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Psychedelic-assisted therapy for death acceptance in terminal illness: A scoping review

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REVIEW ARTICLE

ABSTRACT

Background and Aims: Mental health challenges such as depression, anxiety, and existential distress are common among individuals with terminal illness. Preliminary evidence suggests that death acceptance may protect against these issues, but there is limited research on the role of psychedelic-assisted therapy in fostering death acceptance. This scoping review aims to explore the potential of psychedelic-assisted therapy to promote death acceptance among terminally ill patients. *Methods:* A scoping review was conducted, examining studies published between 1990 and 2023. The review included studies on psychedelic-assisted therapy for death acceptance and closely related constructs, such as psychological flexibility, existential distress, and demoralization in terminally ill populations. *Results:* Findings indicate that psychedelic-assisted therapy may lead to significant and lasting reductions in anxiety, depression, and existential distress. These improvements appear to be mediated by enhanced death acceptance. The therapy may also increase psychological flexibility and reduce demoralization, supporting better mental health outcomes for terminally ill individuals. *Conclusions:* Psychedelic-assisted therapy represents a promising approach to improving quality of life for terminally ill patients by fostering acceptance of their prognosis and mortality. However, further research is needed to confirm these findings. The development of standardized measurement tools and consideration of patient demographics, such as age and spiritual beliefs, are recommended.

KEYWORDS

psychedelic-assisted therapy, terminal illness, death acceptance, existential distress, psychological flexibility

INTRODUCTION

Receiving a terminal diagnosis can be an emotional and challenging experience for individuals and their loved ones. Globally, 56.8 million people require palliative care annually, including 25.7 million at the end of life (World Health Organization, 2020). In the United States, hospice care serves about 1.8 million people annually, providing essential support to terminally ill patients and their loved ones through the patient's death (National Hospice and Palliative Care Organization, 2022).

Existential distress and mental health disorders, such as depression, anxiety, and suicidal ideation, profoundly affect hospice and palliative care (HPC) patients, with prevalence rates ranging from 30 to 69% (Mitchell et al., 2011). Existential distress manifests as hopelessness, loss of meaning, demoralization, spiritual confusion, and a diminished will to live (Beaussant et al., 2021; Hua & Bhatarasakoon, 2024). Left untreated, these issues exacerbate physical pain, poor quality of life, and a desire for hastened death (Hua & Bhatarasakoon, 2024; Kissane, Bobevski, & Grassi, 2022).

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Death acceptance (DA), defined as the recognition and embrace of one's mortality, is considered critical in mitigating existential distress and improving the quality of end-of-life experiences (Cobbs, Lynne, & Manfredi, 2024; Kübler-Ross, 1969). Low DA correlates with death denial, anxiety, depression, and demoralization, ultimately diminishing the potential for a meaningful death and life quality (Abraham, Kutner, & Beaty, 2006; Thompson et al., 2009). Psychological flexibility, or the capacity to adapt to adversity while maintaining core values, may foster DA and psychological resilience (Ding & Zheng, 2022).

Current treatments for existential distress, including psychotherapy and pharmacotherapy with selective serotonin reuptake inhibitors (SSRIs), have shown mixed efficacy and practical limitations (Beaussant et al., 2021; Grassi, Caruso, Hammelef, Nanni, & Riba, 2014). Recent research highlights the potential of psychedelic-assisted therapy (PAT) to alleviate existential distress and promote psychological well-being in seriously ill patients (Reiff et al., 2020). PAT involves the use of substances like psilocybin or MDMA (3,4-Methylenedioxymethamphetamine) in a controlled setting to facilitate emotional processing and insight (Nutt, Erritzoe, & Carhart-Harris, 2020). Emerging studies suggest that psychedelics may work through neuroplasticity, anti-inflammatory effects, and profound psychological and spiritual experiences (Nichols, Nichols, & Hendricks, 2023).

Psychedelics have been used in Indigenous spiritual practices for thousands of years, yet Western research has only begun to examine the therapeutic potential of these substances in recent decades (Williams, Romero, Braunstein, & Brant, 2022). While PAT may be promising for hospice and palliative care patients, particularly in addressing existential distress, depression, and anxiety related to a serious prognosis, research is still in its infancy (Cornish et al., 2025).

Objectives

This review primarily aims to assess whether PAT is associated with improvements in DA in seriously or terminally ill patients, compared to standard approaches or no intervention, across diverse study designs. Secondarily, this review also seeks to evaluate outcomes related to DA and psychological mechanisms of acceptance, incorporating studies with healthy samples to illuminate potential universal mechanisms that may underpin how PAT could foster improvements in acceptance and attitudes toward death across diverse populations. Given the limited literature on the intersection of PAT in the HPC demographic, a scoping review is appropriate to capture the breadth and complexity of the available, diverse evidence (Kazi, Chowdhury, Chowdhury, & Turin, n.d.).

METHODS

Protocol and registration

This scoping review adheres to the protocols outlined by the Preferred Reporting Items for Scoping Reviews (PRISMA-ScR) (Tricco et al., 2018), though it was not pre-registered.

Eligibility criteria

This scoping review includes studies published in full-text, peer-reviewed journals in English. Search criteria followed the PICOS format (Becky Alford, 2025).

Included studies. Open-label and pilot studies, randomized and non-randomized controlled trials, longitudinal follow-up studies, case reports, and mixed methods studies conducted following a quantitative parent trial were included in the review.

Eligibility requirements for terminal illness samples. In this review, we use the term 'serious or terminal illness' to reflect the spectrum of life-limiting conditions commonly encountered in hospice and palliative care, including advanced cancer and chronic, life-threatening illnesses. Eligibility requirements for terminal illness samples included: participants who were seriously or chronically ill, receiving palliative or hospice care services, or had a terminal (life-limiting) diagnosis; participants received a classic psychedelic agent as a treatment intervention in conjunction with psychological support; primary or secondary outcomes measured DA, broader constructs of acceptance, or closely related proxy measures, or these constructs were explored through qualitative interpretation in the study's results or discussion.

