MINNESOTA

Psychedelic Medicine Task Force

LEGISLATIVE REPORT

01/01/2025

Psychedelic Medicine Task Force

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As requested by Minnesota Statute 3.197: This report cost approximately $150,396 to prepare, including staff time, printing and mailing expenses.

Contents

Glossary of terms and acronyms

Terms

Biopiracy: Exploitation of biological materials (plants, fungi, animals) that seeks to patent or restrict general use, often for financial gain.

Breakthrough Therapy designation: A process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).

Critical periods of development: Periods during development when the brain is especially responsive to experiences (or lack of experiences) which can have lasting effects on both the structure of the brain and behavior.

Cultural appropriation: The unacknowledged and inappropriate adoption of customs, practices, ideas, etc. from one, typically minority, culture, often perpetuated by the majority group.

Cultural genocide: The systematic destruction of traditions, values, language, etc. of one group by another, typically by a dominant or majority group.

Drug exceptionalism: An ideology suggesting that some drugs are eligible for reform while others should remain prohibited, with these categories often politically or culturally motivated.

Drug schedules: The classification system formed by the Controlled Substances Act which regulates controlled substances. There are five categories, or schedules (I, II, III, IV, V), based on a substance's accepted medical use, potential for abuse or addiction, and harmfulness.

Ecological validity: Ensuring experimental findings are representative and generalizable to the broader population.

Effectiveness: Describes if a treatment can produce the intended results in "real world" settings, as it would be used outside of clinical trials.

Efficacy: Describes if a treatment produces the expected result under strictly controlled circumstances, as in a clinical trial.

Entheogen: A psychoactive, hallucinogenic substance, especially when derived from plants or fungi and often used in religious, spiritual, or ritualistic contexts.

Functional unblinding: In a clinical trial, the ability of either the participant or the investigator to correctly guess the treatment group the participant has been assigned to, usually due to apparent drug effects.

Indigenous reciprocity: Recognizing that the relationships between Indigenous and non-Indigenous peoples must be based on mutual respect, understanding, and benefit.

Mystical experiences: Unique phenomenological experiences that are often reported to induce significant and persisting changes in the experiencer's worldview.

Neuroplasticity: The brain's ability to form and reorganize synaptic connections, particularly in response to learning, experience, or following injury.

New Drug Application: The vehicle through which investigators submit a formal request to the Food and Drug Administration to review clinical data to approve a new drug or treatment.

Phase I Trial: A type of clinical trial designed to explore dosage, safety and side effects of a potential new treatment in normal volunteers. Also used to gather feasibility data for a specific patient population, or to conduct basic science research on mechanisms of action.

Phase II Trial: A type of clinical trial designed to explore the efficacy and side effects of a potential new treatment. Includes up to several hundred participants and lasts months to years.

Phase III Trial: A type of clinical trial designed to further study the efficacy of a potential treatment, as well as additional monitoring of adverse events. Recruits hundreds to thousands of participants and can last several years. Required for the submission of a New Drug Application to the Food and Drug Administration.

Principal Investigator: A credentialed researcher (MD, PhD, DO, etc.) who is authorized to run a clinical trial according to FDA, DEA, and IRB requirements.

Psychonaut: Someone who explores their psyche/mind with psychedelics, like an astronaut explores space.

Schedule I: The most tightly controlled classification of drugs, defined as those with no currently accepted medical use and a high potential for abuse. MDMA, psilocybin, and LSD are all currently classified in this schedule.

Schedule II: The second most tightly controlled classification of drugs, defined as having some accepted medical use, but still considered to have a high potential for abuse which may lead to severe psychological or physical dependence. Fentanyl is currently classified in this schedule.

Schedule III: Drugs with a moderate to low potential for physical and psychological dependence. Marijuana (cannabis) is in the process of being considered for reclassification to this schedule at the time of report writing. Ketamine is currently on this schedule.

Set and Setting: A term popularized by Timothy Leary and Richard Alpert (also known as Ram Dass) relating to the mindset (set) and the physical location (setting) one has when entering into a psychedelic experience.

