

Critical Review

The Role of Psilocybin-Assisted Psychotherapy to Support Patients With Cancer: A Critical Scoping Review of the Research

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Treatments for addressing psychiatric mental health issues in vulnerable patients with cancer are established. Yet, many patients persist with unrelenting psychological difficulties despite intervention. There is growing interest in the role of psilocybin-assisted psychotherapy for managing treatment-resistant mental health challenges in patients with cancer. Psilocybin is a naturally occurring compound derived from certain mushroom species that can induce entheogenic experiences or an altered state of consciousness. Reed's Self-Transcendence Theory provides a holistic lens to examine existential concerns and mental health in individuals who perceive their illness as potentially life threatening, such as those with cancer. This scoping literature review used Arksey and O'Malley's template to evaluate research examining psilocybin-assisted psychotherapy for patients with cancer. Eight articles met inclusion/exclusion criteria (four quantitative, two mixed methods, and two qualitative). Review findings indicated that the majority of patient experiences were positive, centering on themes of death acceptance, reflection, and broadened spirituality. Although psilocybin-assisted psychotherapy is in early stages of clinical testing, it thus shows promise for carefully screened patients with cancer who have persistent existential suffering. It will be critical for investigators to tailor this emerging intervention to select patients and for clinicians to be engaged in assessment of outcomes and efficacy.

Keywords: *cancer; psilocybin-assisted psychotherapy; anxiety; depression; existential concerns*

Introduction

Cancers are the second leading cause of death internationally with about 17 million people newly diagnosed yearly (Brant & Silbermann, 2021). A diagnosis of cancer and its associated treatment is a significant stressor that heightens the potential for psychological problems. The growth of integrative oncology resources has improved self-management options for mental health care. Yet, many individuals persist with unrelenting psychological suffering.

Poor mental health in patients with cancer has been associated with adverse health outcomes, including reduced survival and quality of life, along with

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greater symptom burden and even nonadherence to treatment (Lehto et al., 2018). Given persistent problems associated with treatment-resistant anxiety and depression among patients with cancer, there is a heightened need for new approaches. One potential strategy is psilocybin-assisted psychotherapy. Psilocybin is a naturally occurring compound derived from certain mushroom species that when ingested can induce entheogenic experiences. For this article, “entheogenic” is defined as an altered state of consciousness for spiritual purposes. It is important that nurses, as part of the interdisciplinary health team, are knowledgeable about ongoing research regarding such adjunct therapies as awareness of their impact expands (Penn, 2021). Therefore, a critical review using a scoping methodology was conducted to examine research evaluating psilocybin-assisted psychotherapy to address existential issues affecting mental health in patients with cancer.

Background and Significance

It is estimated that 25%–30% of patients with cancer meet criteria for a psychiatric disorder in spite of diligent clinical expertise in managing ongoing psychological distress (Grassi et al., 2017). Anxiety and/or depressive disorders in patients with cancer often include underlying existential components, which can be challenging to address and can even be overlooked in a medicalized approach (Bauereiß et al., 2018; Karlsson et al., 2014). Existential concerns may reflect an individual’s struggle to find meaning, purpose, and value with living and may coincide with a loss or lack of spiritual well-being (Johnson et al., 2021). It is established that many cancer patients with anxiety and/or depressive disorders derive symptom improvement from traditional psychotherapeutic options, including pharmaceutical agents, cognitive-behavioral interventions, psychotherapy, supportive-existential interventions, and integrative therapies—such as mindfulness meditation (Grassi et al., 2017). Notwithstanding these advances, however, many patients with cancer either do not respond to clinical interventions for ongoing depression and anxiety or they experience a relapse of symptoms. Furthermore, a diagnosis of cancer places high demands on the long-term coping capacity of individuals in their treatment trajectory, potentially comprising of active treatment, remission and cure, disease recurrence, and end of life (Grassi et al.,

2017). Given the limits of traditional psychotherapies for some patients, there has been an increased integration of complementary modalities that incorporate spiritual practices to augment established approaches to improve mental health. Such approaches provide opportunities to seek meaning and purpose from life experiences and to experience deeply personal connections with self, others, nature, and the sacred (Bossis, 2021).

Spirituality is a unique experience for each individual and has been associated with feelings and experiences that connect the individual to a sacred source, or an awareness of the infinite with awe (Johnson et al., 2021). Spiritual encounters can result in enhanced connection, heightened awareness, acceptance, and capacity to express humanness, and are thus frequently associated with healing (Johnson et al., 2021). When patients are distressed by psychological symptoms, it can be difficult to tap into their spiritual resources. One way to facilitate access to spiritual support is through psilocybin-assisted therapy. This type of psychotherapy can induce personally relevant spiritual experiences that are highly individualized. Such experiences hold promise for the advancement of mental health resources among people with cancer (Bossis, 2021).

Psilocybin is a compound derived from psilocybe mushroom species that can induce altered consciousness experiences, especially when ingested in a controlled supportive environment with the intention to heal. The ingestion of psilocybin in a therapeutic context has been associated with mystical experiences that increase perceived wellbeing and elicit personal transformative encounters among people with cancer (Griffiths et al., 2018).

