

RESEARCH ARTICLE

“To Have the Encounter with Our Own Finiteness in that Existential Way”: Descriptions of Existential Experience in Patients with Cancer and Major Depression Participating in Psilocybin-Assisted Group Therapy

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Abstract

Background: Cancer poses an existential threat for patients and caregivers. Psilocybin-assisted therapy (PAT) has emerged as a potential tool to meet these existential needs, yet little is known about how patients describe this element of their cancer journey, and how it might be affected by PAT, especially in the group therapy context.

Purpose: To explore how patients with cancer and depression describe their existential journey through the experience of cancer and group PAT.

Methods: Grounded in the Conceptual Model of Existential Experience in Adults with Advanced Cancer, this study is a qualitative analysis of existing data from semi-structured exit interviews with participants ($n = 28$) of the psilocybin trial, “The Safety and Efficacy of Psilocybin in Cancer Patients with Major Depressive Disorder” (NCT04593563). This study uses a qualitative descriptive approach paired with template analysis to analyze interview transcripts.

Results: Our analysis revealed three overarching themes: (1) Participants described cancer prompting a deepened lived understanding of their mortality, as well as a re-prioritization of their attention, relationships, and efforts; (2) Therapeutic intentions for participating in the PAT trial went beyond relief of depression and extended to gaining a new perspective toward existential worries and building spiritual resources; (3) Participants described the lasting effects of PAT as a healing, unfolding transformation, noting an enhanced sense of meaning, agency, aliveness, and connectedness.

Discussion: Our findings provide important insights into the existential experiences of people with cancer and depression, as well as the potential role of PAT, in a novel group therapy context, in addressing existential suffering and fostering personal growth.

Keywords: cancer, existential experience, group therapy, major depressive disorder, psilocybin-assisted therapy, psychedelics, qualitative analysis

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Introduction

Serious illness, such as cancer, affects all aspects of life, leading to losses and threats of losses that can provoke fundamental existential challenges for patients and their caregivers.^{1–4} Existential challenges often relate to an individual's struggle to find meaning, purpose, and belonging when confronted with the boundaries of life and the fragility of existence.^{5–7} Existential suffering results when a person is unable to cope with these fundamental challenges and is characterized by distressing thoughts and emotions, including feelings of hopelessness, fears about dying, and loss of meaning and purpose.⁷ Demoralization syndrome, a state of profound existential suffering, occurs in up to 13–23% of people with serious illness.^{8,9} It has been associated with decreased quality of life, elevated symptoms of depression and anxiety, worsening physical symptoms, and a wish for hastened death.^{8,10–12}

Despite its commonality and impact, the existential needs of patients with cancer (e.g., to search for hope and connection) often go unaddressed in our current health care system.^{13–15} Evidence-based treatments for existential suffering remain limited. The ability of current targeted psychotherapeutic interventions, which bolster meaning and tend to existential concerns in people living with cancer,^{16,17} demonstrates only modest benefit.¹⁸ Further, conventional approaches to the management of psychological conditions, combining pharmacological and psychotherapy, often require extended periods to take full effect. The pharmacological treatments, in particular, can carry potentially burdensome side effects, posing a barrier to engagement and effectiveness for individuals in more advanced phases of serious illness.^{19,20} Patients living with cancer need more effective, faster acting, and accessible interventions to address their unmet existential needs.

Psilocybin-assisted therapy (PAT)—combining brief psychotherapeutic approaches with psilocybin, a classical serotonergic psychedelic that induces non-ordinary states of consciousness—has shown promise to safely and effectively address both psychological and existential distress in life-threatening illness.^{21–28} Clinicians working with people with serious illness are interested in innovative approaches, like PAT, to address existential distress and improve quality of life.¹⁵ This therapeutic approach has found a renewed relevance in recent years, though Indigenous tribes have long recognized plant-based hallucinogenic substances as sacred for their healing properties and promotion of mystical experiences.^{29,30} However, the individual patient PAT treatment model requires substantial resources, typically involving two trained facilitators to provide psychotherapeutic support throughout the preparatory, dosing, and

integration sessions. This treatment model presents limitations to the accessibility and scalability of PAT, due to the scarcity of appropriately trained personnel as well as time and costs of individual therapy.³¹

To overcome limitations in the scalability of PAT, the first study assessing the feasibility, safety, and efficacy of PAT simultaneous administration for patients with cancer and major depressive disorder was recently conducted ($n = 30$; see Methods for details).³² Results suggest psilocybin-assisted group therapy was safe, feasible, and clinically meaningful in patients with cancer and depression, where 80% of patients achieved a sustained response of depressive symptoms and 50% achieved full remission of depressive symptoms at 8 weeks. Further, quantitative findings from this study demonstrate participants experienced psycho-social-spiritual growth as measured by the NIH-HEALS (National Institutes of Health, Healing Experiences in All Life Stressors scale).^{33,34} A qualitative analysis of patient experiences in this study suggested that the group approach, in addition to being acceptable, fostered a sense of belonging and connection, and deepened meaning and self-transcendence through the shared psilocybin experience and group integration.³⁵

While the therapeutic outcomes are promising, much remains unknown regarding the underlying mechanisms of the profound psychedelic-mediated psycho-existential changes of PAT. In-depth qualitative examinations of the existential experiences of participants of PAT can provide a more complete understanding of the link between PAT and its effects, as these methods are well suited to explore questions related to participants' inner experiences and behavior change within complex multifaceted environments.³⁶ Further, qualitative research can generate hypotheses to drive future research into understudied phenomena, such as the novel psilocybin-assisted group therapy context. The objective of the present study was to explore how the trial's participants describe their individual existential journey through the experience of cancer and group PAT. Understanding the existential experiences of participants in this novel psilocybin-assisted group therapy context is a critical step in better supporting this often-neglected element of the cancer trajectory, as well as shedding light on potential group synergistic effects within this innovative therapeutic approach.

