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Mapping an Agenda for Psychedelic-Assisted Therapy Research in Patients with Serious Illness

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Abstract

Background: With support from the Radcliffe Institute for Advanced Study at Harvard University, we convened researchers representing palliative care, psychosocial oncology, spiritual care, oncology, and psychedelic-assisted therapies. We aimed to define priorities and envision an agenda for future research on psychedelic-assisted therapies in patients with serious illness. Over two days in January 2020, participants engaged in an iterative series of reflective exercises that elicited their attitude and perspectives on scientific opportunities for this research.
Objectives: The aim of the study is to identify themes that shape priorities and an agenda for research on psychedelic-assisted therapy for those affected by serious illness.
Methods: We collected data through preconference interviews, audio recordings, flip charts, and sticky notes. We applied thematic qualitative analysis to elucidate key themes.
Results: We identified seven key opportunities to advance the field of psychedelic-assisted therapies in serious illness care. Four opportunities were related to the science and design of psychedelic-assisted therapies: clarifying indications; developing and refining therapeutic protocols; investigating the impact of set and setting on therapeutic outcomes; and understanding the mechanisms of action. The other three pertained to institutional and societal drivers to support optimal and responsible research: education and certification for therapists; regulations and funding; and diversity and inclusion. Additionally, participants suggested epistemological limitations of the medical model to understand the potential value and therapeutic use of psychedelics.
Conclusions: Medicine and society are witnessing a resurgence of interest in the effects and applications of psychedelic-assisted therapies in a wide range of settings. This article suggests key opportunities for research in psychedelic-assisted therapies for those affected by serious illness.

Keywords: anxiety; depression; existential distress; palliative care; psychedelics; serious illness

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> This work will benefit many people who are facing difficult questions about their mortality and own personal meaning in life, and hopefully help them transition with more peace and understanding.
>
> Kerry Pappas
> Seminar participant
> Volunteer in the Johns Hopkins Psilocybin Cancer Study

Introduction

People with serious illness commonly experience psychological, existential, and spiritual distress that negatively impacts their quality of life and other health care outcomes.[1–4] More than 30% of patients with cancer meet criteria for mood disorders such as anxiety or depression[5] and 13%–18% present clinically relevant demoralization, a syndrome characterized by hopelessness and helplessness due to a loss of purpose and meaning.[6] These proportions increase in patients with advanced disease, who may lose the will to live when they feel that their existence is no longer meaningful.[7] Targeted pharmacological, psychological, and spiritual care interventions may alleviate some of these symptoms.[8–14] However, most clinical trials have shown only small to moderate effect sizes.

Psychedelic-assisted therapies have gained interest as a potential novel therapeutic modality because preliminary evidence suggests their profound impact on psychological, existential, and spiritual outcomes in serious illness.[15–24] These therapies combine the consciousness-expanding properties of psychedelics with psychotherapy to facilitate processing and relief of psychological and existential issues.[25] In seriously ill patients, preliminary studies have demonstrated clinically significant and persistent reductions in depression or anxiety, as well as sustained benefits in existential distress, spiritual well-being, and quality of life.[21,22] However, it remains to be determined in larger and more homogeneous studies whether, to what extent, for which populations, and with which therapeutic protocols psychedelic-assisted therapies can improve psychosocial and existential outcomes in seriously ill patients.

Experts in serious illness care have expressed both optimism and concern about psychedelic-assisted therapies and advocate for rigorous research integrated with high-quality psychosocial and palliative care.[26–30] Previously articulated concerns relate to potential risks of adverse effects, such as delirium or worsening of psychological distress, and to potential ethical issues arising from dynamics between providers and patients (e.g., the challenges of cocreating truly informed consent, minimizing conflicts of interest, and avoiding practicing outside the provider's scope of competency).[27,28] Rapid evolution in the legal and regulatory status of psychedelics has heightened the urgency of obtaining scientific evidence to inform future standards of care of psychedelic-assisted therapies.[31–33] This is particularly true for those with serious illness and who may not only have particular vulnerabilities to these therapies but may also derive substantial benefit.

