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PSYCHEDELIC-ASSISTED THERAPY FOR TREATING MENTAL HEALTH DISORDERS

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EXECUTIVE SUMMARY

In the United States, half of all people will be diagnosed with a mental health disorder in their lifetime, and depression is the leading cause of years of life lost due to disability worldwide.¹ Given the burden of mental health disorders, it is vital to explore all treatment options to improve population health. Although they are classified by the Drug Enforcement Administration (DEA) as Schedule I substances—a designation reserved for drugs with no current accepted medical purpose and high abuse potential—psychedelics show significant promise in treating mental health disorders. This paper describes the current evidence for using psychedelics as a treatment for mental health disorders, explores the existing policy landscape and offers suggestions for future psychedelic policy.

1. Department of Economic and Social Affairs, "Mental Health and Development," United Nations, last accessed April 28, 2022. <https://www.un.org/development/desa/disabilities/issues/mental-health-and-development.html>; Office of Disease Prevention and Health Promotion, "Mental Health and Mental Disorders," U.S. Department of Health and Human Services, last accessed April 28, 2022. <https://health.gov/healthy-people/objectives-and-data/browse-objectives/mental-health-and-mental-disorders>.

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A number of clinical trials have assessed the use of different psychedelics to treat a wide range of mental health disorders, including depression, post-traumatic stress disorder (PTSD) and substance use disorders. Most of these trials combine psychedelic doses with guided therapy, which is often referred to as psychedelic-assisted therapy.² There are relatively few clinical trials that have reported outcomes on psychedelic-assisted therapy; however, the initial results are extremely promising. Clinical research combined with observational studies demonstrate the relatively low abuse potential and low toxicity of psychedelics, which makes them even more appealing as a therapeutic option.³

Although more research into psychedelic-assisted therapy is needed to refine methodology, some jurisdictions are already legalizing or decriminalizing certain psychedelics. The most prominent example of this is in Oregon, which legalized the use of psychedelics for therapeutic use in 2020.⁴ Several cities have also legalized possession and use of psychedelics,

2. Brian Pilecki et al., "Ethical and legal issues in psychedelic harm reduction and integration therapy," *Harm Reduction Journal* 18:40 (April 7, 2021). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769>.

3. Rafael Guimarães dos Santos et al., "The Use of Classic Hallucinogens/Psychedelics in a Therapeutic Context: Healthcare Policy Opportunities and Challenges," *Risk Management and Healthcare Policy* 14 (March 5, 2021), pp. 901-910. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943545>; Richard Matzopoulos et al., "Psychedelic Mushrooms in the USA: Knowledge, Patterns of Use, and Association With Health Outcomes," *Frontiers in Psychiatry* 12:780696 (Jan. 3, 2022). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8761614>; Vince Polito and Richard J. Stevenson, "A systematic study of microdosing psychedelics," *PLoS One* 14:2:e0211023 (Feb. 6, 2019). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6364961>; Matthew W. Johnson et al., "The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substances Act," *Neuropharmacology* 142 (November 2018), pp. 143-166. <https://www.sciencedirect.com/science/article/pii/S0028390818302296>; Anne K. Schlag et al., "Adverse effects of psychedelics: From anecdotes and misinformation to systematic science," *Journal of Psychopharmacology* 36:3 (Feb. 2, 2022), pp. 258-272. <https://journals.sagepub.com/doi/full/10.1177/02698811211069100>.

4. "Oregon Measure 109, Psilocybin Mushroom Services Program Initiative (2020)," Ballotpedia, 2020. [https://ballotpedia.org/Oregon_Measure_109_Psilocybin_Mushroom_Services_Program_Initiative_\(2020\)](https://ballotpedia.org/Oregon_Measure_109_Psilocybin_Mushroom_Services_Program_Initiative_(2020)).

with other states considering similar policies.⁵

This paper sets out to familiarize policymakers with the existing body of research on psychedelics use for the treatment of mental health disorders. Additionally, the paper will highlight several factors for policymakers to consider when developing policies associated with psychedelic medicine. These factors include the need for more research into psychedelic medicine; the need to educate and increase the mental health workforce; and the need to ensure equity and access.

INTRODUCTION

Mental health disorders account for 7.4 percent of the global disease burden, translating to about 970 million cases and a global economic cost of \$1 trillion per year.⁶ Individuals with mental health disorders often face significant stigma and marginally effective treatment options.⁷ Many current pharmaceutical treatments take upwards of seven weeks to become effective—if they do—and many people experience intolerable side effects that negatively impact treatment adherence.⁸ New treatments are needed to address the individual and societal toll of mental health disorders.