Methods

Study design and participants

We used a qualitative descriptive approach^{37,38} to analyze existing data from the Acceptability of Psilocybin-Assisted Group Therapy in Patients with Cancer and Depression Study (ACCEPT study). As described more fully elsewhere,³⁵ the ACCEPT study was a qualitative

study conducted concurrently with the parent clinical trial entitled “The Safety and Efficacy of Psilocybin in Cancer Patients with Major Depressive Disorder” (NCT04593563). The parent clinical trial was a single-center, phase 2 open-label PAT study among adults diagnosed with co-occurring cancer and major depression. Study participants completed a multi-visit PAT protocol, where three to four patients at a time underwent group preparation sessions, simultaneous treatment with 25 mg of psilocybin, and group integration sessions, along with individual care. The simultaneous individual psilocybin treatment session occurred in separate, adjacent rooms with a 1:1 therapist/participant ratio. Two lead therapists located in a different room monitored the session in real time by video to assist if necessary.

The ACCEPT study used convenience sampling, where all 30 participants who had completed the parent clinical trial were eligible and 28 consented to participate. Data included semi-structured exit interviews with trial participants. Participants completed informed consent for the ACCEPT study separate from the parent clinical trial. The study was approved by the Advarra institutional review board. The consolidated criteria for reporting qualitative research guidelines were used (see Supplementary Data).³⁹

Procedures

Semi-structured interviews were conducted with each study participant from January to November 2021 and occurred within 2.9 months (range: 2.1–5.1) after participants’ psilocybin dosing day (the interview guide has previously been published³⁵). Interviews were conducted virtually via secure videoconferencing platform (Zoom). The ACCEPT study principal investigator (Y.B., a hematological oncologist, palliative care physician, and investigator with significant experience in qualitative research) conducted all interviews. Interviews were audio-recorded and transcribed using a human-generated transcription service (GoTranscript). Participants did not receive compensation for their participation in the ACCEPT study. The ACCEPT study semi-structured interview guide was developed to elicit participants’ perspectives on different aspects of the parent clinical trial, including their existential experience, grounded in the conceptual framework of acceptability.⁴⁰

Analytic approach

We (E.C.T., S.A.M., Y.B., M.L., B.G., and K.N.) used a combined inductive and deductive approach to coding, using template analysis (April 2021 to December 2022).⁴¹ The initial ACCEPT study coding template was based on the conceptual framework of acceptability,⁴⁰ as well as concepts of set and setting fundamental to therapeutic research on psychedelics.^{42,43} To uphold credibility and minimize potential bias, some of the authors (E.C.T.,

S.A.M., Y.B., Z.S., J.S., and M.A.) validated and refined the initial coding template after two coders independently coded the first eight transcripts. Investigators then coded transcripts independently, looking for descriptive code-level saturation by identifying patterns of topics across transcripts,⁴⁴ meeting biweekly to iteratively refine the codebook, reach consensus about coding differences, and discuss theme development and interrelationships. Then, grounded in the Conceptual Model of Existential Experience in Adults with Advanced Cancer,⁶ the research team (led by E.C.T., a palliative care nurse practitioner and researcher with expertise in qualitative research) iteratively arranged and rearranged descriptive codes into broader existential themes to achieve meaning saturation.⁴⁴ This conceptual model was derived from qualitative literature involving adults with advanced cancer and their own descriptions of existential experience. Based on this model, we defined existential experience as including any discussion concerned with confronting the boundaries of life—that is, mortality or the fragility of existence—and the process of facing fundamental existential challenges related to the parameters of existence (death, responsibility, isolation, and meaninglessness).^{5,6,45} In this process, we attended to the notion of “dynamic integration,” that fundamental existential concerns result in conflict and growth, and present possibilities for developing existential maturity.⁴⁶

Poetic analysis^{47,48} was used as a tool during analysis to engage with data reflexively,⁴⁹ to intensify and evoke deeper meanings, crystallizing and representing themes. Poems were created using poetic transcription,⁵⁰ which is an analytic approach used during *in vivo* coding that uses the participants’ own language to create a poem, uncovering the “organic poetry” in everyday discourse. Rules of poetic transcription allow that words can be repeated, endings can be added and dropped, verb tenses can be changed, and data can be presented in the first or third person, to refine and define the core meaning of the theme. To bolster trustworthiness,^{51,52} study authors engaged in regular peer debriefing, and the first author kept analytic memos creating an audit trail for transparency and dependability.⁵³ Qualitative data were managed using Dedoose software (version 9.0.54).

Results

Twenty-eight adults with cancer and co-occurring depression participated in semi-structured interviews that lasted 90 min (range: 56–190) on average. Participants averaged 56.2 years (standard deviation = 11.4) and were mostly female (67.8%) and White (82.1%). The majority (54%) had incurable cancer, with over two-thirds (67.8%) having received more than one line of cancer therapy prior to enrollment. Over one-third (37.8%) presented with more than three lifetime episodes of depression.

