Feature Article

A Rapid Review of Psychedelic-Assisted Therapy in the Context of Palliative Care

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Psychedelic-assisted therapy (PAT) involves supported experiences with psychedelic medicines in carefully curated environments. Early evidence suggests possible utility of PAT for addressing psychosocial-spiritual-existential concerns, yet gaps remain in understanding findings related to PAT's role in palliative care. This rapid review aims to synthesize current literature on applications of PAT in the context of palliative care. Through a systematic process, we identified 34 articles published between January 2021 and July 2024. Protocols varied yet included common components of participant screening, preparation, dosing, and integration. Psilocybin was the most commonly studied compound. Results support safety and initial efficacy of PAT for psycho-spiritual-existential outcomes among carefully screened and highly homogonous samples of patients with serious illness (predominantly cancer). Current efforts and challenges around integrating PAT into systems of palliative care were highlighted. Additional work is needed to (1) explore PAT's safety and efficacy within more diverse samples and contexts, (2) train palliative care providers on PAT, (3) determine systems of care delivery best suited for translation of PAT into practice, and (4) begin developing policy solutions to support safe and equitable access to PAT. Because many patients lack access to basic psychosocial-spiritual-existential care, careful consideration is needed around integration of PAT.

KEY WORDS

palliative care, policy, psilocybin, psychedelic, psychedelic-assisted therapy, psychosocial-spiritual-existential, rapid review, serious illness, supportive care

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M. Miller received research support from the Office of the Vice Chancellor for Research and Graduate Education, University of Wisconsin-Madison, with funding from the Wisconsin Alumni Research Foundation. W.E.R. is partially supported by NIH)/National Cancer Institute (NCI) Comprehensive Cancer Center award number P30CA008748. A.P. has received research support from the Multidisciplinary Association for Psychedelics Studies, Usona Institute, and Filament.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jhpn.com).

DOI: 10.1097/NJH.0000000000001096

Psychedelic-assisted therapy (PAT) has emerged as a potentially useful psychosocial-spiritual-existential intervention in the palliative care context.[1-3] Across settings where legal PAT occurs (predominantly research trials and specialized clinics), PAT involves informed consent, comprehensive preparation, at least 1 experience with a psychedelic substance, and 1 or more postpsychedelic integration sessions.[3,4] Psychedelic-assisted therapy experiences are facilitated by practitioners with specialized training in PAT, often including nurses, to ensure a safe therapeutic process.[3-6] Although there currently is no set regulatory standard for PAT practitioners,[7] specialized training in PAT can be obtained through various certificate programs, universities, nonprofit organizations, and for-profit companies. Legality of PAT is complex, with status differing by location, substance, and regulatory context.[8] As the field of PAT continues to evolve, it is important to explore the nuances of this unique intervention and its relevance to palliative care nursing.

Many people with serious illness struggle with psychosocial-spiritual-existential concerns, in addition to physical

symptoms.[9-11] Early evidence yields promising results for PAT among people with serious illness.[3] For example, people with cancer undergoing PAT have reported decreases in depression, anxiety, and death anxiety, and increases in quality of life and spiritual well-being.[1,12] Qualitative findings explore lived experiences with PAT among people with serious illness to uncover potential underlying psychological processes.[13] Although PAT may also have applications in hospice, most research in this area has focused on the context of palliative care. As this field continues to grow, calls for additional investigation have been made to understand optimal psychedelic substances, dose, number of sessions, safety profile (especially within the context of serious illness), and efforts to address clinical trial diversity.[1,2,12]

Psychedelic-assisted therapy research is rapidly expanding,[14] requiring a deeper understanding of this unique intervention to inform nursing roles and responsibilities. Thus, the objectives of this review were to (1) present an overview of how PAT is being administered in palliative care, (2) describe the impacts of PAT in palliative care, and (3) provide implications for PAT across palliative care practice, policy, and research.

METHODS

Search Strategy

A rapid review of the literature[15] was completed to uncover evidence related to PAT in palliative care. Systematic searches were conducted in June and July 2024 across PubMed and PsycINFO using standard search terms and Medical Subject Headings (see Supplemental Table 1, http://links.lww.com/JHPN/A110) to identify peer-reviewed research published in or after January 2021. Searches were also conducted to identify relevant gray literature from professional organizations and legislative measures.