Shamanism: A religious practice of some Indigenous peoples that involves a practitioner interacting with the spirit world through altered states of consciousness, such as trance.

Tribal Sovereignty: The unique status of the Minnesota tribes and their absolute right to existence, self-governance, and self-determination. Minnesota Statute § 10.65.

Acronyms

ADA: Americans with Disabilities Act

AIRFA: American Indian Religious Freedom Act

BDNF: Brain-derived neurotrophic factor

CDC: Centers for Disease Control and Prevention

CEC: Church of the Eagle and the Condor

CSA: Controlled Substances Act

DEA: Drug Enforcement Administration

FDA: U.S. Food and Drug Administration

FTC: Federal Trade Commission

GAD: Generalized anxiety disorder

GCP: Good Clinical Practice

GMP: Good Manufacturing Practices

HHS: Department of Health and Human Services

HIPAA: Health Insurance Portability and Accountability Act

IHS: Indian Health Services

IRB: Institutional Review Board

LSD: Lysergic acid diethylamide

MAPS: Multidisciplinary Association for Psychedelic Studies

MDD: Major depressive disorder

MDH: Minnesota Department of Health

MDMA: 3,4-methylenedioxymethamphetamine

MIAC: Minnesota Indian Affairs Council

MMB: Minnesota Department of Management & Budget

NIDA: National Institute of Drug Abuse

NIH: National Institutes of Health

NIMH: National Institute of Mental Health

PI: Principal Investigator

PTSD: Post-traumatic stress disorder

RCT: Randomized controlled trial

RFRA: Religious Freedom and Restoration Act

RTT: Right to Try Act

SME: Subject matter expert

TRD: Treatment-resistant depression

UDV: The União do Vegetal church

Executive summary

The Minnesota legislature created the Psychedelic Medicine Task Force to advise it on the legal, medical, and policy issues associated with the legalization of psychedelic medicine in the state. Within that legislation and this report, "psychedelic medicine" means 3,4-methylenedioxymethamphetamine (MDMA), lysergic acid diethylamide (LSD), and psilocybin, which can be synthetic or with psilocybin, found naturally in certain mushrooms (often referred to as "magic mushrooms"). The task force met once a month between November 2023 and December 2024 to discuss the scientific, cultural, and legal considerations of the legislative charge, as well as questions of cost, access, and equity. Smaller working groups also met outside of the larger monthly meeting. The task force regularly consulted subject matter experts, both during full task force meetings and working groups. The report this task force produced is a product of the shared perspectives and experiences of its appointed members, and not of any one individual nor of any of the state agencies that served on it.

Recommendations

By a two-thirds supermajority vote of its members, the task force recommends the Minnesota legislature:

1. Create a state-regulated clinical program for the therapeutic administration of psilocybin-containing mushrooms.
2. Remove criminal penalties for the personal use and possession of psilocybin-containing mushrooms.
3. Allocate funding for more research into the health benefits of MDMA, psilocybin, and LSD.

The task force considered additional proposals that did not reach a two-thirds supermajority, including:

1. The removal of criminal penalties for the personal use and possession and noncommercial (without remuneration) cultivation and sharing of psilocybin-containing mushrooms.
2. Remove criminal penalties for the personal use and possession of MDMA, synthetic psilocybin, and LSD.
3. The creation of a state-regulated program for the clinical administration of MDMA and LSD.
4. Creating a regulated, adult use market for psilocybin-containing mushrooms.

Each recommendation could be implemented together, depending on the views of the public, the MN legislature, the governor, and state agencies. That is, these recommendations complement each other, and are neither mutually exclusive nor "all or nothing" proposals. Instead, the task force considers this report to be a guide for the MN legislature on how to approach and understand the subject of psychedelic medicines. The task force anticipates its recommendations can be rolled out incrementally as scientific and medical understanding, federal and state laws, and perception by the general public develop around psychedelic medicines. Consequently, this report includes proposals that were considered but did not pass by a two-thirds majority, for reference, should the state wish to consider them in the future.