To facilitate a concerted, interdisciplinary, and international research effort, we convened an exploratory seminar entitled ''Researching Psychedelic-Assisted Therapies in Patients with Serious Illness: Defining a Path Forward.'' We brought together researchers with expertise in palliative care, psychedelic-assisted therapy, oncology, psychology, and spiritual care research to define priorities and envision an agenda for future research on psychedelic-assisted therapies in patients with serious illness. This article reports on the findings from a qualitative analysis of audio recordings and written outputs of this conference.

Methods

Seminar design and agenda

The Radcliffe Institute for Advanced Study at Harvard University hosted the seminar over two days in January 2020. We invited 19 participants with expertise in palliative care, psychology, psychiatry, oncology, spiritual care, and psychedelic research (Table 1). One participant was a patient with advanced cancer who had participated in the Johns Hopkins psilocybin-assisted therapy trial for patients with cancer.

Before the meeting, we conducted phone interviews with each participant to understand their expectations and to refine the seminar agenda. Participants agreed to review the state of the science and to engage in a two-day interdisciplinary discussion to collectively brainstorm ideas, define priorities, and map an agenda for future research.

Based on findings from our study exploring multidisciplinary views on psychedelic-assisted therapy, we designed the seminar agenda to elicit participant attitudes and their perspectives on scientific opportunities and priorities for psychedelic research in serious illness.[20] We used structured processes (e.g., importance/likelihood and creative matrices) to iteratively generate ideas relevant to the seminar topic, identify key opportunities in various domains of research, and understand their priorities and interconnections.[34] Table 2 shows the seminar agenda as well as framing questions driving group discussions. This study was determined Not Human Subject Research by the Dana-Farber Cancer Institute's Office for Human Research Studies, and therefore no IRB review was required.

Data collection, analysis, and reporting

All large and half-group sessions were audio recorded. In the small group sessions, we used flip charts and sticky notes systematically to document the discussion, and two of the authors (B.G. and C.S.-P.) took extensive notes throughout the seminar. Y.B., B.G., and C.S.-P. reviewed all notes taken during the seminar, and using Dedoose qualitative analysis software (version 8.3.19), one of us (Y.B.) categorized the recorded data by theme.

We then organized, reduced, and categorized data, using a free and open grid to promote the emergence of codes and themes that best captured and regrouped the essential meanings of participants' perspectives and ideas.[35,36] Final conceptualization emerged following discussion of these findings with coauthors and some of the participants. All participants were offered the opportunity to review the article.

Results

We identified seven topic areas representing key opportunities to advance the field of psychedelic-assisted therapies in serious illness care. Four opportunities were related to the design and science of psychedelic-assisted therapies: patient and caregiver outcomes, therapeutic protocols, therapeutic setting, and mechanisms of action. The other three pertained to institutional and societal drivers that may support optimal

