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How Should We Expand Access to Psychedelics While Maintaining an Environment of Peace and Safety?

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Abstract

Psychedelics have long been used by individuals seeking peace and a sense of wellness. This article examines widespread adoption of ketamine as a proxy for psychedelics. For ketamine, there is a need to protect vulnerable persons from exploitation that should be balanced against risks of hypermedicalization. This article suggests strategies for striking such a balance, including by carefully differentiating between persons with psychiatric illnesses, such as treatment-resistant depression, who could benefit from psychedelics, and persons using psychedelics for peace and wellness under careful guidance.

Wellness Pursuits in Clinical Settings

Various methods are used to achieve an individual sense of peace and wellness in modern clinical and nonclinical settings, including meditation, prayer, dietary changes, self-reflection, and substance-mediated peace experiences. These practices have varying degrees of published evidence to support their efficacy, but virtually all methods of attaining peace are heavily marketed—sometimes with strong claims to being the correct, or even the only, method of attaining peace if properly followed. The marketing of personal peace and wellness can take advantage of the vulnerabilities of people who are desperate to feel better at any cost and who might in fact be seeking these resources during an episode of psychiatric illness. A wide variety of clinicians, therapists, coaches, guides, and other leaders in health and wellness practices are positioned to wield their credibility over these practices for personal gain. Often, those who are critical of the medicalization of psychedelic experiences have just as much—or more—financial incentive to market their methods. In this article, we discuss the case of ketamine treatment to explore the ethical obligations of health professionals to be aware of the benefits, detriments, and economic interests at play in the growth of modern psychedelic administration as a peace and wellness practice.

Brief History of Psychedelics

Psychedelics are a heterogeneous group of compounds that produce a profound effect on mood and consciousness. Historically, psychedelics have been defined exclusively by 5HT-2A receptor antagonism, with recent debates considering a broader definition that includes compounds that induce psychedelic-like experiences (such as ketamine,

cannabis, and 3,4-methylenedioxymethamphetamine, or MDMA).[1] While systematic evaluation of psychedelics' therapeutic benefit primarily started in the mid-20th century in Western medicine, many psychedelic compounds have been utilized by Indigenous communities for centuries.[2] Extensive research in the 1950s and 1960s led to greater interest in utilizing these compounds alone or in conjunction with psychotherapy to treat psychiatric illness.[3] With the discovery of lysergic acid diethylamide (LSD) and the isolation of other psychedelic compounds, research on the potential therapeutic benefits of psychedelics continued until the passage of the Controlled Substances Act of 1970, which criminalized the majority of psychedelic compounds.[4] A resurgence of scholarly work at the beginning of the 21st century has resulted in renewed interest in the clinical use of psychedelics, accompanied by considerable popular interest in psychedelics not only to treat psychiatric illness, but also to facilitate peace and wellness practices in diverse settings and for other uses outside of the clinical context, including recreational use.

There is growing consensus within the psychiatric field supporting the use of psychedelics in clinical practice, potentially representing a substantial shift in perspective.[5] This growing support has coincided with the biotechnology sector's renewed interest in commercializing psychedelics and in developing new psychedelic compounds for clinical use.[6] Most medications with psychedelic potential are still only in an investigational stage of development—except ketamine, which was approved by the US Food and Drug Administration (FDA) in 1970 for use as an anesthetic agent and was later found to induce an acute mental state similar to that of classic psychedelics.[7,8] Given widespread clinical use of ketamine, we contend that it is a compelling proxy for the coming wave of potential psychedelic treatments. Furthermore, aspects of the commodification of ketamine practices could offer a cautionary tale about the ethics of access to psychedelics.

Ketamine Use and Commodification

Due to ketamine's ubiquitous use as an anesthetic, its incorporation in clinical practice for other indications following early displays of efficacy has been rapid. Currently, intravenous racemic ketamine and intranasal esketamine (an enantiomer) are used in clinical practice for treatment-resistant depression, defined as depression that persists despite trials with 2 conventional antidepressive regimens.[9] Recommending ketamine to patients, however, is complicated by access, variable quality of programs and treatments, patient ability to pay out of pocket, and potential for recreational use.