Our analysis revealed three overarching themes that shed light on the existential journey of patients with cancer and depression during group PAT. Participants described a deepened lived understanding of their mortality through the cancer experience, as well as a reckoning with and a re-prioritization of their attention, relationships, and efforts. Their therapeutic intentions for participating in the PAT trial went beyond relief of depression and extended to gaining a new perspective toward existential worries and building spiritual resources to work toward desired states. Lastly, they described the lasting effects of PAT as an unfolding, healing transformation, noting an enhanced sense of meaning, agency, aliveness, and connectedness. See Table 1 for additional exemplary quotations organized by theme and subtheme, and Tables 2 and 3 to relay themes through poetic representations.

Theme 1: Cancer prompted a lived understanding of mortality and a grappling with priorities

Many participants emphasized the shock of their cancer diagnosis as “a hit in the head” (P26) or “instant death” (P17), saying after their diagnosis, “my mortality feels closer” (P8). They described vaguely having been aware of the idea of death before but, after their cancer diagnosis, reckoning with the “truth” about time in a different way (Table 1), more tangibly living the reality that they could die from this disease (Table 2).

We all have the illusion, even though it's not true, of this infinite time that stretches before us. Suddenly, I'm having to confront the fact that I don't know how much time I have, and I don't know how that time is going to be. (P1)

Participants described the emotional distress and “existential angst” (P15) this lived understanding of mortality could evoke, describing sadness, depression, anxiety, anger, and fears—about recurrence, leaving their loved ones behind, and dying.

You think about death anytime, but just knowing that you have this diagnosis and always knowing that a cancer diagnosis for a lot of people, you could lose your life to the disease. I was really, I guess, sad. I was really sad. (P31)

At the same time, participants described that this confrontation with their mortality could present an “opportunity,” “an invitation” (P26), “a catalyst” (Table 1), a “wake-up call” (P32) to reckon with who they were and how they were living their life.

It's like you wake up in the morning and it used to be that you felt like you had this time bomb in your body, and you know that sooner or later it's going to go off and you're going to be screwed and all that other stuff. It's like I think I have, which is this tremendous

opportunity again that I had to try to make the most of what I'm doing in as many ways as possible. Who I am, what I'm doing, and I have a golden opportunity to do so. (P5)

This re-examination could lead participants to “retake stock and reprioritize everything in life,” (P29), uncovering new or “dormant” priorities (P5) and redirecting how they spent their time, efforts, and relationships. Participants described changing jobs, deepening or abandoning spiritual practices, nurturing relationships with themselves and others, as well as ending relationships, and overall, being more mindful of how and with whom they spent their time (Table 1).

I think I realized that I had to take ownership of my mind, that I was living per society expectations, but that was not really necessarily doing what I wanted. It was really a wake-up call for me. Following that, I made some significant changes into my life. I actually left my partner at the time because the life that he wanted and the life that I wanted were not aligned anymore and I decided to be even more disciplined and more refined into my meditation practice, into my yoga practice. I really wanted after cancer to dive into that and get to know myself better. (P32)

Theme 2: Motivations for participation: Gaining new perspectives and bolstering strengths

Even though the PAT trial focused on depression management, participants described their therapeutic intentions as extending beyond relief of depression. These motivations encompassed seeking relief or wanting to gain a new perspective toward existential worries. Participants described wishing to reduce their “horrible cancer anxiety” (Table 1); feel “more comfortable” (P7), “come to terms” (P17), or “prepare for” (P24) death and dying; and work with their grief and fears surrounding actual or anticipated losses.

I was going through a bit of anxiety thinking about death. I was thinking about how the Western society has a weird relationship with death in terms of it's almost like, from my perspective, brush it under the rug [...] I don't like it really and it seems to me that there's got to be—I know that there's different ways [...] I was thinking that maybe a dose of a psychedelic could reset that thinking somehow, maybe bring some answers. (P3)

Participants hoped to gain “a new way of looking” (P25) at these anxieties and fears to help them in their daily lives.

I had in my mind, okay these are the psychological issues that I'm dealing with, these are the things that are problems for me, and coping with cancer, coping with life,

Table 1. Quotations Organized by Theme and Subtheme

Theme 1: Cancer prompted a lived understanding of mortality and a grappling with priorities

Deepened, lived experience of mortality

In that time, I guess when I was really sick, I started thinking, “Well, I could die. This is just reality.” They immediately write terminal on your forms. I thought, “You always vaguely think about death,” in a way in that way that most people do as this may never happen to me delusionary way, but that was gone entirely for me. I knew that there was that possibility. It wasn’t like I was giving up because I never did. I thought, “This is a reality that I must face because whether or not, whenever it comes, it comes in a year, or two, or five or whatever. This is my truth now. I have this disease. I can’t run from it.” (P13)

I’ve always known what I care about. It’s made me cognizant in a different way about time. That it has. It’s ridiculous. This is where Dr. [Name], even though what he said to me was very jarring that first time that I met with him, and he gave me the diagnosis, it’s so true. It’s plain, and everyone knows it, but we archive it in the back of our brains. You don’t know you can go out today, and you could die out on the street, but a cancer diagnosis makes it tangible. (P18)

Both emotionally distressing and an invitation to reckon with who they were and how they were living their life