Despite the need for new treatments, psychiatric pharmaceutical development has slowed significantly.⁹ Many of the recently introduced psychiatric pharmaceuticals constitute small changes to the chemical structure of existing drugs or revised methods of drug delivery. These changes rarely pro-

duce significant improvements in efficacy. Some researchers, however, are looking beyond the existing classes of psychiatric drugs. Psychedelics represent one new area of consideration for treating mental health disorders.

Western exploration of psychedelics began in the 1950s.¹⁰ Despite the positive finding of early psychedelics researchers, sensationalized media coverage and recreational use in the 1960s resulted in psychedelic drugs being classified as Schedule I by the DEA and the United Nations Convention on Psychotropic Substances, a classification reserved for substances with no currently accepted medical use and high abuse potential. Schedule I substances are illegal to use or possess, making it difficult for researchers to obtain and study these substances and stifling research into the medical use of these substances.¹¹

It was not until the 1990s that clinical trials on the use of psychedelics for treating mental health disorders resumed.¹² Initially, positive outcomes led the Food and Drug Administration (FDA) to classify both 3,4-methylenedioxymethamphetamine (MDMA or ecstasy) and psilocybin as “breakthrough therapies” in 2017 and 2019, respectively, allowing for an expedited drug development and approval process.¹³ As a result of publishing more clinical trials, interest in psychedelic medicine continues to grow. Although there is great optimism about psychedelic medicine, especially for the treatment of mental health disorders, psychedelic-assisted therapy researchers are still establishing best practices for delivering treatment. Furthermore, sound regulatory models and jurisdictional oversight are necessary to ensure patient safety once psychedelic medicine is ready for broad application.

This paper will describe the current state of psychedelics research for the treatment of mental health disorders, explain the policy landscape surrounding psychedelics and

5. See, e.g., “Denver, Colorado, Initiated Ordinance 301, Psilocybin Mushroom Initiative,” Ballotpedia, May 2019. [https://ballotpedia.org/Denver_Colorado_Initiated_Ordinance_301_Psilocybin_Mushroom_Initiative_\(May_2019\)](https://ballotpedia.org/Denver_Colorado_Initiated_Ordinance_301_Psilocybin_Mushroom_Initiative_(May_2019)); Noel Gallo, “Agenda Report: Decriminalizing Entheogenic Plants,” City of Oakland, May 15, 2019. <https://www.decriminalizenature.org/media/attachments/2019/11/20/decrim-resolution.pdf>; “Ann Arbor decriminalizes magic mushrooms, psychedelic plants,” AP News, Sep. 26, 2020. <https://apnews.com/article/ann-arbor-plants-featured-ca-state-wire-mi-state-wire-b0ce69ca0961c150e0f900e8ea4cf432>; Andrew Beaujon, “Magic Mushrooms Are Decriminalized in DC as of Today,” *Washingtonian*, March 15, 2021. <https://www.washingtonian.com/2021/03/15/magic-mushrooms-are-decriminalized-in-dc-as-of-today/>; Jon Blistein, “Massachusetts City Moves to Decriminalize Natural Psychedelics,” *Rolling Stone*, Jan. 15, 2021. <https://www.rollingstone.com/culture/culture-news/somerville-massachusetts-psychedelics-magic-mushrooms-decriminalize-1115198/>; Tiffany Kary, “Seattle Votes to Decriminalize Psilocybin and Similar Substances,” *Bloomberg*, Oct. 4, 2021. <https://www.bloomberg.com/news/articles/2021-10-04/seattle-votes-to-decriminalize-psylocybin-and-similar-substances>.

6. Elena Argento et al., “Psychedelic-Assisted Psychotherapy After COVID-19: The Therapeutic Uses of Psilocybin and MDMA for Pandemic-Related Mental Health Problems,” *Frontiers in Psychiatry* 12 (Sept. 6, 2021). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8450400/>; Alize J. Ferrari et al., “Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019,” *The Lancet Psychiatry* 9:2 (Feb. 1, 2022), pp. 137–150. [https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366\(21\)00395-3/fulltext](https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(21)00395-3/fulltext).