Eligibility criteria for healthy samples (secondary aim). Outcomes related to DA or closely related constructs (psychological flexibility, decentering, mindfulness, etc.) were reported, with focus on mechanisms of acceptance; studies examined psychological flexibility as a factor facilitating acceptance or DA, whether subjectively described or quantitatively measured. Psychological flexibility is the ability to stay present, open to thoughts and challenging emotions, and act in alignment with personal values rather than being driven by short-term impulses or avoidance (Yildirim, Dilekçi, & Manap, 2024).

Excluded studies. Study interventions using entactogens (e.g., MDMA), dissociative anesthetics (e.g., ketamine), cannabinoid substances, micro-dosing of psychedelics, and animal and tissue/cellular studies. See Table 1 for further details.

Search strategy and information sources

A comprehensive literature search was conducted on January 20, 2023, with guidance from a University of California, San Francisco research librarian. The search was updated on February 19th, 2025, with no changes to the search strategy or yielded results. Four databases were searched using identical eligibility criteria: PubMed, PsychInfo, CINAHL, and Embase. Three main search syntaxes were used, including all relevant or synonymous terms: (1) psychedelic-assisted therapy, (2) terminally ill/hospice/palliative care, and (3) existential distress/DA.

A date limit was set restricting results to studies published between 1990 and 2023, as historical studies on PAT in cancer patients, terminally ill, or end-of-life patients from

Table 1. PICOS eligibility criteria

PICOS	Inclusion	Exclusion
Population	– Terminally, seriously, or chronically ill individuals – Palliative care patients – Healthy participants without comorbidities	None
Intervention	– Psychedelic-assisted therapy utilizing classic serotonergic psychedelics: – psilocybin, LSD, ayahuasca, 5-MeO-DMT, DMT	– Ketamine – Cannabinoids – MDMA – Micro-dosing of psychedelic substances
Comparison	– No control – Placebo – very low dose of psychedelic intervention – SSRIs – Healthy participants results	None
Study Design	– Randomized and non-randomized controlled studies – Pilot and open-label studies – Long-term follow-up studies – Mixed methods studies, case studies, and qualitative studies as follow-up to a quantitative parent study	– Animal studies; reviews; commentaries; conference papers; fMRI or genetic studies that exclude measures on acceptance or existential distress
Publication Criteria	– English language – Full text article – Peer-reviewed – Date limits: 1990–2023	– Unpublished dissertations – Retracted studies – Studies in language other than English – Studies with unavailable full-text articles

the "first wave" of psychedelic research have been previously reviewed (Maia, Beaussant, & Garcia, 2022; Reiche et al., 2018; Ross, 2018; Schimmel et al., 2021). Search filters applied were clinical trials, full text, and English as the published language in all databases. See Table 2. Electronic Search.

Selecting sources of evidence

Eligible articles identified through database searches were uploaded to Zotero reference management software for citation organization and storage (*Zotero | Your Personal Research Assistant*, n.d.). A two-phase screening process was conducted: (1) screening titles and abstracts for eligibility and (2) a full-text review. Duplicate articles were manually removed. Figure i. outlines the screening process of eligible studies.

Data charting process and data items

All relevant data from eligible studies were charted in a standard Microsoft Excel spreadsheet according to the PRISMA-ScR checklist (Page et al., 2021). Detailed study characteristics, including the year of publication, first author, study design, sample size, psychedelic intervention, measurement of acceptance or related constructs, and main findings were abstracted. Demographic characteristics of the study samples, such as mean age, gender, and baseline clinical diagnosis, were also recorded. See Table 3 for a detailed breakdown of these study characteristics.

Synthesis of results

The eligible literature from the search results is examined to address the main research question, using a narrative-descriptive approach to encompass the full scope of the identified evidence. When possible, findings were organized by population type (seriously or terminally ill versus healthy/non-terminal samples) and outcome measurement approach to highlight distinctions between directly measured DA, proxy measures, and related constructs. See Table 3 for a concise presentation of the evidence of the review.

RESULTS

Study selection and characteristics

In addition to obtaining one cross-referenced article, 225 articles were yielded from the search results across the four databases. After removing six duplicates, 220 article titles and abstracts were screened for eligibility. Fifty-one studies were deemed irrelevant to the PICOS question and were removed, leaving 169 articles for full-text manual review. One hundred sixty studies were excluded for reasons listed in the PRISMA Flow Diagram (Fig. 1). A total of 9 studies met the PICOS eligibility criteria and were retained for review. See Table 3 for a list of eligible studies that have been included and reviewed.

Medical status and illness context

Terminally ill samples (N = 5 studies). Five out of the nine studies involved participants with existential or psychiatric distress associated with a serious or terminal illness (Agin-Liebes et al., 2020; Anderson et al., 2020; Gasser, Kirchner, & Passie, 2015; Griffiths et al., 2016; Malone et al., 2018).

Non-terminal psychiatric samples (N = 2 studies). Two studies included participants with self-reported depression

Table 2. Electronic search strategy

2a PubMed Search
Date of Updated Search: February 19, 2025
Date Range: published between 1990 and 2023.

#	Search Query	Results
1	("Hallucinogens"[Mesh] OR "Hallucinogens" [Pharmacological Action] OR "Lysergic Acid Diethylamide"[Mesh] OR lsd[tiab] OR psilocybin*[tiab] OR Dipropyltryptamine[tiab] OR Hallucinogen*[tiab] OR psychedelic*[tiab]) NOT (ketamine OR MDMA OR cannab*)	331
2	("Depression"[Mesh] OR "Adjustment Disorders"[Mesh] OR "Major Depressive Disorder 1" [Supplementary Concept] OR "Anxiety"[Mesh] OR depress*[tiab] OR anxiet*[tiab] OR existential*[tiab] OR psychol*[tiab] OR stress*[tiab] OR distress*[tiab] OR "fear of death"[tiab] OR "Demoralization"[Mesh] OR "Psychological Distress"[Mesh] OR "Mental Disorders"[Mesh])	117,493
3	("Palliative Care"[Mesh] OR "Hospice and Palliative Care Nursing"[Mesh] OR "Palliative Medicine"[Mesh] OR "Neoplasms"[Mesh] OR "Terminal Care"[Mesh] OR palliative[tiab] OR terminal*[tiab] OR life-threaten*[tiab] OR end-of-life[tiab] OR cancer*[tiab] OR dying[tiab] OR tumor[tiab] OR advanced malignanc*[tiab] OR hospice[tiab])	130,043
4	#1 AND #2 AND #3	10
5	Ineligible studies after manual screening	5
6	*Total studies included in results*	5
7	*Filters applied:* Full text, Clinical Trial, Randomized Controlled Trial, English	

