

New Meta-Analytic Results Informing a Prospective Trial of Psilocybin for Cancer-Related Existential Distress

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Request for Proposals Psychedelics

Abstract: Objective: Terminal cancer patients experience profound existential distress, significantly impairing their quality of life. This study presents new meta-analytic findings on the effectiveness and safety of psilocybin-assisted therapy for alleviating cancer-related existential distress. By synthesizing data from prior trials, this research provides critical insights to guide the design of a prospective clinical trial, marking a step in advancing therapeutic options for terminally ill patients.

Methods: A comprehensive search of MEDLINE, APA PsycINFO, Cochrane database, Embase, and Scopus was conducted from inception to August 26, 2024 to identify randomized controlled trials (RCTs), open-label trials, qualitative studies, and case reports evaluating psilocybin for cancer-related distress. Quantitative data were pooled using a random-effects meta-analysis to calculate standardized mean differences (SMDs). Heterogeneity was assessed using the I^2 statistic, and subgroup analyses were performed to compare RCTs with open-label trials. Qualitative data were thematically analyzed to capture patient-centered experiences. Study quality was evaluated using the Cochrane Risk of Bias tool for RCTs and the Methodological Index for Non-Randomized Studies (MINORS) criteria. The study was registered with PROSPERO (CRD42024511692).

Results: Fourteen studies met the inclusion criteria, comprising three RCTs, five open-label trials, five qualitative studies, and one case report. The meta-analysis revealed significant reductions in depression (pooled SMD: -3.08, 95% CI: -10.34, 4.17, $I^2=94.8\%$) and anxiety (pooled SMD: -1.74, 95% CI: -16.86, 13.38, $I^2=96.5\%$) at early evaluation (~3 weeks). At late evaluation (~6 months), pooled effect sizes for depression (-3.39, 95% CI: -34.69, 27.90, $I^2=95.9\%$) and anxiety (-3.22, 95% CI: -36.03, 29.59, $I^2=96.0\%$) also demonstrated substantial heterogeneity. Subgroup analysis showed larger effect sizes in open-label trials than RCTs, with significant differences in depression ($p<0.001$) and anxiety ($p<0.001$). Psilocybin therapy demonstrated improvements in psychological and existential distress, with mild, transient adverse effects. Thematic analysis revealed psilocybin fostered existential relief and enhanced emotional and spiritual well-being. Participants had increased self-compassion, acceptance of mortality, and a deeper sense of meaning to life.

Conclusion: This study presents new meta-analytic findings on psilocybin-assisted therapy for

cancer-related existential distress, demonstrating its potential to reduce depression and anxiety while enhancing emotional well-being. Despite high heterogeneity, analyses revealed themes of existential relief and deeper life meaning. These findings are directly informing the development of our own prospective pilot clinical trial at our cancer center, designed to investigate psilocybin therapy in advanced cancer patients with severe existential distress, aiming to improve their quality of life.

Learning Objectives:

Learning Objective 1 Understand the effectiveness of psilocybin therapy for reducing cancer-related distress.

Learning Objective 2 Recognize key outcomes, such as existential relief and enhanced emotional well-being.

DISCLOSURE

Financial Relationships

Disclosure No, I have nothing to disclose.