Throughout all the cystoscopies and everything that I was having, the wedge resection, people were saying, “How are you? How are you [Patient name]?” All the family and friends. I said, “Yes, I’m fine.” Indeed, physically, I was fine. I was able to cope with it, but emotionally I was a wreck inside, and somehow, they were not asking me that question. Maybe they were afraid to see me break down, and I wasn’t able to tell them that emotionally, I’m having a lot of problems coping. One day I just started crying in my bedroom just on my own. [Patient’s wife] was there and she said, “What the hell is going on with you?” I said, “I can’t hold it anymore. It’s like I’ve been holding it back for months. I’m afraid. I’m afraid of dying. I’m afraid of this stupid disease, it’s come back.” (P17)

The most helpful thing for me has been to look at cancer as an invitation, so that helps me to be curious about it. I learned a lot about myself and I’ve really slowed down a lot and become more aware and grateful. However, cancer very well, according to my oncologist, may kill me. Take me out of my body. My main problem with that [chuckles] is that, I feel like a kid, like a poor three or four-year-old who’s at a really fun birthday party and I don’t want to go home. (P26)

Reckoning with and re-prioritizing attention, relationships, efforts

The cancer diagnosis in my view was almost a catalyst for me to do some really hard internal and mental, to do a really hard re-examination and to do the deep dive into understanding my past and understanding more. (P6)

The one thing that it has helped me with is just enjoying the day. I hate this one expression about killing time. It’s not about killing time. It’s about taking it for what it is, trying to find the best aspects of the day, dealing with the very complicated, and that mostly is my work. It’s just like taking it one day and enjoying it and making the most out of it. It sounds very cliché-ish, but that’s what that diagnosis has helped me with. (P18)

Theme 2: Therapeutic intentions for PAT extended to gaining new perspectives on existential worries and bolstering strengths

Seeking relief, new perspectives toward existential worries

I think my hopes were that I would get rid of some of this horrible cancer anxiety and that I would feel more comfortable with the idea of death. I’m not sure that that happened. It’s hard to sort out the whole thing. (P7)

I guess in relation to the cancer, I was trying to deal with my fears of pain, of sorrow, having to say goodbye to everything, to people, and to the earth, to everything. I’m not afraid of where I’m going because I assume I’m going where everybody’s going. But the act of dying, the very act of declining that way. (P13)

Building spiritual resources to work toward desired states

For me, 100% cancer has been a- just for lack of a better word, I’m just going to keep saying spiritual, a spiritual journey. In that, I don’t believe that it’s a spiritual underpinning, it’s a spiritual cause. I don’t mean a punishment or anything like that. There’s no physiological reason that I have this cancer. Excuse me, that I had that cancer. For me, it’s a spiritual, like, what are you trying to learn? What are you trying to work out here through this? For me, the solution or the healing would be a spiritual one. That’s just what makes sense to me. Listening to him talk about what psilocybin can do, particularly when he was talking about experiencing oneness. I was just like, “That’s it. That’s what I want.” I was also really hoping to find peace. If I could somehow experience the oneness and come to peace with potentially, my daughter not having a mom, that was my motivation. (P33)

I think that was really my greatest hope was that also that I could feel some connection to other people. I had read a lot about psilocybin, and, well, I had talked to people who had done ayahuasca and they had the sense that they were connected to the universe, and that they were connected to people who were part of this great system. I felt like I had none of that. I had no feeling of being connected to people or I felt very apart and an observer in life, rather than a participant really. I thought that the experience might help me to open up to even nature or something like that and feel connected to the world in some way. That was one of my hopes with that. (P27)

(continued)

Table 1. (Continued)

Theme 3: Lasting effects of PAT were an unfolding, healing transformational process

A healing transformation

For me, the dosing day was really transformational. It had really a deep impact. It's a beautiful gift, I really see that as a gift. (P32)

It was a very profound experience. It was definitely transformative in a lot of ways. (P14)

Very anxious and depressed and had, in general, just a lot of body pain. That's how I would describe life before. Then after the experience, it was definitely life-changing [. . .] I just feel like I'm living a much richer and fuller life now. There's a lot of potential for healing with psilocybin, I think for people in general and cancer patients in particular. (P29)

Enhanced sense of meaning

I would say that in my sense I think it did provide a good level of reassurance. I think it gave me a sense and it still does. I think a sense of grounding that what I am going through is a process that is I guess the word journey is the one that comes to mind quick that it gave me a renewed sense of purpose, but it also gave me a renewed sense of worth. (P23)

Those are all experiences within our conscious state. Your consciousness is everything around you. It's a part of that and it's okay.

It's something to accept as a part of being a part of this cosmos, a part of this world, existence as it is. The main ego tends to focus too much on itself, on what I want. Me, me, me, me, me. You learn to relinquish that a little bit and say, "Take a backseat for a little bit. Let's just carry on with life, because every moment in life is precious." (P17)

Increased sense of agency and freedom

At some point, I'm going to have a recurrence and I'm going to have to go through who knows what kind of hellish medical treatment or not have medical treatment available. I don't know, but right now it's kind of easy, but I know that it'll get tough again in the future. That I do have this as a resource. Based on the couple of more minor experiences that I've had recently with the bleeding and the oncologist, I think that I have definitely more resources to deal with these obstacles when they come up, resources that I got from psilocybin. (P14)

It helped me. It's definitely helped me to be more at peace with and aware of this idea of life and death not being mutually exclusive.