Table 1. Exploratory Seminar Leaders and Participants

Exploratory seminar leaders	
Yvan Beaussant, MD, MSc Instructor in the Medicine Psychosocial Oncology and Palliative Care Department, Dana–Farber Cancer Institute Harvard Medical School	Justin Sanders, MD, MSc Instructor in the Medicine Psychosocial Oncology and Palliative Care Department, Dana–Farber Cancer Institute Harvard Medical School
Cofacilitators	
Benjamin Guérin, MA Independent researcher in history and philosophy Author, poet, and ceramist	Claudia Schwarz-Plaschg, PhD Marie Skłodowska-Curie Fellow, Department of Science and Technology Studies, University of Vienna
Exploratory seminar participants	
Manish Agrawal, MD Medical Oncologist Co-Director of Clinical Research at the Aquilino Cancer Center in Maryland	Anthony Back, MD Professor of Medicine, Division of Medical Oncology, University of Washington Co-Director, Cambia Palliative Care Center of Excellence Co-Founder, VitalTalk
Tracy Balboni, MD, MPH Associate Professor of Radiation Oncology at Harvard Medical School Director of the Supportive and Palliative Radiation Oncology Service at the Dana–Farber/Brigham and Women's Cancer Center	Craig Blinderman, MD, MA Director of the Adult Palliative Medicine Service at Columbia University Medical Center/New York-Presbyterian Hospital Associate Professor of Medicine in the Department of Medicine, Columbia University, College of Physicians and Surgeons
Anthony Bossis, PhD Clinical Psychologist Clinical Assistant Professor of Psychiatry NYU School of Medicine	Ilana Braun, MD Assistant Professor, Psychiatry, Harvard Medical School Chief, Division of Adult Psychosocial Oncology, Psychosocial Oncology and Palliative Care, Dana–Farber Cancer Institute
William Breitbart, MD Chairman, Jimmie C. Holland Chair in Psychiatric Oncology Attending Psychiatrist, Psychiatry Service in the Department of Psychiatry and Behavioral Sciences Memorial Sloan Kettering Cancer Center	Ira Byock, MD, FAAHPM Emeritus Professor of Medicine at the Geisel School of Medicine at Dartmouth Founder and Chief Medical Officer of the Institute for Human Caring, a component of Providence St. Joseph Health
Robin Carhart-Harris, PhD Faculty of Medicine, Department of Brain Sciences Founder of the Centre for Psychedelic Research Imperial College London	Mary Cosimano, MSW Director of Clinical Services for the Center for Psychedelic and Consciousness Research Department of Psychiatry, Behavioral Pharmacology Research Unit (BPRU) Johns Hopkins University School of Medicine
Rick Doblin, PhD Founder and Executive Director Multidisciplinary Association for Psychedelic Studies (MAPS)	Charles Grob, MD Professor of Psychiatry and Pediatrics at the UCLA School of Medicine Director of the Division of Child and Adolescent Psychiatry at the Harbor–UCLA Medical Center
Franklin King IV, MD Director, Training and Education, Center for Neuroscience of Psychedelics, Massachusetts General Hospital Instructor, Harvard Medical School	Kerry Pappas Volunteer and invited guest of the Johns Hopkins Psilocybin Research Study
William Richards, STM, PhD Psychologist Johns Hopkins Center for Psychedelic and Consciousness Research	Zachary Sager, MD, MA Advanced Fellow New England Geriatric Research Education and Clinical Center (NEGRECC) VA Boston Healthcare System
Karen Steinhauser, PhD Professor, Departments of Population Health Sciences and Medicine, Duke University Medical Center Senior Fellow with the Duke University Center for Aging and Health Scientist with the Center for Health Services Research in Primary Care, VA Medical Center, Durham	James Tulsky, MD Chair, Department of Psychosocial Oncology and Palliative Care at Dana–Farber Cancer Institute Chief, Division of Palliative Medicine, Brigham and Women's Hospital Professor of Medicine, Harvard Medical School
Monnica Williams, PhD, ABPP Canada Research Chair in Mental Health Disparities Associate Professor, School of Psychology, University of Ottawa Clinical Director of the Behavioral Wellness Clinic, LLC, Tolland, CT	

