The Long Road Toward Equitable MDMA Treatment in the United States

Zofia Kozak, MD, and Scott T. Aaronson, MD

A recent New York Times article[1] described favorable findings from the most recent clinical trial investigating 3,4-methylenedioxymethamphetamine (MDMA) for moderate-to-severe posttraumatic stress disorder (PTSD).[2] The article described next steps in the regulatory process for MDMA, as Lykos Therapeutics (formerly Multidisciplinary Association for Psychedelic Studies, or MAPS) has compiled data from 18 phase II and III trials and submitted a new drug application (NDA) to the US Food and Drug Administration (FDA) for the review and possible approval of MDMA-assisted therapy (MDMA-AT) for PTSD. As of February 13, 2024, the FDA officially accepted this NDA, granting it priority review status.

MDMA research has had to confront significant legal restrictions and social stigma to get to this point. MDMA was first synthesized in 1912 at Merck Pharmaceuticals. It was initially studied only in animal models and was then resynthesized in 1960 by 2 Polish chemists.[3] Although MDMA was likely used recreationally starting in the 1960s, human research did not begin until the 1970s. MDMA enjoyed several years of use in psychotherapeutic settings before being outlawed in the United States in 1985 as a Schedule 1 drug.[4] MAPS was formed by Rick Doblin in 1986, with the intention of conducting further scientific investigation into MDMA's therapeutic potential following its ban. However, early research efforts were thwarted, as MDMA became mired with scientific hesitancy and doubt. Questions of its clinical utility, potential for its abuse, and risk of patient exploitation due to associated hypersuggestible states resulted in a scientific dark age in the United States, with no domestic scientific investigation of MDMA until the first MAPS-funded trial was published in 2011.[5]

Despite its complicated history, MDMA is now undergoing regulatory review to be approved as a psychiatric treatment in the United States. To obtain FDA approval, an investigational drug must complete phase I, II, and III clinical trials demonstrating efficacy and population-level safety and submit an NDA, which the FDA reviews to make a final regulatory decision.[6] Safety and efficacy data from early clinical trials on MDMA allowed this new wave of research to skip the early safety trials and immediately begin phase II trials in the United States, culminating in the completion of multisite phase III clinical trials investigating MDMA-AT for PTSD, with favorable results. In the first phase III trial, 67% of participants experienced a complete remission of symptoms at the primary study end point (18 weeks after baseline), no longer qualifying for a diagnosis of PTSD.[7] This stands in contrast with current standards of care for PTSD, such as prolonged exposure, which is associated with PTSD remission in 14%–40% of participants.[8,9] Approval for MDMA is actively being negotiated, following the NDA submission to the FDA in December 2023.[10] However, there is a significant risk that under-resourced communities will lack access to MDMA if, and when, it becomes legally available. Trauma disorders are widespread in underserved communities, contributing to significant morbidity and mortality,[11] and these communities stand to benefit the most from addressing underlying trauma disorders. However, they may be the least likely to have access to MDMA-AT. The rollout of esketamine for depression in the United States provides an important historical example underscoring this argument. The FDA approved the nasal spray esketamine for treatment-resistant depression in 2019. Since its approval, socioeconomic disparities in accessing this medication have been well documented.[12]

Questions of Insurance Coverage for MDMA-AT

Thus far, every single MAPS-funded MDMA clinical trial has included a robust psychotherapeutic framework composed of 3 preparatory sessions, either 2 or 3 dosing sessions, and multiple integration sessions. The positive outcomes from the trials are thought to be at least in part due to skilled therapists providing psychotherapy, acting synergistically with the MDMA itself. As MDMA progresses through the regulatory approval process, questions remain about how this framework will be implemented and regulated. While the FDA has a broad scope of regulatory authority, there is no precedent for it regulating a psychotherapeutic framework associated with a novel drug, and it is unclear how it would do

so. If it elects to do so, providers may be required to participate in the risk evaluation and mitigation strategy (REMS), an FDA supervisory drug safety program for drugs with significant safety risks. REMS programs are operationally complex, as many require prescriber training and certification and may require dispenser certification and patient enrollment.[13] This may impede access to medications under REMS, as prescribers may be hesitant to prescribe these medications with such administrative burdens. Insurance companies and other payors will be tasked with ensuring MDMA is delivered with psychotherapy, and given the high costs associated with delivering psychotherapy, they may elect not to cover this (despite one study suggesting cost benefits with MDMA-AT[14]). Importantly, even if the FDA approves MDMA-AT, insurance companies are not required to pay for these services despite the American Medical Association approving new Current Procedural Terminology (CPT) billing codes for psychedelic-assisted therapy. It is also worth noting that the current MAPS model for MDMA-AT optimizes for safety, thus requiring an intensive number of resources in the form of therapist hours, prescriber time, and facility needs. With increasing safety data from trials, investigating newer (and less resource-intense) models of delivering MDMA-AT will be needed.