Like that little kid at the birthday party, you don't really have to be that pissed because there's more of a party just might be in a different way. It's going to be a different context. You're going to take the experiences you've had and that you know and the main thing actually that one of the biggest things that came out of the psilocybin was this idea of time can thinking that I'm always like, oh, I won't have enough time to do this or to see this or to be with my kids for this. What I realized is, yes, you'll always have enough time. Time doesn't end. The state of your body might change but time doesn't end. If I can rest in that, I'll sob in that thought, but if I can really believe in that thought, it's a huge relief. That's even why I was rushing before having cancer, it was because oh, I don't have time. I have to, oh, I have to make the lunches before. No, there's time. There's just time. You're right now actually there's no such thing as time. There is no time. That's life, you can't run out of it so you don't have to worry about it. (P26)

You're right now actually there's no such thing as time. There is no time. That's life, you can't run out of it so you don't have to worry about it. (P26)

Feeling more alive, more oneself, more whole

I feel like I'm becoming more alive than I've been all my life. I am finally getting born at 79 years old. [. . .] I live in this world. I am still very much a part of it. (P4)

I don't know that I really came up with any new insights I hadn't thought of before, but they were only in my head. They were only intellectual. I was like the student who memorizes a bunch of stuff to spit it out on the test the next day, and then poof, it's gone.

What the psilocybin experience helped me to do was to be like the student who really absorbs it, and connects this new information with other things and just really incorporates it into what they know. It took what was in my head and it connected it with my heart, my gut, my soul. It just really helped to make it real and to make it whole. (P14)

Increased sense of connectedness

If we go back to liminal space, I think that it's now starting to lessen, but there was a while that it opened up a space in which I was a little more outside of my relationships looking in. They coincided with the final group session was right after the holidays. I would be sitting sometimes watching the hubbub around me at the holidays with little kids running and playing and family, just having conversations and be outside of it and thinking, "I don't know if I'll be here next year, or the year after that." Feeling the sadness of it, but also the fact that it was okay because holidays, to me, are those times. They are an invitation to memory and to ritual. The ritual gives us that. For me, both of my parents died at Christmas and so there is a history of loss that's also associated to celebration. Of course, nobody else is thinking that they're just happily having another Christmas. It was precious, but it took me a little outside of it. There is some loss entangled in that, but overall, I think it gave me a deeper sense of what I was having in that moment. (P1)

There's some sense of, I don't know really, this expression is so overused because I make fun of it sometimes just because it's so overused. There is a sense that I'm more interested in being authentic about who I am in the world. That when people ask me what I want to do as if I want to become famous again or some worldly thing like that. First of all, I'm not as good-looking as I was when I was younger. That joking aside, I'm not a young man. I'm not in that game but, I'm still a musician and I work with really fascinating people. How it affected me is more that I want to have a bigger heart about love towards myself, really. (P13)

I had this heightened perception of nature and even now, I try to go for a walk every day, some days it's hard because it's really cold and snowy here, but today it's beautiful. It sounds silly, but I feel like really connected to the trees and the bushes and they talk to me and I'm just really aware of how beautiful nature is. (P7)

(continued)

Table 1. (Continued)

Unfolding over time, bolstered by the group
 How it evolved, I think was just over time with my own spiritual work. The way I look at psilocybin is like it was the icing on the cake. I already had the cake made, the cake was already really, really good, and all the ingredients were just right and organic. Then the psilocybin was the icing. (P33)
 I didn't really feel and I can't remember if it was any shorter, but I do remember one of my colleagues in the cohort, [group member name], saying that his wife was saying he was now [group member name] 2.0. I just remember that and how much it had changed him, and I just felt so wonderful for him, for that. I didn't have the same feeling, the intensity or the transformative-ness that he had had, but I just felt really happy. (P16)

PAT, psilocybin-assisted therapy.

coping with relationships, all that. These are the issues I'd like to address because, this is where I want to get to psychologically by the time I die and more importantly, this is how I want to live until then. (P14)

In addition to mitigating or alleviating existential worries, participants described wanting to build spiritual

resources, expanding their tools and language to work toward desired states. Many participants described spiritual aspirations such as searching for peace, meaning, "oneness," and "connection" with themselves, others, nature, and the larger universe (Table 1).

I was hoping that the psilocybin would alleviate the depression by creating new neural pathways in the brain and creating synapses where there were none. I had watched several documentaries, one of the science of psilocybin [...] I wanted to be the woman in that segment with the salt and pepper hair, who said, "I am no longer worried about dying. I am not afraid anymore." [...] That's what I was looking for, that peace, that inner peace. (P8)

Overall, finding relief and tools for coping with the existential distress that colored their cancer experience was central to participants' motivations to partake in the trial. They shared they weren't hoping "to heal something broken necessarily" (P1), but they wanted to try to add something new to make sense of themselves and their lives with cancer.

