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Psychedelic-Assisted Therapies and Serious Medical Illness

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Disclosures

We have no conflicts of interest.

YB received research grants from Sunstone Therapies and Cy Biopharma to conduct studies on psilocybin-assisted therapy

Serious illness



A condition that carries a high risk of mortality, negatively impacts quality of life and daily function, and/or is burdensome in symptoms, treatments, or caregiver stress



Knaul FM et al. Lancet Commission on *Palliative* Care and Pain Relief Study Group. The Lancet. 2017.

The burden of serious illness goes beyond the physical symptoms



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Health Care in America: The Experience of People with Serious Illness:

People with serious illness experience distress over and above the physical symptoms of their specific condition

62%

feel anxious, confused, or helpless

48%

have emotional or psychological problems caused by their condition

32%

reported feeling left out, lacking in companionship, or isolated from others



A Century of Advancing Health Care for All

The New York Times

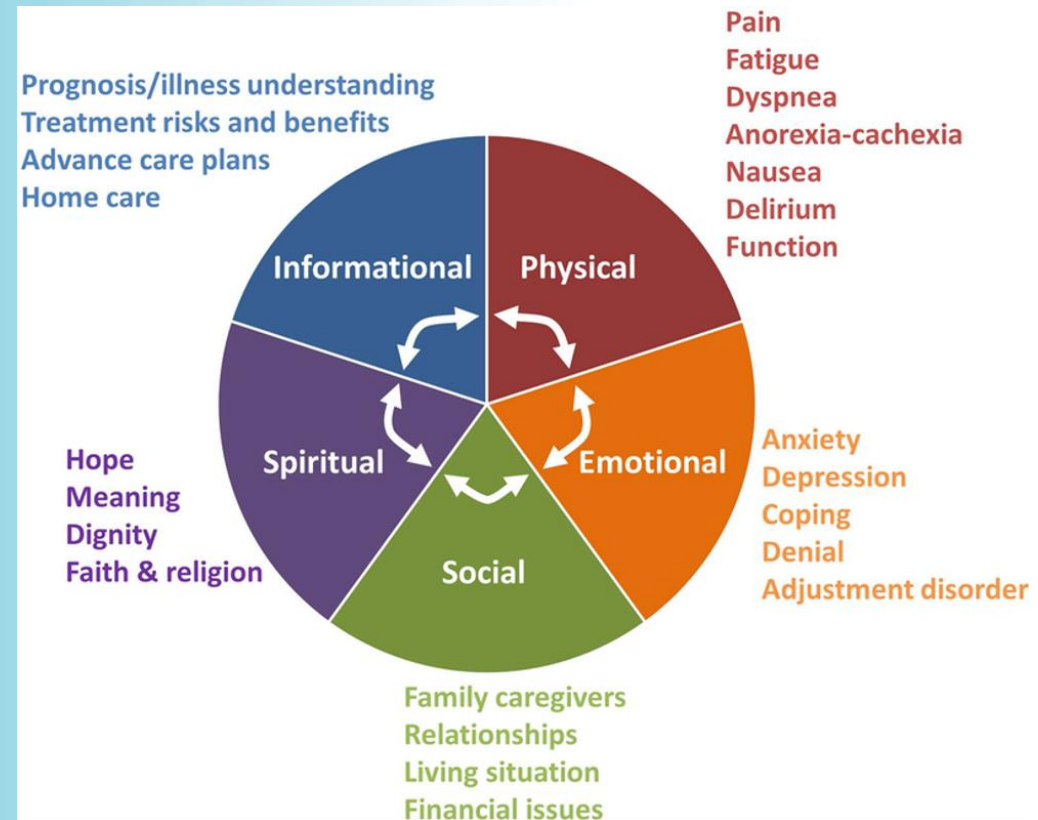


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The burden of serious illness goes beyond the physical symptoms

- Fundamental aspect of care
- Improved disease-related outcome and quality of life
- High prevalence of emotional, spiritual, existential distress
 - ~30-40% with significant mood or anxiety issues
 - **Transdiagnostic constructs**