Table 2. Exploratory Seminar Agenda

	Session	*Framing questions*
1. Building the community	1.1. Historical perspective *(didactic presentation)*	Putting psychedelic research in patients with serious illness in a historical perspective, what lessons can we learn from the pioneers' experience?
	1.2. Discussion with study participant *(LG)*	What drove you to enroll in this trial? What was your experience of cancer at that time? What was the therapeutic experience like? What happened in the days or weeks that followed and what did you personally draw from this experience? What according to you is the long-term effect of this treatment?
	1.3. Eliciting biases *(cynics and believers, process by pair+LG discussion)*	What are the pros and cons to researching psychedelic-assisted therapies in patients with serious illness?
	1.4. Eliciting hopes and fears *(importance/likelihood matrix in SG+LG discussions)*	What are the worst/best possible outcomes that we can imagine as a result of the psychedelic research in palliative care?
2. Level setting	2.1. State of the science *(didactic presentation+LG discussions)*	What do we know? What are the lessons for future research?
	2.2. Unmet needs in patients with serious illness *(importance/likelihood matrix in SG+LG discussions)*	What are the most important opportunities to improve care and outcomes for patients with serious illness using psychedelics?
3. Exploring	3.1. Research questions *(SG+LG discussions)*	What are the main research questions in specific domains of serious illness care?
	3.2. Emerging primary questions *(half group discussions)*	How might psychedelic research inform the understanding of the existential or spiritual experience of serious illness? How might we reconcile the tension between the psychological experience with psychedelics and the neuropharmacological paradigm in a way that can help the design of psychedelic protocols?
4. Defining a path forward	4.1. Primary issues *(Creative Matrix)*	How might we develop psychedelic research responsibly for patients with serious illness?
	4.2. Serious psychedelic speed dating	How would we collaborate in this area?
	4.3. Priorities	What are the big ideas for next steps in this research area? What SMART goal will you accomplish in the next 6 months that will contribute to this work?

LG, large group; SG, small group.

and responsible research: education and certification for therapists, regulations and funding, and diversity and inclusion. Additionally, seminar participants proposed that there may be inherent limitations of the medical model in comprehending psychedelic experiences and suggested that psychedelic-assisted therapies might shift perspectives on what the biomedical model considers pathologic.

Design and science of psychedelic-assisted therapies

Clarify indications for psychedelic-assisted therapies in patients with serious illness. Participants considered numerous psychosocial and palliative care outcomes as potential therapeutic targets for psychedelic-assisted therapy. They called for a concerted effort to standardize outcome measures across studies, which would optimize the efficacy of data analysis.

Table 3 presents patient and family's outcomes discussed by participants at the intersection between palliative and psychedelic research and reports examples of corresponding research questions articulated by participants.

Participants expressed particular interest in the potential for psychedelic-assisted therapies to address the existential and spiritual dimensions of suffering experienced by patients with serious illness. Evidence linking psychedelics to existential and spiritual experiences provoked discussion about the potential for psychedelics to help understand the nature of such distress among those with serious illness and disentangle and define what we mean by spiritual and existential issues as both terms tend to get conflated. As one participant remarked, ''Maybe psychedelic-assisted therapies could help map the landscape of existential distress.''

In addition, participants highlighted the need to monitor and address potential disruptive effects of these therapies on relationships and decision making. For example, one

TABLE 3. EXAMPLES OF PATIENTS/FAMILY OUTCOMES AND CORRESPONDING RESEARCH QUESTIONS AT THE INTERSECTION BETWEEN PSYCHEDELIC-ASSISTED THERAPIES AND SERIOUS ILLNESS CARE SUGGESTED BY PARTICIPANTS