2b EMBASE Search
Date of Updated Search: February 19, 2025
Date Range: published between 1990–2023

#	**Search Query**	**Results**
1	'psychedelic agent'/exp OR 'psilocybin'/exp OR 'psilocybin' OR 'lysergide'/exp OR hallucinogen* OR psychedelic* OR lsd OR dipropyltryptamine NOT 'endocannibanoids' NOT 'cannabis' NOT 'cannabinoid'	3,515
2	'depression'/exp OR 'adjustment disorder'/exp OR 'anxiety'/exp OR 'demoralization'/exp OR depress* OR anxiet* OR existential* OR psychol* OR distress* OR 'fear of death'	**253,516**
3	'hospice'/exp OR 'neoplasm'/exp OR 'terminal care'/exp OR palliative OR terminal* OR 'life-threaten*' OR 'end-of-life' OR cancer* OR dying OR 'advanced malignan*' NOT 'animal'/exp NOT 'human'/exp	**275,660**
4	#1 AND #2 AND #3	1
5	Ineligible studies after manual screening	1
6	*Total studies included in results*	0
7	Filters applied: (sources) excluded Medline (PubMed) results and preprints (publication types) include: articles	

2c Web of Science
Date of Updated Search: February 19, 2025
Date range: published between 1990 – 2023

#	**Search Query**	**Results**
1	Hallucinogens OR "Lysergic Acid Diethylamide" OR lsd OR psilocybin OR Dipropyltryptamine OR Hallucinogen OR psychedelic NOT (ketamine OR MDMA OR cannab*)	3,840
2	Depression OR "Adjustment Disorders" OR "Major Depressive Disorder 1" OR "Anxiety" OR depress* OR anxiet* OR existential* OR psychol*OR stress* OR distress* OR "fear of death" OR "Demoralization" OR "Psychological Distress" OR "Mental Disorders"	353,645
3	"Palliative Care" OR "Hospice and Palliative Care Nursing" OR "Palliative Medicine" OR "Neoplasms" OR "Terminal Care" OR palliative OR terminal* OR life-threaten* OR end-of-life OR cancer* OR dying OR tumor OR "advanced malignan*" OR hospice (All Fields) not animals OR humans (All Fields)	1,766,513
4	#1 AND #2 AND #3	182
5	Ineligible studies after manual screening	179
6	*Total studies included in results*	3
7	Filters applied: article, open access, English	

2d PsychInfo
Date of Updated Search: February 19, 2025
Date range: published between 1990–2023

(continued)

Table 2. Continued

#	Search Query	Results
1	Hallucinogens OR "Lysergic Acid Diethylamide" OR lsd OR psilocybin OR Hallucinogen OR psychedelic	305
2	Depression OR "Adjustment Disorders" OR "Major Depressive Disorder 1" OR "Anxiety" OR depress* OR anxiet* OR existential* OR psychol*OR stress* OR distress* OR "fear of death" OR "Demoralization" OR "Psychological Distress" OR "Mental Disorders"	22,140
3	"Palliative Care" OR "Hospice and Palliative Care Nursing" OR "Palliative Medicine" OR "Neoplasms" OR "Terminal Care" OR palliative OR terminal* OR life-threaten* OR end-of-life OR cancer* OR dying OR tumor OR "advanced malignan*" OR hospice	28,663
4	#1 AND #2 AND #3	31
5	Ineligible studies after manual screening	31
6	*Total studies included in review*	0
7	Filters applied: articles, scholarly journals, full text, peer reviewed, evidence-based healthcare, case studies	

or anxiety symptoms without a serious or life-limiting comorbidity (Davis, Barrett, & Griffiths, 2020) or diagnosed with treatment-resistant depression (Watts, Day, Krzanowski, Nutt, & Carhart-Harris, 2017).

Healthy samples (N = 2 studies). Two studies included only healthy participants, with no reported mental or medical diagnoses (Griffiths et al., 2018; Murphy-Beiner & Soar, 2020).

Participant characteristics

The selected nine studies included a total of 1,222 participants with a median sample size of 20 (IQR = 50.5). The relatively large survey study (N = 985) serves as an outlier (Davis et al., 2020). Mean age across studies was 46 years (SD = 10.9), with two studies reporting age ranges only [30–64 years (Watts et al., 2017) and 20s through 60s (Malone et al., 2018)].

Demographics across all included studies

Gender representation varied, with two studies reporting 60% female participants (Agin-Liebes et al., 2020; Griffiths et al., 2018), two reporting predominantly male samples (60 and 72% male) (Davis et al., 2020; Gasser et al., 2015), one with exclusively male participants only (Anderson et al., 2020), and the remaining studies showing near-equal gender distribution (Agin-Liebes et al., 2020; Griffiths et al., 2016; Malone et al., 2018; Murphy-Beiner & Soar, 2020; Watts et al., 2017). Only one study included data on transgender or nonbinary identification (6%) (Davis et al., 2020). One study reported exclusively gay-identified participants (Anderson et al., 2020). Gasser et al. (2015) did not report any demographic data on race/ethnicity or education; the remaining eight studies reported white/Caucasian and highly educated samples. Only four studies reported religious or spiritual beliefs (Agin-Liebes et al., 2020; Gasser et al., 2015; Griffiths et al., 2018; Malone et al., 2018); five reported marital status (Anderson et al., 2020; Davis et al., 2020; Gasser et al., 2015; Griffiths et al., 2016; Malone et al., 2018); and four reported work status (Gasser et al., 2015; Griffiths et al., 2018; Malone et al., 2018; Watts et al., 2017). Participant demographics are summarized in Table 4.

