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VIEWPOINT

Psychedelics in Addiction Treatment— Navigating a Sociopolitical Rift

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The human toll of substance use disorders (SUDs) has become catastrophic, demanding innovative approaches to address the growing crisis. While this reality has coincided with a resurgence of interest in the use of psychedelics in treating addictions, the current infrastructure of psychedelics research faces a complex juxtaposition with the multidimensional social, economic, and political factors shaping the SUD epidemic. As we navigate an evolving terrain and reflect on a history of drug policies that have frequently lacked empirical support, it is critical for psychedelics researchers to maintain vigilance regarding how our work fits into the broader framework of drug addiction as a disorder defined not only by dysregulation of neural circuitry, but also by systemic forces less visible within conventional clinical research. We identify avenues through which researchers, practitioners, and sponsors of psychedelic science may support the field's alignment with principles of health equity core to addiction medicine.

Center Cultural Inclusivity in Psychedelics Clinical Research

At a population health level, experiences of trauma underlying the development of addictions are often rooted within sociostructural exposures and policies that propagate inequality, systemic racism, isolation, and despair.^{1,2} Yet, published clinical trials of psychedelic therapies have largely failed to enroll individuals most impacted by these structural undercurrents.³ A systematic review of psychedelic studies conducted between 1993 and 2017 (N = 282) underscored a stark reality: only 2.5% of participants were Black and 2.1% Latino, while 82.3% were non-Hispanic White.³ While recent years have brought heightened attention to the imperative of achieving balanced racial and ethnic representation in psychedelic research, significant disparities persist.⁴

Recommendations and deliberate attempts to address this issue have included designing clinical trials in collaboration with community-based stakeholders serving racial and ethnic minoritized patients, integrating strategies to reduce enrollment barriers faced by low-income participants, and improving diversity among investigators, therapists, and staff involved in psychedelics research.⁴ However, the maintenance of exceptionally strict eligibility criteria across psychedelic clinical trials has compounded their systematic omission of patients facing social challenges. Trials commonly exclude adults with histories of cardiac disease, physical disability, or family histories of psychotic illness—conditions associated with social disadvantage. Most have also excluded people who use illicit substances and, among trials focused on SUD treatment, nearly all have excluded individuals who routinely use multiple substances, despite

epidemiologic data indicating widespread polydrug use⁵ and a recognition that psychedelics carry therapeutic potential across multiple SUDs. Thus, while eligibility restrictions are important for assuring safety and interpretability of some clinical effects, research addressing the prevailing SUD crisis necessitates a more judicious equilibrium between participant selectivity and real-world generalizability.

Expand Public Funding for Psychedelics Research

The degree of racial homogeneity found among participants of psychedelic studies falls short of guidelines mandating inclusion of racial and ethnic minority groups set forth by the National Institutes of Health, highlighting 1 of several harmful downstream effects of the near-total cessation of federal funding for psychedelics research between 1970 and 2020. Encouragingly, the National Institutes of Health and US Food and Drug Administration (FDA) have recently revived such funding, advancing the field's growth potential and providing opportunities to design studies that are more explicitly aligned with public health priorities. Several states have also instituted policies and allocated funding for psychedelics research, supporting the development of initiatives that may better address local needs.

While this progress is promising, considerable groundwork remains before psychedelics may be safely disseminated in clinical settings to treat SUDs. Prior to obtaining FDA approval in 2002, sublingual buprenorphine, an effective pharmacotherapy for opioid use disorder, was evaluated in 3 phase 3 randomized clinical trials (RCTs), which collectively enrolled 1224 participants.⁶ Meanwhile, recently published findings from US psychedelic trials for SUD treatment are limited to a single phase 2 RCT of psilocybin for alcohol use disorder (AUD) (n = 95) and 2 small psilocybin pilot studies for AUD (n = 10) and tobacco use disorder (n = 15).⁷ Streamlining regulatory hurdles associated with conducting research with Schedule I substances may reduce administrative burdens among sponsors and expand clinical investigations in this domain. For example, following the demonstration of preliminary efficacy in early-phase trials, breakthrough therapy designations could be routinely considered for programs developing psychedelic drugs as treatments for SUDs, expediting later phase trials. Furthermore, if a Schedule I substance receives a breakthrough therapy designation for a specific medical indication, from a public health perspective, it would be beneficial to subsequently treat it as a Schedule II drug, eliminating the ongoing need to maintain a Schedule I research registration. Such a change to the Controlled Substances Act had notably

received bipartisan support when proposed in the Breakthrough Therapies Act.

Recognize the Unique Value of Observational Data

While RCTs have long been considered the gold standard for establishing the therapeutic efficacy of medications, clinical trials of psychedelics have drawn criticism due to ineffective blinding and challenges in maintaining fidelity to manualized psychotherapy. However, in contrast to most drug development candidates, psychedelics have already been used by nearly one-fifth of US adults.⁵ Consequently, while clinical trials remain critical to elucidating the safety and efficacy of psychedelics within a medicalized model, observational studies examining their therapeutic uses outside of clinical settings may offer insights into how psychedelics may be safely accessed by real-world populations.

This is particularly important in an era marked by evolving policies regarding psychedelic legalization and decriminalization. As these drugs become increasingly available, shifting focus to high-quality data collection via observational cohorts may allow for a more comprehensive understanding of the benefits and harms associated with psychedelic use, particularly among vulnerable populations. The concurrent development of efficient, centralized systems for pharmacovigilance reporting of psychedelics may similarly support the identification of safety signals to inform public health responses.

Avoid Reliance on a Strictly Medical Model

Even if some psychedelic drugs receive FDA approval in the near term, overreliance on a medicalized model is likely to preclude access among racial and ethnic minoritized patients and those with SUDs, who already experience barriers accessing medical care.² In 2021, fewer than 5% of patients in the US with AUD accessed any form of treatment and fewer than 1% received

evidence-based AUD medications.⁵ Analogously, while the FDA approval of buprenorphine expanded opioid use disorder treatment access by authorizing office-based prescribing of an opioid-based maintenance medication, considerable racial disparities in buprenorphine use ensued.^{2,6}

Moreover, all modern US psychedelic clinical trials include components of psychotherapy administered by licensed clinicians, yet high-quality therapy is cost prohibitive for many people with severe addictions. The brief psychotherapy models used in clinical trials are also potentially concerning for treating SUDs, which are considered chronic relapsing disorders and require ongoing supportive care—particularly during abstinence, when return to drug use may pose overdose risks. Therefore, studies exploring the use of psychedelics in combination with nonclinical models of psychosocial support, such as community-based peer support networks, may contribute meaningfully to the literature.

Advocate for Policies That Address Addiction Comprehensively

While psychedelic therapies may be uniquely equipped to address the complex neuropsychiatric mechanisms that underly drug addiction, we have significant work ahead of us to ensure that their potential is not eroded by existing frameworks of neuroscience, biotechnology development, regulation and marketing—which have produced significant racial disparities in addiction treatment access.² We must also avoid repeating a history of attempting to use a siloed pharmacologic solution to address the sociopolitical and structural issues that have shaped this mental health crisis.¹ Instead, studying the role of psychedelics in addiction treatment should occur in partnership with advocacy for evidence-based policies that reduce harms from drug use, expand access to existing SUD treatments, mitigate socioeconomic disparities, and foster trust among communities most impacted by the war on drugs.

ARTICLE INFORMATION

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