The national landscape regarding psychedelic medicine is rapidly evolving. Because of this, there could be changes in research, federal policy, religious practice, or other areas that may alter best practices, alterations that may even render parts of this report obsolete or irrelevant in the future. This task force cannot accurately

predict where these fields will go, and so it encourages lawmakers to stay flexible and adapt to the rapid pace at which this field continues to evolve.

Guiding principles

The task force followed a number of guiding principles to engage in discussions. The full description of these principles can be found in Appendix C. Briefly, they are:

- Scientific and research rigor
- Collaboration and inclusivity among the task force
- Accountability to the public and integrity
- Awareness in evaluation
- Practicality
- Social equity
- Engagement with the public whenever possible

Scientific research

The Department of Health hired a research scientist to review the scientific literature the task force is charged with summarizing. It discussed as a group what types of research it would include in its report. After identifying all of the health conditions for which each drug has shown potential in treating, for the purposes of the legislative charge, it focused on the "efficacy" of each drug as demonstrated through randomized controlled trials (RCTs). The task force then directly compared how "effective" the medicines are in treating these health conditions, comparing them to the gold standards of care currently being used to treat those health conditions (*e.g.*, psychotherapy, antidepressant medications). Detailed summaries of these results are in the Scientific Literature Review section and in Appendix H.

While many scientific studies have been published about psychedelic medicines and their potential for healing, the majority of these are population studies, review articles, anonymous online survey studies, or open label trials without a placebo control group—the difficultly of using placebos to study psychedelic medicine is discussed at length in this report—and so only studies with a placebo control were used for the task force's criteria for inclusion in the report's scientific literature review. Those other types of works are discussed in the Community Research section and in Appendix I.

All three of these psychedelic medicines have received Breakthrough Therapy designation by the Food and Drug Administration (FDA), yet none have received FDA approval at the time of this report writing, and thus remain on Schedule I under the federal Controlled Substances Act (CSA). Very promising evidence is emerging from RCTs for MDMA as a potential treatment for post-traumatic stress disorder (PTSD), psilocybin as a potential treatment for alcohol use disorder and depression (both major depressive disorder and treatment-resistant depression), and LSD as a potential treatment for anxiety disorders and alcohol use disorder.

Comparisons with standard treatments identified that each psychedelic medicine performed better than or equal to standard treatments, based on effect sizes as available. Effect sizes are a measure of how well the drug works compared to a placebo control and can be directly compared between studies to determine which is

potentially more effective. However, there are some concerns whether efficacy can be accurately measured in RCTs with psychedelic medicines because placebo controls that can successfully blind people to which drug they are taking do not work when studying many existing psychoactive medicines, and are especially challenging for psychedelic medicines, given the obviousness of their effects to both patient and scientist.

Additionally, comparing the effect sizes from the psychedelic medicine RCTs to those of standard lines of treatment ("effectiveness") should be done with caution: the RCTs investigating psychedelic medicine are relatively new, and have only evaluated a few hundred people over a handful of clinical trials, while current standard treatments have evidence from hundreds of trials, from likely thousands of participants, over many decades. As such, the difference in scale of quantities of data make direct comparison of effectiveness difficult at this stage in the research.

Legal research

The MN legislature also asked the task force to explore a variety of legal pathways to mitigate conflicts with federal law. Several of the federal statutes the task force analyzed offered, at least nominally, federally lawful pathways to create a clinical or research program for psychedelic medicines; however, the agencies that administer these pathways have, for decades, kept them effectively closed. Without the benefit of these pathways, any type of state-regulated program would inherently conflict with federal laws—laws controlling psychedelic medicines as Schedule I drugs, not approving them for medical use, and preventing their interstate sourcing. Changes to these federal laws would be required to make any state-regulated programs with psychedelics fully legal, but this would require an act of Congress.