Geographical context

Six studies were conducted in the United States (Agin-Liebes et al., 2020; Anderson et al., 2020; Davis et al., 2020; Griffiths et al., 2016, 2018; Malone et al., 2018), though one cross-sectional survey study reported that 35% of their sample lived outside the U.S. (Davis et al., 2020). One study was conducted in Switzerland (Gasser et al., 2015), and two in the United Kingdom (Murphy-Beiner & Soar, 2020; Watts et al., 2017). All included studies were published between 2015 and 2023, despite the date filter extending back to 1990.

Study design

Study designs varied as follows:

- 1 single-arm, open-label pilot study
- 2 double-blind, randomized controlled trials (one with a crossover design)
- 1 quantitative observational study
- 2 qualitative follow-up studies to parent trials
- 1 mixed-methods follow-up study to a parent trial
- 1 international cross-sectional survey study

Two studies (Agin-Liebes et al., 2020; Malone et al., 2018) were follow-ups to the same parent trial (Ross et al., 2016).

Types of psychedelic interventions

All interventional studies incorporated psychotherapeutic support as an adjunct during psychedelic treatment. Three studies utilized psilocybin as the active psychedelic treatment (Anderson et al., 2020; Griffiths et al., 2016, 2018) while three conducted follow-up investigations to psilocybin parent trials (Agin-Liebes et al., 2020; Malone et al., 2018; Watts et al., 2017). One study (Gasser et al., 2015) conducted a follow-up to an LSD parent trial (Gasser et al., 2014). One cross-sectional survey (N = 985) captured online participants who self-reported histories of at least a one-time use of LSD (42%), psilocybin mushrooms (38%), or other psychedelics substances (20%) such as mescaline, ayahuasca, DMT (N,N-Dimethyltryptamine) (Davis et al., 2020) One study

Table 3. Study characteristics

Authors/Year	Study Design/ location/sample size (*N*)	Mean (SD) age Sex	Type of psychedelic Intervention (+control)	Serious or terminal illness (Y/N)	DA or related outcomes measured	Main findings
Agin-Liebes et al. (2020)	Long-term follow-up to parent study (Ross et al., 2016) NYU $N = 15$	53 (16) Female 60%	6.5 mo to 4.5 yr follow up to parent trial of single dose psilocybin (0.3 mg/kg) with psychotherapeutic support (Niacin 250 mg)	Yes: Cancer-related psychiatric distress	DAS DS	- Significant within-subject decreases in demoralization ($p = .001$) and death anxiety ($p = .05$) from baseline to up to 4.5 years suggesting increased DA
Anderson et al. (2020)	Open-label pilot study; UCSF; $N = 18$	59 (4) Female 0%	1 psilocybin dose (0.3–0.36 mg/kg) with 8–10 group therapy visits	Yes: demoralized older long-term AIDS survivor gay men	DS-II	- clinically meaningful change in demoralization from baseline to 3-month follow-up
Davis et al. (2020)	Cross-sectional survey; Johns Hopkins; $N = 985$	32 (13) Female 28%	Personal hx of having taken a dose of a single psychedelic: psilocybin, LSD, ayahuasca, mescaline, DMT, etc.	No: Personal report of depression and/or anxiety only	AAQII	- psychological flexibility and acceptance from PAT fully mediated and was moderately correlated with reductions in depression/anxiety
Gasser et al. (2015)	Mixed Methods f/u to parent study (Gasser et al., 2014) Switzerland $N = 10$	52 (9) Female 36% (demographics from parent trial of $N = 11$)	12 months following completion of LSD-assisted therapy of either low or high dose	Yes: anxiety associated with life-threatening disease	QCA	themes found: - transcending fear of death leading to acceptance - serenity and acceptance of difficulties and circumstances - a "depatterning" of attachment to physical/mortal life
Griffiths et al. (2018)	Double-blind RCT Johns Hopkins $N = 75$	42 (n/a) Female 60%	2 doses psilocybin, initiation of program of meditation; 3 different doses correlating with 3 levels of spiritual support	No: healthy participants	Death Acceptance subscale of the LAP-R	- no significant difference in death acceptance reported
Griffiths et al. (2016)	Double-blind crossover RCT; Johns Hopkins $N = 51$	56 (1) Female 49%	Low dose and high dose of psilocybin per tx group: crossed over at 5 weeks between sessions with 6-week follow-up	Yes: Anxiety and/or depression associated with life-threatening cancer	Death Acceptance subscale of the LAP-R	- significant increase in DA: 1. between groups 2. between post-session 1 and post-session 2 3. between Baseline and 6 months - DA sustained at 6- months

(continued)

Table 3. Continued

Authors/Year	Study Design/ location/sample size (*N*)	Mean (SD) age Sex	Type of psychedelic Intervention (+control)	Serious or terminal illness (Y/N)	DA or related outcomes measured	Main findings
Murphy-Beiner and Soar (2020)	Observational study; University of East London $N = 48$	38 (7) Female 54%	One-time ayahuasca ingestion in a naturalistic or ceremonial setting; assessed before and 24 hrs after drinking ayahuasca	No: Healthy participants	FFMQ EQ	- 2 out of 3 of the acceptance facets of the FFMQ increased: non-reactivity and - no significant difference for the acceptance facet of non-judgement
Watts et al. (2017)	Qualitative f/u study to parent study; Imperial College London; $N = 20$	Range: 30–64 yrs Female 46%	Semi-structured interviews at 6-month follow-up after open-label trial of psilocybin-assisted therapy	No: TRD	Thematic analysis	- Potential psychological mechanisms found: 1. from disconnection to connection 2. from avoidance to acceptance - PAT favored among participants compared to traditional treatments
Malone et al. (2018)	Mixed methods f/u to parent trial (Ross et al., 2016) NYU $N = 4$	Range: 20s through 60s Female 25%	Parent trial: double-blind, crossover- single-dose psilocybin (0.3 mg/kg) or niacin	Yes: Adjustment disorders, anxiety, or GAD with cancer diagnosis	Interpretive Phenomenological Analysis	- major theme of DA found - fear of or poor DA transcended into acceptance

Abbreviations: NYU (New York University); UCSF (University of California, San Francisco); RCT (randomized controlled trial); MDD (major depressive disorder); TRD (treatment-resistant depression); GAD (generalized anxiety disorder); LSD (lysergic acid diethylamide). DMT (N,N-dimethyltryptamine); QCA (Qualitative Content Analysis); LAP-R (Coherence and Death Acceptance subscales of the Life Attitude Profile – Revised); AAQII (Acceptance and Action Questionnaire II); FFMQ (Five Facet Mindfulness Questionnaire); EQ (Experiences Questionnaire); DS (Demoralization Scale); DS-II (Demoralization Scale); DA (death acceptance).