7. Argento et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8450400/>.

8. Maxemiliano V. Vargas et al., “Psychedelics and Other Psychoplastogens for Treating Mental Illness,” *Frontiers in Psychiatry* 12 (Oct. 4, 2021). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8520991/>; Toby Lea et al., “Perceived outcomes of psychedelic microdosing as self-managed therapies for mental and substance use disorders,” *Psychopharmacology* 237:5 (May 2020), pp. 1521–1532. <https://pubmed.ncbi.nlm.nih.gov/32043165/>.

9. Jason B. Luoma et al., “A Meta-Analysis of Placebo-Controlled Trials of Psychedelic-Assisted Therapy,” *Journal of Psychoactive Drugs* 52:4 (2020), pp. 289–299. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7736164/>.

10. Franklin King 4th and Rebecca Hammond, “Psychedelics as Reemerging Treatments for Anxiety Disorders: Possibilities and Challenges in a Nascent Field,” *Focus (American Psychiatric Publishing)* 19:2 (June 2021), pp. 190–196. <https://pubmed.ncbi.nlm.nih.gov/34690582/>; Maurizio Coppola et al., “Psilocybin for Treating Psychiatric Disorders: A Psychonaut Legend or a Promising Therapeutic Perspective?,” *Journal of Xenobiotics* 12:1 (Feb. 7, 2022), pp. 41–52. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8883979/>; Peter S. Hendricks et al., “Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population,” *Journal of Psychopharmacology* 29:3 (2015), pp. 280–288. <https://pubmed.ncbi.nlm.nih.gov/25586402/>.

11. Hendricks et al. <https://pubmed.ncbi.nlm.nih.gov/25586402/>; Pilecki et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769/>.

12. Erwin Krediet et al., “Reviewing the Potential of Psychedelics for the Treatment of PTSD,” *The International Journal of Neuropsychopharmacology* 23:6 (2020), pp. 385–400. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311646/>; Mason Marks, “A Strategy for Rescheduling Psilocybin,” *Scientific American*, Oct. 11, 2021. <https://www.scientificamerican.com/article/a-strategy-for-rescheduling-psilocybin/>.

13. “Breakthrough Therapy,” U.S. Food and Drug Administration, Jan. 4, 2018. <https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy>; Guimarães dos Santos et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943545/>; Krediet et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311646/>; Yasemin Saplakoglu, “FDA Calls Psychedelic Psilocybin a ‘Breakthrough Therapy’ for Severe Depression,” *Live Science*, Nov. 25, 2019. <https://www.livescience.com/psilocybin-depression-breakthrough-therapy.html>.

provide policy considerations for preparing for broad application of psychedelic-assisted therapy.

PSYCHEDELICS AS A TREATMENT FOR MENTAL HEALTH DISORDERS

Psychedelics, molecules with “mind-manifesting” properties, can be broken up into three categories of compounds: psychedelics, entactogens and dissociatives.¹⁴ Classical psychedelics include lysergic acid diethylamide (LSD), peyote, mescaline, N,N-dimethyltryptamine (DMT) and psilocybin.¹⁵ Entactogens include MDMA or ecstasy and dissociatives include ketamine.¹⁶ Psychedelics affect the perception of sensory stimuli; increase introspection and self-awareness; alter the sense of time; facilitate mystical experiences; and induce a blissful, joyous or euphoric state.¹⁷ For the purposes of this paper, the term “psychedelics” refers to psilocybin, LSD, DMT and MDMA, unless otherwise specified. Although one form of ketamine, esketamine, has been FDA approved as a therapeutic for treatment-resistant depression, ketamine’s status as a Schedule III substance places it outside of the scope of this paper due to its legal status and accepted use as a medical anesthetic.¹⁸ This is in contrast to other psychedelics, which are Schedule I drugs and have no current accepted medical use.

Clinical Evidence for Psychedelic-Assisted Therapy for the Treatment of Mental Health Disorders

From the 1950s through the 1970s, there was significant scientific exploration into the use of psychedelics in medicine. The results from this era are promising, although most of the experimental data lacked the methodological rigor expected from scientists today.¹⁹ Clinical trials using psychedelics have explored their potential for treating PTSD; depression; tobacco and alcohol use disorders; obsessive-compulsive disorder (OCD); and anxiety and depression in patients with terminal cancer diagnoses.²⁰