Yet the state has options with precedent that can minimize its conflicts with federal law. Consequently, the task force's recommendations are designed to eliminate or reduce conflict with the federal government and its laws as much as possible. Two recommendations (creating a state-regulated program for the clinical administration of psilocybin-containing mushrooms and allocating funding for more research into the health benefits of MDMA, psilocybin, and LSD) can fit within federal statutes relating to clinical trials with controlled substances (e.g., researchers obtaining DEA licenses for the use of Schedule I drugs, Investigational New Drug [IND] applications). Administrative or judicial exemptions to the CSA from the DEA could be requested to allow for state programs to operate, though this has never been granted for any such state programs, and exemptions to the CSA have only been granted for religious use of psychedelic medicines.

Another federal statute, the Right to Try Act, is intended to make Schedule I drugs available to patients with few other options, but requests have long been blocked by the DEA; a federal appeals court ruling on psilocybin for end-of-life care is currently pending before the Ninth Circuit Court of Appeals (*AIMS v. DEA*). Pharmaceutical companies conducting clinical trials can make psychedelic medicines available through the Expanded Access program, but to qualify, the company must design its Expanded Access program similar to its clinical trials, which center research rather than patient outcome, and are very limited in scope and access.

The state can also petition the US Attorney General (AG) or the Department of Health and Human Services (HHS) to establish a research program, but other than methadone, which was granted approval under these conditions in the 1970s, no other example of such a program could be found at the time of report writing. There is one pathway showing promise relating to federal-state synergy: Oregon has begun to collect data from psilocybin

service centers with federal protections through a research study at Oregon Health Sciences University (OHSU). By doing so, they can protect psychedelic medicine patient data confidentiality and track public health outcomes of its state-regulated psilocybin clinic program. Refer to Appendix G for more details of these legal pathways and navigating conflicts with federal laws.

Regulatory considerations

On the subject of regulation—how the state's psychedelic medicine laws might actually be written and structured—the task force was instructed by its legislative members to provide only general guidelines, given that most of this work will be done by the MN legislature itself if and when a bill from these recommendations is drafted, revised with stakeholder input, and heard in committee. As with other states that have passed laws on psychedelic medicines, working groups, advisory committees, and further scientific research will be needed to develop and implement regulations. It will also be important for Minnesota to watch other states—learning from their innovation, implementing their successes, and avoiding their failures.

Currently, Colorado and Oregon are pioneering regulation of psychedelic medicines. While Oregon has created a market for the supervised administration of psilocybin at dedicated service centers, its tight regulatory structure has created problems of cost (and thus access), as well as complications ensuring the protection of medical professionals' licenses. In some cases, people pay far more for a psilocybin service center than they would to see a licensed physician, while many facilitator training programs are making more money than the facilitators themselves. Some service centers are closing due to high overhead costs imposed by state regulation, and many have found their niche catering to out-of-staters willing to pay a premium for access to the nation's only psilocybin service centers rather than serving Oregonians. Colorado's program is still in development and taking a different approach from Oregon. Colorado has yet to launch their program, as of report writing, given a long rule-making process and uncertainty about how much conflict with federal laws they will encounter.

Minnesota can learn lessons from Oregon and Colorado. For example, Oregon's tight restrictions requiring that psilocybin be administered in a dedicated brick-and-mortar location, with maximal staffing requirements and controls at all points across the business, drive up costs. Likewise, funding the regulator using only licensing fees creates further expense on the provider and, consequently, on their clients. Appendix K summarizes the status of psychedelic medicine in these and other states.

Finally, many Tribal nations, both the Ojibwe and Dakota nations within the borders of Minnesota and other tribes and bands across the country, may have extensive experience with psychedelic medicines. For example, the first exemption for use of a Schedule I drug for religious purposes, peyote (containing the Schedule I drug mescaline), was obtained by the Native American Church, an award won over the reluctance of DEA and only by force of the Supreme Court. Three other exemptions for religious use have been granted for psychedelic medicines, all for ayahuasca (containing the Schedule I drug dimethyltryptamine), two of which are protected by the Brazilian government and one formed in Arizona by a group with various Indigenous backgrounds. The MN legislature will serve Minnesotans in this field only if it deepens its partnership with these sovereign nations that have used peyote, and other Indigenous communities that use psilocybin-containing mushrooms and commits to learning from their unique perspectives and practices.

