

# Research and Implementation of Psychedelic-Assisted Therapy in the Veterans Health Administration

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Proactively preparing for the approval of PATs for clinical use allows the VA to stay on the leading edge of health care and creates opportunities ... to optimize delivery of emerging treatment modalities.

The past decade has seen an accelerating revival in research supporting various psychedelic-assisted therapies (PATs) (1). Currently the strongest body of evidence involves PATs with psychotherapy augmented with 3,4-methylenedioxymethamphetamine (MDMA) for posttraumatic stress disorder (PTSD) (2–5), and psilocybin for both major depressive disorder (MDD) and treatment-resistant depression (TRD) (6–9). The Food and Drug Administration (FDA) has designated each of these PATs as a “breakthrough therapy.” As current research shows promise for leading to potential regulatory changes and clinical access, the Department of Veterans Affairs (VA), as the nation’s largest integrated health care system, must engage in strategic planning for a potential future where PAT is a clinical reality.

The VA has a long history of pioneering health care advancements and is committed to providing the best health care and effective treatment options for veterans. By preparing in advance of potential FDA approval, the VA aims to be able to provide timely and safe access to novel treatments for the veterans who are most likely to benefit. Thus, the VA convened the “State of the Art (SOTA) Conference: Psychedelic Treatments for Mental Health Conditions” in September 2023 to address two major objectives: 1) determine next steps for potential VA system-wide clinical implementation of MDMA and psilocybin; and 2) establish a strategic framework for the VA to conduct psychedelic research. Invited SOTA participants included 72 VA researchers, clinicians, and policy leaders from across the country as well as representatives from other key stakeholder federal agencies, including the Department of Defense, National Institutes of Health, Substance Abuse and Mental Health Services Administration, Office of the Assistant Secretary for Health, and FDA.

SOTA participants were divided into four workgroups: 1) Preclinical Research; 2) Clinical Research; 3) Clinical

Practice Logistics and Implementation; and 4) System-Wide Clinical Decision-Making and Scale. Each workgroup discussed and developed a list of considerations for VA leadership. This report organizes these considerations by theme. We aim to not only detail the considerations developed by the SOTA workgroups but also expand on the next steps that the VA has since taken to support psychedelic research and prepare for potential clinical implementation.

## POTENTIAL PRECLINICAL AND CLINICAL RESEARCH PRIORITIES

Although there is a growing foundation of evidence with MDMA, psilocybin, and other psychedelics, optimizing the delivery of PAT with these treatments will require further preclinical and clinical research. Box 1 summarizes the potential preclinical and clinical research priorities that were identified through the SOTA workgroups. These potential priorities may be used to inform future psychedelic research funded by the VA and other agencies.

## POTENTIAL CLINICAL IMPLEMENTATION AND SYSTEM-WIDE SCALE

PAT represents a paradigm shift in clinical care (13) with treatment protocols that require substantially different resource utilization and clinical workflows than traditional mental health services. Anticipated demand from veterans may initially outweigh available resources to deliver PAT (14). Increased access to PAT in medical settings may help mitigate the risk of spillover to non-prescribed use of psychedelic drugs and its associated morbidity and mortality (15), thus further underscoring the importance of ensuring access to PAT. Box 2 summarizes the considerations that were discussed at SOTA to inform a framework for possible clinical implementation and scale.

## SOTA OUTCOMES

Following SOTA, VA leaders testified before the House Veterans Affairs Committee, Subcommittee on Health in a

## BOX 1. Potential preclinical and clinical research priorities

### Mechanisms and frameworks

- Clarify the molecular, cellular, and network-level mechanisms of action.
- Investigate biomarkers that are both clinically feasible and predictive of treatment outcomes.
- Establish complete profiles of pharmacokinetic and pharmacodynamic drug-drug interactions that are clinically relevant for each psychedelic.
- Consider a transdiagnostic approach based on treating underlying processes as opposed to a diagnosis.
- Utilize a biopsychosocial model to understand mediators and moderators of treatment response and safety, i.e., evaluate biological, psychological, and social markers that may impact outcomes of efficacy and safety.

### Safety

- Collect actionable safety data that is systematic, comprehensive, and includes longitudinal adverse event monitoring.
- Clarify the impact of PAT on precipitation of addiction or non-prescribed substance use.

### Efficacy and therapeutic modality

- Determine how the safety and efficacy of PAT is impacted by concomitant medications, recent discontinuation of medications, comorbidities, sex, age, and other patient-level characteristics.
- Clarify optimization of dose, supplemental doses, timing, number/frequency of dosing sessions, and durability of effect.
- Conduct component analyses to determine what aspects of the therapeutic modality are necessary to optimize safety and efficacy.

- Determine what forms of therapy will be optimal to augment the psychedelic for various indications and patient characteristics.
- Evaluate strategies that improve efficiency and scalability to treat more veterans by optimizing resource allocation without compromising safety and efficacy. Strategies that still require further evaluation include incorporating group preparation, integration, and medication sessions; simultaneously dosing several individuals in multiple rooms; reducing the number of medication sessions per course of treatment; and/or eliminating supplemental doses (10–12).