Table 2. Poetic Transcription Illustrating Theme 1: Cancer Prompted a Lived Understanding of Mortality and a Grappling with Priorities

Verbatim transcription	Poetic condensed transcription
Participant: [...] that sense of having to suddenly try to make sense , to incorporate it into some narrative about who I was , and what I was , and come to grips with a future that was changed . We all have the illusion even though it's not true of this infinite time that stretches before us . Suddenly, I'm having to confront the fact that I don't know how much time I have , and I don't know how that time is going to be .	<i>Suddenly</i> [I] try to make sense About who I was What I was Come to grips With a future changed We have the illusion Though it's not true Of infinite time Stretching before us
Having to think about how to talk to my family, to make my wishes clear, and to have the best quality of life I can for as long as I can then figure out how I want to die. It was that rush in the initial phase. Now, I've had the gift of this time to have a variable relationship to it, but I would say that it is a constant relationship to it. It is like having a conjoined twin . Death and I are in this co-existing space where sometimes, it's absolutely fine, and I'm aware of it, and it's not a problem, and other times, I would love to just be able to ignore it. I can't because there's no day that goes by that I don't contemplate my own death.	<i>Suddenly</i> I confront the fact I don't know How much time I have I don't know How that time is going to be <i>Suddenly</i> I had the gift of time To have a relationship A constant relationship Like having a conjoined twin Death and I (P1)

This is a poem created using poetic transcription⁵⁰ to condense and combine parts of the transcript to distill and reveal the core meaning. Bolded text is used to illustrate how the poetic condensed transcriptions correspond to the verbatim transcriptions.

Theme 3: Lasting effects of PAT were an unfolding, healing transformational process
 Overall, many participants emphasized the positive benefits they received from PAT, with lasting effects many participants described as "healing," "life-changing," and "transformative" (Table 1).

It's a big improvement. I feel like I'm fully living my life now. It's not as narrow and one-dimensional as it was before. (P25)

Many participants described it as a "180" (P33), with less anxiety and depression, as well as decreased hopelessness and grief. They described feeling more alive, with a new understanding of their potential and the potential for the future.

All of a sudden, an entire [...] An entire part of my psyche my spirituality and everything else has been opened up to explore. Now I see a way forward. (P5; Table 3)

Table 3. Poetic Transcription Illustrating Theme 3: Lasting Effects of PAT Were an Unfolding, Healing Transformational Process

<i>Verbatim transcription</i>	<i>Poetic condensed transcription</i>
<p>Since then what I've learned is – I've been searching for this spirituality. I had lived in the confines of traditional religion and all that other stuff all this time. I have just completely – At this point, I've completely gotten fed up by all the nonsense. In this whole transactional approach to spirituality that basically never made sense. What it was is like – The thing I learned is I have to commit to the things that I already knew. I knew these things, but I didn't have the courage or the mental – For some reason, it just caused this mental break. . . . I knew that was wrong. I always knew it was wrong. That just was wrong for me. As a person who was searching for that spiritual connection, I continued and it was painful and long and useless. Then somehow, all the things that I knew were real. Like the fact that there has to be something out there, there has to be enlightenment, there has to be something greater than myself that basically that exists. I was looking for it in the outside world. I thought it existed somewhere out there. I finally realized that it's here. It's in me. My mind, my soul is in here. Somewhere in there, but it's not out there and these people can't help me.</p>	<p>I've been searching for this spirituality I had lived in the confines of traditional religion I've completely gotten fed up</p> <p>I learned I have to commit To the things that I already knew</p> <p>I knew these things But I didn't have the courage It just caused this mental break</p> <p>As a person Searching for that spiritual connection I continued It was painful Long Useless</p> <p>Then somehow All the things that I knew were real I was looking for it in the outside world I thought it existed somewhere out there</p> <p>I finally realized that it's here It's in me My mind My soul is in here (P5)</p>

Bolded text is used to illustrate how the poetic condensed transcriptions correspond to the verbatim transcriptions. PAT, psilocybin-assisted therapy.

It is important to note that some participants shared that their “existential angst” had not improved as much as they hoped, though they often identified other benefits.

I think my hopes were that I would get rid of some of this horrible cancer anxiety and that I would feel more comfortable with the idea of death. I'm not sure that that happened. It's hard to sort out the whole thing. [. . .] I didn't feel less depressed or less anxious, but I did have this extreme connection with nature as a result of this study. (P7)

Participants described transformation in dimensions that reflected fundamental existential challenges, noting: (1) an enhanced sense of meaning; (2) increased sense of agency and freedom; (3) feeling more alive, more oneself, more whole; and (4) increased sense of connectedness.

Enhanced sense of meaning

First, participants described PAT helped them to uncover more intense meaning. They explained how PAT supported them in discovering a renewed sense of purpose

and worth, as well as finding more profound appreciation for everyday moments (Table 1).

I find more intense meaning in music, in my interactions with people and what I read, in nature. I'm obsessed with watching trees blow now. It's not a psychedelic thing, it's not like a traces or a trace or something, it's just that I just find it enchanting. It's beautiful. I was driving home in the rain and there was a truck in front of me and usually I would be annoyed and try to get around the truck, but the spray of the water was just so beautiful coming off of its tires. That kind of thing I'm able to really enjoy very small moments. [. . .] I know that I have meaning from my meditation and the time that I spend with people and the time I spend in nature. I found my meaning and it feels endless, I can find it endlessly. It's not a project, it's endlessly available to me. (P15)

Increased sense of agency and freedom

Participants also described how PAT enabled them to develop new resources and tools for coping with cancer and death anxiety, in this way experiencing increased agency and freedom in response to their evolving

oncological condition. These tools often included a changed perspective, including more comfort with uncertainty, a new ability to live in the moment, and greater acceptance of the place of sickness and dying within life.

I don't think it has changed my attitude towards cancer. I think it has changed my attitude towards my fear of being sick in general and dying. This is more the part that has changed where I think it does relieve some pressure. [...] It's okay to be scared and it's okay to die. (P32)

Many participants described these as resources they got from psilocybin (Table 1). In particular, participants described developing a new relationship with death. Several participants described gaining an awareness that life and death are not mutually exclusive.