Therapeutic targets/outcomes	*Examples of research questions*
Existential/spiritual distress	• What is the impact of psychedelic-assisted therapies on spiritual well-being? • Which aspects of existential or spiritual distress are affected by psychedelic-assisted therapies? • What factors predispose to positive response? • Could psychedelic-assisted therapies help understand the trajectory of spiritual journeys? • What is existential distress and how to measure it?
Trauma	• Could psychedelic-assisted therapies help with trauma accumulated throughout life? • Can psychedelic-assisted therapies treat trauma related to the diagnosis and treatment of serious illness? • Are pre-existing and illness-related trauma symptoms equally responsive to psychedelic-assisted therapies? • Is there a specific presentation (symptom cluster) of trauma that psychedelic-assisted therapies might be particularly helpful with? • What are the opportunities for post-traumatic growth with psychedelic-assisted therapies?
Communication	• How do psychedelic-assisted therapies affect patient–physician communication? • Do patients become better communicators in their families? • Does psychedelic-assisted therapy improve the quality of relationships with family? • If MDs/oncologists prescribe psychedelic-assisted therapies, do they improve end-of-life communication (e.g., difficult conversations)
Coping	• Do psychedelic-assisted therapies increase proactive/functional coping, as opposed to dysfunctional coping strategies? • What kind of coping does psychedelic-assisted therapies help with (e.g., meaning-focused coping (Lazarus/Folkman) vs. medical bills)?
Anxiety and depression	• What type of anxiety do psychedelic-assisted therapies help with? • Which symptoms of anxiety and depression improve, stay unchanged, or worsen postconsolidation? • How do psychedelic-assisted therapies impact ruminations and how does that relate to improvement of anxiety/depression? • Comparative trial against other treatments (e.g., benzodiazepines and antidepressants) • How long does the therapeutic effect last? • What is the importance of environment in long-term outcomes?
Loneliness/ isolation	• Do psychedelic-assisted therapies change loneliness or isolation to emotional connectedness and relational embeddedness? (quality + quantity of social support, objective and subjective) • Do psychedelic-assisted therapies increase capacity to connect/sense of connection? • Do they modify satisfaction with loneliness? (difference between loneliness and aloneness) • What integration network could be put in place to decrease loneliness and isolation?
Pain	• How do psychedelic-assisted therapies affect perception of pain? • How do psychedelic-assisted therapies affect intensity of pain? • Are psychedelics coanalgesics?
Empowerment/ engagement/ decision making	• Can psychedelic-assisted therapies affect end-of-life priorities and shared decision making? • Would going through psychedelic-assisted therapy lead to greater goal-concordant care? • Do people's values shift? How does that affect informed consent? • Will this lead to more effective use of resources? • Are patients more engaged with their treatments? Is disengagement coming at the right time? • Can psychedelic-assisted therapies help with decisional conflict patient/families?
Caregivers/families	• Do psychedelic-assisted therapies improve the quality of relationships with family? • Do psychedelic-assisted therapies increase quality and content of communication with family/caregivers • How do psychedelic-assisted therapies affect bereavement outcomes? • Do psychedelic-assisted therapies conducted in patients improve family outcomes? • Do psychedelic-assisted therapies conducted in families improve patient/families' outcomes? • Does psychedelic-assisted therapy in dyad patient/family caregiver improve outcomes?

participant wanted to look into any negative relational outcomes in psychedelic trials as literature on other profound experiences such as near-death experiences suggests that divorce is not uncommon in that population.

They suggested that caregiver outcomes (e.g., mental health, quality of life, and bereavement) might be affected by psychedelic-assisted therapies: indirectly, because of the effect on patients' symptoms and communication; or directly, if protocols involve conjoint therapy (in which both patient and caregiver receive the intervention). They raised the possibility of caregiver inclusion in study trials.

Develop and refine therapeutic protocols according to indication. Our data suggest ways in which therapeutic protocols might be developed, refined, and standardized in the setting of serious illness care.

Important pharmacological issues for research include assessment of the indications and relevant precaution for different psychedelic drugs. For example, some participants noted that shorter-acting psychedelics such as dimethyltryptamine or ketamine at doses inducing psychedelic effects, used in a psychotherapeutic setting, might prove useful in frail patients for whom a six-hour psilocybin session could be challenging. Participants also proposed that studies compare psychedelic medications with each other and with current standards of care (''this might be palliative care or meaning-centered therapy or whatever is relevant'') to improve methodological rigor in particular, as the use of placebo is poorly applicable and relevant in psychedelic studies.

Participants also highlighted the importance of manualizing psychotherapeutic protocols to help standardize psychological support during preparation, drug sessions, and integration. They suggested the opportunity to synergistically combine psychedelic-assisted therapies with existing evidence-based psychotherapeutic approaches in serious illness care (e.g., meaning-centered therapy or acceptance and commitment therapy) and considered their potential role alongside spiritual care interventions (e.g., chaplaincy care). In addition, they suggested research to understand the relative effects of various modalities, such as individual therapy (classically one or two therapists for one patient), group therapy, or conjoint therapy. As one participant articulated, ''The model that we are using in 2020 is the one that was developed 20 years ago. And, it may be the right thing, you may need two therapists for x amount of time and all of that, but maybe there are a lot of other ways to do this. What are the minimum necessary pieces?''