Most modern clinical trials follow a similar treatment protocol for psychedelic-assisted therapy. The process consists of three phases: preparation sessions, treatment sessions and integration sessions.²¹ The goal of preparation sessions is to build trust between patients and clinicians, encouraging the development of an open mindset that promotes “letting go” of psychological resistance.²² Treatment or dosing sessions involve the patient receiving the psychedelic substance. Most clinical trials consist of one or two dosing sessions during which patients are given a psychedelic dose high enough to elicit an altered state of consciousness.²³ Treatment sessions often last six to eight hours and focus on the patient’s inner experience in a non-directive way.²⁴ During treatment sessions, researchers focus on “set” (the psychological state of the patient) and “setting” (the environment in which the substance is used).²⁵ After the treatment sessions, clinicians conduct one or more integration sessions where the patient processes feelings and experiences from the treatment sessions and works to create lasting change.²⁶ To ensure patient safety, all sessions are usually conducted with two therapists.²⁷ Though there are relatively few completed clinical trials with published results, there are at least 50 active phase two or phase three clinical trials—which assess the efficacy and side effects of a treatment—on psychedelics as of April 2022.²⁸

One of the most anticipated studies compared psilocybin to escitalopram (a common antidepressant) in 59 people with long-standing moderate-to-severe depression.²⁹ The study found no difference in the antidepressant effects of psilocybin compared to escitalopram.³⁰ Additionally, the percentage of patients reporting anxiety, dry mouth, sexual dysfunction, or reduced emotional responsiveness was lower in the psilocybin group.³¹ This suggests that psilocybin produces

14. Vargas et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8520991>.

15. Grant M. Jones and Matthew K. Nock, “Lifetime use of MDMA/ecstasy and psilocybin is associated with reduced odds of major depressive episodes,” *Journal of Psychopharmacology* 36:1 (January 2022), pp. 57-65. <https://pubmed.ncbi.nlm.nih.gov/34983261>; Vargas et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8520991>.

16. Vargas et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8520991>.

17. Guimarães dos Santos et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943545>.

18. Drug Enforcement Administration, “Drug Fact Sheet: Ketamine,” Department of Justice, April 2020. <https://www.dea.gov/sites/default/files/2020-06/Ketamine-2020.pdf>.

19. Neil M. Weston et al., “Historic psychedelic drug trials and the treatment of anxiety disorders,” *Depression and Anxiety* 37:12 (December 2020), pp. 1261-1279. <https://pubmed.ncbi.nlm.nih.gov/32627308>; Peter S. Hendricks et al. <https://pubmed.ncbi.nlm.nih.gov/25586402>.

20. Krediet et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311646>.

21. Pilecki et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769>.

22. Leor Roseman et al., “Quality of Acute Psychedelic Experience Predicts Therapeutic Efficacy of Psilocybin for Treatment-Resistant Depression,” *Frontiers in Pharmacology* 8:974 (Jan. 17, 2018). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5776504>.

23. Roseman et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5776504>; Pilecki et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769>.

24. Ibid.

25. Ibid; Guimarães dos Santos et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943545>.

26. Pilecki et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769>.

27. Ibid.

28. U.S. National Library of Medicine, “Clinicaltrials.gov,” The National Institutes of Health, last accessed May 4, 2022. https://clinicaltrials.gov/ct2/results?cond=&term=psychedelic&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&qndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e.

29. Robin Carhart-Harris et al., “Trial of Psilocybin versus Escitalopram for Depression,” *New England Journal of Medicine* 384 (April 15, 2021), pp. 1402-1411. <https://www.nejm.org/doi/full/10.1056/nejmoa2032994>.

30. Ibid.

31. Ibid.

results that are at least comparable to the current standard of treatment while potentially mitigating side effects.³² Trials of psilocybin among people with life-threatening cancer diagnoses have shown that the effects of psilocybin-assisted therapy can last at least 4.5 years, and 60 to 80 percent of trial participants had clinically significant reductions in anxiety and depression.³³

Several trials using MDMA to treat PTSD have also shown promising results. One recent study found that 67 percent of participants with PTSD no longer met the diagnostic criteria for PTSD two months after MDMA-assisted therapy.³⁴ Less robust evidence exists for the treatment of tobacco- and alcohol-use disorders though several studies have shown high abstinence rates after psilocybin-assisted therapy.³⁵ Across clinical trials, there have been no serious adverse events reported, and side effects have been fleeting and included headache, anxiety, nausea and confusion.³⁶