I could have a sense of having everything I needed even though I was going to die. We often set those up in antithetical ways, and to find a way to merge them. It didn't feel transformational in the sense that it wasn't stuff that I had never thought of before or seen before, but it brought so many elements of it into a wonderful and terrifying collision in the moment [...] Seems like the whole point of this is to have the encounter with our own finiteness in that existential way. (P1)

Feeling more alive, more oneself, more whole

Similar to when they were diagnosed with cancer, many participants described how PAT served as a catalyst to shift their way of being in the world, with revitalized and reimagined priorities and values enabling a feeling of being more alive, more oneself, and more whole.

This experience was not so much about overcoming depression or anxiety or any of those kinds of things in a clinical way, as it was to really just rejuvenate how I wanted to go about living and in interacting. (P23)

Some participants described a “new spiritual aspect” of their life (P7), a “subconscious realm” (P27), a deepened faith, or a renewed creative energy. For many, PAT gave them access to knowledge they already had, and of who they were, but in a deeper way (Table 1).

I think in the larger existential and philosophic ways, it felt like a continuation of where I already was, but it allowed me to be in relationship to it differently. So that when I came out with almost, I don't know, buzzwords more. [...] To come back to, “You have everything you need in this moment, right now and you are loved.” Those could go on people's T-shirts. They're not profound unless I allow them to be. I think the psilocybin gave me access to that in a much deeper way that moved it from a bumper sticker to something that I really hold inside of me now, that when I touch it, it's familiar. (P1)

Increased sense of connectedness

The last transformational dimension participants emphasized was an increased sense of connectedness in their relationships with self, others, and nature/the wider universe. Participants described more openness, empathy, and a new capacity for love.

There's this new capability to love and be loved. That translates into being more loving, being more affectionate, being more patient, keeping more connected, being more vulnerable, being more supportive, being less critical, being more accepting, being more joyful, more playful. (P33)

This could result in changed relationships with individuals in their lives, such as partners, parents, and children, as well as more generally changing their approach to relationships (Table 1). Participants also described changed relationships with themselves.

Just got to put that down and just accept that you are, I am like everyone else too just a damaged, flawed, bruised, beautiful little spark of humanity. Just accept that and just let go of beating myself over the head with my guilt baggage for all the mistakes I made. (P14)

Unfolding over time, bolstered by the group

Participants described healing as a “work in progress” (P18), bringing together experiences related to their cancer, the psilocybin experience itself, and therapy in the context of the trial, which continued through the process of integration.

I had said something to the breast surgeon that I was doing the psilocybin. She said something interesting to me. She said, “Did it help?” [...] I said, “It's not like that. It's not like you take it, and it's a one-shot deal.” I said, “It's unfolding. It's still unfolding.” [...] It was something to have available and life-changing that it was. I don't know if everybody really understands that it's not—The payoff is so long. (P30)

Participants described the effects of PAT as nonlinear in their realization over time, and suggested that one experience with PAT could be deepened or consolidated with additional treatments.

Initially I didn't feel depressed at all, my anxiety was much lessened, but I have become more anxious, I have to say. Especially when I started to have this trouble breathing, where I couldn't get up a flight of stairs without having to stop and catch my breath. That has made me anxious because to me it means that my disease has progressed even further. That I am closer to my own mortality. I'm still afraid of dying, I'm not going to lie. What am I afraid of? I don't know [...] I would do [PAT] again. If there's a chance that I might get over my fear of death I would do it again in one minute. (P8)

Participants explained how being part of the group was one way of integrating and continuing the healing of the experience, even if they had experiences that were different from their group members (Table 1).

I think the integration really helps, hearing other people's stories [...] You feel that you're not suffering in this alone. [...] We're all part of one big family, so if they are praying for me, they are rooting for me, in some ways, it's emboldening me, it's helping me, it's making my life so much better. The integration helps in that sense. You are part of a community that's suffering or healing together, both things help. (P17)

Discussion

Semi-structured interviews with participants in a trial of group PAT provide important insights into the existential experiences of people with cancer and depression, as well as the potential role of psilocybin-assisted therapy in addressing existential suffering and fostering personal growth.

Participants described that through group PAT they experienced a recalibration of their relationships with cancer and dying, new understandings about themselves, and heightened feelings of connectedness. This study adds to the literature by looking at the entire cancer and PAT therapy context, which allowed us to illustrate how group PAT fit into participants' cancer journey and ongoing integration. Theme one highlights that even in patients who meet criteria for major depressive disorder, psycho-existential experience is not easily reduced to psychiatric diagnosis, but is marked by a wide range of intense, deep, and dynamic affects in reactions to the threat and burden of cancer.^{3,6} This finding supports the idea that psycho-existential distress is difficult to recognize and distinct from depression.^{11,54} Theme two illustrates that these wide-ranging existential worries motivated participants to partake in PAT, and importantly, that participants were seeking tools to bolster their spiritual strengths. Together, these findings underscore the need for a space of existential exploration and healing in serious illness care,^{55,56} and the possibility that psilocybin may enhance existing approaches.^{16,17,57}

