

Strategies For Improving Diversity In Psychedelics Research

By **Kyle Mack and Julia Markov** (August 18, 2022, 4:32 PM EDT)

The American Psychiatric Association issued an official position statement in July related to the medicinal use of psychedelic, and other psychoactive drugs that produce feelings of empathy, for mental health conditions.[1]

It comes at a time when societal and governmental interests in this burgeoning space are increasing at what seems to be an exponential rate.

The statement, which suggests that "[c]linical treatments should be determined by scientific evidence in accordance with applicable regulatory standards and not by ballot initiatives or popular opinion," comes swiftly on the heels of an analysis by the APA regarding the ethical and practical implications of psychedelics in the field of psychiatry.[2]

While this latter document outlines bases for the APA's concerns regarding social and political movements related to psychedelics, it also touches upon existing challenges in psychedelics research and how they potentially affect the integration of psychedelics into the practice of psychiatry.

One challenge the APA highlights is that of diversity inclusion in clinical trials. Diversity within research is essential in all therapeutic sectors to ensure real-world applicability and generalizability of study results, but it is perhaps particularly important in the emerging therapeutic psychedelics space.

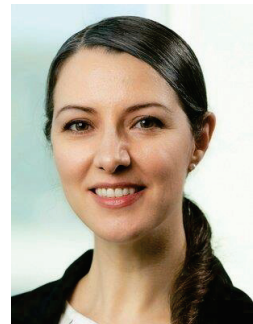
The National Institutes of Health recently noted that "knowledge gaps in psychedelics research persist due to the lack of participant diversity in clinical trials to date" in a June letter to Sen. Brian Schatz, D-Hawaii, regarding psychedelics research.[3]

For therapeutic psychedelics, the knowledge gaps go beyond understanding how a drug behaves pharmacologically in different populations — a challenging enough feat in and of itself — as nonpharmacological factors are also at play.

The NIH's response letter explains that "a person's subjective experience of a psychedelic drug varies depending on their mental state at the time that the drug is administered and the setting in which they have the experience." [4]



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Studying how the psychedelic therapeutic response varies across different racial, ethnic and other underrepresented populations — and how it is influenced by unique biological and sociocultural factors — is key not only to optimizing these promising new therapeutics, but also advancing health equity.

In this article, we focus on diversity challenges encountered in both psychedelics research and psychedelic therapy, as well as how efforts by the U.S. Food and Drug Administration, legislators and the NIH to promote diversity can be combined with other strategies to help stakeholders ensure psychedelic therapies are safe and effective for everyone, including underrepresented populations.

Diversity Challenges in Clinical Trials and Other Areas of Psychedelics Research

Available published data on participants in psychedelic studies reveal the racial and ethnic disparities in study participants as compared to the general U.S. population.

For example, a 2018 study published in BMC Psychiatry[5] evaluated the ethno-racial breakdown in 18 psychedelic studies conducted between 1993 and 2017 and found that, of the total 282 participants, 82.3% were non-Hispanic white, while only 2.5% were Black, 2.1% were Latino, 1.8% were Asian, 4.6% were Indigenous, 4.6% were mixed race, 1.8% were "other" and 8.2% were "unknown." [6]

Contrast this to the ethno-racial breakdown of the U.S. population, which was, as of July 2021, 59.3% non-Hispanic white, 13.6% Black, 18.9% Hispanic or Latino, 6.1% Asian, 1.3% American Indian and Alaska Native, 0.3% Native Hawaiian and other Pacific Islander, and 2.9% two or more combined races.[7]

Perhaps compounding the problem is the historical challenge of minority inclusion in other areas of psychedelics research and practice, including among scientists and other staff involved in recruiting for and conducting clinical trials, therapists, business and academic leadership, and even editorial boards.[8]

Therapeutic Response to Psychedelics Isn't Just Influenced by Pharmacological Factors

Biological differences in how individuals process drugs can affect pharmacological response.

For example, genetic variations across different races that influence how a drug is metabolized in the body could affect the safety and efficacy of a particular therapy for certain racial or ethnic groups.[9]

Drug response can also be influenced by sociocultural factors.[10] Most notably, sociocultural factors may affect set and setting — a concept in psychedelic therapy where nonpharmacological factors influence psychedelic experience.[11][12]

Set typically describes the patient's mindset and expectations. Response to psychedelics therapy is best achieved with a positive mindset and a willingness to submit to the experience.

Mistrust of the health care system due to history of discrimination and exploitation, as well as inequities in drug-related arrests and prosecutions, may negatively alter mindsets and expectations.[13]

Setting refers to the environment in which psychedelic therapy occurs.

Perhaps the most important factor shaping the environment, and thus drug response, is the therapeutic relationship. Culturally insensitive therapists, or therapists who have not personally experienced similar

sociocultural struggles as the patient, may fail to recognize or offer the proper supportive care necessary for optimal response.

