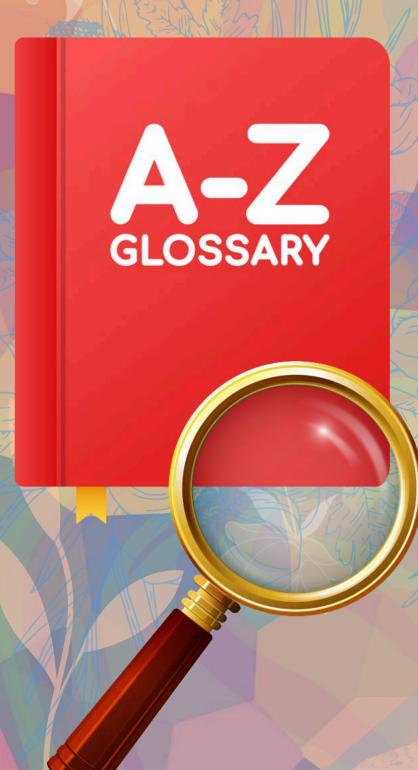
PSYCHEDELIC RESEARCH SNAPSHOT

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



KEY DEFINITIONS



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
- ketamine-based studies (25% LSD, 24% psilocybin, 5% DPT, 3% MDMA, 2% ayahuasca)
- 12% RCTs (most studies were uncontrolled experiments, 43% of RCTs were psilocyin-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 60s-80s outcomes)
- ketamine (affective + clinical outcomes) '07-'18
 + psilocybin (most comprehensive outcomes)
- 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 for psychological suffering associated with the end of life

Kratina, S., Strike, C., Schwartz, R., Nayfeh, A., Jopling, S., Lo, C., & Rush, B. (2025).

Social Science and Medicine Journal (Pre-Proof)