Theme three sheds light on the mechanisms of therapeutic effect for how PAT can address existential suffering and foster existential growth in dimensions of meaning, agency, aliveness, and connectedness. Our findings build upon previous philosophical work surrounding existential experience, supporting psychiatrist Irvin Yalom's emphasis on four key existential challenges: (1) aliveness/finitude, (2) freedom/responsibility, (3) isolation/connection, and (4) meaning/meaninglessness.⁵ Notably, we found that PAT offered many participants an invitation to engage with these existential challenges in different ways, leading

to unexpected and novel insights. PAT participants often recognized these previously conceived dualities as not mutually exclusive, merging in particular ideas surrounding life and death. This therapeutic insight is in line with previous foundational research, which described the notion of paradoxicality and reconciliation as a feature of psychedelic mystical experiences.⁵⁸

Our findings align with previous qualitative work, supporting that improvements in anxiety and depression seen in cancer with PAT may relate to "positive, transcendent, and life-affirming" aspects of PAT.^{59,60} Emanuel and colleagues⁴⁶ describe how navigating serious illness in a supportive relational container can assist individuals to face mortality or other fundamental stressors of life-threatening illness and integrate them within the rest of their life, moving toward existential growth or maturity. This process has been characterized by meaning-making, appreciation for daily life, increased fulfillment, a sense of connectedness, and moving toward a feeling of wholeness.⁶¹ Our findings support the idea that PAT may assist with this process of developing existential maturity,⁶² and further, that the group therapy context may provide a supportive, safe holding environment for this important work.^{35,46,63} Interestingly, our findings also suggest that while the benefits of PAT on psycho-existential distress may occur rapidly after dosing, they also unfold over time in a nonlinear way. This highlights a dynamic tension between the often-cited "fast-acting" potential of psychedelic therapies⁶⁴ and the more gradual, integrative nature of their full therapeutic impact. Participants described initial shifts in mood, anxiety, or perspective soon after dosing, but also emphasized that deeper healing, insight, and existential processing emerged gradually—amplified through ongoing reflection, integration practices, and support from the group. Rather than a singular, discrete intervention, PAT was experienced as a catalyst for an evolving process of transformation, which may be especially important in the context of serious illness where time may be limited but inner work continues. These findings suggest that the promise of PAT lies not only in the immediacy of symptom relief but also in its capacity to initiate and support a sustained trajectory of existential growth and meaning-making.

This study extends our previous findings that the group PAT context is acceptable and offers synergistic group benefits³⁵ into the existential realm, suggesting that being part of the group enabled and supported participants' ongoing integration and transformation. In the context of resource limitations faced by health systems considering the integration of PAT (e.g., time, cost, and adequately trained personnel), our findings that the existential transformation and healing in this setting are similar to that described in individualized models^{59,65} underscore group PAT as a model to increase access and scalability.

Study findings should be interpreted in light of study strengths and limitations. First, the open-label design of the parent trial favored enrollment of participants motivated to engage in a psilocybin trial; this combined with the fact that two participants of the parent trial did not respond to our invitations to participate in the qualitative study indicates potential self-selection bias toward positive experiences. Future work examining the experiences of individuals who did not achieve a sustained response in their depressive symptoms may permit greater understanding of this effect. Second, the sample included English-speaking, predominantly White participants, influencing transferability of findings. PAT research intentionally including more racially, ethnically, and linguistically diverse patient populations is warranted, given existing racial disparities in the development of and access to psychedelic medicine³⁰ and cultural differences in existential experience and expression.⁶⁶ Lastly, findings from this study represent retrospective reports from participants, making insights into psychological therapeutic mechanisms limited by participant recall bias. Future investigations of actual PAT sessions themselves (i.e., preparatory, dosing, and integration sessions) can help elucidate how existential experience manifests and is supported through patient-therapist therapeutic alliance.⁶⁷ One unique strength of the study was the use of poetic analysis as a tool during analysis. Others have written about how poetic analysis can be used as a tool to bolster reflexivity, deepening analysis by asking investigators to slow down and pay closer attention to their own feelings and reflections during coding.^{48,68} In this way, poetic analysis provided space for existential exploration within our own research process. We suggest that this analytic approach is well-suited to complement investigations into the inner worlds of PAT participants. It could be used in future work to continue to explore the existential experiences of individuals with PAT both inside and outside clinical trials.

Conclusions

PAT is a promising intervention to address psycho-existential distress in patients with cancer and depression. Our findings add to the evidence that an intervention combining individual and group therapy sessions with simultaneous administration of psilocybin offers opportunities for existential transformation and healing similar to and perhaps beyond individual PAT.^{21–26} Our findings further highlight dimensions of patients' existential journey through the experience of cancer and group PAT, deepening our language and tools for understanding cancer patients' existential experience and offering ways to improve how we provide whole-person serious illness care.

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Authors' Contributions

E.C.T.: Conceptualization, formal analysis, methodology, writing—original draft, and writing—review and editing. S.A.M.: Formal analysis, writing—original draft, and writing—review and editing. K.N.: Formal analysis and writing—review and editing. Z.S.: Formal analysis, methodology, and writing—review and editing. J.S.: Conceptualization, formal analysis, investigation, methodology, and writing—review and editing. M.L.: Formal analysis and writing—review and editing. B.G.: Formal analysis and writing—review and editing. K.R.: Investigation, methodology, and writing—review and editing. J.A.T.: Conceptualization, methodology, and writing—review and editing. M.A.: Conceptualization, formal analysis, investigation, methodology, and writing—review and editing. Y.B.: Conceptualization, formal analysis, investigation, methodology, writing—original draft, and writing—review and editing.

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Supplementary Material

Supplementary Data

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