Inclusion and Exclusion Criteria

All authors developed inclusion/exclusion criteria by consensus (see Supplemental Table 2, http://links.lww.com/JHPN/A110), and then a subset of authors reviewed each title/abstract accordingly (M. Miller, M. Myers, A.M., S.N.). Full-text articles were then each reviewed by at least 2 authors (M. Miller, M. Myers, A.M., S.N.) to determine inclusion/exclusion. Covidence[16] was used to complete literature screening. Reasons for exclusion were tracked throughout. During screening, questions or disagreements were resolved by discussion between 2 or more authors until consensus was reached.

Data Extraction

Article title, author(s), publication date, country of origin, funding source(s), purpose, study design, sample inclusion/exclusion criteria, participant characteristics, PAT method(s), outcomes, and results/key findings were extracted from each article using Covidence.[16] Team members independently extracted data; a second team member verified accuracy.

RESULTS

Characteristics of Included Publications

Initial searching yielded 2215 records. Nine records were identified through hand searching and gray literature searches. After removing duplicates, 2204 records (titles and abstracts) were screened for relevance. Full-text versions of each publication (n = 104) were then assessed based on inclusion/exclusion criteria. Ultimately, 34 publications were included in this rapid review. See Supplemental Figure 1, http://links.lww.com/JHPN/A111, for a modified Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram, with reasons for exclusion. See Supplemental Table 3 for a summary of included articles and Supplemental Table 4 for an overview of best practices for nurses, http://links.lww.com/JHPN/A110.

Articles in this rapid review included quantitative studies (n = 3),[17-19] qualitative studies (n = 4),[20-23] a multiple-methods study (n = 1),[24] study protocols (n = 2),[25,26] reviews and/or commentaries (n = 19),[2,14,27-43] case studies (n = 2),[44,45] and gray literature pieces (n = 3).[8,46,47] Publications primarily originated from the United States (n = 20).[2,8,14,18-24,27,28,30,31,35,36,38,42,46,47] When funding information was included (n = 14),[2,17,19-21,23-26,30,34,38,40,48] it was primarily awarded by nonfederal sources, including private donations. Across studies, participants were most commonly female, White, highly educated, and facing cancer diagnoses. Publications primarily focused on psilocybin-assisted therapy (n = 11).[17-19,21,22,24,27,36,42,44,45] Some focused on 3,4-methylenedioxymethamphetamine–assisted therapy (n = 1),[25] ketamine-assisted therapy (n = 1),[47] and lysergic acid diethylamide–assisted therapy (n = 1).[26] Others focused on multiple psychedelic substances.[2,8,14,20,23,28-32,34,35,37-41,43,48]

PAT Administration

Overview of PAT Administration

Across publications, PAT administration was described as involving multiple steps: participant screening, informed consent, preparation, 1 or more supervised psychedelic sessions, and postsession integration. Participants in PAT trials were screened using a comprehensive set of inclusion and exclusion criteria that were developed by each study team.[19,24-26] Inclusion criteria varied yet often required some level of baseline distress associated with life-threatening illness, diagnosis of a serious or incurable illness (such as cancer), life expectancy > 3 months, and willingness to refrain from medications or activities that could impede the safety of the intervention.[19,24-26] Exclusion criteria often addressed comorbidities that posed safety risks in the context of PAT, such as liver dysfunction,

certain cardiovascular conditions, uncontrolled psychiatric comorbidities, or active suicidality.[19,24-26]

Preparation

All studies included an informed consent process that involved discussion of PAT, as well as potential benefits and risks. Across studies, 1 to 3 preparation sessions were held before psychedelic dosing, each with a duration of 1 to2 hours per session and 1 to 2 practitioners (often nurses and/or other mental health practitioners with specialized training in PAT) per participant.[19,21,24,25,44,45] Preparation sessions included focusing on mindset, intention, building rapport, and providing psychoeducation.[19,21,24,25,44,45] Preparation sessions occurred in both individual and group settings, or a combination of both.[19,21,24,25,44,45] When group preparation sessions were used, they incorporated a supportive expressive group therapy style.[19,24]