Ancient cultures have used plants and fungi capable of inducing altered states of consciousness (ASC) for healing, rituals and rites, and death-rebirth experiences throughout recorded history (Doyle, 2012; Rosa et al., 2019; Schultes & Hoffman, 1979). Termed entheogenic, these plants and fungi can alter neurocognitive mechanisms leading to experiences of self-transcendence, reduction of egocentric concerns, and heightened freedom that broadens perspectives and fosters development of awe and wonder for life (Nichols, 2020). During the 1950s and 1960s, investigators began to uncover the potential of psychedelic-assisted therapies to ease mental health concerns and existential suffering (Kast, 1966; Kurland et al., 1972). Although much of this research elicited promising results, the concurrent nonmedical use of

psychedelics and associated political and cultural upheavals brought about an abrupt ban on this research for years (Byock, 2018).

The recent expansion of interest in this area warrants an update given an increasing number of studies exploring the application of psilocybin-assisted therapy in healthcare (McCorvy et al., 2016; Watts et al., 2017). Studies evaluating the efficacy of psilocybin for managing treatment-resistant depression have also shown promising findings (Watts et al., 2017). In an open-label clinical trial that was conducted in England, participants reported enhanced mental health at 6 months follow-up (Watts et al., 2017). Participants have indicated that psilocybin augmented their perceptions of connection and of open acceptance of life, a mechanism that contributed to lowered depression (Watts et al., 2017). Clinicians and researchers engaged in psychedelic-assisted therapy have emphasized the importance of screening, trained supervision, and carefully considered environments by which to conduct the treatments in order to reduce risks and enhance positive outcomes from this therapy (Byock, 2018). These same mechanisms could potentially be helpful for people with advanced cancer, and the literature examining such applications is growing.

Theoretical Underpinnings

The Theory of Self-Transcendence provides a framework for understanding and facilitating integration of human issues associated with living, growing older, and the inevitability of death. The theory posits that self-expansion via adoption of transformative perspectives provides an avenue for the individual to place life's challenges into a meaningful structure that supports wellbeing and a holistic sense of connectedness and unity. Broadening perspectives via boundary expansion can support the development of a mature approach to accepting death, a heightened appreciation for life, and the unknown. In nursing, Reed (2018) identified self-transcendence as a vital capacity for mental health and developmental adaptation when faced with vulnerability such as life-threatening illness and/or mortality confrontation. Thus, self-transcendence emphasizes both wellbeing and vulnerability. Wellbeing is defined as a sense of wholeness and health in relation to one's own perceptions. Indicators of wellbeing include hopefulness, sense of meaning, self-positivity, and satisfaction

with life. Vulnerability in the self-transcendence model refers to the personal awareness of death and/or painful life events that can be invoked by challenges such as illness, disability, loss and grief, aging, and other serious life events (Reed, 2018). Given the essential nature of the themes of self-transcendence, wellbeing, and vulnerability to spiritual growth and their strong relevance to patients with cancer facing the end of life, Reed's theory is compelling from a holistic nursing perspective, prompting an evaluation of what is known about psilocybin-assisted therapy to support patients with cancer who resist traditional treatment modalities.

While attention to the use of psychedelic-assisted therapy for alleviating mental health problems has shown resurgence, limited nursing inquiry has been conducted. It has been pointed out that there is a pressing need for evaluating new strategies to alleviate psychological suffering among patients with cancer who persist with unrelieved mental health distress (Lehto et al., 2018; Grassi et al., 2017). For patients with cancer, additional therapeutic approaches are needed that address personalized fears associated with death and dying, and to place the cycle of life in a context that makes sense (Karlsson et al., 2014). Furthermore, therapies that build the capacity for distressed individuals to widen their spiritual lens and that carry the potential to alleviate existential angst may produce mental health benefits beyond established approaches (Johnson et al., 2021). The need for novel treatments for anxiety, depression, and existential distress among people with cancer leads researchers to evaluate the state of the science relative to psychedelic-assisted psychotherapy as a viable intervention.

Purpose

Using a self-transcendent lens, the purpose of this critical scoping literature review was to evaluate the state of the science relative to the use of psilocybin-assisted psychotherapy to improve the mental health patients with cancer who may be experiencing existential concerns.

Methods

Arksey and O'Malley's (2005) template for conducting a scoping review to depict the state of the science was used. Scoping reviews are a valuable methodology for guiding an appraisal of research

literature in areas that have not been comprehensively evaluated in relation to a phenomenon and are more broad and inclusive than systematic reviews (Arksey & O'Malley, 2005). The Preferred Reporting Item for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews (PRISMA-ScR) methodology was used to organize the search and to identify the research ultimately used for the scoping review (Liberati et al., 2009; Tricco et al., 2018; Figure 1). The PRISMA-ScR checklist was also used to enhance methodologic rigor and reporting of this review (Tricco et al., 2018). The five stages articulated by Arksey and O'Malley (2005) to evaluate the research around a specific area comprise—stage 1: identifying the research question and eligibility criteria; stage 2: identifying relevant publications; stage 3: selecting publications; stage 4: charting the data; and stage 5: collating, summarizing, and reporting the results.

Stage 1: Identifying the Research Question and Eligibility Criteria

The aim of this review was to determine the state of the science relative to the evaluation of psilocybin-assisted psychotherapy for addressing mental health symptoms and existential concerns among vulnerable patients facing cancer. Inclusion criteria were studies published in English that included patients with cancer as the study sample and evaluated the use of psilocybin-assisted therapy to improve mental health outcomes. Exclusion criteria were articles that focused on (1) psychiatric diagnoses that were unrelated to mental health and cancer; (2) other hallucinogenic substances, such as lysergic acid diethylamide; (3) study protocols; (4) noncancer patient populations, including healthy samples; (5) commentaries; (6) provider focus and attitudes; (7) effects from usage such as mysticism; and (8) medication or bio-pharmacy mechanisms.

