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Introducing psychedelics to end-of-life mental healthcare

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Early evidence suggests psychedelics could help alleviate end-of-life anxiety and depression. Yet there has been little study or discussion of their integration into hospice and palliative care settings, where patients often have complex comorbidities and medication regimens. The authors discuss relevant clinical challenges and approaches.

Technology allows medicine to prolong life despite life-threating illness. Consequently, patients spend more time in the 'end of life' phase of care. During this period, they often experience anxiety, depression or a sense of impending mortality. These symptoms do not arise only because of pain or other symptoms; they often stem from limitations that symptoms place on independence, social interaction and engagement with meaningful activities[1]. For some, this psychological distress, which includes doubts regarding one's purpose in life, is the primary motivator for seeking palliative care.

There is limited but compelling evidence that psychedelic substances — especially psilocybin — could reduce anxiety, depression and existential distress in patients near the end of life[2]. Psychedelics are a diverse class of compounds that can cause acute and chronic emotional, cognitive and perceptual change. Some psychedelics, such as psilocybin and ibogaine, are produced by plants or fungi. Many are considered sacred by Indigenous communities and used in healing and religious ceremonies. Other psychedelics, such as lysergic acid diethylamide (LSD), were synthesized by Western scientists in the twentieth century.

Although their therapeutic mechanisms of action are unknown, psychedelics may promote cognitive flexibility and new perspectives on one's circumstances, which has been hypothesized to occur in the context of treating major depressive disorder, for example[3]. Study participants often report feeling more connected to nature, family and society[4]. Some researchers believe that psychedelics could also improve physical symptoms such as pain. However, even without affecting physical symptoms or functional impairments, psychedelics might reduce end-of-life anxiety and depression.

Nevertheless, adopting psychedelics in palliative settings raises ethical concerns[5]. We highlight five of the most important, including selecting appropriate candidates, determining how and when to broach the subject, obtaining informed consent, minimizing the risk of unpleasant or traumatic psychedelic experiences and reducing the risk of coercion or abuse of vulnerable patients (Box 1). These ethical challenges require prompt attention.

Selecting candidates

Existing clinical trials may be of limited use in identifying candidates for end-of-life psychedelic treatment. Clinical trials have uniformly imposed relatively restrictive eligibility criteria. Most have attempted to exclude participants with multiple medical comorbidities, complex drug regimens and severe socioeconomic stressors[6]. Accordingly, study participants might not reflect the diversity of populations with life-threatening illness, many of whom have complex medication regimens and comorbidities, such as serious psychiatric conditions[7]. Additionally, trials have excluded persons presumed to be at risk for negative long-term consequences of psychedelic use due to underlying psychiatric illness or related family histories. For instance, persons with borderline personality disorder are thought to be at elevated risk of severe psychological regression and increased suicidal ideation if administered psychedelics[8]. Similarly, those with pre-existing psychotic disorders, or a family history thereof, are believed to be at increased risk for prolonged psychosis[9]. Although understandable in early clinical trials, where researchers were reintroducing psychedelics to Western science, these exclusion criteria lack empirical support, and the effects of psychedelics on excluded populations should be assessed in randomized controlled trials.

The strict exclusion criteria of psychedelic trials have multiple implications. They suggest that mounting evidence on the efficacy of psychedelic treatments for existential distress may not fully extend outside clinical trials. Insofar as the benefit of psychedelics derives from an existential reorientation, terminally ill persons with cognitive impairments or serious psychiatric conditions may be less likely to receive those benefits—we can only speculate until trials include these populations. In addition, limited generalizability means the risk of harm from psychedelic medicines, though apparently minimal in clinical trials, may be greater in hospice, palliative care or general clinical practice. Finally, the lack of generalizability raises difficult questions regarding equity. Given that persons with terminal illnesses and those with complex psychiatric, medical or socioeconomic conditions can experience severe existential distress, should they not also have opportunities to receive psychedelic treatments, even if they may be at increased risk for adverse events? To further complicate this question, potential harms and benefits should be evaluated in the context of an individual's prognosis and available alternatives.

These delicate balancing questions are beset by countervailing intuitions. Suppose a patient with a terminal illness has other health conditions or a medication regimen that could significantly increase the risk of serious adverse events if they received psychedelic treatment. On one hand, the potential relief of severe existential distress may outweigh the risk. On the other, these risks may loom larger given the importance of best utilizing what remaining time patients have. For instance, it would be tragic if psychedelic treatment made one's remaining weeks unbearable due to worsened anxiety, depression or psychosis. To better inform these decisions, psychedelic trials should

BOX 1

The challenges of integrating psychedelics into end-of-life mental healthcare

Challenges	Recommended approaches
Selecting appropriate candidates for end-of-life psychedelic treatment	Tailor recommendations to individual patient prognosis, priorities and available alternatives. To increase the quality and quantity of evidence to guide clinical decision making, increase the diversity of psychedelic clinical trials to better reflect populations in hospice and palliative care, including people with serious, life-threatening illnesses and complex medication regimens and comorbidities.
Determining when and how to broach the subject of psychedelic interventions	Discuss potential psychedelic treatment with patients, families and caregivers early in hospice or palliative care planning. Have frank conversations regarding decision-making capacity and the role of healthcare proxies and advanced directives in end-of-life psychedelic treatment.
Obtaining informed consent for psychedelic treatment in hospice or palliative care settings	Evaluate medical decision-making capacity. Thoroughly discuss potential benefits and risks, including the risk of symptom exacerbation and increased susceptibility to coercion and abuse. Review advanced directives and consult with healthcare proxies.
Minimizing the risk of traumatic psychedelic experiences	Train hospice and palliative care practitioners to be skilled psychedelic researchers and clinicians. Include unconventional treatment settings and timeframes in clinical trials to understand how they affect the patient experience. Use role-playing and virtual reality simulations to help prepare patients for the perceptual effects of psychedelics. Teach patients coping skills to alleviate the distress of challenging psychedelic experiences and rehearse those behaviors before a psychedelic experience.
Reducing the risk of coercion or abuse of vulnerable patients during or following psychedelic treatment	Educate patients, family members and caregivers on the risk of patient coercion and abuse. Account for the atypical settings in which end-of-life care may be provided.

carefully include more diverse cohorts, including end-of-life patients with complex backgrounds and conditions.