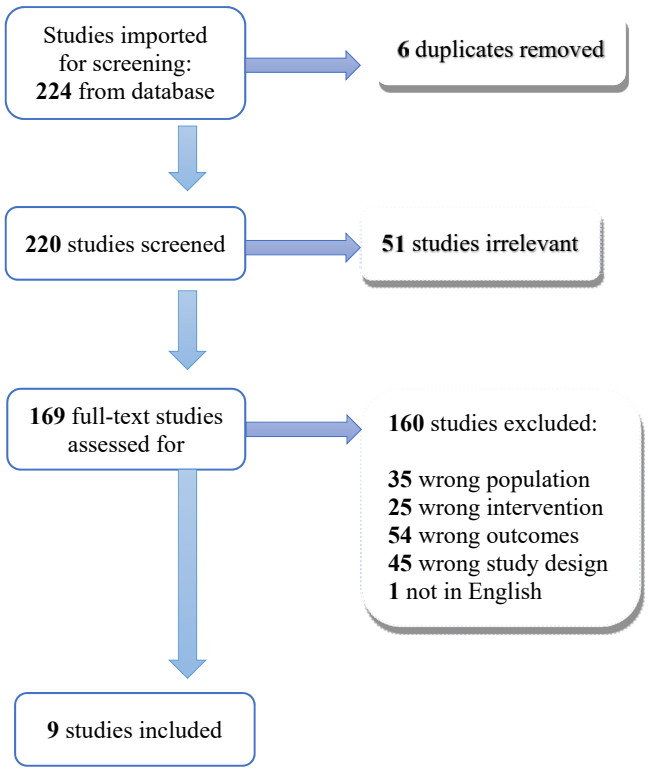

Fig. 1. PRISMA flow diagram of study selection

assessed participants who had ingested ayahuasca in a naturalistic, ceremonial setting (Murphy-Beiner & Soar, 2020).

Four studies compared high-dose versus low-dose psychedelic interventions or conducted follow-ups on these comparison studies (Gasser et al., 2015; Griffiths et al., 2016, 2018; Watts et al., 2017). Only one study explicitly compared a psychedelic treatment group (psilocybin, 0.3 mg/kg) versus a non-psychedelic control (Niacin 250 mg) (Agin-Liebes et al., 2020).

OUTCOMES

Measurements of death acceptance: direct versus proxy measures

A critical distinction must be made in interpreting the findings: only two of the nine included studies explicitly measured DA using a validated, death-acceptance-specific instrument (Griffiths et al., 2016, 2018). The remaining seven studies assessed related but distinct constructs, including demoralization, death anxiety, psychological flexibility, mindfulness, and decentering (Agin-Liebes et al., 2020; Anderson et al., 2020; Davis et al., 2020; Gasser et al., 2015; Malone et al., 2018; Murphy-Beiner & Soar, 2020; Watts et al., 2017). While these constructs are related to acceptance processes, they should not be treated as direct equivalents without theoretical justification.

Directly measured death acceptance (N = 2 studies). Both studies by Griffiths et al. (2016, 2018) used the DA subscale of the Life Attitudes Profile-Revised (LAP-R) as the primary outcome measure. The LAP-R is a 48-item self-report instrument designed to measure six dimensions of one's sense of meaning and purpose in life, with evidence of validity, reliability, and acceptability across age groups (Erci, 2008; Reker, 2001). The DA subscale specifically captures the degree of fear of death and acceptance of death as a natural part of the life cycle.

Griffiths et al. (2016) applied the LAP-R subscale to participants with depression or anxiety associated with life-threatening cancer. Participants received low-dose (1 or 3 mg/70 kg) or high-dose (22 or 32 mg/70 kg) psilocybin, with a 6-week follow-up between sessions. The reported findings showed significant between-group differences: the high-dose group had a mean LAP-R DA score of 36.17, compared with 29.14 in the low-dose group ($p < 0.05$). Significant within-group improvements were reported from baseline to six months: the high-dose group improved from 29.09 to 36.25; the low-dose group improved from 28.05 to 34.95. DA improvements were sustained at the six-month follow-up.

The Griffiths et al. (2018) study, on the other hand, was a double-blind RCT that examined healthy participants (no serious illness or psychiatric diagnosis) randomized to three spiritual intervention conditions with varying dose levels and support. The authors reported no significant difference in DA within or between groups. This was the only study included in the review that reported no significant changes in DA or related constructs.

The contrast between these two studies is notable-they both used the same outcome measurement (the DA subscale of the LAP-R), yet only the study with terminally ill participants demonstrated significant DA improvements. This suggests that DA changes in the context of PAT may be specific to individuals confronting actual mortality rather than a universal effect across populations.

Proxy measures and related constructs ($N = 7$ studies)

The remaining seven studies captured elements of acceptance through constructs theoretically related to DA, such as psychological flexibility, demoralization, death anxiety, mindfulness, and decentering. While these constructs are conceptually linked to acceptance processes, they represent inferred or theorized pathways to DA rather than direct measurement of DA itself.