Other areas of regulatory consideration include, but are not limited to:

- Removing the ineffective and punitive criminal penalties for use and possession of psychedelic medicines.
- Mandating public safety education and first responder education and training.
- Upholding regulations to prevent commercial manufacturing and sales.
- Regulating the supply of psychedelic medicines.
- Developing a dual licensure program for licensed professionals.
- Establishing training and licensing for facilitators.
- Gathering data on safety monitoring and adverse event reporting.
- Creating incentives for business start-ups, including equity licenses, to reduce barriers to entry.
- Allocating funding for eligible investigator-initiated clinical trials.
- Consulting with Tribal nations in the development of new laws and regulations.
- Allowing for the legacy (e.g., existing underground) market to move into a state-regulated legal space, with incentives for equity licenses and business start-up to reduce barriers to entry.
- Exploring intersection with "compelling government interests" for enforcing Minnesota's CSA and religious freedom protected by the First Amendment of the US Constitution, the American Indian Religious Freedom Act (AIRFA), and the Religious Freedom Restoration Act (RFRA).

Policy considerations

Given the rapidly evolving nature of the psychedelic medicine landscape, it was not possible for the task force to develop deep foundations of public policy. Instead, the state will need to make ongoing efforts to monitor and adapt to this landscape to create a safe and legal pathway to access to psychedelic medicines. This may involve ongoing work groups to monitor public perception, nationwide legislation, clinical trials, and changes in scheduling and FDA approval.

Potential considerations for future working groups include, but are not limited to:

- Equity, access, and justice, including issues related to people's engagement with state-regulated programs and to federal benefits or employment, and parental or custody issues.
- Creating a path toward expunging drug records related to psychedelic medicines.
- Prioritizing the legacy market to become involved.
- Continuously consulting with Tribal nations in the development of policy.
- Priority access to services and licensing for Tribal nations.
- Ensuring Tribal sovereignty is maintained.
- Ensuring that psychedelic medicine is accessible, including in compliance with Americans with Disabilities Act.

Tribal nation sovereignty

The task force learned from legal subject matter experts about Public Law 83-280 (18 U.S.C. § 1162, 28 U.S.C. § 1360, and 25 U.S.C. §§ 1321–1326), which states that county and state jurisdiction can be enforced on Tribal lands if the matter is criminal in nature. Civil and regulatory matters can be handled by each reservation's government. However, two of the eleven Tribal nations within Minnesota boundaries, Red Lake and Bois Forte, are exempted from Public Law 280, and thus are only subject to the criminal jurisdiction of the federal

government. Regulation and enforcement of civil matters is decided independently by each of these Tribal governments. Overall, recommendations that remove criminal penalties for possession and use of psychedelic medicines in Minnesota would remove barriers for Tribal nations to create their own psychedelic medicine programs and would protect them from interference by the county and state, while allowing tribes to negotiate compacts with state and federal agencies.

Veteran affairs

More than 100 Minnesota veterans die by suicide each year, more than 2.5 times the rate of civilians, driven by vastly higher instances of PTSD, depression, addiction, and traumatic brain injury. So deep is this crisis that more veterans have died by suicide than in all wars since September 11, 2001. Because the current legal options for treatment are not sufficiently serving veterans, many seek alternative options to find relief, either outside of the US where some psychedelic medicines are legal or decriminalized, in state-regulated programs in Oregon and soon Colorado, and, most often, from illegal underground sources. The costs of international travel alone make the option of retreats in countries like Costa Rica, Brazil, or even Mexico impossible for many veterans. Other state-regulated programs are often expensive luxury retreats, and most working-class or disabled veterans still do not have the time or resources for these programs. Minnesota's pursuit of access to psychedelic medicine must center the experiences of veterans and their quests for relief.