Stage 2: Identifying Relevant Publications

The literature search was led by a health sciences librarian. Databases included CINAHL, PsycINFO Web of Science, Cochrane, and PubMed databases. For PubMed, the MeSH headings “Psilocybin”[Mesh] and “Neoplasms”[Mesh] were used and searched with associated keywords. In CINAHL, subject

headings were used when available, along with associated keywords. Searches were duplicated and consistent across all databases. The following search combinations were used: (“Psilocybin”[Mesh] OR psilocybin) AND (Cancer* OR “Neoplasms”[Mesh] OR neoplasm* OR oncolog* OR tumor OR maligna* OR “cancer patient” OR “cancer patients”). Psilocybin AND (Cancer* OR oncolog* OR tumor* OR maligna* OR neoplasm* OR “cancer patient*” Or (MH “Neoplasms”) OR (MH “Cancer Patients”) OR (MH “Oncology”). Manual searching was also conducted following the database search, during which reference lists of relevant reviews and original studies were screened. Searches were conducted in March 2020 and updated in June 2021 to identify relevant research published from 2000 to the present.

Stage 3: Selecting Publications

A total of 343 articles were retrieved from database searching and 16 were retrieved through hand searching. The search yielded both qualitative and quantitative studies, commentary papers, and reviews. After removal of duplicates, 222 records remained. Of the remaining articles, 76 were deleted based on titles that indicated a lack of relevance, an additional 57 following abstract review, and 81 papers following screening of the full texts. Exclusions occurred primarily due to a focus on other populations, such as psychiatric mental health and addiction emphasis, or due to being nonresearch studies. After completing the screening process, eight articles were identified as meeting the established criteria and were thus included in the review. Consensus was achieved by discussion after independent evaluation of the reviewed articles by the authors. Rationales for determining article exclusion are provided in Figure 1.

Stage 4: Charting the Data

A data charting form was developed including columns for (a) author name and date, (b) sample, (c) study design, (d) assessment, (e) intervention, and (f) key findings. This standardized information was extracted from each publication using a descriptive analytical method. The quality of evidence was not appraised, as is the standard practice among scoping reviews (Arksey & O'Malley, 2005).

