi.org/10.2139/ssrn.1464837

Greif, A., & Šurkala, M. (2020). Compassionate use of psychedelics. Medicine, Health Care and Philosophy, 23(3), 485–496. https://doi.org/10.1007/s11019-020-09958-z

Griffiths, R R, Richards, W. A., Johnson, M. W., McCann, U. D., & Jesse, R. (2008). Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. Journal of Psychopharmacology, 22(6), 621–632. https://doi.org/10.1177/0269881108094300

Griffiths, R R, Richards, W. A., McCann, U., & Jesse, R. (2006). Psilocybin can occasion mystical-type experiences having sub-stantial and sustained personal meaning and spiritual significance. Psychopharmacology, 187(3), 268–283. https://doi.org/10.1007/s00213-006-0457-5

Griffiths, Roland 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), 1181–1197. https://doi.org/10.1177/0269881116675513

Griffiths, Roland R., Johnson, M. W., Richards, W. A., Richards, B. D., Jesse, R., MacLean, K. A., Barrett, F. S., Cosimano, M. P., & Klinedinst, M. A. (2018). Psilocybin-occasioned mystical-type experience in combination with meditation and other spiritual practices produces enduring positive changes in psychological functioning and in trait measures of prosocial attitudes and be-haviors. Journal of Psychopharmacology, 32(1), 49–69. https://doi.org/10.1177/0269881117731279/ASSET/IMAGES/LARGE/10.1177_0269881117731279-FIG2.JPEG

Hausfeld, R. (2019). Will MDMA-assisted psychotherapy be covered by health insurance? Psymposia. https://www.psymposia.com/magazine/mdma-insurance/

Hauskeller, C., Artinian, T., Fiske, A., Schwartz Marin, E., González Romero, O. S., Luna, L. E., Crickmore, J., & Sjöstedt-Hughes, P. (2022). Decolonization is a metaphor towards a different ethic. The case from psychedelic studies. Interdisciplinary Science Reviews, 0(0), 1–20. https://doi.org/10.1080/03080188.2022.2122788

Hawker S, Payne S, Kerr C, Hardey M, Powell J. Appraising the Evidence: Reviewing Disparate Data Systematically. Qualitative Health Research. 2002;12(9):1284-1299. doi:10.1177/104973230223825

INCB. (2022). Narcotic Drug Report 2021.

Johnson, M. W., Richards, W. A., & Griffiths, R. R. (2008). Human hallucinogen research: guidelines for safety. Journal of Psy-chopharmacology (Oxford, England), 22(6), 603–620. https://doi.org/10.1177/0269881108093587

Johnson, Matthew W. (2021). Consciousness, Religion, and Gurus: Pitfalls of Psychedelic Medicine. ACS Pharmacology and Translational Science, 4(2), 578–581. https://doi.org/10.1021/acsptsci.0c00198

Johnson, Matthew W., Garcia-Romeu, A., & Griffiths, R. R. (2017). Long-term follow-up of psilocybin-facilitated smoking ces-sation. American Journal of Drug and Alcohol Abuse, 43(1), 55–60. https://doi.org/10.3109/00952990.2016.1170135

Kaelen, M., Roseman, L., Kahan, J., Santos-Ribeiro, A., Orban, C., Lorenz, R., Barrett, F. S., Bolstridge, M., Williams, T., Williams, L., Wall, M. B., Feilding, A.,

Muthukumaraswamy, S., Nutt, D. J., & Carhart-Harris, R. (2016). LSD modulates music-induced imagery via changes in parahippocampal connectivity. European Neuropsychopharmacology : The Journal of the European College of Neuropsychopharmacology, 26(7), 1099–1109. https://doi.org/10.1016/J.EURONEURO.2016.03.018

Katzung, B. G. (2017). Chapter 32: Drugs of Abuse. In M. H. Education (Ed.), Basic & Clinical Pharmacology (13th ed., pp. 552–566). Lange.