The burden of serious illness goes beyond the physical symptoms



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Fear of cancer recurrence

Death anxiety

Demoralization

Hopelessness

Spiritual distress

Desire for hastened death

Dignity-related distress

Meaning

Social connectedness

Quality of life

Spiritual well-being

Death transcendence

Optimism



Current interventions have limited efficacy on distress outcomes

Interdisciplinary palliative care (SW, spiritual care, nursing), psychiatry

Psychotherapies

Supportive
Behavioral
Existential
Expressive

Pharmacotherapies

Antidepressants, anxiolytics
Antipsychotics & mood
stabilizers

Integrative

Body work
Meditation
Creative therapies
Nutrition
Spiritual Care

← Psychedelic-assisted therapies →

All layered on a patient with serious, dynamic medical illness
(altered physiology, polypharmacy)

Early psychedelic research in patients with serious medical illness

1964 – 1977



Early therapeutic signals on cancer pain → QOL / psycho-existential distress

Kast, E.C. and Collins, V.J. (1964). **Study of Lysergic Acid Diethylamide as an Analgesic Agent.** *Anesthesia & Analgesia*.

Kast, E.C. (1966). **LSD and the dying patient.** *Chicago Medical School Quarterly*.

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Psychotherapeutic process / set & setting; mystical experience; death anxiety / psycho-existential distress

Pahnke W. et al. (1969). **LSD-assisted psychotherapy with terminal cancer patients.** *Psychedelic Drugs*.

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Contemporary psychedelic research in patients with serious medical illness **2011-**



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Grob, C. et al. (2010) **Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer.** *Archives of General Psychiatry.*

Gasser, P. et al. (2014). **Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases.** *Journal of Nervous and Mental Disease.*

Griffiths R.R. et al. (2016) **Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: a randomized double-blind trial.** *Journal of Psychopharmacology.*

Ross, S. et al. (2016) **Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial.** *Journal of Psychopharmacology.*

Anderson BT et al. (2020) **Psilocybin-assisted group therapy for demoralized older long-term AIDS survivor men: An open-label safety and feasibility pilot study.** *EClinical Medicine*

Wolfson PE et al. (2020) **MDMA-assisted psychotherapy for treatment of anxiety and other psychological distress related to life-threatening illnesses: a randomized pilot study.** *Sci Rep*

Agrawal et al. (2023) **Psilocybin-assisted Group Therapy in Patients with Cancer Diagnosed with a Major Depressive Disorder.** *Cancer*

Lewis et al. (2023) **HOPE: A Pilot Study of Psilocybin Enhanced Group Psychotherapy in Patients with Cancer.** *Journal of Pain and Symptom Management* 2023





Key findings

- 1- Rapid, substantial effect on psycho-existential distress, improving quality of life and spiritual well-being
- 2- Effect is mediated by subjective experience
- 3- Effect is sustainable
- 4- Data on group approaches is promising



Unique characteristics of the intervention

Behavioral



Pharmacologic



Set



Setting



Acceptability of the psilocybin experience

- Intensity and demandingness of the effect – seen as integral to the healing process
- Tension between resistance and surrender
- Vulnerability, dependence, and suggestibility felt towards the setting