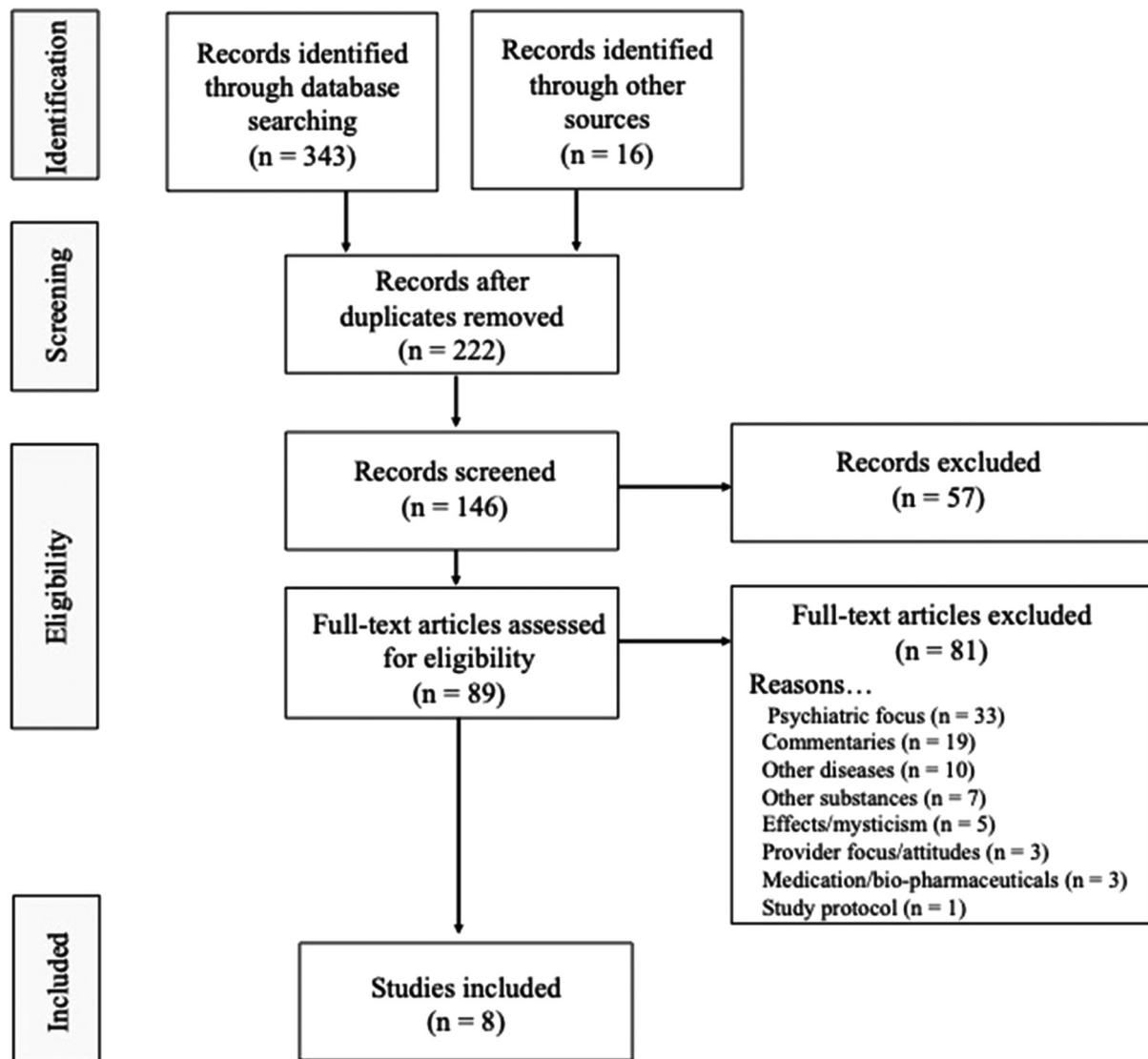


Figure 1. Preferred Reporting Item for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews diagram of search strategy.

Stage 5: Collating, Summarizing, and Reporting the Results

Table 1 depicts information relative to the eight articles in this review. Participants in the studies included patients with cancer who experienced anxiety, depressive symptoms, and adjustment and/or depressive disorders. Of the eight articles, there were four quantitative, two qualitative, and two mixed methods studies. Participants in six of the included studies were part of research conducted by a national team of researchers housed at New York University led by Dr. Stephen Ross. This team is currently evaluating the use of psilocybin-assisted therapy to alleviate mental health distress for patients

with cancer. The other two studies were randomized double-blind pilot studies led by other research teams (Griffiths et al., 2016; Grob et al., 2011).

Sample sizes across the included studies ranged from 4 to 51 participants. All of the studies included patients with cancer who were experiencing mental health symptoms of anxiety and/or depression, or adjustment disorders. All studies followed a similar procedure, including preparatory sessions, psilocybin-assisted therapy, and follow-up integration sessions, which were supported by well-trained psychedelic-assisted therapists.

Quantitative studies (n = 4): One quantitative study was a feasibility/acceptability pilot with 12 participants (Grob et al., 2011). Two were randomized

Table 1. Studies Included in the Review.

Publication	Sample	Design	Assessment	Intervention	Key findings
Agin-Liebes et al. (2020)	N=15 patients with cancer, an average of 3.2- and 4.5-year following psilocybin administration; 25–73 years; (mean = 52); 60% female; 93.33% non-Hispanic White. At enrollment of the initial study, all met criteria for cancer-related adjustment disorder with anxious and/or depressed features or anxiety disorder	Mixed methods; long-term follow-up from initial study (Ross et al., 2016). Quantitative measures along with qualitative interviews, written narratives, and clinician notes from a double-blind controlled trial	Long-term follow-up from the initial psilocybin study (Ross et al., 2016). Follow-up points were at mean 3.2 years and mean 4.5 years. <ul style="list-style-type: none"> The Hospital Anxiety and Depression Scale (HADS) Beck Depression Inventory (BDI)-II State-Trait Anxiety Inventory (STAI) Death Anxiety Scale (DAS) Hopelessness Assessment in Illness (HAI) Demoralization Scale (DS) World Health Organization Quality of Life-Brief Version (WHOQOL-BREF) Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being (FACIT-Sp-12) Persisting Effects Questionnaire (PEQ) Mystical Experience Questionnaire (MEQ-30) 	Single-dose psilocybin (0.3 mg/kg) or niacin, both in conjunction with psychotherapy. Reported findings are from mean 3.2 and 4.5 years postintervention	<ul style="list-style-type: none"> Reductions in anxiety, depression, hopelessness, demoralization, and death anxiety were sustained at the first and second follow-ups. Within-group effect sizes were large At the second (4.5 year) follow-up approximately 60%–80% of participants met criteria for clinically significant antidepressant or anxiolytic responses Participants overwhelmingly (71%–100%) attributed positive life changes to the psilocybin-assisted therapy experience and rated it among the most personally meaningful and spiritually significant experiences of their lives
Belser et al. (2017)	N=13 patients with clinically elevated anxiety associated with cancer diagnosis; 22–69 years (mean = 50); 46% female; 92% white; projected life expectancy of	Qualitative study of participant experiences in psilocybin-assisted psychotherapy	<ul style="list-style-type: none"> Semi-structured interviews using interpretative phenomenological analysis 	Moderate dose of psilocybin and adjunctive psychotherapy with an emphasis on the process of meaning-making	<ul style="list-style-type: none"> General themes found in all or nearly all transcripts: relational embeddedness, emotional range, the role of music as conveyor of experience, meaningful visual phenomena, wisdom lessons, revised life priorities, and a

(continued)

Table 1. (continued)