Kious, B., Schwartz, Z., & Lewis, B. (2022). Should we be leery of being Leary? Concerns about psychedelic use by psychedelic researchers. Journal of Psychopharmacology. https://doi.org/10.1177/02698811221133461

Ko, K., Knight, G., Rucker, J. J., & Cleare, A. J. (2022). Psychedelics , Mystical Experience , and Therapeutic Efficacy : A Systematic Review. 13(July), 1–12. https://doi.org/10.3389/fpsyt.2022.917199

Kuypers, K. P. C., Ng, L., Erritzoe, D., Knudsen, G. M., Nichols, C. D., Nichols, D. E., Pani, L., Soula, A., & Nutt, D. (2019). Microdosing psychedelics: More questions than answers? An overview and suggestions for future research. Journal of Psy-chopharmacology, 33(9), 1039–1057. https://doi.org/10.1177/0269881119857204

Langlitz, N., Dyck, E., Scheidegger, M., & Repantis, D. (2021). Moral Psychopharmacology Needs Moral Inquiry: The Case of Psychedelics. Frontiers in Psychiatry, 12(August), 1–6. https://doi.org/10.3389/fpsyt.2021.680064

Lattin, D. (2010). The Harvard Psychedelic Club: How Timothy Leary, Ram Dass, Huston Smith, and Andrew Weil killed the Fifties and ushered in a new age for America. In The Harvard Psychedelic Club: How Timothy Leary, Ram Dass, Huston Smith, and Andrew Weil killed the Fifties and ushered in a new age for America. HarperOne/HarperCollins.

Lebedev, A. V., Lövdén, M., Rosenthal, G., Feilding, A., Nutt, D. J., & Carhart-Harris, R. L. (2015). Finding the self by losing the self: Neural correlates of ego-dissolution under psilocybin. Human Brain Mapping, 36(8), 3137–3153. https://doi.org/10.1002/HBM.22833

Letheby, C. (2016). The epistemic innocence of psychedelic states. Consciousness and Cognition, 39, 28–37. https://doi.org/10.1016/j.concog.2015.11.012

Letheby, C., & Mattu, J. (2021). Philosophy and classic psychedelics: A review of some emerging themes. Journal of Psychedelic Studies, 5(3), 166–175. https://doi.org/10.1556/2054.2021.00191

Levin, A., Nagib, P. B., Deiparine, S., Gao, T., Mitchell, J., & Davis, A. K. (2022). Inconsistencies between national drug policy and professional beliefs about psychoactive drugs among psychiatrists in the United States. International Journal of Drug Policy, 108, 103816. https://doi.org/10.1016/j.drugpo.2022.103816

Lüscher, C., & Ungless, M. A. (2006). The mechanistic classification of addictive drugs. PLoS Medicine, 3(11), e437. https://doi.org/10.1371/journal.pmed.0030437

Lutkajtis, A. (2019). Lost Saints: Desacralization, Spiritual Abuse and Magic Mushrooms. Fieldwork in Religion, 14(2), 118–139. https://doi.org/10.1558/FIRN.40554

Lyons, T., & Carhart-Harris, R. L. (2018). Increased nature relatedness and decreased authoritarian political views after psilo-cybin for treatment-resistant depression. Journal of Psychopharmacology, 32(7), 811–819. https://doi.org/10.1177/0269881117748902/ASSET/IMAGES/LARGE/10.1177_0269881117748902-FIG1.JPEG

MacLean, K. A., Johnson, M. W., & Griffiths, R. R. (2011). Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. Journal of Psychopharmacology, 25(11), 1453–1461. https://doi.org/10.1177/0269881111420188

MAPS. (2021). MAPS Code of Ethics for Psychedelic Psychotherapy.

MAPS Public Benefit Corporation. (2022a). MAPS MDMA Therapy Training Program. https://mapspublicbenefit.com/training/about-the-program/

MAPS Public Benefit Corporation. (2022b). MAPS PBC Completes Second Phase 3 “MAPP2” Trial of MDMA-Assisted Therapy for Treatment of PTSD. https://mapspublicbenefit.com/press-releases/mapp2-completion-announcement/

Marcus, O. (2022). 'Everybody's creating it along the way': ethical tensions among globalized ayahuasca shamanisms and therapeutic integration practices. Interdisciplinary Science Reviews, 0(0), 1–20. https://doi.org/10.1080/03080188.2022.2075201

Mathai, D. S., Lee, S. M., Mora, V., O'Donnell, K. C., Garcia-Romeu, A., & Storch, E. A. (2022). Mapping consent practices for outpatient psychiatric use of ketamine. Journal of Affective Disorders, 312(November 2021), 113–121. https://doi.org/10.1016/j.jad.2022.06.036