Many jurisdictions are creating paths outside the conventional healthcare system, which patients might utilize to alleviate depression and anxiety at the end of life. In the USA, Oregon has licensed centers for supervised non-medical psilocybin consumption. Colorado will license similar centers in 2025. Because these programs have fewer exclusion criteria than clinical trials, people with complex medical conditions may utilize them toward the end of life.

Oregon and Colorado have also reduced or eliminated criminal penalties associated with psychedelics. Meanwhile, in countries such as Jamaica, Mexico, Peru and The Netherlands, some psychedelics are unregulated, making these attractive locations for retreat centers, where tourists consume psychedelics with little or no medical oversight. Palliative care clinicians should be aware that patients may attempt to access psychedelics in these and other settings, which could represent a risk for vulnerable individuals.

Because jurisdictions around the world either do not regulate psychedelics or are reducing legal restrictions, clinicians should understand that they might not be the sole gatekeepers of access to psychedelics. They may have to treat patients whose psychedelic experiences outside the medical system went awry or advise those contemplating psychedelic use outside the medical system on risk mitigation.

Informed consent

What should an ethical approach to informed consent for psychedelic use look like at the end of life? Obtaining informed consent to receive psychedelics is already complex given difficulties in predicting outcomes. This population heaps on additional challenges. Many persons with serious, life-threatening illness may have at least partial or temporary reductions in cognitive capacity — whether due to neurodegenerative illness such as Alzheimer's dementia, delirium associated with severe illness or medication effects.

To best address this complexity, the prospect of psychedelic treatment should be introduced early, allowing all involved to thoroughly consider it while maximizing the chance that patients have sufficient capacity to understand the risks. Psychedelics remain stigmatized and widely misunderstood. Accordingly, patients and caregivers may have strong preconceived notions regarding their use. Suggesting psychedelic medicine when a patient's condition has progressed or is deteriorating could intensify conflict and confusion. Raising the topic early helps ensure competence to make informed decisions.

The relevant risks are not merely physical or psychological. They may also be legal and financial. Because psychedelics can alter how people perceive interpersonal relationships, there is potential for coercion and abuse of vulnerable patients at the end of life — for example, influencing patients to make large financial gifts[10] or abruptly amend their wills. During the informed consent process, clinicians should discuss these risks.

For patients with diminished medical decision-making capacity, family members might make healthcare decisions on their behalf. However, because of the intense and somewhat unpredictable nature of psychedelic experiences, and the potential to exacerbate patient distress, one potential precaution is to avoid psychedelics in patients with diminished capacity unless they have signed a healthcare proxy or advanced directive authorizing their use. Even then, clinicians should proceed cautiously.

Reducing the risk of abuse and adverse events

Practitioners of psychedelic medicine often refer to 'set' and 'setting', the mindsets in which patients approach psychedelics and the physical environments in which they are administered. These variables are believed to influence safety and efficacy. Psychedelic trials often use therapeutic environments arranged to promote comfort and relaxation. However, in palliative care settings, psychedelics might be administered in skilled nursing facilities or patients' homes, where conditions are less predictable and easily controlled, potentially increasing the risk of adverse events, including patient coercion and abuse.

Training hospice and palliative care practitioners to be skilled psychedelic researchers and clinicians may help reduce the risk of adverse outcomes in vulnerable populations and unconventional environments. Relevant training may include spiritual, religious and existential aspects of psychedelic medicine. Including atypical settings in psychedelic clinical trials will improve our understanding of how these variables affect outcomes.

Some researchers hypothesize that technologies such as virtual reality could simulate psychedelic experiences and reduce risk by setting optimal patient expectations. Introducing the prospect of psychedelic therapy early in hospice or palliative care increases the likelihood that technological aids could be employed. Similarly, role playing and honest discussions regarding risk may help reduce psychedelic-associated morbidity. People who routinely use psychedelics report learning to talk themselves through challenging experiences. It is likely that these coping skills can be taught if adequate time is allocated, and patients remain competent to learn them.

The accelerated timeframes of end-of-life care might also affect the risks. Typically, psychedelic treatment includes multiple integration sessions where patients process their substance-induced experiences. The importance of integration to reducing adverse effects has not been fully established. Nevertheless, in the latter stages of hospice or palliative care, there may be inadequate time for significant integration, which could increase the risk of adverse outcomes. Accordingly, clinical trials of psychedelics should attempt to include both unconventional therapeutic settings, and timeframes for patient preparation and integration, to determine how they influence outcomes.

Conclusion

Because clinical trials of psychedelic therapies typically exclude patients with complex medical conditions, their results might not be fully applicable to populations who could benefit from psychedelics at the end of life. To fill this knowledge gap, future research should modify conventional approaches to psychedelic therapeutics, adapting them to patients who are more acutely ill. Trials should also study the accelerated timeframes associated with end-of-life care, and varied clinical settings, including patients' homes and skilled nursing facilities. In the meantime, uncertainty regarding the use of psychedelics at the end of life makes adequate patient education and informed consent paramount.

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