Randomized, controlled clinical trials are considered the gold-standard of evidence in medical research. They do, however, have some limitations in the context of psychedelic-assisted therapy—notably it is difficult to find an adequate control treatment. Since psychedelics produce clear characteristic cognitive effects, it is possible for participants and researchers to guess which is the control (placebo) group and which is the treatment group, which may nullify blinding, therefore biasing the results toward more positive outcomes based on expectations.³⁷ Additionally, small sample sizes and strict criteria for viable participants in the trials may limit the generalizability of clinical trial results.³⁸

Safety and Acceptability of Psychedelic Use for Mental Health Disorders

Observational research offers a view into real-world use of psychedelics that suggests patient acceptability. An estimated 32 million people in the United States have used psychedelics at least once.³⁹ In the 2020 Global Drug Survey, about 6 percent of respondents reported using psychedelics to self-treat mental health conditions during the previous year.⁴⁰ Additionally, the same survey found that legal, regulated treatment with psychedelics was of interest to 90 percent of people who reported having a supervised, psychedelic experience in an uncontrolled setting.⁴¹ Finally, a different survey of psychedelic users found that 62 percent who had been diagnosed with a mental health disorder used psychedelics as a replacement or enhancement to psychiatric medications or psychotherapy.⁴²

Research also indicates that classical psychedelics show low abuse potential and toxicity. In clinical trials of psychedelic-assisted therapy, serious adverse events have not been reported and side effects have been minimal.⁴³ A trend known as microdosing also demonstrates the low toxicity and abuse potential of classical psychedelics. Microdosing involves taking a small dose of a psychedelic substance, one that does not impair normal functioning, on a set schedule (often every third day).⁴⁴ Since people who micro dose are exposed to psychedelics regularly, albeit at low levels, the habit shows the relative safety of classical psychedelics. The most commonly microdosed psychedelics are psilocybin and LSD.⁴⁵

MDMA, on the other hand, may have a higher abuse potential than classical psychedelics, though its abuse potential is not as high as many other substances.⁴⁶ Acute toxicity and abuse have not been observed in medically supervised use of

32. Ibid.

33. Argento et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8450400>.

34. Ibid.

35. Argento et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8450400>; Teresa Reynolds Sousa et al., “Psychedelics and hallucinogens in Psychiatry: finding new pharmacological targets,” *Current Topics in Medicinal Chemistry* (Dec. 1, 2021). <https://pubmed.ncbi.nlm.nih.gov/34852736>.

36. Martin L. Williams et al., “Translating Psychedelic Therapies From Clinical Trials to Community Clinics: Building Bridges and Addressing Potential Challenges Ahead,” *Frontiers in Psychiatry* 12:737738 (Nov. 4, 2021). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8599345>; Hendricks et al. <https://pubmed.ncbi.nlm.nih.gov/25586402>; Krediet et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311646>; Sally E. Meikle et al., “Psilocybin-assisted therapy for depression: How do we advance the field?,” *The Australian and New Zealand Journal of Psychiatry* 54:3 (March 2020), pp. 225-231. <https://pubmed.ncbi.nlm.nih.gov/31752499>; Coppola et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8883979>.

37. Weston et al. <https://pubmed.ncbi.nlm.nih.gov/32627308>; William R. Smith and Paul S. Appelbaum, “Two Models of Legalization of Psychedelic Substances: Reasons for Concern,” *JAMA* 326:8 (Aug. 24 2021), pp. 697-698. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8753745>; Meikle et al. <https://pubmed.ncbi.nlm.nih.gov/31752499>; Suresh D. Muthukumaraswamy et al., “Blinding and expectancy confounds in psychedelic randomized controlled trials,” *Expert Review of Clinical Pharmacology* 14:9 (September 2021), pp. 1133-1152. <https://pubmed.ncbi.nlm.nih.gov/34038314>.

38. Smith and Appelbaum. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8753745>; Pilecki et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769>.

39. Pilecki et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769>.

40. Argento et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8450400>.

41. Ibid.

42. Toby Lea et al., “Perceived Outcomes of Psychedelic Microdosing as Self-Managed Therapies for Mental and Substance Use Disorders.” <https://pubmed.ncbi.nlm.nih.gov/32043165>.

43. Carhart-Harris et al. <https://www.nejm.org/doi/full/10.1056/nejmoa2032994>; Williams et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8599345>; Coppola et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8883979>; Krediet et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311646>.