Ketamine's use as a peace and wellness adjunct as well as its use in the clinical setting is restricted by its regulatory and legal status, which results in substantial costs to people looking to access this treatment. Racemic ketamine remains an FDA Schedule III controlled substance indicated only for use in induction and maintenance of anesthesia. Administration of racemic ketamine in the wellness or psychiatry realms falls under off-label use, with little-to-no insurance coverage. Intranasal esketamine received FDA approval in 2019 for use in adults with treatment-resistant depression, in combination with conventional antidepressants.[10] Although FDA approval may have improved esketamine's potential for insurance coverage, treatment prices for both esketamine and racemic ketamine remain upwards of $500 or more per session, often with protocols that include up to a dozen sessions or more.[11,12]

Ketamine's growth in the mental health sphere has been rapid, and it is now offered in a variety of settings—including clinics associated with major health centers, clinics run by

large corporations, and independent mental health clinics—and can be taken at home, with or without virtual monitoring. The numerous settings in which ketamine is offered raise considerable concerns about the consistency and quality of treatment.[13] These concerns include the level of experience of the clinicians administering the infusion, access to medications to manage complications, and access to a prescribing clinician to manage complications. The variable quality of treatment is best exemplified by the difference between receiving ketamine in an experienced infusion center with clinicians available to manage complications and receiving ketamine in the home setting. Complications of ketamine administration that might require clinical management or closer observation include transient blood pressure changes, oversedation, and lightheadedness.[14] Clinics in which ketamine is administered without significant infusion experience or guardrails might have the benefit of lower maintenance costs but could compromise patient safety. Restricting ketamine use only to clinical environments with greater resources and experience, however, could limit access as well as increase costs for the patient.

The growth of access to ketamine is in no small part due to private interest in managing treatment-resistant depression and other psychiatric illness, which incurs tens of billions of dollars in direct and indirect costs annually.[15] The variety of settings in which ketamine is offered, financial interests in marketing ketamine, and substantial advertisement of ketamine services by private equity-funded ketamine startups makes it difficult for physicians to responsibly recommend treatment centers, and so they rely primarily on reputation. The increased prescribing of ketamine, though well intentioned, has led to marketing for many off-label indications, and at times patients might be getting treatments when there is no clinical indication at all.[16]

Contextualizing Psychedelic Use

Current concerns about ketamine treatment, access, and recreational use can serve as a proxy for those of other psychedelics as they are submitted to the FDA for approval for psychiatric indications. There has been a huge growth of interest in legislation concerning decriminalization and rescheduling of psychedelics over the past decade, as exemplified by the first-ever 2023 congressional hearing on psychedelic-assisted psychotherapy for use in military veterans.[4,17] As these medicines become FDA approved, questions remain about insurance coverage and the potential expense incurred by people who might be in a vulnerable state and who could instead choose to access less reliable sources of these medicines outside of the regulated market. As exemplified by cannabis in New York State, the unregulated market dominates consumption when price is a concern, despite increased availability of regulated products.[18] It is also likely that clinicians and private companies will develop and market their own methods of psychedelic administration without substantial evidence to support them—mirroring practices that have proliferated with ketamine. These risks might be mitigated by credentialing or licensing and by requiring implementation of a Risk Evaluation and Mitigation Strategy (REMS) program. REMS is an FDA program that provides closer monitoring of and guidelines for administration of medications with potentially adverse effects.[19] This program could mitigate some risks related to quality and safety of administration, and a REMS program has been in place for intranasal esketamine since its approval in 2019.[20] A highly regulated market provides greater protections but comes at the cost of potentially restricting access and reducing the number of sites capable of administering the drug. Despite the pitfalls of a more regulated market for psychedelics, an unregulated market allows opportunistic practitioners to prey on those seeking treatment or wellness pursuits at any cost.