Publication	Sample	Design	Assessment	Intervention	Key findings
	at least 1 year; stages I–IV; varied cancer types; high education levels				<p>desire to repeat the psilocybin experience</p> <ul style="list-style-type: none"> • Typical themes found in the majority of transcripts: exalted feelings of joy, bliss, and love; embodiment; ineffability; alterations to identity; a movement from feelings of separateness to interconnectedness; experiences of transient psychological distress; the appearance of loved ones as guiding spirits; and sharing the experience with loved ones posttreatment • Variant themes found in a minority of participant transcripts: lasting changes to sense of identity, synesthesia experiences, catharsis of powerful emotion, improved relationships after treatment, surrender or “letting go,” forgiveness, and a continued struggle to integrate experience
Griffiths et al. (2016)	N = 51 cancer patients with life-threatening diagnoses and/or symptoms of depression and/or anxiety; mean = 56.3 years; 49% female; 94% white; 65% recurrent or metastatic disease; varied cancer types; high education levels	Randomized double-blind, crossover trial	<p>Participants, staff, and community observers rated participant moods, attitudes, and behaviors throughout the study</p> <ul style="list-style-type: none"> • Blood pressure (BP)/heart rate (HR) • Monitor Rating Questionnaire • Hallucinogen Rating Scale (HRS) • 5-Dimension Altered States of Consciousness (5D-ASC) • Mysticism Scale (experience-specific 9-point scale) • States of Consciousness Questionnaire (SOCQ) • MEQ-30 • GRID-Hamilton Depression Rating Scale (GRID-HAM-D-17) 	<p>Very low (placebo-like) dose (1 or 3 mg/70 kg) versus a high dose (22 or 30 mg/70 kg) of psilocybin administered in counterbalanced sequence with 5 weeks between sessions and a 6-month follow-up</p>	<ul style="list-style-type: none"> • Large decreases in clinician- and self-rated measures of depressed mood/anxiety, increases in quality of life, meaning and optimism, decreases in death anxiety • At 6-month follow-up, changes were sustained, with ~80% continuing to show clinically significant decreases in depressed mood/anxiety • Participants attributed improvements in attitudes about life/self, mood, relationships, and spirituality to the high-dose experience, with >80% endorsing moderately or greater increased wellbeing/life satisfaction • Community observer ratings showed corresponding changes • Mystical-type psilocybin experience on session day mediated the effect of psilocybin dose on therapeutic outcomes

(continued)

Table 1. (continued)

Publication	Sample	Design	Assessment	Intervention	Key findings
Grob et al. (2011)	N=12 patients with advanced stage cancer and anxiety; 36–58 years; 92% female; varied cancer types	Double-blind, placebo-controlled pilot study	<ul style="list-style-type: none"> • Hamilton Anxiety Rating Scale (HAM-A) • BDI • HADS • STAI • Profile of Mood States (POMS) • Brief Symptom Inventory (BSI) • McGill Quality of Life (MQOL) • Life Orientation Test-Revised (LOT-R) • Life Attitude Profile-Revised (LAP-R)—Death Acceptance • LAP-R-Coherence • Death Transcendence Scale (DTS) • Purpose in Life (PIL) Test • Safety/efficacy assessments • BDI • POMS • STAI • Brief Psychiatric Rating Scale (BPRS) • 5D-ASC 	Moderate dose (0.2 mg/kg) of psilocybin	<ul style="list-style-type: none"> • No clinically significant adverse events • STAI trait anxiety subscale demonstrated a significant reduction in anxiety at 1 and 3 months after treatment • BDI revealed an improvement of mood that reached significance at 6 months • POMS identified mood improvement after treatment with psilocybin that approached but did not reach significance
Malone et al. (2018)	N=4 patients with cancer-related anxiety and depression; 20–60 years; 50% female; varied cancer types and stages; 100% white; high education levels; subset of participants from a larger quantitative study	Mixed methods; quantitative measures along with qualitative interviews, written narratives, and clinician notes from Ross et al., double-blind controlled trial (case reports)	<ul style="list-style-type: none"> • In-depth qualitative interviews • Clinician notes • HADS • BDI • STAI 	Single-dose psilocybin (0.3 mg/kg) or niacin in conjunction with psychotherapy	<ul style="list-style-type: none"> • Personal narratives extended beyond cancer diagnosis itself, frequently revolving around themes of self-compassion and love, acceptance of death, and memories of past trauma • Specific details or narrative content differ substantially • Results demonstrate the personalized nature of subjective experiences elicited through treatment with psilocybin, particularly with respect to spiritual/psychological needs of each patient

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Table 1. (continued)

Publication	Sample	Design	Assessment	Intervention	Key findings
Ross et al. (2021)	N = 11 patients with cancer-related anxiety and depression; 48–71 years (mean = 60.3); 63.6% female; varied cancer types and stages; 90.9% white; relatively high education levels; subset of participants from a larger quantitative study	Secondary analysis of data from a double-blind, placebo-controlled, crossover trial (Ross et al., 2016)	<ul style="list-style-type: none"> A composite score representing Suicidal Ideation with items from the BDI-II and the BSI DS BDI-II Hopelessness HAI FACIT-Sp-12 	Single-dose psilocybin (0.3 mg/kg) or niacin, both in conjunction with psychotherapy	<ul style="list-style-type: none"> Psilocybin-assisted psychotherapy produced rapid and sustained improvements in depression, demoralization, and hopelessness Psilocybin-assisted psychotherapy may be an effective anti-suicidal intervention following cancer diagnoses, due to positive impacts on hopelessness, demoralization, and meaning-making Preliminary results indicate that psilocybin treatment is a potentially effective alternative to existing antidepressant medications in patients with cancer who are suicidal. Further investigation among patients with elevated levels of depression and suicidality is warranted
Ross et al. (2016)	N = 29 patients with cancer-related anxiety and depression; 22–75 years (mean = 56.3); 62% advanced cancer; varied cancer types; 62% female; 90% white; high education levels	Double-blind, placebo-controlled, crossover trial	<ul style="list-style-type: none"> Adverse event monitoring BP/HR HADS BDI STAI DS HAI DAS DTS WHOQOL-BREF FACIT-spiritual wellbeing MEQ-30 PEQ 	Single-dose psilocybin (0.3 mg/kg) or niacin, both in conjunction with psychotherapy	<ul style="list-style-type: none"> Prior to crossover, psilocybin produced immediate, substantial, sustained improvements in anxiety/depression and led to decreases in cancer-related demoralization and hopelessness, improved spiritual wellbeing, and increased quality of life At 6.5-month follow-up, psilocybin was associated with enduring anxiolytic and antidepressant effects (approximately 60–80% of participants continued with clinically significant reductions in depression or anxiety), sustained benefits in existential distress and quality of life, and improved attitudes towards death The psilocybin-induced mystical experience mediated the therapeutic effect of psilocybin on anxiety and depression
Swift et al. (2017)	N = 13 patients with clinically elevated anxiety associated with a	Qualitative study of participant	Semi-structured interviews,	The original quantitative study employed a double-blind, crossover,	<ul style="list-style-type: none"> 10 themes, focused specifically on