McCoy, M. S., & Emanuel, E. J. (2017). Why There Are No "Potential" Conflicts of Interest. JAMA, 317(17), 1721–1722. https://doi.org/10.1001/jama.2017.2308

Mcintyre, R. S., Rosenblat, J. D., Sc, M., Nemeroff, C. B., Ph, D., Sanacora, G., & Ph, D. (2021). Synthesizing the Evidence for Ketamine and Esketamine in Treatment-Resistant Depression : An International Expert Opinion on the Available Evidence and Implementation. 16, 383–399. https://doi.org/10.1176/appi.ajp.2020.20081251

Metzner, R. (1998). Hallucinogenic Drugs and Plants in Psychotherapy and Shamanism. Journal of Psychoactive Drugs, 30(4), 333–341. https://doi.org/10.1080/02791072.1998.10399709

Miceli McMillan, R. (2021a). Global bioethical challenges of medicalising psychedelics. Journal of Psychedelic Studies, 5(2), 57–64. https://doi.org/10.1556/2054.2021.00188

Miceli McMillan, R. (2021b). Prescribing meaning: Hedonistic perspectives on the therapeutic use of psychedelic-assisted meaning enhancement. Journal of Medical Ethics, 47(10), 701–705. https://doi.org/10.1136/medethics-2020-106619

Miceli McMillan, R. (2022). Psychedelic injustice: should bioethics tune in to the voices of psychedelic-using communities? Medical Humanities, 48(3), 269–272. https://doi.org/10.1136/medhum-2021-012299

Michaels, T. I., Purdon, J., Collins, A., & Williams, M. T. (2018). Inclusion of people of color in psychedelic-assisted psychotherapy: A review of the literature. BMC Psychiatry, 18(1), 1–14. https://doi.org/10.1186/s12888-018-1824-6

Mintz, K. T., Gammer, B., Khan, A. J., Shaub, G., Levine, S., & Sisti, D. (2022). Physical Disability and Psychedelic Therapies: An Agenda for Inclusive Research and Practice. Frontiers in Psychiatry, 13(May), 1–7. https://doi.org/10.3389/fpsyt.2022.914458

Mocanu, V., Mackay, L., Christie, D., & Argento, E. (2022). Safety considerations in the evolving legal landscape of psychedel-ic-assisted psychotherapy. Substance Abuse: Treatment, Prevention, and Policy, 17(1), 1–6. https://doi.org/10.1186/s13011-022-00468-0

Morton, J. (2005). Ecstasy: pharmacology and neurotoxicity. Current Opinion in Pharmacology, 5(1), 79–86. https://doi.org/10.1016/j.coph.2004.08.007

Muthukumaraswamy, S. D., Forsyth, A., & Lumley, T. (2021). Blinding and expectancy confounds in psychedelic randomized controlled trials. Https://Doi.Org/10.1080/17512433.2021.1933434, 14(9), 1133–1152. https://doi.org/10.1080/17512433.2021.1933434

Nichols, D. E. (2004). Hallucinogens. Pharmacology & Therapeutics, 101(2), 131–181. https://doi.org/10.1016/j.pharmthera.2003.11.002

Noorani, T. (2020). Making psychedelics into medicines: The politics and paradoxes of medicalization. Journal of Psychedelic Studies, 4(1), 34–39. https://doi.org/10.1556/2054.2019.018

Nour, M. M., Evans, L., & Carhart-Harris, R. L. (2017). Psychedelics, Personality and Political Perspectives. Https://Doi.Org/10.1080/02791072.2017.1312643, 49(3), 182–191. https://doi.org/10.1080/02791072.2017.1312643

D. Health Administration of Veterans Affairs, V., Health Strategic Healthcare Group, M., & Center for Posttraumatic Stress Disorder, N. (2017). It Is Time to Address the Crisis in the Pharmacotherapy of Posttraumatic Stress Disorder_ A Consensus Statement of the PTSD Psychopharmacology Working Group. Biological Psychiatry, 82, e51–e59. https://doi.org/10.1016/j.biopsych.2017.03.007

Page, L. A., Rehman, A., Syed, H., Forcer, K., & Campbell, G. (2021). The Readiness of Psychiatrists to Implement Psychedel-ic-Assisted Psychotherapy. Frontiers in Psychiatry, 12(November), 1–8. https://doi.org/10.3389/fpsyt.2021.743599