Investigate the impact of setting on therapeutic outcomes. Participants highlighted both the need to specify setting elements for research protocols and the need for research to help refine standards for optimal therapeutic settings for people affected by serious illness. They considered interdisciplinary care and certain elements of treatment facilities and locations as major aspects of this research to be further examined as empirical data link such factors to safety and efficacy of serious illness care and/or psychedelic-assisted therapies.

Integrating psychedelic research into interdisciplinary care models emerged as a major theme of this seminar. There were concerns about ''how psychedelic-assisted therapy might meet palliative care needs if other treatments, approaches, and modalities that are out there are not optimally being utilized, accessed, or implemented.'' Thus, participants envisioned a model of research and therapy involving collaborations between mental health, palliative care, geriatrics, and/or spiritual care professionals, along with specialists from relevant disciplines (e.g., hematology–oncology, geriatrics, and neurology). They highlighted the paramount importance of conducting this research in patients whose psychosocial and palliative care needs have been addressed by interdisciplinary teams according to current best standards of care.

Participants also specified criteria they considered the most important for treatment spaces. These included comfortable, quiet, safe, and esthetic rooms separated from other activities in the building and equipped with audio systems. While some participants articulated that research data should be obtained to define treatment space-related standards of care, others estimated that these elements of the setting were important and consensual enough to warrant their regulation from the outset.

When participants were asked to imagine potential negative outcomes that might derive from the reopening of psychedelic research in patients with serious illness, inappropriate and harmful settings due to improper structures, poor screening, and poor preparation of patients were a major concern. However, participants were equally concerned that the cost related to a psychedelic-assisted therapy setting might constitute a factor of inequality for low-resource and/or underserved populations. Some emphasized that insurance or institutions should absorb the cost of setting to help prevent potential discrimination.

Understand mechanisms of action and foster translational research. Participants identified the need to better understand psychedelic-assisted therapy mechanisms of action in the context of serious illness care. They suggested that uncovering mechanisms of actions would continue to require complementary approaches such as phenomenology, psychology, neuroimagery, and neurobiology and called for translational designs and mixed methods involving interdisciplinary teams to advance this research, foster development of clinical applications, and improve safety and efficacy. Examples of research questions suggested by participants in this domain included the following: Is the effect related to drug, psychotherapy, or their combination? What is the phenomenology of traumatic resolution in patients with serious illness with psychedelic-assisted therapies? Is dissolution of ego (or neural correlates) necessary for resolution of trauma or amelioration of effects?

Institutional and societal drivers

Integrate education and certification for therapists. Rapid growth of psychedelic research after several decades of stagnation necessitates education and certification programs. Some participants expected regulatory changes more supportive of psychedelic research in the near future and anticipated a fast-growing need for health care professionals trained both in psychedelic-assisted therapies and serious illness care. Issues that emerged included curricula (e.g., training should include mentorship, peer groups, and supervision), certifications (e.g., psychedelic-assisted therapy training for facilitators should be regulated/standardized), and diversity (e.g., require effective diversity training of all clinicians and training therapists who represent the community).

Participants also discussed the relevance of therapists' first-hand experience of psychedelics, considered by some as ''an important and the quickest way to learn this work for the therapist.'' As psychedelic use is currently illegal for non-research purposes in most states and countries, some participants suggested an opportunity for policy updates to support this aspect of the training of future therapists. One said: ''We will not understand the true potential of this [therapy] without having guides having had the experience. We need a legal route for this. Guides not knowing the experience would miss many opportunities.''

As an alternative, some suggested that therapists might at least have experience with expanded states of consciousness through other means (e.g., meditation and other spiritual practices, hypnosis, and holotropic breathwork) to enhance delivery of safe and effective psychedelic-assisted therapies.