### Clinical trial methodology

- Select comparators that aim to minimize functional unblinding.
- Measure and report blinding success.
- Manage, measure, and report expectancy for both participants and therapists.
- Incorporate qualitative approaches.
- Involve input from veteran patient stakeholders.
- Ensure VA patients with representative demographic diversity and clinical complexity are recruited in future studies.

### Facilitating future VA research

- Release Requests for Applications (RFAs) to support clinical trials that evaluate safety and efficacy of PATs in veteran populations while also addressing aforementioned research priorities.
- Release implementation science RFAs potentially through the VA's Health Services Research and Development Service and/or fund evaluation efforts via VA's Quality Enhancement Research Initiative or Partnered Evaluation Initiative.

November 2023 hearing focused on these emerging psychedelic therapies. SOTA informed VA's Office of Research and Development decision to issue a Request for Applications (RFA) in January 2024 focusing on MDMA or psilocybin for the treatment of mental health conditions such as PTSD or depression (16). In April 2024, the VA chartered an Integrated Project Team (IPT) of experts from across the VA to help strategically plan for future research and clinical implementation.

The IPT consists of four workstreams that will address research, clinical implementation, training, and evaluation. These workstreams will support the development of a comprehensive plan to implement PAT for mental health treatment in VHA. While the framework developed can be used as a foundation to support the clinical deployment of multiple psychedelic agents that have been studied in therapeutic contexts, the IPT's initial work will focus on MDMA-assisted therapy for PTSD.

## STRENGTHENING PARTNERSHIPS AND COLLABORATIONS

SOTA provided a critical opportunity for interagency partnerships and collaboration, which should continue as the field evolves. SOTA participants realized the importance of tracking the rapidly evolving trends in data, drug development, and safety. In one example, SAMHSA has begun to build partnerships to analyze, monitor, and enhance data systems which will allow the development of risk reduction programming – working together with federal partners to set data strategies and to learn from analyses of implementation, as the VA, the states, and other partners take action to reach those most vulnerable with potentially lifesaving services.

The VA has long-standing relationships with its many academic affiliates, several of whom have been leading the field of psychedelic research. Several VA principal

## BOX 2. Potential clinical implementation and System-Wide Scale priorities

### Foundational strategic planning

- Establish a VA psychedelic implementation task force to track evolving internal and external practice standards.
- Build collaborations with external stakeholders and community partners.
- Develop a strategic communication plan that involves all relevant internal and external stakeholders.

### Safety monitoring and data

- Ensure national data capture to facilitate program evaluation and learning from best practices.
- Establish system-wide safety monitoring and pharmacovigilance and develop measurement-based infrastructure.
- Develop a mechanism to monitor safety related to PAT system-wide with considerations for care in the community.
- Identify appropriate clinical outcome measures and system-wide methodology to capture data over time, including common definitions.

### Training, access, and enterprise scalability

- Develop a high-quality workforce to deliver PAT to veterans.

- Determine the optimal team-based care model(s) for PAT
- Identify minimum training requirements for eligible practitioners.
- Support an internal training and supervision program utilizing current VA Evidence-Based Psychotherapy expertise.
- Ensure equitable access, which may be achieved in part by stratifying access via a scarce resource allocation model with a focus on equity.

### Clinical operations

- Develop VA-wide practice standards that help guide site-level implementation.
- Create PAT directives, standard operating procedures, tools, and any other applicable guidance to facilitate safe and equitable access to PAT for veterans.
- Develop a strategic implementation plan using a hub-and-spoke model, starting with pilot sites to ensure phased and scalable implementation that actively balances safety versus access.
- Foster interdisciplinary teams and inter-facility communities of practice.
- Overall, establish the infrastructure needed to support potential field implementation and sustainment in VA.

investigators with affiliations to these academic psychedelic research programs have already been conducting psychedelic research with the VA, primarily funded through private philanthropy and non-profit psychedelic research support organizations. Expanding the opportunity for VA-funded research through its recently published RFA will help build upon this existing foundation of expertise and further strengthen the partnerships with those academic institutions.

Finally, moving forward strategically with both research and planning for future potential clinical implementation of psychedelic treatments provides the occasion for the VA to create new collaborations with community organizations and industry. This provides the VA the opportunity to better identify innovative, emerging treatments that may improve care for veterans.

## CONCLUSIONS

With the possibility of PATs receiving FDA approval soon, it is advantageous for the VA to explore strategies to further veteran-centered research and to prepare for future potential clinical implementation. Proactively preparing for the approval of PATs for clinical use allows the VA to stay on the leading edge of health care and creates opportunities to partner with interagency colleagues, academic affiliates, and

community and industry partners to optimize delivery of emerging treatment modalities.

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