This could be especially problematic if there is a lack of understanding of race-based trauma.[14] Music, lighting, decor and artwork within the treatment area also work to shape the therapeutic psychedelic experience.[15]

Additional research is needed to explore how these elements may influence the therapeutic response and how they can best be incorporated into the therapeutic setting to optimize treatment efficacy.[16]

Recent Efforts by FDA, Legislators and the NIH Hope to Improve Diversity

In April, the FDA took an additional step toward its ongoing aim of promoting diversity in clinical trials generally, by issuing a new draft guidance titled "Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials." [17]

The draft guidance is the most recent among several guidance documents the administration has issued aimed at increasing clinical trial diversity. It lays out the overall framework for the content and format of a race and ethnicity diversity plan, which sponsors of a medical product should submit early in clinical development to promote enrollment of more participants in clinical trials from underrepresented racial and ethnic populations.

While the emphasis is on race and ethnicity, the FDA suggests sponsors also consider other underrepresented populations, such as sex, gender identity, age, socioeconomic, disability, pregnancy, lactation and comorbidity status.

Additionally, the FDA's Office of Minority Health and Health Equity created the diversity in clinical trials initiative, which includes public education and outreach and will use strategies such as "educational materials in multiple languages, a dedicated webpage with public service announcements and videos, social media outreach and ongoing stakeholder engagement, collaborations and partnerships" to promote diversity.[18]

Legislators are also taking steps to help increase clinical trial diversity.

The Diverse and Equitable Participation in Clinical Trials Act,[19] a bipartisan bill introduced to Congress in February, if passed, would require sponsor applicants for new drug and devices to report clinical trial enrollment targets by demographic subgroups, including race and ethnicity among others, and submit a diversity action plan for how they will meet such targets.

In addition, the FDA would have authority to mandate post-approval studies and surveillance when demographic subgroup data is insufficient.

The NIH already mandates inclusion of women and minorities in NIH-funded clinical research.[20] Specifically with regard to the therapeutic psychedelics space, the NIH has noted that it "aims to develop guidance to help the field address the lack of participant diversity." [21] Such guidance would be a welcome tool in this area.

Another helpful NIH resource is the NIH Workshop on Psychedelics as Therapeutics: Gaps, Challenges and Opportunities held in January, which included recorded sessions exploring how the contributions of

set and setting can be considered in psychedelic clinical trial designs.[22]

The FDA's draft guidance, alongside the proposed congressional legislation and the anticipated NIH guidance, may accelerate progress in increasing diversity in all areas of pharmaceutical research, including psychedelics.

Additional Strategies to Improve Diversity

When designing clinical trials, psychedelic drug sponsors can consider making trial participation as accommodating as possible to promote inclusion of participants of color.

Strategies such as reducing frequency of study visits, assisting in travel, incorporating telehealth or using mobile health providers to visit patients at their home when applicable, and providing rooms for overnight stays — especially if treatment sessions are lengthy — may be effective ways of increasing diversity among study volunteers.[23][24]

In addition to improved diversity training, broader recruitment of therapists from underrepresented groups will be needed. Sponsors should invest in community engagement and collaborations where nonclinician members of the community can serve as participant recruiters, protocol design consultants and as advisers in institutional review boards.[25]

It is crucial to strive for improving diversity at all levels where patients can see their community represented through researchers, therapists and other staff.

Amending the way clinical trials are designed and reported may also help fill the knowledge gaps referenced by NIH.

This may include, among other things:

- Publishing the diversity breakdown of participants in all studies;
- Powering studies for predefined subgroup analyses when possible;
- Promoting collaboration between researchers to pool data or build registries in order to collect large enough samples to detect outcomes for underrepresented populations; and
- Specifically evaluating the effects of set and setting on treatment outcomes and how they are shaped by sociocultural factors.[26]

Additionally, the scientific and cultural contributions of indigenous people and other underrepresented groups should be recognized, highlighted and incorporated into practice.[27] Fully utilizing this diverse knowledge base could inform study designs and treatment plans that will ultimately improve the generalizability of study findings.[28]

Lastly, it is never too early for stakeholders to develop plans for ensuring equitable access to these groundbreaking therapies once they are FDA-approved.

As an example, the Multidisciplinary Association for Psychedelic Studies, in anticipation of a possible future FDA approval of MDMA-assisted therapy, has created a health equity program, which includes a fundraising goal and allocation strategy of \$5.5 million to four initiatives:

1. Scholarships for training therapists, supervisors and trainers from historically marginalized communities;
2. Treatment access funds to support clinics and patients in the expanded access program;
3. Outreach and education to build an inclusive community; and
4. Hiring team members dedicated to integrating health equity principles.[29]

Although plans for equitable access will undoubtedly differ among stakeholders, it is paramount to have strategies in place so that no one in the population is disadvantaged from attaining the full health potential of these promising psychedelic therapies.