Change of regulation and funding mechanisms to support the research effort. Participants highlighted the impact of regulatory and funding hurdles on clinical research on psychedelic-assisted therapy in most countries. As health authorities have recently given encouraging signs of opening in supporting 3,4-methylenedioxymethamphetamine (MDMA) and psilocybin-assisted therapy trials in Post-Traumatic Stress Disorder (PTSD) and depression, respectively,[32,33] participants were generally optimistic that future psychedelic research in patients with serious illness would entail similar support and oversight as well as federal funding opportunities guided by collectively defined priorities. Some of them suggested involving regulatory agencies—for example, the Food and Drug Administration (FDA) in the United States—early in the development of research protocols to collect data in ways that support regulatory approval.

Some also suggested a role for regulatory and funding agencies to promote ethical research, particularly in terms of representation of and accessibility for patients from racialized and underserved populations. For example, one participant suggested ''Funding should be tied to studies being inclusive and proportionate re: minority participant populations and study staff.''

Finally, in the context of an increasing number of legalization/decriminalization initiatives in cities, states, or countries,[37] some participants suggested that a medical model of psychedelic-assisted therapy might coexist with a community-based model of psychedelic use, for example, when they are used for personal growth or in a religious setting. Harm reduction programs and other bridges between communities and institutions were mentioned as responsible responses to this trend.

Built-in diverse and inclusive research. As highlighted in previous sections, this crosscutting theme was part of the discussions about patient and family outcomes, therapeutic protocols, therapeutic settings, education and certification of therapists, and regulation and funding. Participants suggested ways in which psychedelic research might be inclusive of diverse and/or underserved populations of patients with serious illness, for example, by involving more therapists of color (scholarships), including nontraditional sites with more diverse populations, or enabling access through coverage by all major insurances and charitable care for anyone.

Psychedelic research was also conceived as an opportunity to amplify the voice of people who have been marginalized and to acknowledge the living heritage psychedelic-assisted therapies receive from indigenous cultures (e.g., ''Learn from the lessons of the past regarding knowledge and experience of indigenous models'').

Psychedelic-assisted therapies and the medical model

Central to this seminar was the goal of mapping and operationalizing responsible forward movement in the science of psychedelic-assisted therapies for patients with serious illness. Consequently, participants discussed psychedelic-assisted therapy as a potential biomedical intervention amenable to a mechanistic approach of health and science, as exemplified by the following quote: ''We need a mechanistic model to do good science in this area. The more we can know what it is that we are measuring and what are the components of the intervention, the easier it is to study this in ways that are reproducible. That's where we get to efficiency.''

However, participants also questioned the appropriateness of the sole medical model to approach the science and therapeutic use of psychedelics, particularly in the setting of serious illness and end of life, underlining further the necessity of a multidisciplinary approach. They questioned the ability of scientific methods to adequately capture phenomena such as spiritual experiences, the value of pathologizing the spiritual or existential dimension of suffering, and the validity of considering psychedelic-assisted therapy as a biomedical intervention designed to address medically framed indications or symptoms. For example, one participant said: ''Maybe we're fundamentally dealing with a different sort of therapy that is more holistic in orientation and we need a whole different paradigm to even be asking the right questions.'' In addition, another said: ''The whole idea of spiritual distress is a very medically bounded way of looking at spirituality. We really need to step back and ask: what is the trajectory of the spiritual experience that people go through? Something that is less about assuming there is some sort of diagnostic cutoff for spiritual distress… because I feel that in a way it's the wrong paradigm for this.''

Discussion

This article highlights findings from a two-day symposium hosted by the Radcliffe Institute for Advanced Study at Harvard University, convening an interdisciplinary group of 23 clinicians, researchers, and one patient. The aim of this seminar was to define priorities and envision an agenda for future research on psychedelic-assisted therapies in patients with serious illness. Our in-depth qualitative analysis of iterative discussions and related outputs suggests key opportunities for research at the intersection between serious illness care and psychedelic-assisted therapies.