Dosing Sessions

Psychedelic substance and dosage varied across publications. Psilocybin, the most commonly studied substance, was dosed orally ranging from 0.2 to 1 g or 2.5 to 5 g of dried mushrooms, or 20 to 25 mg psilocybin capsules. Weight-based dosing followed standards set in previous study protocols, at a ratio of 0.3 mg/kg.[13,49] Dosages were most often standardized across participants in the context of clinical trials.[19,24,25] Psychedelic dosing sessions were delivered in comfortable environments, created to minimize the clinical setting in favor of a more living-room–like environment, generally accompanied by eyeshades and headphones with predetermined music.[19,24,25,44,45] No matter the substance, there was a strong emphasis on the therapeutic process. During psychedelic sessions, participants were often encouraged to be present with their internal experience as it unfolded.[19,24,25,44,45] Nondirective psychological support occurred most commonly in person by trained practitioners.[19,21,24,25,45] Practitioners were from multiple disciplines and included physicians, social workers, nurses, psychotherapists, psychologists, and counselors, often with specialized training in PAT.[19,21,24-26,43-45] Protocols predominantly included 1 single dosing session in a clinic-based environment[19,24,25,45]; however, 1 publication involved psilocybin dosing over 4 to 5 separate occurrences in naturalistic environments with a loved one as a guide,[36] whereas another publication involved 13 microdoses of lysergic acid diethylamide both in clinic and at home.[26] Psychedelic session length was not reported, but 1 systematic review identified sessions generally lasting between 6 and 14 hours.[43]

Postsession Integration

Most publications describing PAT also highlighted the use of postsession integration after psychedelic dosing sessions.[19,21,24-26,36,38,43-45] Across publications, there was a range of 1 to 7 postpsychedelic integration sessions,[19,24,25,36,43,45] most commonly using approximately 3 integration sessions with a trained practitioner.[19,24] Integration sessions were focused on revisiting intentions, reflection on the psychedelic experience, consolidation of memories related to the experience, and developing meaning. Integration was delivered in both group and individual settings, largely in-person.[19,21,24-26,36,45]

PAT Outcomes

Four publications explored feasibility, acceptability, and safety of PAT.[17,19,21,24] High acceptability of PAT was reported,[17,21] PAT in a group setting was found to be a safe and feasible alternative to individual sessions that could address accessibility and scalability issues,[19,21,24] and no serious adverse events were reported across studies.[2,19,21,24,26,43] Results revealed that PAT yielded rapid and sustained reductions in depression, anxiety, hopelessness, death anxiety, demoralization, and existential distress, and improvements in spiritual well-being and overall quality of life.[13,19,21,44,45] Participants have reported PAT as one of the most meaningful experiences of their lives.[14,45]

Importantly, 1 participant across studies reported "major worsening" of psychosocial-spiritual-existential symptoms.[44] Of note, they received PAT through Canada's compassionate access program, which is often less regulated than clinical trial settings (eg, lack of clearly defined practitioner training, varied symptom and safety assessments, less stringent inclusion criteria),[44] emphasizing a need for additional focus on PAT's safety and efficacy. Other publications highlighted the need for a tempered approach to prioritizing access to PAT, citing concerns around potentially enhancing stress during an already difficult time of life, and/or diverting focus and resources away from ensuring equitable access to basic palliative care and other evidence-based psychosocial-spiritual-existential interventions.[14,48]

Across reviews and commentaries, publications explored implications of PAT for existential distress and medical assistance in dying (MAiD),[29,34] and the potential of PAT as an alternative or complement to opioid use at the end of life.[41] In addition, corollaries between PAT and palliative care delivery models were described, highlighting how drawing upon insights gained through development of modern hospice and palliative care models may support the implementation of human-centered high-quality PAT.[38] Across publications, topics related to equity were discussed, such as the importance of centering diversity in future PAT trials and honoring Indigenous traditions that inform current PAT practice.[2,20,26,29,38] Barriers to PAT delivery, including cost, legal ambiguities, social stigma, lack of professional integration pathways, and limited regulatory guidance, were also explored.[2,22,23,38,42]

Translation of PAT Into Clinical Practice

Some publications raised concerns about standardization of PAT delivery given its varied subjective effects.[2,23,28,38]

Psychedelic-assisted therapy's promise in treating existential distress was explored, potentially as an alternative to controversial interventions such as palliative sedation and MAiD.[29,37] Palliative providers reported uncertainty about psilocybin's risks and benefits, whether practitioners who want to facilitate PAT sessions would require a new specialty, and whether PAT should be individualized or protocolized.[22,23] Given the unique legal status of PAT, most publications in this review reported on findings from PAT provided in the context of clinical trials, where session costs were not charged to participants (they were provided for free as part of study protocols)[19,24-26]; therefore, questions remain about cost and affordability once PAT becomes more widely available. When exploring PAT outside the context of a research setting, practical issues were discussed such as legal ambiguities, social stigma, lack of professional training pathways, and limited regulatory guidance.[27] In addition, publications in this review explored the contrast of PAT's relational, existential, and nonlinear approach with the need to fit into current medical systems.[20,23,36,38] Finally, the necessity of multidisciplinary collaboration (nurses, psychotherapists, physicians, spiritual care providers, etc) in PAT delivery was mentioned across publications.[2,23,38,47,50]