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[1] See Jonathan E. Alpert, William M. McDonald, Charles B. Nemeroff & Carolyn Rodriguez, Position Statement on the Use of Psychedelic and Empathogenic Agents for Mental Health Conditions ("Position Statement"), Am. Psychiatric Ass'n (July 2022), <https://www.psychiatry.org/getattachment/d5c13619-ca1f-491f-a7a8-b7141c800904/Position-Use-of-Psychedelic-Empathogenic-Agents.pdf>.

[2] See Gregory S. Barber & Charles C. Dike, Resource Document on Ethical and Practical Implications of Psychedelics in Psychiatry, Am. Psychiatric Ass'n, (June 2022), <https://psychiatry.org/getattachment/998071b6-138e-40d1-a482-e7b8e85d4f90/Resource-Document-Psychedelics-in-Psychiatry.pdf>.

[3] See Letter from the NIH to the Honorable Brian Schatz (June 15, 2022), <https://s3.documentcloud.org/documents/22076083/response-from-nimh-nida-re-psychedelics-research-061522.pdf>.

[4] Id.

[5] See Timothy I. Michaels, Jennifer Purdon, Alexis Collins & Monnica T. Williams, Inclusion of people of color in psychedelic-assisted psychotherapy: a review of the literature, BMC Psychiatry, 2018;18(1):245.

[6] Id.

[7] See United States Census Bureau, QuickFacts: Race and Hispanic Origin (July 1, 2021), <https://www.census.gov/quickfacts/fact/table/US>.

[8] See Jamilah R. George, Timothy I. Michaels, Jae Sevelius & Monnica T. Williams, The psychedelic

renaissance and the limitations of a White-dominant medical framework: A call for indigenous and ethnic minority inclusion, *Journal of Psychedelic Studies*, 2020;4(1):4–15.

[9] See for example A. Ramamoorthy, MA Pacanowski, J. Bull & L. Zhang, Racial/Ethnic Differences in Drug Disposition and Response: Review of Recently Approved Drugs, *Clinical Pharmacology & Therapeutics* 2015;97(3), 263-273 (2015). (Showing that 21% (35/167) of new molecular entities (NMEs) approved by the FDA between 2008-2013 reported racial/ethnic differences in pharmacokinetics, safety, efficacy, dosing, or pharmacogenetics).

[10] See Coedelic-Assisted Psychotherapies, *Experimental and Clinical Psychopharmacology*, 2021;29(5):539-554.

[11] See Logan Neitzke-Spruill, Race as a component of set and setting: How experiences of race can influence psychedelic experiences, *Journal of Psychedelic Studies*, 2020;4(1):51-60.

[12] See Fogg et al., *supra* note 10.

[13] *Id.*

[14] *Id.*

[15] *Id.*

[16] *Id.*

[17] See FDA, Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials; Draft Guidance for Industry; Availability (Apr. 2022), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/diversity-plans-improve-enrollment-participants-underrepresented-racial-and-ethnic-populations>.

[18] See FDA, FDA Takes Important Steps to Increase Racial and Ethnic Diversity in Clinical Trials (Apr. 13, 2022), <https://www.fda.gov/news-events/press-announcements/fda-takes-important-steps-increase-racial-and-ethnic-diversity-clinical-trials>.

[19] See Diverse and Equitable Participation in Clinical Trials Act (DEPICT Act), H.R. 6584, 117th Cong. (2022), <https://www.congress.gov/bill/117th-congress/house-bill/6584/text?r=8&s=1>.

[20] See NIH, Inclusion of Women and Minorities as Participants in Research Involving Human Subjects (Feb. 9, 2022), <https://grants.nih.gov/policy/inclusion/women-and-minorities.htm>.

[21] See Letter from the NIH, *supra* note 3.

[22] See NIH, NIH Workshop on Psychedelics as Therapeutics: Gaps, Challenges and Opportunities (Jan. 12-13, 2022), <https://www.niaaa.nih.gov/news-events/meetings-events-exhibits/nih-workshop-psychedelics-therapeutics-gaps-challenges-and-opportunities>.

[23] See FDA, Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry (Nov. 2020), <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enhancing-diversity-clinical-trial-populations-eligibility->

criteria-enrollment-practices-and-trial.

[24] See Michaels et al., *supra* note 5.

[25] See George et al., *supra* note 8.

[26] See Fogg et al., *supra* note 10.

[27] See George et al., *supra* note 8.

[28] *Id.*

[29] See MAPS, Introducing our Health Equity Program, <https://maps.org/health-equity/?campaign=health-equity&allocation=health-equity> (last visited Aug. 3, 2022).