Beaussant et al., Cancer 2023

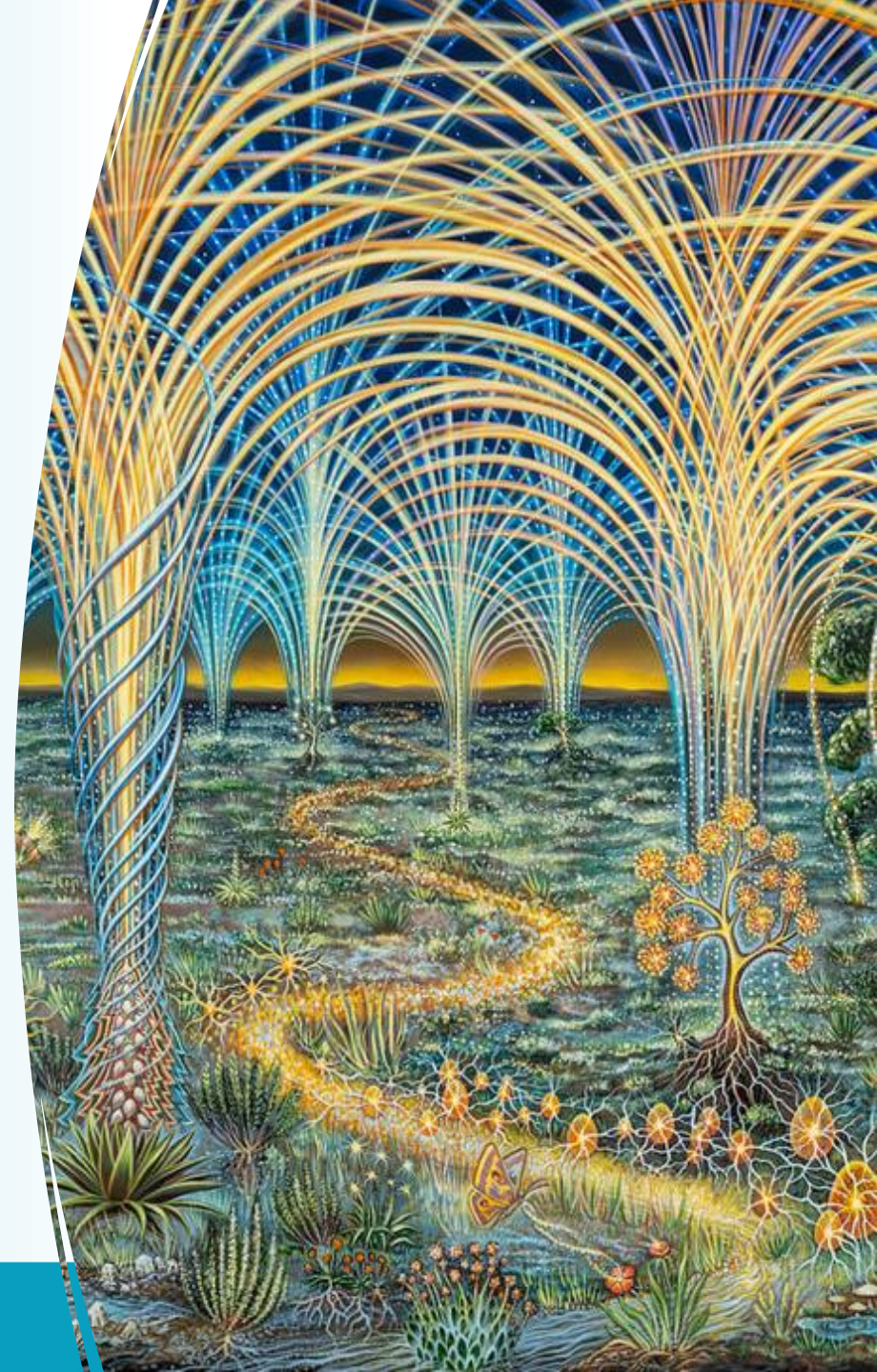


Ongoing studies in patients with serious medical illness

Title	Institution	Treatment
A Phase 2b, Randomized, Double-blind, Placebo-controlled, multi-center Study of the Effects of Psilocybin-assisted Psychotherapy on Psychiatric and Existential Distress in Advanced Cancer	NYU Langone Health	Psilocybin
Pragmatic Trial of Psilocybin Therapy in Palliative Care (PT2PC): A Multi-center Triple-blind Phase 2 Randomized Controlled Trail of Psilocybin Therapy for Demoralized Adults Near the End of Life	UCSF	Psilocybin, Ketamine
Lysergic Acid Diethylamide (LSD) in Palliative Care (LPC)	Basel University	LSD
Pilot Study of Psilocybin-Assisted Therapy for Demoralization in Patients Receiving Hospice Care	Dana-Farber Cancer Institute	Psilocybin
Feasibility Phase 2 Study of Psilocybin-Assisted Therapy for Opioid-Refractory Cancer Pain in Patients with Advanced Cancer	Dana-Farber Cancer Institute	Psilocybin
The Safety and Efficacy of Psilocybin in Cancer Patients With Major Depressive Disorder	Maryland Oncology Hematology	Psilocybin
MDMA-assisted Therapy for Adjustment Disorder (AD) in Dyads of Patients With Cancer and a Concerned Significant Other	Sunstone Medical	MDMA
Study of Psilocybin Enhanced Group Psychotherapy in Patients With Cancer	University of Utah	Psilocybin
Psilocybin Combined With Multidisciplinary Palliative Care in Demoralized Cancer Survivors With Chronic Pain	Emory University	Psilocybin
Ketamine-Assisted Psychotherapy Viability in Treating Cancer-Related Emotional Distress	Northwell Health	Ketamine