Veterans in the US have been at the forefront of advocating for access to psychedelic medicines for many years. As dedicated service members who have fought for this country, veterans shoulder a disproportionate burden of trauma and other health complications as a consequence of their service. While they have sacrificed their minds, bodies, and sometimes their lives in defense of the US Constitution, they are unable to enjoy the liberties that it provides for them. That veterans have to travel internationally or be forced to come into conflict with federal law is unacceptable in light of the healing attributes of this medicine. A few advocacy organizations have been helping veterans gain access to psychedelic medicines where it is more accessible, including the Heroic Hearts Project, Reason for Hope, and Veterans Exploring Treatment Solutions (VETS).

Public education

Part of the task force's legislative charge was to develop an education plan surrounding its recommendations. One theme that emerged during the task force's work is the deep need for broad public education regarding psychedelic medicines. Many communities that could benefit from psychedelic medicines still have much to learn about their history, use, the state of the science, and what is happening in other countries and states where access is allowed in some form, especially given the increased media attention. So too must the public learn about the unique qualities, benefits, and risks of these medicines.

In its discussions, the task force recognized the need to educate healthcare providers, law enforcement and first responders, interested patients, and parents. Tribal communities without a history of using psychedelic medicines could also benefit from a public education campaign to ease fears related to introducing new drugs into a community facing the devastating effects of the opioid crisis. Public education campaigns targeted at the MN legislature, educators, spiritual communities, lawyers, and many other communities will also be beneficial. Through the course of public education, it will be important to root the message in science and public-health-based evidence rather than fear.

Looking towards the future

The task force would like to highlight some noteworthy, recent developments that the MN legislature should be aware of related to psychedelic medicines:

- Ongoing clinical trials and scientific research and new drug applications to the FDA.
- Federal legislation to broaden therapeutic access to psychedelic medicines, including bills introduced for the Breakthrough Therapies Act (S.5123) and the Right to Try Clarification Act (H.R.1825).
- Ongoing court cases against the DEA to allow access to psychedelic medicines under the Right to Try Act, additional religious exemptions from plant medicine churches, etc.
- Learning from existing state-regulated programs and ongoing legislation in other states creating new programs.
- Drug policy positions in future administrations (state and federal), and authority of administrative agencies, such as the DEA and FDA.
- Pending DEA rescheduling hearing for cannabis, based on new two-part test implemented by HHS to evaluate accepted medical use based on physician recommendations in state medical programs, which may or may not contribute to similar approaches for evaluating rescheduling recommendations for psychedelic medicines being implemented in state medical programs.

Introduction

In accordance with Minnesota Session Laws (Laws of Minnesota, 2023, chapter 70, article 4, section 99), the Psychedelic Medicine Task Force was established to advise the Minnesota legislature on the legal, medical, and policy issues associated with the legalization of psychedelic medicine in the state of Minnesota. For the purposes of this task force, "psychedelic medicine" was defined to mean MDMA, psilocybin, and LSD. The task force's duty was to conduct comprehensive research into how to legalize these three substances in Minnesota while reducing conflicts with federal laws, as well as to summarize the scientific literature about their potential medical benefits for common health conditions and compare those to standard treatments often used for those health conditions. Throughout the process, the task force solicited the opinions of a number of subject matter experts, including lawyers, Indigenous people, drug policy experts, regulators from Oregon and Colorado (two states that have already legalized psilocybin and other natural psychedelic medicines), and pharmaceutical companies involved in clinical trials and the FDA approval process. Several task force members were actively engaged in community outreach to the groups they represent, to help inform an equitable approach to accessing psychedelic medicines for different communities. In the task force discussions, members had some debate around the concept of "medicine." Many communities use this word in a way that does not always translate to "medical" when it comes to culturally competent healthcare. This perspective was most effectively communicated to the task force by members representing Tribal nations speaking up about what medicine means to their communities, and this sentiment is echoed in a more holistic approach to medicine (e.g., food as medicine).