Page, M. J., McKenzie, J. E., Bossuyt, P., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E., 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 Me-dicina Fluminensis (Vol. 57, Issue 4, pp. 444–465). https://doi.org/10.21860/medflum2021_264903

Peterson, A., Tagliazucchi, E., & Weijer, C. (2019). The ethics of psychedelic research in disorders of consciousness. Neuroscience of Consciousness, 2019(1), 1–8. https://doi.org/10.1093/nc/niz013

Petranker, R., Anderson, T., & Farb, N. (2020). Psychedelic Research and the Need for Transparency: Polishing Alice's Looking Glass. Frontiers in Psychology, 11(July), 1–6. https://doi.org/10.3389/fpsyg.2020.01681

Phelps, J. (2017). Developing Guidelines and Competencies for the Training of Psychedelic Therapists. Journal of Humanistic Psychology, 57(5), 450–487. https://doi.org/10.1177/0022167817711304

Pilecki, B., Luoma, J. B., Bathje, G. J., Rhea, J., & Narloch, V. F. (2021). Ethical and legal issues in psychedelic harm reduction and integration therapy. Harm Reduction Journal, 18(1), 1–14. https://doi.org/10.1186/s12954-021-00489-1

Plesa, P., & Petranker, R. (2022). Manifest your desires: Psychedelics and the self-help industry. International Journal of Drug Policy, 105. https://doi.org/10.1016/j.drugpo.2022.103704

Preller, K. H., Herdener, M., Pokorny, T., Planzer, A., Kraehenmann, R., Stämpfli, P., Liechti, M. E., Seifritz, E., & Vollenweider, F. X. (2017). The Fabric of Meaning and Subjective Effects in LSD-Induced States Depend on Serotonin 2A Receptor Activation. Current Biology, 27(3), 451–457. https://doi.org/10.1016/j.cub.2016.12.030

Rucker, J. J., & Young, A. H. (2021). Psilocybin: From Serendipity to Credibility? Frontiers in Psychiatry, 12(April), 1–5. https://doi.org/10.3389/fpsyt.2021.659044

Rush, A. J., Trivedi, M. H., Wisniewski, S. R., Nierenberg, A. A., Stewart, J. W., Warden, D., Niederehe, G., Thase, M. E., Lavori, P. W., Lebowitz, B. D., McGrath, P. J., Rosenbaum, J. F., Sackeim, H. A., Kupfer, D. J., Luther, J., & Fava, M. (2006). Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: A STAR*D report. American Journal of Psychiatry, 163(11), 1905–1917. https://doi.org/10.1176/AJP.2006.163.11.1905

Saveanu, R., Etkin, A., Duchemin, A.-M., Goldstein-Piekarski, A., Gyurak, A., Debattista, C., Schatzberg, A. F., Sood, S., Day, C. V. A., Palmer, D. M., Rekshan, W. R., Gordon, E., Rush, A. J., & Williams, L. M. (2015). The International Study to Predict Op-timized Treatment in Depression (iSPOT-D): Outcomes from the acute phase of antidepressant treatment. Journal of Psychiatric Research, 61, 1–12. https://doi.org/10.1016/J.JPSYCHIRES.2014.12.018

Schatzberg, A. F. (2015). Development of New Psychopharmacological Agents for Depression and Anxiety. The Psychiatric Clinics of North America, 38(3), 379–393. https://doi.org/10.1016/J.PSC.2015.05.009

Schleim, S. (2022). Grounded in Biology: Why the Context-Dependency of Psychedelic Drug Effects Means Opportunities, Not Problems for Anthropology and Pharmacology. Frontiers in Psychiatry, 13(May), 11–13. https://doi.org/10.3389/fpsyt.2022.906487

Schmid, Y., & Liechti, M. E. (2018). Long-lasting subjective effects of LSD in normal subjects. Psychopharmacology, 235(2), 535–545. https://doi.org/10.1007/s00213-017-4733-3

Smith, W. R., & Appelbaum, P. S. (2021). Two Models of Legalization of Psychedelic Substances: Reasons for Concern. JAMA - Journal of the American Medical Association, 326(8), 697–698. https://doi.org/10.1001/jama.2021.12481

Smith, W. R., & Appelbaum, P. S. (2022). Novel ethical and policy issues in psychiatric uses of psychedelic substances. Neuro-pharmacology, 216(February), 109165. https://doi.org/10.1016/j.neuropharm.2022.109165