Psychological flexibility and decentering (N = 2 studies). The Murphy-Beiner and Soar (2020) study was a quantitative observational study that examined healthy participants engaging in an ayahuasca ceremony in a naturalistic setting. The Five Facet Mindfulness Questionnaire (FFMQ), a 39-item self-report measure, was used to assess mindfulness and attentional presence (Takahashi, Saito, Fujino, Sato, & Kumano, 2022; Wang et al., 2024). Two of the five FFMQ facets are considered emotional acceptance components: non-judgment and non-reactivity (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006; Murphy-Beiner &

Table 4. Participant demographics

Authors/year	% Past Psychedelic use	Race/ethnicity	Religious or spiritual practices	Education level	Marital status
Agin-Liebes et al. (2020)	47%	White/Caucasian 93% Asian 7%	Atheist/agnostic 33% Jewish 20% Catholic 7% Other faiths 26% Unreported 14%	Part college 13% 4-year college 27% Graduate school +60%	
Anderson et al. (2020)	Median = 5	White 78% Black/African American 6% Multiracial 17% Hispanic/Latino 6%		College or more 72%	Single 44% Married or Partnered 44% Divorced or Separated 11%
Davis et al. (2020)	100%	White/Caucasian 84% Black/African American 1% Asian 2% Native/Pacific Islander 1% Mixed race/other 12%		High school or less 17% Some college 44% College 24% Graduate school +16%	Never married 51% Married 22% Living with partner 20% Divorced or separated 7%
Gasser et al. (2015)	25%		Protestant 18% Catholic 9% Buddhist 9% Not religious 64%		Married/living w/partner 56% Single 18% Divorced or separated 27%
Griffiths et al. (2018)	25%	White/Caucasian 85%; Black/African American 5%; Asian 9%	Practiced meditation 31%	College/graduate school +89%	
Griffiths et al. (2016)	45%	White/Caucasian 94% Black/African American 4% Asian 2%		High School 2% College 45% Graduate school +53%	Married or living with partner 69%
Murphy-Beiner and Soar (2020)	87%	Caucasian 67%		College or beyond 83%	
Watts et al. (2017)	25%	Caucasian 75% Black/African American 15% Hispanic/Latino 5% Asian 5%		High School 20% College 45% Graduate school +35%	
Malone et al. (2018)	25%	White/Caucasian 100%	Atheist/Agnostic 75% Christian 25%	Part College 25% College 25% Graduate school +50%	Never married 50% Married 25% Partnered 25%

Soar, 2020). The findings indicated a significant increase in non-reactivity between baseline and 24-h post-ayahuasca ($p < .05$); no significant difference in non-judgment ($p > .05$); and a significant increase in decentering, as measured by the Experience Questionnaire.

A primary construct of psychological flexibility, decentering is the ability to observe thoughts, feelings, and experiences from a detached observer perspective rather than automatically identifying with them (Bennett et al., 2021). Decentering theoretically facilitates acceptance by reducing experiential avoidance and enabling individuals to view unwanted experiences as temporary events of the mind (Bennett et al., 2022; Hamilton & Barnhofer, 2024; Soler et al., 2021). However, enhanced mindfulness and decentering in healthy individuals may operate differently than in those facing a serious or terminal illness.

The Davis et al. (2020) study was a cross-sectional survey of non-terminal participants who self-reported depression or anxiety symptoms along with a history of psychedelic use, in which psychological flexibility was assessed using the Acceptance and Action Questionnaire II (AAQII). Although the AAQII was designed to measure psychological *inflexibility*, respondents were asked to rate changes in psychological flexibility before and after their recalled psychedelic experience. The study's path analysis indicated that psychedelic-induced psychological insight ($p < 0.001$; $r = .46$) and acute mystical experiences ($p = 0.01$; $r = .09$) directly increased psychological flexibility. The authors also reported increased psychological flexibility fully mediated and was moderately correlated with reductions in depression and anxiety ($p < 0.001$; $r = -.62$). The authors propose that increased psychological flexibility, by promoting present-moment engagement and alignment with personal values, may help individuals better accept difficult circumstances. However, this mechanism is hypothesized rather than directly tested in a terminal illness context.

Demoralization and death anxiety (N = 2 studies). While demoralization and death anxiety are not direct measures of DA, research indicates that higher levels of DA predict lower levels of these constructs in individuals with serious illness (Philipp et al., 2019). This suggests an inverse relationship-DA may serve as a protective quality against such suffering (Philipp, Mehnert, Müller, Reck, & Vehling, 2020). Agin-Liebes et al. (2020) conducted a long-term follow-up study examining cancer patients ($n = 15$) with anxiety who received psilocybin therapy in a randomized controlled trial. The study team measured demoralization using the Demoralization Scale (DS) and death anxiety using the Death Anxiety Scale (DAS). The reported findings include significant within-subject improvements in demoralization from baseline to the 4.5-year follow-up ($p = .001$) and in death anxiety from baseline to follow-up ($p = .05$), indicating that these improvements were sustained long-term after their psilocybin therapy. Due to the small sample size, the results were underpowered to detect anything other than large within-subject effects and for subgroup or mediation analyses. While the DS and DAS measure existential distress rather than DA directly, reductions in demoralization and death anxiety may reflect enhanced DA as an underlying mechanism. Hence, this remains an inference rather than a direct measurement.

Anderson et al. (2020) single-arm, open-label pilot study examined psilocybin-assisted group therapy for demoralized older long-term AIDS survivor gay men ($n = 18$). The Demoralization Scale-II (DS-II), a 16-item refined version of the original 30-item DS (Robinson et al., 2016), was used. A clinically meaningful within-subjects reduction in demoralization from baseline to the 3-month follow-up was observed. The DS-II includes a "meaning and purpose" subscale and a "distress and coping ability" subscale, with the latter capturing the individual's capacity to adapt to and accept distressing circumstances. However, this is a component of a broader demoralization measure and not a direct DA assessment (Belar et al., 2019; Robinson et al., 2016).