Examining the dual clinical and other uses of psychedelics might further aid our understanding of the evolving regulatory environment of psychedelics in general. Nonclinical uses of psychedelics are those that have not reached a particular evidence-based standard that is the result of the typically rigorous pharmaceutical approval process. Both recreational use of psychedelics and personal use of psychedelics for peace and wellness fall under nonclinical use, but the latter might have therapeutic potential similar to that of psychedelic use in a clinical environment. However, the home or community environment for nonclinical uses of psychedelic experiences, even if therapeutic, would not offer the clinical responsiveness and protections of formalized clinics. Special protections and considerations in psychedelic treatment and use are critical for people with severe psychiatric illness or who have significant medical complexity. However, if psychedelic usage is only kept within the confines of specific clinics, there is a risk of gatekeeping, leaving vulnerable people seeking peace and wellness—regardless of whether they carry a psychiatric diagnosis—to pay a high price. Price is of great concern in general when it comes to psychedelic treatment, and there is interest in developing alternatives to traditional treatment that offer greater affordability and increased access, such as group-based treatment.[21] While research is still ongoing, there is also a popular perception that psychedelics benefit the wellness of healthy individuals as well as those with psychiatric disease.[22] Thus, it is worth distinguishing between people who might benefit from psychedelics to treat specific illnesses in a more controlled clinical setting and people who might benefit from psychedelics as a peace and wellness pursuit. Both might receive treatment in regulated clinics, but the latter might bear unnecessary costs if other psychedelics follow the route of ketamine.

The interplay between safety and access is further complicated by a subset of patients who might experience psychological harm from long-term use of psychedelics, such as anxiety, social disconnection, or depersonalization.[23] These potential harms might necessitate closer long-term monitoring of patients who experience complications as well as closer monitoring during psychedelic administration. Is it possible to have safe, appropriate access for patients who are at higher risk while working toward ethical and safe use outside of traditional clinical settings? Extending access might require creative solutions, group-based treatment, new types of treatment models, or development of psychedelic medicines that can be adapted to different settings. It should start with discerning which patients are at higher risk and need treatment in a clinical setting and which patients might be able to safely use psychedelics in less controlled environments.

Conclusion

The landscape of psychedelic experiences for treatment and for peace and wellness pursuits is evolving rapidly. What guidance should clinicians and therapists give to patients who are interested in these medicines? Additional education, with an emphasis on harm reduction, will be critical for all involved in the clinical setting and, in particular, for psychiatrists. There are many well-intentioned clinicians offering treatment with unproven products or making claims in the peace and wellness space that are not justified by the literature. Clinicians have a responsibility to educate patients and caution against perceptions that these medicines are a panacea, as well as to give clear safety recommendations for patients with clinically and psychiatrically complex illnesses. As clinicians develop and market their own methods of psychedelic administration, guidelines, limitations, and licensing will be necessary to maintain patient protection.

Determining the risks and benefits of psychedelic use for people who have been—and who have not been—diagnosed with a psychiatric illness is a complex challenge, but one

with great promise in the pursuit of peace and wellness, as well as within the scope of clinical treatment. These determinations are inextricably intertwined with issues of inequality in access, marketing and risks of false promises, off-label use, and gatekeeping in medicalization that could delay or prevent crucial benefit for people who are in need.