Equitable Access to MDMA Treatment Hinges on the Willingness of Medicare to Cover It

As stated above, more research is needed to identify cost-effective models for administering MDMA-AT. However, if MDMA-AT is approved within the current MAPS model, including a mandatory associated psychotherapeutic component, it is possible that health insurances will not cover this combination due to large costs associated with psychotherapy. This will likely result in the creation of a large industry of private, for-profit clinics that will deliver the evidence-based combination (preparation sessions, psychotherapy during the dosing session, and integration sessions) to those who can afford it, rendering this evidence-based approach out of reach for marginalized communities. If MDMA is approved as a standalone medication (ie, without a required psychotherapeutic component), insurances may either elect to cover MDMA but pay for fewer hours of psychotherapy than there is currently evidence for (again, creating an opening for for-profit clinics to deliver the full spectrum of therapy to those who can afford it) or choose not to cover psychotherapy at all, leaving those who cannot afford or access concurrent psychotherapy to receive substandard treatment. Either way, it appears that the key to ensuring an equitable rollout will be to lobby the Centers for Medicare and Medicaid Services for coverage of MDMA treatment with concurrent psychotherapy. As the largest US health care payer, Medicare's coverage decisions often precede Medicaid and private health plan reimbursement and inform how they pay for physician services.[15,16] If Medicare does not cover this treatment—and as a result, if Medicaid does not cover this treatment—it will be rendered irrelevant for marginalized communities who stand to gain the most from it, echoing the notion of the "Inverse Care" law, where those who stand to benefit the most from a treatment are paradoxically the least likely to obtain it.

It is also worth noting that even if Medicaid agrees to cover MDMA-AT, the degree to which it will be available and accessible by individuals will vary from state to state. Medicaid programs are quite heterogeneous across states, and state Medicaid administrators have significant autonomous decision-making authority. The extent to which MDMA-AT would be implemented would largely depend on the individual administrator's implementation of eligibility criteria as well as on details of reimbursement rates.

Cultural Barriers to MDMA-AT

It is critical to acknowledge that even if reasonable CPT codes are created and Medicaid covers MDMA-AT, marginalized communities face the same structural barriers to accessing MDMA treatment as they do in accessing general mental health care. Practical issues of transportation costs, difficulty taking time off from work, and lost wages from time off all directly interface with cultural issues, such as mistrust of the medicolegal system due to historical abuses within the medical system and mistrust of illicit drugs following the War on Drugs.[17] A recent qualitative research study assessing Black therapist's experiences of MDMA highlights this point, with one therapist describing fear of doing MDMA (even within a research program) due to fears of possible legal repercussions.[18] Additionally, it is important to consider that many marginalized communities have racially related PTSD, and it will be critical to ensure that facilitators and therapists have culturally informed training to reduce the risk of retraumatizing patients within a health care setting.[18]

Conclusion and Recommendations

We are currently at a critical juncture, with MDMA (and classic psychedelics such as psilocybin) being negotiated outside of the research setting and into clinical psychiatry. There is a great need for effective, organized, and thoughtful advocacy to ensure the priorities of privatized interests do not crowd out the equitable distribution of these treatments. We must have an eye toward ensuring that MDMA-AT is equitably available to all patients, particularly those who stand to benefit the most. This is further explored in the recommendations below.

Recommendation #1: Explicitly State "Equity" as an Organizational Priority. Understandably, there may be hesitance from the American Psychiatric Association (APA) leadership to take a formal stance on MDMA-AT, given its current legal status. However, it would be prudent to recognize and get ahead of the groundswell, as the FDA has officially accepted the NDA for MDMA. Latency in taking a public position creates a leadership vacuum in the rapidly evolving regulatory space. This provides privatized enterprises leverage to roll out initiatives without accountability from the APA, the professional organization that most visibly advocates for mental health needs. A public position on the issue can be taken with a statement from APA leadership explicitly stating that equitable access to MDMA-AT is an organizational priority, along with forming positions within the organization with the stated objective of advocating for equitable access to MDMA-AT. A further step that will be needed is advocacy for joint approval of MDMA with psychotherapy (eg, drug + therapy) as a single treatment, rather than as separate treatments. Future clinical trials will help elucidate the appropriate number of therapy sessions necessary to balance treatment efficacy with treatment cost.

Recommendation #2: Lobby Medicare for Reimbursement. The most obvious way for MDMA-AT to become available to marginalized communities is to ensure that state Medicaid programs cover it, which can only happen if federal Medicare approves the treatment. This will pave the way for private insurances to follow suit and increase accessibility to MDMA-AT in under-resourced communities. For this to happen, persistent lobbying efforts on behalf of medical professional organizations are needed. Given the heterogeneity in Medicaid coverage of approved therapies across states, policies promoting uniform coverage of MDMA-AT across different Medicaid programs will be needed to ensure parity. If insurances elect not to cover MDMA-AT, the almost-certain privatization of MDMA-AT will result in a model maximizing profits for pharmaceutical and privately owned companies at the expense of population-level health objectives. We need effective lobbying of Medicare at the federal level and Medicaid programs at the state level for equitable access to MDMA-AT.

Recommendation #3: Ensure Training Therapists From Marginalized Backgrounds Is a Funding and Organizational Priority. Given the history of medically related trauma and the prevalence of racialized trauma within marginalized communities, it is imperative to create a safe environment for these individuals during MDMA treatment. Specifically, it will be critical to train therapists in culturally informed approaches to prevent the risk of perpetuating racialized medical trauma.

Acting on these 3 recommendations will take us a few steps closer toward an equitable rollout of MDMA-AT.

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Author Affiliations: Department of Psychiatry, University of Maryland School of Medicine, Baltimore, Maryland (Kozak); Institute for Advanced Diagnosis and Therapeutics, Sheppard Pratt Hospital System, Baltimore, Maryland (Aaronson).

Corresponding Author: Zofia Kozak, MD, Department of Psychiatry, University of Maryland School of Medicine, 22 S Greene St, Baltimore, MD 21211 (zofia.kozak.md@gmail.com).

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