In part, the impetus behind this legislation is that Minnesota faces a persistent and worsening health crisis, particularly in mental health, with both providers and patients feeling despair about the lack of effective treatment options. In recent years, clinical trials have begun investigating psychedelic medicine, including MDMA, psilocybin, and LSD, as a treatment for chronic, often treatment-resistant, health conditions. Psychedelic medicines, such as naturally occurring psilocybin-containing mushrooms, have been used by Indigenous cultures for thousands of years for spiritual and religious ceremonies, and for community healing. LSD and psilocybin have been used by the general population in the US since at least the 1950s, and MDMA since at least the 1970s. These substances have been shown to be relatively physically safe when used in a controlled environment, with most risks for their use focused on the psychological distress and existential or spiritual components, while also being described as profoundly healing and life-changing. For more information, please see the Scientific literature review section.

Clinically, these psychedelic medicines are being re-invented by the pharmaceutical industry (e.g., synthetic psilocybin, as well as MDMA and LSD) and are being tested in clinical trials where promising evidence has demonstrated they are helpful in alleviating the suffering associated with chronic mental health and other medical conditions. All three drugs have been given "Breakthrough Therapy" status by the FDA and are being evaluated with large-scale clinical trials. The goal of these trials is FDA approval of the treatments. It should be noted that the FDA recently decided not to approve MDMA for PTSD due to some concerns about lack of sufficient safety data, as well as complications around testing efficacy (measuring against a placebo) due to concerns about functional unblinding. There will likely need to be at least one more large phase III clinical trial exploring MDMA as a treatment for PTSD to address these concerns before FDA approval. However, the clinical

trial process is an imperfect system for evaluating the full scope of usefulness of a medication in the general population, and even more so for psychedelic medicines.

Psychedelic medicines are currently federally classified as Schedule I controlled substances and are illegal outside of the context of FDA-approved clinical trials or use as sacraments by specific churches that have been granted exemptions by the Drug Enforcement Agency (DEA) for religious use. Therefore, until they are federally rescheduled, or broader special exemptions are granted to allow their use in other contexts, any state-regulated program will be in violation of federal law. This is similar to how Minnesota's medical and adult-use cannabis programs are in conflict with federal drug laws. However, after extensive review and consultation with lawyers in the space, regulators from Oregon and Colorado, and drug policy experts, the task force found that there is a spectrum of protections from federal conflicts that each recommendation may be able to accommodate to reduce the risk that a new program in Minnesota would trigger extra attention from the federal government.

One such avenue for their use that is currently legal is clinical trials in different patient populations, though this is an imperfect solution for providing access, as clinical trials are science experiments, not healthcare. As states like Oregon and Colorado have begun to adopt programs with naturally derived psychedelic medicines, doing more clinical trials in Minnesota is an option if the state feels uncomfortable pushing the federal boundary for state-regulated access, knowing there is a track record for doing so without inciting federal consequences with medical cannabis programs. Another discussion was the concept of states as labs, which includes experimenting with drug policy reform to test the boundaries of violating federal laws while exercising state sovereignty under the Tenth Amendment and anticommandeering laws. A template for states as labs is the introduction of these state-regulated programs with Schedule I drugs. With psychedelic medicine, there is an appetite for states to pursue state-regulated programs that are in violation of federal laws enforced by the DEA and the FDA, similar to cannabis. Alternative and innovative federal-state partnerships may be explored to help find a better way for state programs to access psychedelic medicines and monitor public safety and effectiveness at improving health outcomes, while complying with federal laws and protecting citizens who engage in state programs with psychedelic medicines from additional consequences related to job security, housing, child custody, and other concerns.

Drug policy reform, public health experts, and medical doctors agree that decriminalization of possession and use of personal amounts of drugs, which include the three psychedelic medicines discussed in the legislation and this report, should happen first or in addition to any other legalization or regulations that may occur. Related to this, it is imperative to continue to educate the public, and other impacted and interested stakeholders, on the principles and best practices for safety around engaging with psychedelic medicines, either as a user, facilitator, cultivator, regulator, or any other entity.