DISCUSSION

This rapid review aimed to synthesize recent literature related to the integration and impact of PAT in palliative care and identify multilevel implications. Findings of the review showed the PAT field is rapidly advancing with scientific and related literature addressing patient outcomes and clinical implications for multidisciplinary clinicians, as well as broader societal and resource utilization issues. A key issue is the time- and resource-intensive nature of PAT required to ensure the full package of associated care (ie, screening, consent, preparation, supported psychedelic session[s], and postsession integration).[4] Given that many patients with serious illness continue to lack access to basic psychosocial-spiritual-existential care,[51] fundamental questions remain about how to allocate resources to ensure advancement of PAT delivery in equitable, effective, and sustainable ways while considering just allocation of human, fiscal, and physical resources. In the context of significant resource limitations faced by health systems and practicing clinicians (eg, time, cost, adequately trained staff), group PAT[19,21,24,26] may be a viable alternative to individual delivery to reduce demand while increasing access and scalability. However, significant questions remain regarding how to best structure and provide group PAT for optimal outcomes.[52]

Homogeneity of PAT study participants (eg, White, highly educated) is evident.[1] Thus, although PAT safety continues to be validated among carefully screened patient populations in controlled clinical trial environments,[19,21,24] generalizability of related safety and physical outcomes to more diverse samples (including diversity across cultural, racialized, sexual, sex, social identities, etc) is unclear. Evidence for efficacy of PAT across outcomes (eg, depression, anxiety, death anxiety, demoralization, quality of life, spiritual well-being) has also been established in previous studies using similarly homogeneous samples.[13,19,21,44,45] Although logistical and systemic challenges of equitable PAT implementation and more inclusive recruitment and accrual practices are not well described, lack of diversity remains a common thread that needs timely attention as PAT obtains increased scientific investment.

With increased societal and political focus on MAiD nationally and globally,[53] further exploration of PAT as a novel intervention to decrease a desire for hastened death is warranted, given evidence for its role in alleviating psychosocial-spiritual-existential suffering.[1,3,19,24] In summary, although results reflect encouraging clinical outcomes as a result of PAT, additional examination of how to best translate this unique intervention into clinical care with the development of interprofessional and nursing guidelines to drive safe and resource-conscious care is needed. Careful policy considerations pertaining to PAT at institutional, local, and national levels will be essential, while also considering changing regulations about nonmedical use of psychedelics across many states, to prioritize safety with medically indicated access for patients in need.

CONCLUSION

Implications for Practice

Psychedelic-assisted therapy is an increasingly acceptable palliative intervention and may be a reasonable option to offer patients experiencing psychosocial-spiritual-existential suffering before proceeding to MAiD. The following implications for practice were identified in this rapid review:

- With appropriate screening, informed consent, and risk mitigation, PAT can often be safely deployed, even in medically fragile palliative care patients.
- PAT calls for a multidisciplinary approach to care with practitioners who have received training in psychedelic therapies.
- Palliative care patients often report psychosocial-spiritual-existential suffering. Extant clinical trials of PAT show salutary benefits for depression, anxiety, and existential distress and warrant replication in larger trials.

Implications for Policy

There are significant gaps in policy-related knowledge. Moving forward, regulations and funding mechanisms should support and facilitate rigorous and inclusive research efforts, including consideration of rescheduling and/or potentially decriminalizing psychedelics and updating breakthrough

therapy designation laws. The following implications for policy were identified in this rapid review:

- Developing policies must include guidelines on professional ethics for psychedelic practice to ensure public safety.
- Data on state-level challenges, including legal ambiguities and limited regulatory guidance, should be collected and shared across relevant parties to inform best practices in a quickly evolving legal and regulatory landscape.
- Psychedelics should be included in right-to-try laws, and other expanded access programs, to provide terminally ill persons access to experimental medications that are not yet US Food and Drug Administration approved.
- Policies and funding should prioritize representation, accessibility, and a commitment to the protection of Indigenous rights and sovereignty.

Implications for Research

Rigorous research is needed in all aspects of psychedelic-related care. The following implications for research were identified with this rapid review:

- The roles of nurses and advanced practice nurses should be explored throughout PAT preparation, delivery, and integration in the context of larger health care delivery systems, clinical team dynamics, licensure, and scopes of practice.
- The safety and efficacy of PAT should be evaluated in more diverse population samples to center the experiences of systematically marginalized and minoritized people.
- Community-engaged research approaches that incorporate the experiences of cultural groups that have used psychedelics in traditional healing should be used to inform study design and implementation where appropriate.

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