44. Joseph M. Rootman et al., “Adults who microdose psychedelics report health related motivations and lower levels of anxiety and depression compared to non-microdosers,” *Scientific Reports* 11:1:22479 (Nov. 18, 2021). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8602275>; Polito and Stevenson. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6364961>.

45. Toby Lea et al., “Microdosing psychedelics: Motivations, subjective effects and harm reduction,” <https://pubmed.ncbi.nlm.nih.gov/31778967>; Nadia R.P.W. Hutten et al., “Self-Rated Effectiveness of Microdosing With Psychedelics for Mental and Physical Health Problems Among Microdosers,” *Frontiers in Psychiatry* 10 (Sep. 13, 2019). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6753862>; Rootman et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8602275>.

46. National Institutes on Drug Abuse, “MDMA (Ecstasy) Abuse Research Report: Is MDMA Addictive?,” National Institutes of Health, September 2017. <https://nida.nih.gov/publications/research-reports/mdma-ecstasy-abuse/mdma-addictive>.

MDMA, though MDMA can cause acute toxic effects such as hyperthermia, hypertension, seizure, arrhythmia and psychosis.⁴⁷ Since psychedelic-assisted therapy is performed in a medically supervised setting, these side effects are of less concern because patients can be screened for contraindications and mild side effects, such as hyperthermia, can be managed by medical professionals.⁴⁸

CURRENT PSYCHEDELIC POLICY LANDSCAPE

As of April 2022, no psychedelic has been approved for the treatment of any mental or physical disorder. Although psychedelics are not federally legal, the FDA has granted “breakthrough therapy” status to MDMA for treating PTSD and psilocybin for treating depression.⁴⁹ This status will help pharmaceuticals that use MDMA and psilocybin advance through the FDA’s approval process more quickly.⁵⁰ Nevertheless, some jurisdictions are moving forward with decriminalization or legalization of psilocybin and some other psychedelic compounds.

In May 2019, Denver, Colorado legalized the use and possession of psilocybin-containing mushrooms.⁵¹ Oakland and Santa Cruz, California followed in 2019 and 2020, respectively, by decriminalizing all entheogenic plants and fungi, which includes mushrooms, cacti, iboga-containing plants and/or extracted combinations of plants similar to ayahuasca.⁵² However, in 2021, Santa Cruz rolled back their decriminalization of peyote and mescaline, citing concerns raised by indigenous communities whose use of these plants for spiritual purposes predates western interest in psychedelic medicine.⁵³ Washington, D.C.; Seattle, Washington; Ann Arbor, Michigan; and Somerville and Cambridge, Massachusetts

also decriminalized all entheogenic plants and fungi.⁵⁴ Legislation decriminalizing psychedelics has passed by both ballot initiatives (in Denver and Washington, D.C.) and through city councils (in Santa Cruz, Ann Arbor, Oakland, Seattle, Somerville and Cambridge). Additionally, Washington, Colorado, New York and California are all considering some form of psychedelics legalization.⁵⁵

Oregon also passed a ballot measure to legalize psilocybin for therapeutic use in 2020.⁵⁶ The measure tasked the Oregon Health Authority with creating the programs and regulations to facilitate therapeutic use under the advisement of the Oregon Psilocybin Advisory Board.⁵⁷ This is notable because of the stipulation that psilocybin be used for therapeutic purposes. The measure states that clients must undergo a preparation session with a “psilocybin service facilitator” before they are allowed to purchase, possess and consume psilocybin at “psilocybin service centers.”⁵⁸ This program is slated to begin serving clients in 2023, and Oregon is currently grappling with how to provide and regulate these services.⁵⁹ As is often the case with policy, how Oregon regulates and offers therapeutic access to psychedelics will likely guide how other jurisdictions proceed. Although this measure only allowed for the therapeutic use of psilocybin, there was an additional measure that decriminalized possession of most drugs, including psychedelics, for personal use that passed at the same time.⁶⁰

CONSIDERATIONS FOR THE FUTURE OF PSYCHEDELIC POLICY

Although research on the use of psychedelics for the treatment of mental health disorders is still emerging, efforts to

47. Krediet et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311646>; Smith and Appelbaum. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8753745>.

48. Krediet et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311646>.

49. “Breakthrough Therapy.” <https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy>; Guimarães dos Santos et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943545>; Krediet et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7311646>; Saplakoglu. <https://www.livescience.com/psilocybin-depression-breakthrough-therapy.html>.