Qualitative assessments ($N = 3$ studies)

Three studies employed qualitative analyses illuminating themes of acceptance and DA through participant narratives (Gasser et al., 2015; Malone et al., 2018; Watts et al., 2017). Gasser et al. (2015) conducted a mixed-methods follow-up study to a randomized controlled trial assessing LSD safety and efficacy for anxiety related to a life-threatening disease (Gasser et al., 2014). Qualitative Content Analysis was used to explore participants' nuanced experiences. The Swiss research team reported major themes of transcending a deeply rooted fear of death, leading to a sense of serenity and acceptance of difficulties and life circumstances.

Malone et al. (2018) also conducted a mixed-methods follow-up study and employed Interpretive Phenomenological Analysis to explore the experiences of four cancer patients with varying stages of cancer (stage I to stage IV terminal), who had received psilocybin-assisted therapy in a parent trial (Ross et al., 2016). Key themes reported include self-compassion and a recognition of the universality of birth, aging, sickness, and death. In Malone et al. (2018) and Gasser et al. (2015), the two qualitative studies that included seriously and terminally ill samples, both reported themes of an overwhelming felt sense of love, which some participants reported carried them through their fear or poor DA to acceptance. Unlike broader discussions of the psychedelic experience, these two studies also found that the psilocybin-assisted therapy session did not necessarily focus on the cancer diagnosis itself but rather on these universal existential themes.

The third qualitative study reviewed, Watts et al. (2017), examined non-terminal participants' subjective experiences in a parent trial investigating psilocybin for treatment-resistant depression ($n = 20$). Emotional transformations from disconnection to connection and avoidance of emotion and unpleasant circumstances to acceptance emerged from thematic analysis. First, the intensity of emotion was reported across all participants, followed by a surrender to their depression, and then a felt sense of unity, connection,

and embodiment of love that appeared to facilitate the acceptance of life's complexity. While this study examines emotional acceptance and acceptance of life's complexity in depression, this differs qualitatively from confronting terminal illness and impending death. Nonetheless, these findings suggest that psilocybin treatment may foster feelings of connectedness and acceptance, potentially easing existential distress and improving psychological well-being in seriously ill and end-of-life populations.

Summary of outcome measurement heterogeneity

The heterogeneity of measurements represents both a strength and a limitation. While diverse measurement approaches capture multiple dimensions of "acceptance," they may also create conceptual ambiguity. Only two studies directly measured DA: one showed improvements in DA in a terminally ill sample (Griffiths et al., 2016), whereas the other, in a healthy sample, did not (Griffiths et al., 2018). Four studies were reviewed that used proxy measures theoretically related to DA, including demoralization, death anxiety, psychological flexibility, or decentering (Agin-Liebes et al., 2020; Anderson et al., 2020; Davis et al., 2020; Murphy-Beiner & Soar, 2020). Three studies employed qualitative methods and reported overall themes of general acceptance and DA (Gasser et al., 2015; Malone et al., 2018; Watts et al., 2017). This heterogeneity makes synthesis challenging and raises questions about construct validity. Findings from the proxy measures and qualitative themes should be interpreted as suggestive of potential DA-related mechanisms rather than direct evidence of DA improvement.

DISCUSSION

Overall interpretation

This scoping review explored available literature regarding PAT and its potential to promote DA in terminally ill individuals. Nine studies were reviewed in which changes in acceptance, DA, or related constructs were reported as primary or secondary outcomes or discussed in qualitative analyses. Overall, the findings suggest that PAT may influence how some individuals relate to death and other existential concerns, primarily through effects on demoralization, death anxiety, psychological flexibility, decentering, and meaning in life. However, the small number of studies, heterogeneous designs, and reliance on proxy measures indicate that these results should be interpreted as preliminary signals rather than definitive evidence that PAT reliably enhances DA in individuals with serious or terminal illness.

Death acceptance versus related constructs

A central conceptual issue is the distinction between DA as a directly measured outcome and DA as an inferred or theorized process. Only two included studies used a DA-specific subscale of the Life Attitude Profile-Revised (LAP-R), both conducted by Griffiths et al. (2016, 2018). The remaining studies assessed constructs such as demoralization, death anxiety, psychological flexibility, mindfulness facets, and decentering, which are theoretically related to acceptance but not synonymous with it (Agin-Liebes et al., 2020; Anderson et al., 2020; Davis et al., 2020; Murphy-Beiner & Soar, 2020; Philipp et al., 2020). For example, greater psychological flexibility and decentering can reduce experiential avoidance and support a more open stance toward distressing experiences, yet such changes do not necessarily mean that individuals have accepted their mortality (Bennett et al., 2021, 2022; Hamilton & Barnhofer, 2024; Yildirim et al., 2024). This heterogeneity in measurement raises questions about construct validity and underscores the need for future PAT research to incorporate validated DA instruments, including the LAP-R DA subscale and the Death Attitude Profile, alongside broader well-being measures (Gesser, Wong, & Reker, 1988; Reker, 2001; Wong, Reker, & Gesser, 1994).

Context of terminal illness versus non-terminal samples

Differences between seriously or terminally ill and non-terminal populations further shape the interpretation of PAT's potential to influence DA. Studies involving individuals with life-threatening cancer or serious illness reported sustained improvements in DA or closely related existential outcomes following psilocybin or LSD-assisted interventions (Agin-Liebes et al., 2020; Anderson et al., 2020; Gasser et al., 2015; Griffiths et al., 2016; Malone et al., 2018). In contrast, studies with healthy volunteers or people with non-terminal depression and anxiety primarily showed changes in psychological flexibility, mindfulness, or emotional acceptance, and one healthy-sample trial using the LAP-R found no significant change in DA (Davis et al., 2020; Griffiths et al., 2018; Murphy-Beiner & Soar, 2020; Watts et al., 2017). This pattern suggests that confronting an actual life-limiting condition may be an important contextual factor in how psychedelic experiences are interpreted and integrated. For patients facing serious or terminal illness, these experiences may be more likely to be directed toward questions of mortality, finitude, and meaning, whereas in healthy individuals they may be understood as personal growth or spiritual exploration without fundamentally altering death attitudes. Thus, findings from healthy and non-terminal samples should be regarded as hypothesis-generating mechanisms, not as confirmatory evidence for HPC settings.