Some of these opportunities relate directly to the advancement of clinical and scientific knowledge. Participants described critical patient and caregiver outcomes needing further understanding, definition, and evaluation, particularly through clinical trials and qualitative research. Similarly, they raised important considerations related to therapeutic protocols, therapeutic settings, and mechanisms of action that this research should examine moving forward. All participants agreed on the scientific and clinical relevance of pursuing this research, suggesting a considerable public health opportunity. Accordingly, they described institutional and societal drivers that will facilitate this effort: developing education and certification programs, revising policies around regulation and funding, and building diverse, equitable, and inclusive research programs.

These findings are in accordance with a previous qualitative exploration of experts' perspective on the potential role of psychedelic-assisted therapies in patients with serious

illness and clarify further the research effort that lies ahead to advance scientific and therapeutic knowledge in this field.[27] They also echo a growing chorus of researchers, clinicians, and patients calling for mainstream psychedelic research programs for those affected by serious illness care.[26,30,38–42] Limited efficacy of existing interventions to address psychosocial and existential distress in this population warrants strengthening this line of research. The SARS-COV2 pandemic, by adding layers of psychosocial and existential distress to patients, families, and professionals, underscores further the potential clinical need for psychedelic therapies.[43–48] Furthermore, the pandemic has highlighted new ways in which racial trauma and inequities can compound the negative psychological impact of serious illness.[49]

Participants raised fundamental questions about the potential limits of applying a biomedical model to aspects of psychedelic research that may lie outside traditional scientific frameworks. Such epistemological issues have challenged anthropologists working at the intersection of traditional and Western medical therapies, as well as practitioners of palliative care and psychedelic medicine, given their counterculture origins and shared humanistic ideals.[39] In its evolution from philosophical movement to medical subspecialty, palliative medicine has attempted to balance a biopsychosocial and spiritual approach toward healing while accommodating rigid structures of a professionalized biomedical enterprise.[50–52] Similarly, psychedelic research is rooted in humanistic psychology and integrative medicine and relies on both a biomedical model and a healing art.[53,54] The historian Erica Dyck has proposed that revisiting the relationship between psychedelics and palliative care might be an opportunity to consider the broader context of how biomedicine has handled issues of spirituality in the context of healing and caring.[55]

The spiritual dimension of psychedelic-assisted therapies in the context of serious illness is reflected in surveys and qualitative research reporting cancer patients' experiences.[56,57] Research on spirituality and end of life suggests that the role of research is not to measure the ineffable or determine the existence of a realm that is beyond empirical investigation, but rather to develop measures, observations, and an understanding of human experience of the spiritual as distinct from and relating to other determinants of human well-being.[13] If previous psychedelic research in patients with serious illness has demonstrated the feasibility and pertinence of doing so while valuing the spiritual dimension of psychedelic experiences, our findings highlight the considerable work that remains to discern important outcomes, measures, and implementation strategies. They also suggest that this research might benefit from being both grounded in the biomedical model and integrated in a larger frame of knowledge that includes, for example, the input of humanities and of religious and/or indigenous leaders.[58]

Limitations

However thoughtful our attempt to include a well-rounded cohort of key stakeholders, we have without doubt missed voices of those who have extensive relevant experience and perspectives, including nurses, spiritual care providers, representatives of indigenous groups, the pharmaceutical industry, and regulatory/funding agencies. In addition, the voices of women and people of color were underrepresented.

Exploratory seminars present an opportunity to open the box on challenging or controversial topics. This informed our facilitation and analytic approaches, which have limitations. For example, we may have gained further insights from a more consensus-driven approach (e.g., delphi model) or by focusing more narrowly on specific methods or safety parameters. Our findings might inform such endeavors in future works.

Conclusions

Participants in an exploratory seminar on psychedelic research in patients with serious illness identified key opportunities to advance the field in numerous domains. Such research efforts will advance evidence-based methods for the understanding of patient and family experiences and needs at the end of life, the integration of psychedelic-assisted therapies into serious illness care practices, and the delivery of interdisciplinary care to alleviate psychosocial and existential suffering in those affected by serious illness. For this effort to be meaningful to patients and society, rescheduling of the legal status of psychedelics and federal funds will be an important step.

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