(continued)

Table 1. (continued)

Publication	Sample	Design	Assessment	Intervention	Key findings
	cancer diagnosis; 18–69 years (mean = 50); 46% female; 92% white; varied types and stages of cancer; high education levels	experiences in psilocybin-assisted psychotherapy	interpretative phenomenological analysis	placebo-controlled design (psilocybin 0.3 mg/kg or the active placebo, niacin 250 mg) to evaluate efficacy of psilocybin and adjunctive psychotherapy	<p>cancer, death and dying, and healing narratives</p> <ul style="list-style-type: none"> Participants spoke of: the anxiety and trauma related to cancer and perceived lack of available emotional support; immersive and distressing effects of the psilocybin session, which led to reconciliations with death, an acknowledgment of cancer's place in life, and emotional uncoupling from cancer; spiritual or religious interpretations of their experience; psilocybin therapy helped facilitate a felt reconnection to life, a reclaiming of presence, and greater confidence in the face of cancer recurrence

double-blind trials with 51 (Griffiths et al., 2016) and 29 participants (Ross et al., 2016), respectively. The fourth quantitative study was a secondary data analysis (Ross et al., 2021).

Three of the reviewed studies incorporated a randomized trial design (Griffiths et al., 2016; Grob et al., 2011; Ross et al., 2016). The earliest study (Grob et al., 2011) conducted at University California Los Angeles evaluated 12 patients with advanced stage cancer who had a psychiatric clinical diagnosis of adjustment anxiety disorder related to the cancer diagnosis. A crossover design was used so that all 12 participants randomly received either the psilocybin dosing of 0.3 mg/kg or niacin at one of two experimental sessions. Each session was 6 hr in duration with the research personnel in attendance during the entire encounter. Follow-up continued for 6 months following study participation.

The Griffiths study conducted at John Hopkins University also used a crossover design with 51 patients with clinically diagnosed cancer-related anxiety, adjustment, mixed anxiety/depression, or major depressive disorder. Of these patients, 65% had either recurrent or metastatic cancers of mixed types. The study evaluated a single higher dosage of psilocybin (0.31 mg/kg) in comparison with an active control (low-dose of psilocybin 1 or 3 mg/70 kg) to determine its efficacy, when combined with therapy, in relieving cancer-related anxiety or depression. Participants who were randomized to receive the higher psilocybin dose demonstrated rapid and sustained significant improvements in their anxiety and depressive symptoms related to their cancer diagnoses as compared to those individuals receiving lower dosages. The reduction in anxiety and depressive symptoms was clinically and statistically significant over time.

Ross and his research team at New York University evaluated a single dose of psilocybin (0.3 mg/kg) compared to a 250 mg dose of niacin as a part of psychotherapy in a crossover study for 29 patients with cancer who had been clinically diagnosed with anxiety or adjustment disorders (Ross et al., 2016). This study also found improvements in anxiety and depressive symptoms secondary to psilocybin-assisted therapy, which were most apparent in the participants who were initially randomized to receive the psilocybin first (prior to the crossover to niacin as the second dose). The study also reported robust responses to these symptoms at the 6-month follow-up with improvements maintained in the majority of the sample. A second study conducted a longer-term

follow-up with 15 participants who remained alive and willing to participate 3.2–4.5 years following participation in the psilocybin-assisted psychotherapy study (Agin-Liebes et al., 2020). The findings showed significant sustained benefits over time from participation in psilocybin-assisted psychotherapy across multiple mental health parameters, including reduced anxiety, hopelessness, depression scores, demoralization, and death anxiety, along with improved perceived spiritual wellbeing (Agin-Liebes et al., 2020). The Malone and colleagues study (2018) provided case reports on four participants from the Ross study (2016) and included both individual survey data and semi-structured interview reports. And finally, Ross et al. (2021) reported on a secondary data analysis using a subset of data from a prior double-blind, placebo-controlled, crossover trial (Ross et al., 2016). This secondary analysis found that psilocybin-assisted therapy acutely relieved suicidal ideation and loss of meaning, changes that were apparent as early as 8 hr postdosing and persisted for 6.5 months (Ross et al., 2021).