Mystical-type experiences and mechanisms of change

The role of mystical-type experiences in facilitating DA appears complex and context-dependent. Several studies in this review and the broader literature report that more intense mystical-type experiences-marked by unity, transcendence of time and self, and profound insight-correlate with greater improvements in DA, death transcendence, or

related well-being outcomes (Davis et al., 2020; Gasser et al., 2015; Griffiths et al., 2016; Jylkkä, 2024; Malone et al., 2018). However, other work, including Agin-Liebes et al. (2020), Griffiths et al. (2018), and Sloshower et al. (2023), has failed to find a straightforward association between mystical experience scores and therapeutic change, either due to limited statistical power or because symptom improvement appears mediated by other psychological processes. These inconsistent findings indicate that mystical experiences may not be necessary or sufficient for DA-related benefits and may function as one of several overlapping mechanisms. Future studies should therefore examine not only the intensity of mystical-type experiences, but also how they are framed, emotionally processed, and integrated over time, particularly in the context of serious or terminal illness.

Relationship to existing psychotherapies

When considered alongside established psychotherapies for existential distress, PAT appears as a potentially complementary rather than replacement modality. Interventions such as Dignity Therapy, Meaning-Centered Psychotherapy, Expressive Supportive Therapy, and Cognitive-Behavioral Therapy approaches already provide structured pathways for addressing meaning, identity, and anticipatory grief in patients with advanced illness (Breitbart et al., 2015; Heidenreich, Noyon, Worrell, & Menzies, 2021; Lee & Jeong, 2023; Tang, Nguyen, Bruera, Tanco, & Delgado-Guay, 2020). These therapies can reduce depression, anxiety, and overall distress but are often time-intensive and may be difficult to sustain when patients face significant symptom burden, fatigue, or limited prognosis (Holland et al., 2010).

The rapid onset and durable effects observed in some psychedelic trials suggest that PAT could offer a shorter yet potent window for psychological and spiritual work, within which these existing frameworks might operate more effectively (Agin-Liebes et al., 2020; Griffiths et al., 2016; Reiff et al., 2020). However, direct comparative effectiveness trials are lacking, so it remains unknown whether PAT confers unique advantages over standard psychosocial care or functions best as an adjunct in carefully selected cases.

Ethical and safety considerations

Ethical and safety considerations are paramount when contemplating PAT for seriously or terminally ill populations. Patients referred for psychedelic interventions often experience profound existential suffering, which can complicate assessments of decisional capacity and voluntariness in the consent process (Beaussant et al., 2021; Whinkin, Opalka, Watters, Jaffe, & Aggarwal, 2023). Clinicians must ensure that patients understand both the potential benefits and psychological risks of treatment and that interest in psychedelics is not driven solely by desperation or unrealistic expectations. Timing is also critical: powerful, emotionally intense experiences may require substantial reflection and integration, and patients with limited time or energy may not be able to fully process them, raising the possibility of increased distress or unresolved existential questions near the end of life (Whinkin et al., 2023; Yu et al., 2021). Existing data suggest a generally favorable safety profile in selected medically fragile adults, but sample sizes are small, and older adults with multimorbidity remain underrepresented (Anderson et al., 2020; Johnston, Mangini, Grob, & Anderson, 2023). The development of robust ethical frameworks-including guidelines for screening, consent, integration, and follow-up- is therefore essential as research progresses.

Methodological limitations and implications

Several methodological limitations of the current evidence base constrain the strength of conclusions that can be drawn. Most studies relied on small samples and recruited predominantly white, highly educated participants from North America or Western Europe, limiting generalizability to the diverse populations served in HPC, including BIPOC, LGBTQ+, and HIV + communities. These groups often face compounded structural and cultural barriers to DA (Dācus, Wood, & Ward, 2023; Jackson et al., 2022). Older adults with multimorbidity and non-cancer terminal diagnoses are also underrepresented, despite being highly relevant to palliative care practice (Center for Disease Control and Prevention, 2023; Johnston et al., 2023; National Hospice and Palliative Care Organization, 2022). Additionally, the mix of randomized controlled trials, open-label pilots, observational surveys, and qualitative follow-ups, combined with varied dosing regimens, therapeutic frameworks, and follow-up periods, makes it difficult to compare effect sizes or establish causal mechanisms with confidence. The lack of standardized, validated DA measures across studies further complicates synthesis and threatens construct validity.

Future research directions

These limitations point toward several priorities for future research. Trials that designate DA as a primary endpoint and consistently use validated DA scales, along with measures of psychological flexibility, demoralization, and spiritual well-being, are needed to clarify whether and how PAT directly affects DA (Gesser et al., 1988; Philipp et al., 2020; Wong et al., 1994). Longitudinal designs could illuminate how constructs such as decentering, meaning in life, and mystical-type experiences interact over time to support or hinder DA in terminally ill patients (Bennett et al., 2021; Davis et al., 2020; Soler et al., 2021). Comparative trials testing PAT-augmented interventions against established psychotherapies for existential distress would help determine whether psychedelic approaches offer unique or additive benefits (Breitbart et al., 2015; Heidenreich et al., 2021). Equally important is the intentional recruitment of historically marginalized populations, including the BIPOC, LGBTQ+, and HIV + communities, and individuals with a broader range of terminal diagnoses, to ensure that emerging evidence reflects the diversity of people who might ultimately receive such care (Dācus et al., 2023; Jackson et al., 2022). Parallel work in ethics and implementation

science-addressing informed consent, capacity assessment, integration protocols, and equity of access-will be crucial for guiding any future clinical applications (Beaussant et al., 2021; Whinkin et al., 2023).

Conclusion

Taken together, the studies reviewed here provide cautious optimism that PAT may help some terminally ill individuals cultivate a more accepting and less fear-based relationship with death, but they also make clear that the field remains in an early exploratory phase. DA should be treated not as a firmly established therapeutic target already validated for PAT, but as a promising construct that requires clearer definition, better measurement, and careful integration into the complex psychosocial realities of serious illness and end-of-life care.

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