

PSYCHEDELIC RESEARCH SNAPSHOT

**A scoping review of
variations among
psychedelic
interventions for
psychological suffering
associated with the end
of life (Journal Pre-
Proof)**



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KEY DEFINITIONS



A-Z GLOSSARY

Therapeutic Psychedelic Interventions (TPIs):

Psychedelics used alone, or used with psychotherapy or supportive approaches.

Psychological Suffering:

Includes anxiety, depression, hopelessness, existential distress, loss of meaning, demoralization, and fear of dying.

End-of-Life Illness:

Diagnoses that create a sense of a shortened future (e.g., advanced cancer, HIV/AIDS, severe mental illness with high mortality risk).

AIM

To scope the variation in TPIs addressing psychological suffering associated with end-of-life concerns.

BACKGROUND

- TPIs with psychotherapy are being explored to ease end-of-life distress
- Existing reviews have mostly focused on treatment effectiveness (e.g., reductions in anxiety, depression, PTSD)
- In Canada, TPIs are available through the Special Access Program and via clinical trials; reforms are emerging but remain slow and complex.

RESULTS:

STATE OF THE EVIDENCE

59 studies, spanning six substances

41% ketamine-based studies (25% LSD, 24% psilocybin, 5% DPT, 3% MDMA, 2% ayahuasca)

12% RCTs (most studies were uncontrolled experiments, 43% of RCTs were psilocybin-based)

29% single cases (small sample sizes were common)

70% studies with cancer populations

59% missing race data (most samples reporting race were majority White; limited diversity reporting)

three publication waves

- LSD/DPT (personality, psychiatric outcomes) **60s–80s**
- ketamine (affective + clinical outcomes) + psilocybin (most comprehensive outcomes) **'07–'18**
- broader mix incl. MDMA + ayahuasca **'20–'23**

RESULTS

Biopsychosocial–spiritual Domains

Clinical: vital signs

Psychological: depression, anxiety, demoralization

Spiritual: connectedness, ego dissolution, transcendence

Holistic: combined wellbeing across domains

Settings & Aesthetic Elements

Hospitals: 51%; Music: 38%; Eyeshades: 26%;
73% did not describe room environment

Adverse Experiences

- **66%** of studies reported challenging or adverse experiences: fear, dissociation, anxiety, grief, nausea.
- Typically transient and addressed during integration.
- **41%** viewed as therapeutically meaningful (catharsis, insight).
- Rare severe events: distress relapse, trauma flashbacks, one accidental overdose outside a session.

PROPOSED MECHANISMS

Neurobiological (54%): 79% of ketamine studies and 57% psilocybin studies.

Other mechanisms hypothesized:

Psychological (51%): emotional processing, meaning-making, cognitive flexibility.

Spiritual/Existential (44%): mystical-type experiences, shifts in identity, connectedness.

MODELS OF CARE

Dosing-only: 50% of interventions (mainly ketamine).

Therapeutic: ~50% (includes hybrid models) prep → dosing → integration (psilocybin, LSD, DPT); group therapy only in psilocybin studies.

Aesthetic supports (music, eyeshades, room design): inconsistently reported.

Note: Debate in the literature between whether biomedicalized dosing or holistic psychospiritual care should be the way forward.

DISCUSSION

- Early LSD/DPT work highlighted **connectedness** not captured by current tools, indicating the need for more nuanced social-relational metrics.
- Future work should directly address **complex forms of suffering** beyond anxiety and depression, analyze more specific subgroups.
- End-of-life distress is **multidimensional** (fear, meaninglessness, identity loss); different TPIs may target different aspects.
- Different substances are framed through different research traditions (e.g., ketamine = biomedical, LSD = psychospiritual, psilocybin = mixed models), which shape how mechanisms are described across studies.

CURRENT ISSUES

- Terminology inconsistent.
- No clear thresholds for physical vs. psychological severity.
- Under-reporting obscures true risk profile.
- No single model of psychedelic care; approaches vary widely. Unclear which elements drive improvement.

WHAT'S NEEDED



Standardized Reporting Framework:

- Challenging vs. adverse events
- Severity levels
- Role of set/setting, preparation, and clinician factors

Consistent Reporting:

- Mechanisms of action hypothesized and how it guides model of care
- Intervention components
- Outcomes (across biopsychosocial-spiritual domains)
- Challenging/adverse events



REFERENCE

**A scoping review of variations
among psychedelic interventions
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**Kratina, S., Strike, C., Schwartz, R., Nayfeh,
A., Jopling, S., Lo, C., & Rush, B. (2025).**

**Social Science and Medicine Journal
(Pre-Proof)**



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