50. Yasemin Saplakoglu. <https://www.livescience.com/psilocybin-depression-breakthrough-therapy.html>.

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52. Gallo, “Agenda Report: Decriminalizing Entheogenic Plants.” <https://www.decriminalizenature.org/media/attachments/2019/11/20/decim-resolution.pdf>; York, “Santa Cruz Decriminalizes Natural Psychedelics.” <https://www.santacruzsentinel.com/2020/01/29/santa-cruz-decriminalizes-natural-psychedelics>.

53. Aiyana Moya, “Santa Cruz City Council Removes Peyote from List of Decriminalized Psychedelics,” Good Times, Sep. 16, 2021. <https://www.goodtimes.sc/santa-cruz-city-council-removes-peyote-from-list-of-decriminalized-psychedelics>; Center for the Study of World Religions, “Video: Honoring the Indigenous Roots of the Psychedelic Movement,” Harvard Divinity School, March 15, 2021. <https://cswr.hds.harvard.edu/news/2021/03/18/honoring-indigenous-roots-psychedelic-movement>.

54. “Ann Arbor Decriminalizes Magic Mushrooms, Psychedelic Plants.” <https://apnews.com/article/ann-arbor-plants-featured-ca-state-wire-mi-state-wire-b0ce69ca0961c150e0f900e8ea4cf432>; Beaujon. <https://www.washingtonian.com/2021/03/15/magic-mushrooms-are-decriminalized-in-dc-as-of-today>; Blistein. <https://www.rollingstone.com/culture/culture-news/somerville-massachusetts-psychedelics-magic-mushrooms-decriminalize-1115198>; Deborah Becker, “Cambridge Votes To Decriminalize Psychedelics And All Controlled Substances,” WBUR, Feb. 5, 2021. <https://www.wbur.org/news/2021/02/04/cambridge-votes-to-decriminalize-psychedelics-and-all-controlled-substances>; Kary. <https://www.bloomberg.com/news/articles/2021-10-04/seattle-votes-to-decriminalize-psylocybin-and-similar-substances>.

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60. “Oregon Measure 109, Psilocybin Mushroom Services Program Initiative (2020).” [https://ballotpedia.org/Oregon_Measure_110_Drug_Decriminalization_and_Addiction_Treatment_Initiative_\(2020\)](https://ballotpedia.org/Oregon_Measure_110_Drug_Decriminalization_and_Addiction_Treatment_Initiative_(2020)).

legalize or decriminalize psychedelics are gaining momentum. As jurisdictions begin to allow the use of psychedelics, policies should focus on decreasing regulatory burdens to ensure access and equity in psychedelic-assisted therapies.

Additional Research

Given psilocybin and MDMA's breakthrough therapy status, the National Institutes of Health (NIH) should consider funding clinical trials of these substances as therapeutics. One study that assessed the NIH's recent involvement in such clinical research found that the organization had not directly funded any clinical trials on psychedelic-assisted therapy between 2006 and 2020.⁶¹ As one of the largest public funders of biomedical research, the NIH is well-positioned to accelerate psychedelics research for therapeutic use. This is not without precedent, as funding bodies in Australia, Canada, Israel, New Zealand and the United Kingdom have allocated funds to psychedelics research.⁶² One barrier to the NIH funding research is a rider in the federal appropriations bill that prevents federal funds from supporting "any activity that promotes the legalization of any drug or other substance included in schedule I."⁶³ This rider was first enacted in 1996 and has been renewed every year since, despite recent attempts to remove it.⁶⁴ Eliminating this rider from future appropriations bills would enable the NIH to fund a groundswell of research.

In addition, the Attorney General should convene a multi-disciplinary committee focused on assessing scientific evidence to reschedule psychedelics; without this, the Schedule I status of psychedelics may prevent their widespread adoption.⁶⁵ Such a committee should include, at minimum, experts in medicine, psychology and criminal justice. Additionally, community members, the pharmaceutical industry, patient advocates and other stakeholder voices should be taken into consideration because they are major stakeholders affected by regulation of psychedelics.