Feasibility of Psilocybin-Assisted Therapy in Hospice Patients

PATH Trial





PATH study objectives

Primary objective:

To assess the **feasibility** of psilocybin-assisted therapy in patients with moderate-to-severe demoralization receiving hospice care at home

Secondary objectives:

To explore the **safety** of psilocybin-assisted therapy in this population and its preliminary **efficacy** on demoralization and other patient-reported and family caregiver-reported outcomes



Patients & setting

Inclusion criteria

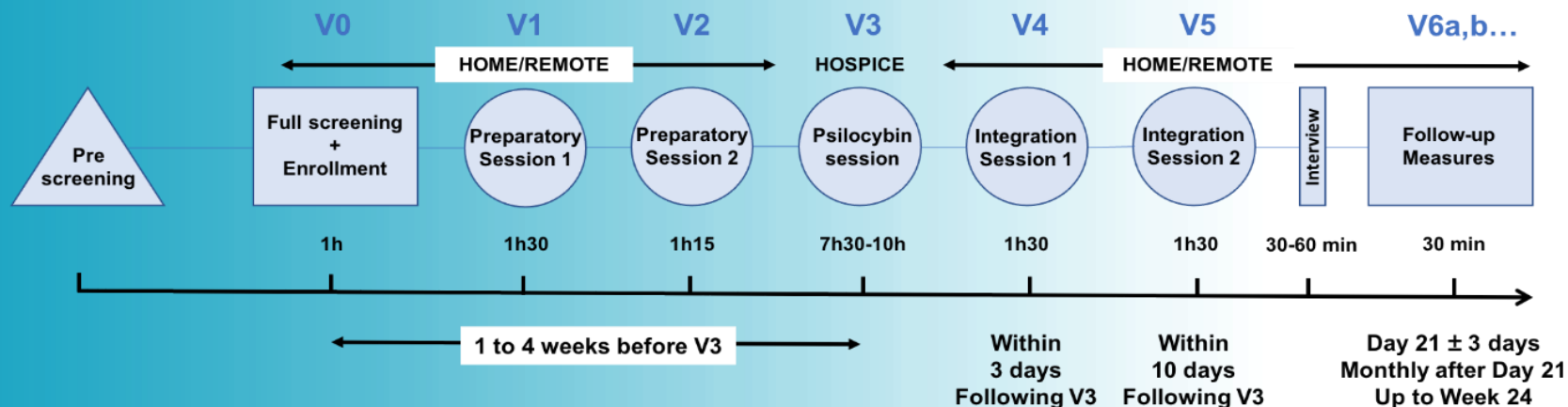
- Patients enrolled in home hospice care at Care Dimensions (5,500 hospice patients served / year)
- Age \geq 21 years
- Any terminal illness
- Palliative Performance Scale \geq 40 %
- Moderate to severe demoralization





Trial Design

- Concurrent mixed-method pilot trial
- n = 15 (at least 10 treated)
- Psilocybin 25mg x1, open-label
- Therapists' dyads (MDs, SW, music therapist)
- Collaboration with IDT at every step
- Patients, family caregivers and hospice staff interviews





Therapeutic approach

- General principles: patient-centered, relational, existentially-based
 - Connection, meaning and transcendence
 - Existential paradoxes: life/death, freedom/responsibility, aloneness/interconnection, meaning/meaninglessness (Yalom)
- Inner-directed on dosing day, music as the third therapist
- Co-construction of therapeutic formulation and intention: participant, family, hospice team, therapy team
- Multi-layered therapeutic container (hospice, therapy team, dyad, space, PATH music program, patient)
- Hand off to hospice team
- Supervision