Qualitative (n = 2): The two qualitative studies reported findings from the same 13 participants (Belser et al., 2017; Swift et al., 2017). Participants participated in in-depth semi-structured interviews (Belser et al., 2017; Swift et al., 2017). Participants (n = 13) appeared to be the same in both the Belser and Swift studies but with different approaches employed to evaluate the study transcripts.

The Belser study evaluated the perceptions and reported experiences that occurred during the psilocybin-assisted psychotherapy utilizing an interpretive phenomenological analysis. Major themes that were identified included feelings of joy, bliss, love, and transient psychological distress. Participants reported feeling less alienated and more interconnected. Perceptions of heightened meaning, wisdom, deeper relatedness, acceptance, forgiveness, emotional release, and positive visual phenomena such as appearances of guiding spirits occurred (Belser et al., 2017).

The Swift and associates (2017) study evaluated the cancer, death and dying, and healing narratives described in the semi-structured interviews to determine psychological mechanisms of action for how psilocybin-assisted psychotherapy led to transformative changes in the psyche. It was noted that participants interpreted their experiences from a religious and/or spiritual perspective, and that the experience fostered a deepened sense of connectedness to life (Swift et al., 2017). The psilocybin journey helped

patients reconcile and face the alienating traumatic and distressing experience of cancer and the realness of death (Malone et al., 2018). Participants derived heightened confidence to face and be present with their life experience, including their diagnosis and management of cancer.

Mixed methods (n = 2): The first mixed methods study (Agin-Liebess et al., 2020) provided information on long-term follow-up of 15 patients who participated in the randomized trial (Ross et al., 2016) that was previously described. The second mixed methods study (Malone et al., 2018) included four participants who had participated in the Ross and colleagues (2016) randomized trial.

Measures: A wide range of instruments was used in the quantitative and mixed methods studies (see Table 1). Traditional measures used to evaluate study outcomes included standardized anxiety and depression measures, and quality of life parameters (Agin-Liebess et al., 2020; Griffiths et al., 2016; Grob et al., 2011; Malone et al., 2018; Ross et al., 2016). Other surveys included in these quantitative studies composed of Mystical Experience Questionnaires, Spirituality, ASC, Death Transcendence, and Hallucinogen Rating Scale. Many of these instruments have been used in previous research and have established psychometric qualities. However, only one study reported the reliability indices for the current study (Agin-Liebess et al., 2020).

Findings from the review suggest that psilocybin-assisted therapy was a positive experience for patients with cancer with preexisting mental health challenges such as depression, anxiety, and adjustment disorders. Psilocybin-assisted therapy appears to be safe among these carefully screened samples of patients, with no reported serious adverse effects from study participation. Sample sizes were small, and evidence was gleaned from the same participants for different studies. All studies were conducted in the United States. Strengths of the studies include use of both quantitative and qualitative methodologies to glean information on intervention outcomes. Importantly, the reductions in mental health symptoms were sustained over time, indicating the long-term effects of the derived benefits with a single dose. If such efficacious results were replicated in larger and more diverse representative samples, the intervention would carry potential to improve the lives for the large numbers of patients with cancer who have treatment-resistant mental health symptoms.

Discussion

This scoping review evaluated the state of the science related to the use of psilocybin-assisted psychotherapy to improve mental health symptoms and address existential concerns among patients facing cancer from a self-transcendent perspective. Findings from the review demonstrated that across studies, a single session of psilocybin-assisted therapy was safe and acceptable. Psilocybin-assisted therapy was found to modify depression and anxiety symptoms, sustained at 6 months and 3.2- and 4.5-year posttreatment (Agin-Liebess et al., 2020; Griffiths et al., 2016). Importantly, the research in this area remains in its early stages with small and nondiverse samples. However, for patients with terminal illness who may have limited time left to live, the expedience of engaging in transformative psychological experiences that enhance personal wellbeing and promote integration of difficult psychological material could be a positive factor when considering the role of psilocybin-assisted therapy as an adjunct to standard treatment.

Participants reported varying personalized accounts centered on death acceptance, reflection, resolution of life traumas, and enhanced spiritual perspectives. These individual testimonies suggest that the psilocybin experience assisted with expansion of self-boundaries in line with Reed's theoretical perspective. Findings from the review support the premise that mental health issues among people with cancer can have deep existential components. By addressing spiritual and existential issues, mental health may be improved. These findings expand possibilities for mental health strategies among patients with cancer relative to more fully addressing spiritual and existential concerns.

It is recognized that spirituality, including religiosity, can be associated with increased perceived meaning and quality of life for patients facing cancer (Flanigan et al., 2019). Participants in these studies indicated that psilocybin-assisted therapy was one of the most significant and spiritually meaningful experiences of their lives (Agin-Liebess et al., 2020). An increasing literature has documented that for many patients, the experience of having cancer can lead to posttraumatic growth and contribute to a renewed sense of purpose and a heightened awareness of the importance of meaningful relationships and connectedness to life (Zhai et al., 2019). Psilocybin-assisted therapy allows patients with cancer an opportunity to

practice *being* with their difficult physical, emotional, and cognitive symptoms such as pain, distress, and lack of coherence, and to potentially reframe and even transcend these situations that are associated with ongoing suffering.