References

1. Nichols DE, Nichols CD, Hendricks PS. Proposed consensus statement on defining psychedelic drugs. *Psychedelic Med (New Rochelle)*. 2023;1(1):12-13.
2. Williams K, Brant S. Tending a vibrant world: gift logic and sacred plant medicines. *Hist Pharm Pharm*. 2023;65(1):8-32.
3. Nichols DE, Walter H. The history of psychedelics in psychiatry. *Pharmacopsychiatry*. 2021;54(4):151-166.
4. Siegel JS, Daily JE, Perry DA, Nicol GE. Psychedelic drug legislative reform and legalization in the US. *JAMA Psychiatry*. 2023;80(1):77-83.
5. Barnett BS, Arakelian M, Beebe D, et al. American psychiatrists' opinions about classic hallucinogens and their potential therapeutic applications: a 7-year follow-up survey. *Psychedelic Med (New Rochelle)*. 2024;2(1):1-9.
6. Aday JS, Barnett BS, Grossman D, Murnane KS, Nichols CD, Hendricks PS. Psychedelic commercialization: a wide-spanning overview of the emerging psychedelic industry. *Psychedelic Med (New Rochelle)*. 2023;1(3):150-165.
7. Mathew SJ, Shah A, Lapidus K, et al. Ketamine for treatment-resistant unipolar depression. *CNS Drugs*. 2012;26(3):189-204.
8. Bowdle TA, Radant AD, Cowley DS, Kharasch ED, Strassman RJ, Roy-Byrne PP. Psychedelic effects of ketamine in healthy volunteers: relationship to steady-state plasma concentrations. *Anesthesiology*. 1998;88(1):82-88.
9. McIntyre RS, Rosenblat JD, Nemeroff CB, et al. Synthesizing the evidence for ketamine and esketamine in treatment-resistant depression: an international expert opinion on the available evidence and implementation. *Am J Psychiatry*. 2021;178(5):383-399.
10. Traynor K. Esketamine nasal spray approved for treatment-resistant depression. *Am J Health Syst Pharm*. 2019;76(9):573.
11. Brendle M, Robison R, Malone DC. Cost-effectiveness of esketamine nasal spray compared to intravenous ketamine for patients with treatment-resistant depression in the US utilizing clinical trial efficacy and real-world effectiveness estimates. *J Affect Disord*. 2022;319:388-396.
12. Nissen N. Closures of ketamine clinics leave some patients scrambling for treatment. *ABC News*. June 3, 2023. Accessed April 30, 2024. https://abcnews.go.com/Health/closures-ketamine-clinics-leave-patients-scrambling-treatment/story?id=99800266
13. Peskin E, Gudin J, Schatman ME. Increased demand for ketamine infusions and associated complexities. *J Pain Res*. 2023;16:295-299.
14. Short B, Fong J, Galvez V, Shelker W, Loo CK. Side-effects associated with ketamine use in depression: a systematic review. *Lancet Psychiatry*. 2018;5(1):65-78.
15. Amos TB, Tandon N, Lefebvre P, et al. Direct and indirect cost burden and change of employment status in treatment-resistant depression: a matched-cohort study using a US commercial claims database. *J Clin Psychiatry*. 2018;79(2):5360.
16. FDA warns patients and health care providers about potential risks associated with compounded ketamine products, including oral formulations, for the

treatment of psychiatric disorders. US Food and Drug Administration. October 10, 2023. Accessed January 12, 2024. https://www.fda.gov/drugs/human-drug-compounding/fda-warns-patients-and-health-care-providers-about-potential-risks-associated-compounded-ketamine
17. McCarthy K. Health Chairwoman Dr Miller-Meeks delivers opening remarks at first-ever oversight hearing on emerging therapies to combat PTSD, veteran suicide, addiction. News release. House Committee on Veterans' Affairs; November 14, 2023. Accessed April 30, 2024. https://veterans.house.gov/news/documentsingle.aspx?DocumentID=6312
18. McPhillips T. Weed is legal in New York, but the illegal market is still booming. Here's why. *PBS News Hour*. March 28, 2023. Accessed January 12, 2024. https://www.pbs.org/newshour/nation/weed-is-legal-in-new-york-but-the-illegal-market-is-still-booming-heres-why
19. Risk Evaluation and Mitigation Strategies: REMS. US Food and Drug Administration. Reviewed May 16, 2023. Accessed June 21, 2024. https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems
20. SPRAVATO® REMS (Risk Evaluation and Mitigation Strategy). SPRAVATO®. Accessed June 21, 2024. https://www.spravatorems.com/
21. Marseille E, Stauffer CS, Agrawal M, et al. Group psychedelic therapy: empirical estimates of cost-savings and improved access. *Front Psychiatry*. 2023;14:1293243.
22. Johnson MW, Hendricks PS, Barrett FS, Griffiths RR. Classic psychedelics: an integrative review of epidemiology, therapeutics, mystical experience, and brain network function. *Pharmacol Ther*. 2019;197:83-102.
23. Evans J, Robinson OC, Argyri EK, et al. Extended difficulties following the use of psychedelic drugs: a mixed methods study. *PLoS One*. 2023;18(10):e0293349.

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