Smith, W. R., & Sisti, D. (2021). Ethics and ego dissolution: The case of psilocybin. Journal of Medical Ethics, 47(12), 807–814. https://doi.org/10.1136/medethics-2020-106070

Solmi, M., Chen, C., Daure, C., Buot, A., Ljuslin, M., Verroust, V., Mallet, L., Khazaal, Y., Rothen, S., Thorens, G., Zullino, D., Gobbi, G., Rosenblat, J., Husain, M. I., De Gregorio, D., Castle, D., & Sabé, M. (2022). A century of research on psychedelics: A scientometric analysis on trends and knowledge maps of hallucinogens, entactogens, entheogens and dissociative drugs. Euro-pean Neuropsychopharmacology, 64, 44–60. https://doi.org/10.1016/J.EURONEURO.2022.09.004

Stauffer, C. S., Brown, M. R., Adams, D., Cassity, M., & Sevelius, J. (2022). MDMA-assisted psychotherapy; Inclusion of transgender and gender diverse people in the frontiers of PTSD treatment trials. Frontiers in Psychiatry, 13. https://doi.org/10.3389/fpsyt.2022.932605

Swainson, J., Thomas, R. K., Archer, S., Chrenek, C., Mackay, A., Baker, G., Dursun, S., Klassen, L. J., Chokka, P., Swainson, J., Thomas, R. K., Archer, S., Chrenek, C., Mackay, A., Baker, G., Dursun, S., Klassen, L. J., Chokka, P., Demas, M. L., … Baker, G. (2019). Expert Review of Neurotherapeutics Esketamine for treatment resistant depression. Expert Review of Neurotherapeutics, 19(10), 1–13. https://doi.org/10.1080/14737175.2019.1640604

Tetlock, P. E., & Mitchell, G. (2009). Implicit Bias and Accountability Systems: What Must Organizations Do to Prevent Dis-crimination? Research in Organizational Behavior, 29, 3–38. https://doi.org/10.1016/J.RIOB.2009.10.002

Thal, S. B., Bright, S. J., Sharbanee, J. M., Wenge, T., & Skeffington, P. M. (2021). Current Perspective on the Therapeutic Preset for Substance-Assisted Psychotherapy. Frontiers in Psychology, 12(July). https://doi.org/10.3389/fpsyg.2021.617224

United Nations. (2002). United Nations Declaration on the Rights of Indigenous Peoples. Trends in the Sciences, 7(8), 44–45. https://doi.org/10.5363/tits.7.8_44

van Amsterdam, J., Peters, G. J. Y., Pennings, E., Blickman, T., Hollemans, K., Breeksema, J. J. J., Ramaekers, J. G., Maris, C., van Bakkum, F., Nabben, T., Scholten, W., Reitsma, T., Noijen, J., Koning, R., & van den Brink, W. (2021). Developing a new national MDMA

policy: Results of a multi-decision multi-criterion decision analysis. Journal of Psychopharmacology, 35(5), 537–546. https://doi.org/10.1177/0269881120981380

Williams, M. L., Korevaar, D., Harvey, R., Fitzgerald, P. B., Liknaitzky, P., O'Carroll, S., Puspanathan, P., Ross, M., Strauss, N., & Bennett-Levy, J. (2021). Translating Psychedelic Therapies From Clinical Trials to Community Clinics: Building Bridges and Addressing Potential Challenges Ahead. Frontiers in Psychiatry, 12(November), 1–7. https://doi.org/10.3389/fpsyt.2021.737738

World Medical Association. (1964). WMA Declaration of Helsinki: ethical principles for medical research involving human subjects. 353(1), 1418–1419. http://www.wma.net/en/30publications/10policies/b3/index.html

Yaden, D. B., Sciences, B., Yaden, M. E., Griffiths, R. R., & Sciences, B. (2022). Psychedelics in Psychiatry—Keeping the Renais-sance From Going Off the Rails. 78(5), 469–470. https://doi.org/10.1001/jamapsychiatry.2020.3672.Psychedelics

Žuljević, M. F., Buljan, I., Leskur, M., Kaliterna, M., Hren, D., & Duplančić, D. (2022). Validation of a new instrument for as-sessing attitudes on psychedelics in the general population. Scientific Reports, 12(1), 1–10. https://doi.org/10.1038/s41598-022-23056-5