Nursing Implications

Interest in the factors contributing to the promotion and maintenance of physical and mental wellbeing during stressful conditions continues to evolve. Psilocybin as an adjunct to psychotherapy may find a therapeutic footing among patients with cancer who seek information about such therapeutics. It is essential that holistic nurses consider their own perceptions about the use of psilocybin as part of a treatment plan. Although the use and interest of such modalities are growing, many health care providers remain skeptical of these treatments. Nurses are in a position to provide evidence-based information to patients who may want to participate in research on psychedelic-assisted therapies. Nurses are well suited to serve as psychedelic-assisted therapy consultants, given the unique, holistic perspective nurses offer (Penn, 2021; Penn et al., 2021; Rosa et al., 2020) across domains of practice, ethics, research, advocacy, policy, and education (Denis-Lalonde, 2020). There has been recent discussion of the role of nursing in psychedelic-assisted therapy, and mounting evidence suggests that holistic nursing skills, knowledge, and values align closely with the necessary traits of a psychedelic-assisted therapist (Penn, 2021; Penn et al., 2021). Skills such as trust enhancement, presence, therapeutic communication of openness, mutual learning, self-care, optimizing therapeutic healing environments, and care of the physical body are each relevant to holistic nursing and psychedelic-assisted therapy (Penn et al., 2021). Optimal training methods must be developed for nurses who participate in psilocybin-assisted therapy, and general information about this therapy could be incorporated into nursing training programs so nurses are able to support patients in making decisions about accessing the therapy. Based on these findings, holistic nurses are encouraged to further explore psilocybin-assisted therapy research, to participate in conferences and training programs, and to explore ways to contribute unique perspectives to this growing field. However, additional theory-guided research is needed to systematically evaluate the real-world applications of this therapy.

There are potential resources available that nurses may access as science in this area expands. For example, the Multidisciplinary Association for Psychedelic Studies (MAPS) (<https://maps.org/>) is a research and educational organization that evaluates medical, legal, and cultural milieus for humans to potentially derive benefits from judicious applications of plant-derived substances, such as psilocybin. Furthermore, organizations such as the California Institute for Integral Studies (CIIS), Center for Psychedelic Therapies and Research, the Organization of Psychedelic and Entheogenic Nurses (OPENurses), and others offer opportunities for nurses to learn about and become involved in psychedelic-assisted therapy work (California Institute for Integral Studies, 2021; Organization of Psychedelic & Entheogenic Nurses, 2020).

Research Implications

Additional research is needed to evaluate which patients might benefit from psilocybin-assisted therapy and which established therapies are best to use in conjunction with psilocybin-assisted therapy. More evidence is needed on how to provide safe and effective access for people with cancer and how to best include and support individuals from diverse backgrounds. Thus, additional research is needed to examine unique therapeutic approaches that consider differences across race/ethnicity, gender, sexual orientation, age-developmental, socio-economic, levels of education and ability, physical abilities, cultural background, and religious preferences. Future research may also explore the efficacy of psilocybin-assisted therapy for grief management, including anticipatory grief among lay caregivers. Furthermore, research is needed to examine how participation in psilocybin-assisted therapy may impact end-of-life decisions and planning for patients with cancer.

On a broader scale, psychedelic-assisted therapy communities are grappling with how to expand access to these therapies in a way that is equitable and that maintains high standards of ethics and integrity; holistic nurses are well served to support these efforts. Although research on psilocybin-assisted therapy is in early stages, the results are promising. Adopting a self-transcendent approach to develop treatment modalities aimed at expanding self-boundaries, facing vulnerabilities, and fostering spiritual growth is central to holistic

nursing and appears to be compatible with a psilocybin-assisted approach.

Limitations

While this scoping review was broad and inclusive of available research on psilocybin-assisted therapy among people with cancer, limitations must be noted. First and foremost, most participants in the research presented were Caucasian and had attained relatively high levels of education. Despite the global nature of cancer and its effects on mental health adaptation, all studies were conducted in the United States; results cannot thus be extrapolated to other populations. Moreover, the reviewed research was primarily conducted and presented from a white, cis-gender, scientific perspective and does not include diverse ways of knowing. Considering that psilocybin mushrooms have been cultivated and ingested in ritual for many years across cultures, such reviews could be greatly expanded by broadening the cultural perspective. We suggest beginning to bridge this gap by establishing cross-cultural partnerships and considering community-based participatory methods for future research. While a broad expanse of literature was screened for this review, because of the vast and varied nature of this content, some studies may have been overlooked. Overall, this review supports the potential promise for psilocybin-assisted therapy as part of holistic cancer care, yet studies are early in their development and results must be interpreted with caution until further evidence is available.

Conclusions

Psychological symptoms remain common in patients with cancer, stimulating ongoing need to examine novel treatments to improve wellbeing among this vulnerable population. Given the spiritual and existential underpinnings of many mental health challenges for patients facing the cancer trajectory, frameworks such as the Self-Transcendence Theory that incorporate broad aspects of mental health are needed to guide intervention development. Psilocybin-assisted therapy remains in the early stages of clinical testing demonstrating early promise as a treatment for cancer-related psychological symptoms associated with adjustment such as depression and anxiety. It is essential that holistic

nurses and health care workers be informed on the state of the science regarding psilocybin-assisted therapy to assist patients who may seek information and to potentially become involved in the safe, ethical administration of this emerging treatment. Given the holistic nature of the nursing approach to patient-centered care, our discipline can contribute unique skills and insights in this growing field.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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