Feasibility



15 patients enrolled

from June 2022 to February 2024

Most hospice patients didn't qualify

10 patients successfully treated

4 dropouts due to illness progression, 1 participant withdrew consent

Medical complexity

Symptom burden, comorbidities and short prognostic

Medications for pain/nausea/depression/anxiety

Oxygen, ostomies



Safety

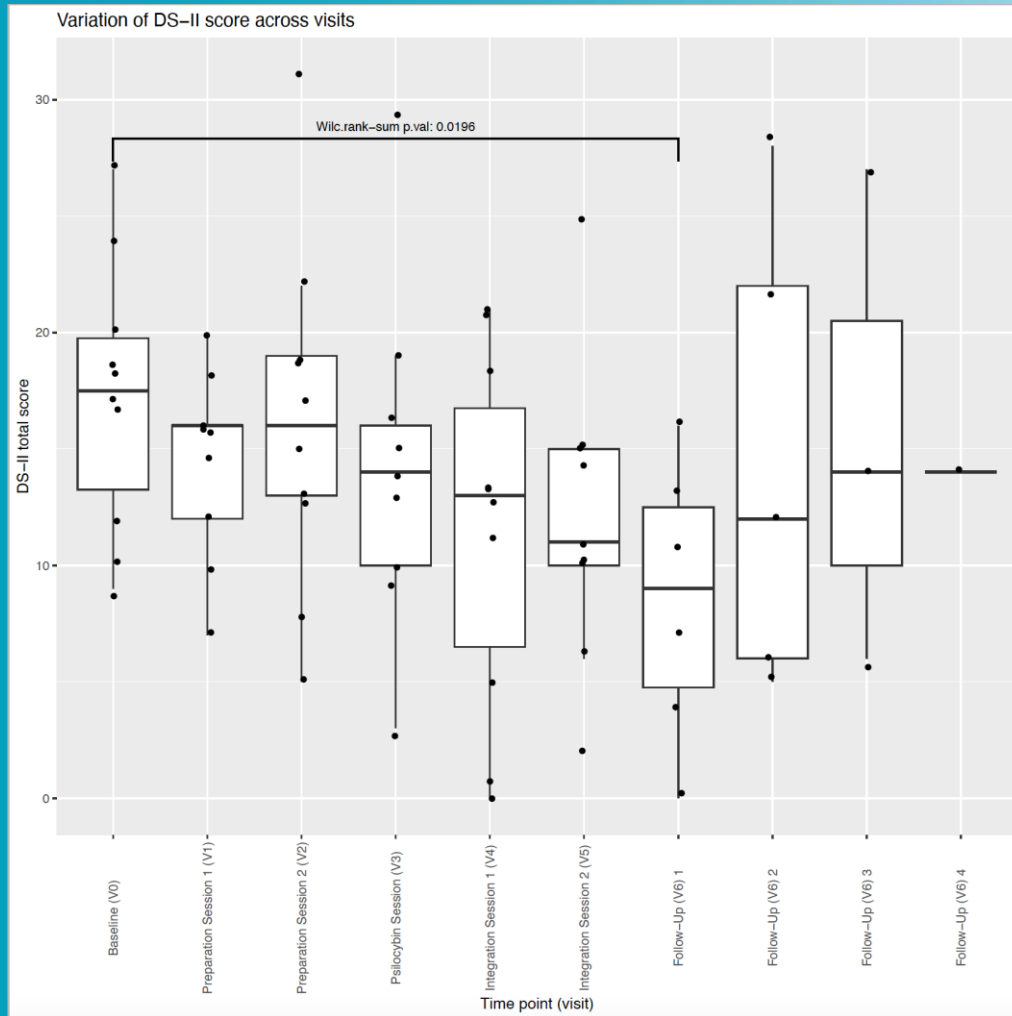


No psilocybin-related serious adverse event

Expected, mild-to-moderate, psilocybin-related adverse event



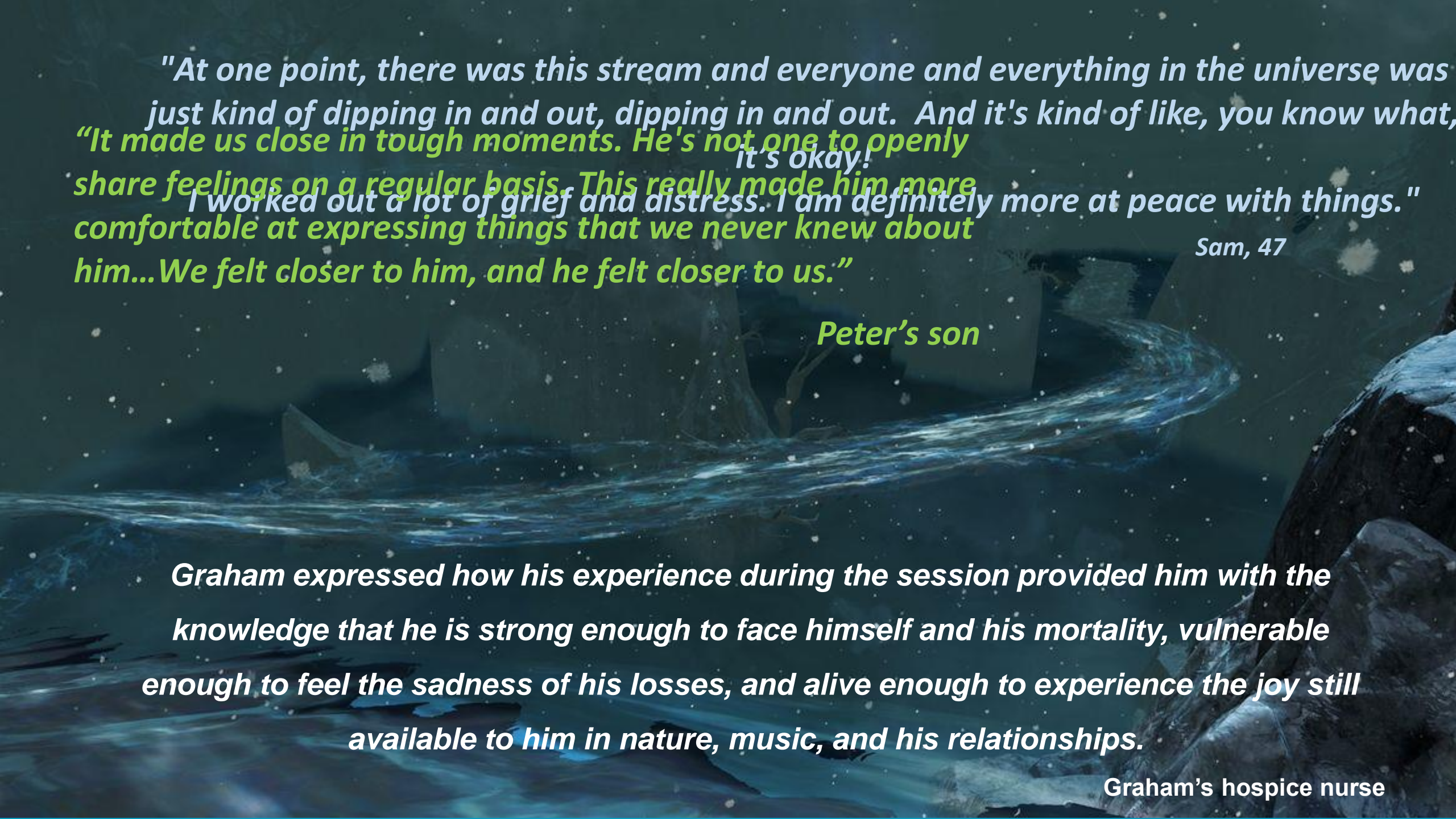
Efficacy



50.8% decrease in demoralization mean score at 3 weeks

DS-II_aggregate_scores

	timepoint	dsii.total.score
1	Baseline (V0)	17.3
2	Preparation Session 1 (V1)	14.444444444444444
3	Preparation Session 2 (V2)	16.2
4	Psilocybin Session (V3)	14.222222222222222
5	Integration Session 1 (V4)	11.6
6	Integration Session 2 (V5)	12
7	Follow-Up (V6) 1	8.5
8	Follow-Up (V6) 2	14.6
9	Follow-Up (V6) 3	15.666666666666667
10	Follow-Up (V6) 4	14



*"At one point, there was this stream and everyone and everything in the universe was just kind of dipping in and out, dipping in and out. And it's kind of like, you know what, **"It made us close in tough moments. He's not one to openly share feelings on a regular basis. This really made him more comfortable at expressing things that we never knew about him...We felt closer to him, and he felt closer to us."***

Sam, 47

Peter's son

Graham expressed how his experience during the session provided him with the knowledge that he is strong enough to face himself and his mortality, vulnerable enough to feel the sadness of his losses, and alive enough to experience the joy still available to him in nature, music, and his relationships.