Mental Health Workforce

As conducted in clinical trials, psychedelic-assisted therapy is a time- and labor-intensive treatment that requires a specialized setting and supervision. There is currently a shortage of mental healthcare workers in the United States,

resulting in unmet need for services.⁶⁶ Given the current state of the mental health workforce, questions have been raised about how accessible psychedelic-assisted therapy may be.⁶⁷ Investing in training programs to increase the supply of new psychiatrists, licensed clinical social workers, professional counselors and other mental healthcare professionals is vital for psychedelic-assisted therapy to be scalable. In addition to educating and licensing new providers, educating current providers is necessary.⁶⁸ Psychedelic-assisted therapy is a specialized treatment, and evidence-based clinical guidelines are necessary.⁶⁹ As more jurisdictions allow the use of psychedelics, it is likely that people will turn to their providers to seek guidance on use of psychedelics, and providers will need education to meet patients' needs.

Equity and Access

Once psychedelic-assisted therapy is offered outside of clinical trials, it will be important to address issues of equity and access. Since it is estimated that one course of MDMA-assisted therapy would total around \$15,000, cost will be a significant barrier to treatment for many people if the treatment is not covered by public and private insurance providers.⁷⁰ Although the cost may seem high, if psychedelic-assisted therapy produces long-lasting results after one to three dosing sessions, as clinical trials suggest, this would make psychedelic-assisted therapy more cost effective than long-term antidepressants.⁷¹

Appropriate Regulatory Mechanisms

At this time, there are no FDA-approved psychedelic medications, so jurisdictions that move forward with allowing therapeutic access to psychedelics need to build appropriate regulatory mechanisms to ensure patient safety. Jurisdictions must first determine what goals they are trying to achieve. Decriminalization or legalization of psychedelic plants removes legal penalties for use and possession, but this path does not provide the regulatory mechanisms that ensure patient safety or therapeutic treatment. If jurisdic-

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64. Ibid.

65. 21 U.S. Code § 872(a)6. <https://uscode.house.gov/view.xhtml?path=/prelim@title21/chapter13&edition=prelim>.

66. Mark Barna, "Mental health workforce taxed during COVID-19 pandemic: Worker shortage hinders access," *The Nation's Health* 51:10 (January 2022), pp. 1-14. <https://www.thenationshealth.org/content/51/10/13>; State Health Facts, "Adults Reporting Unmet Need for Mental Health Treatment in the Past Year," Kaiser Family Foundation, last accessed May 3, 2022. <https://www.kff.org/other/state-indicator/adults-reporting-unmet-need-for-mental-health-treatment-in-the-past-year/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D>.

67. Franklin King 4th and Rebecca Hammond. <https://pubmed.ncbi.nlm.nih.gov/34690582>; Williams et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8599345>.

68. Argento et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8450400>.

69. Mason Marks and I. Glenn Cohen. <https://www.nature.com/articles/s41591-021-01530-3>.

70. Pilecki et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769>; Mason Marks and I. Glenn Cohen. <https://www.nature.com/articles/s41591-021-01530-3>.

71. Guimarães dos Santos et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943545>.

tions have the goal of facilitating access to psychedelics as a therapeutic treatment, they will need to put in place additional regulatory measures.

Jurisdictions will also need to determine how and from where the psychedelics used in psychedelic-assisted therapy will be obtained and develop regulatory measures to govern practitioners providing the psychotherapeutic component of psychedelic-assisted therapy, which is an essential aspect of (just to avoid repeating component) successful treatment.⁷² Establishing which mental health professionals will be allowed to provide or facilitate psychedelic-assisted therapy, how these professionals will be licensed and what happens in cases of professional misconduct or malpractice are also vital to ensuring patient safety. Finally, since the setting in which psychedelic-assisted therapy is performed can impact the patient's experience, there may be a need to provide regulatory guidance regarding building codes.⁷³

The federal government should not be solely responsible for proposed regulatory mechanisms; however, FDA approval of a psilocybin or MDMA-based pharmaceutical may change how jurisdictions want to regulate psychedelic therapies. Mental health and relevant health authorities are also well suited to advance effective practices in collaboration with state licensing agencies. Policymakers should observe how Oregon develops their regulation for therapeutic access to psilocybin, as it will serve as a natural experiment with lessons for other jurisdictions.⁷⁴

CONCLUSION

Psychedelics seem to offer significant promise for treating mental health disorders. Nevertheless, more research is needed to develop the best methods for psychedelic-assisted therapy and to ensure safety for people who want to use psychedelics to treat mental health disorders. As states and localities move forward with the decriminalization or legalization of psychedelic compounds, it is wise for them to consider how best to ensure that people are getting the care they need to support their mental health.

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72. Pilecki et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8028769>.

73. Guimarães dos Santos et al. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7943545>.

74. Ibid.