Graham's hospice nurse



Qualitative findings – acceptability

- **Autonomy** - Protecting vulnerability vs. supporting agency
 - Consenting hospice patients to PAT
 - Dyadic/systemic approach vs. protecting patients' privacy
 - Empowering caregivers who are essential to patients' access
- **Therapeutic effect** – Alleviating suffering vs. Being with suffering – Drug vs Therapy
 - Psycho-existential impact, Relational Impact (family caregivers, hospice staff)
 - Non pharmacological contributors to impact
 - therapeutic relationship
 - attention
 - flexibility/interdisciplinarity
 - Barriers to therapeutic effect
 - Abruptness of the handoff at the end of the intervention
 - disease progression
- **Burden/Safety**
 - Transportation burden vs. safety of medical environment
 - assessment
 - burden for caregiver



Participant 15: “Jackie”

- 76yo F retired banker and museum docent with idiopathic pulmonary fibrosis, not eligible for transplant
- Living alone
- No other comorbidities, but on 5-7L oxygen, tethering her to concentrator. Harder and harder to leave the house.
- Not using medications for symptom management.



P15, “Jackie”: Preparation

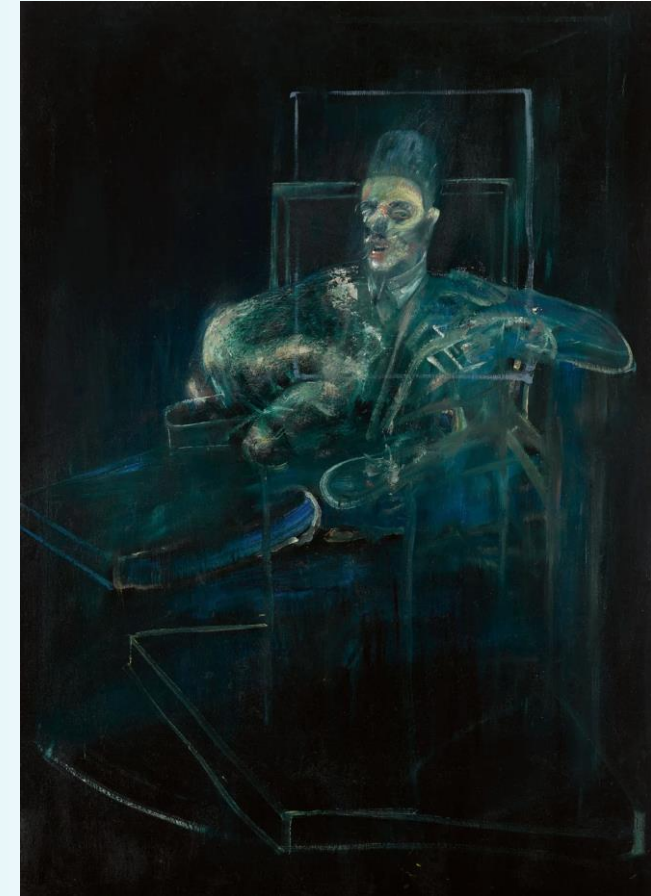
- Demoralization: grief over loss of function
 - "As soon as I adjust, I get hit with another setback"
- Personality style: outgoing, wants to connect with others, also people pleasing
- Exploring her spirituality more
 - Connecting with hospice chaplain





P15, “Jackie”: Dosing

- Did not want to utilize bed, found reclining chair most comfortable
 - Bed signified disease progression
 - Bothered by some of the hospice house accoutrements
- Quiet, introspective, not an outwardly "big" experience
- Connected with meaningful people in her lives, appearance of friends
- Shared lunch together with therapists



Francis Bacon, Pope, 1958



P15, “Jackie”: Integration

- Realization that *she is who she is*
- Growing comfort in being herself, realization that there wasn't something huge missing
- Worsening of depression with disease progression
- Later significant improvement in her mood with time
- Continued connection with friends, hospice chaplain
- Desire to connect with others with similar experience



Bryce Canyon, UT 2020



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Thank you!

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