Lastly is the eventual legalization of naturally derived psychedelic medicines for regulated adult use, as Minnesota has done with cannabis. The public perception may not be there yet; however, great success has been had in Amsterdam with magic mushrooms, and now psilocybin-containing truffles (less potent by weight), where they can be bought at stores called smart shops and consumed in parks around the city, and very few public safety or public health incidents have been noted. Other countries, such as Spain, are exploring models for group cultivation called social clubs that are being pioneered for cannabis, which could lend themselves to other naturally derived medicines people can source or grow themselves within their communities.

Finally, the proposed recommendations can be viewed as a playbook of sorts. The MN legislature can roll out different methods of access to psychedelic medicines as the federal landscape changes, as more states innovate in the area, and as public perception begins to shift.

Legislative charge

The full legislation can be found in Appendix A. Briefly, the legislation directed the task force to:

- Survey existing studies in the scientific literature on the therapeutic efficacy of psychedelic medication in the treatment of mental health conditions including depression, anxiety, PTSD, bipolar disorder, and any other mental health conditions and medical conditions for which a psychedelic medicine may provide an effective treatment option.
- Compare the efficacy of psychedelic medicine in treating the conditions noted above with current available treatments.

As well as develop a comprehensive plan for:

- State and local regulation of psychedelic medicine
- Federal law, policy, and regulation of psychedelic medicine, with a focus on retaining state autonomy to act without conflicting with federal law, including methods to resolve conflicts such as seeking an administrative exemption to the federal Controlled Substances Act under United States Code, title 21, section 822(d), and Code of Federal Regulations, title 21, part 1307.03; seeking a judicially created exemption to the federal Controlled Substances Act; petitioning the United States Attorney General to establish a research program under United States Code, title 21, section 872(e); using the Food and Drug Administration's expanded access program; and using authority under the federal Right to Try Act
- Education of the public on recommendations made to the MN legislature and others about necessary and appropriate actions related to the legalization of psychedelic medicine in the state.

Task force membership

The MN legislation created twenty-three seats for this task force, including representatives from state agencies, the MN legislature, Tribal nations, and members of the public representing health care professionals and patients. For a full roster of all members, please see Appendix B.

Task force operational process

Task force meetings began in November 2023 and were livestreamed and publicly accessible. Meetings occurred monthly in an online format, each lasting approximately three hours. Smaller work group meetings to discuss legal and regulatory topics occurred once or twice monthly between the full meetings.

The first two full meetings focused on the task force's structure, background, chair selection, guiding principles, and grounding background information. The guiding principles, working agreements, and expectations can be found in the full Psychedelic Medicine Task Force Charter, in Appendix C. During the task force's tenure, members were encouraged to hold listening sessions with the populations they represented between meetings and report back to the group, where members were encouraged to discuss and ask questions.

Task force members voted on final recommendations in the September and October 2024 meetings, and the final report was prepared for submission on January 1, 2025. A visual representation of the timeline and responsibilities completed by the task force can be found in Appendix C (see Meeting schedule and work cadence). The task force voted on recommendations, which required a supermajority of two-thirds of members voting in favor to pass. Votes to abstain did not count in the pool of existing votes toward the supermajority. Voting logs for each of the recommendations can be found in Appendix D.

During both the full task force meetings and the smaller work group meetings, a number of subject matter experts (SMEs) and relevant guests from various local and national stakeholder groups were invited to share their expertise and knowledge. Task force members and work groups had additional consultation meetings with many of these contributors. A list of these SMEs, a summary of their contributions, and a grateful acknowledgement of their effort can be found in Appendix E.

Task force members provided personal anecdotes of their experiences with psychedelic medicine in Appendix F. As most of the full monthly meetings included feedback solicited from represented communities, anecdotes and testimonials from these communities are also included in Appendix F. Additionally, because there are a number of possible legal pathways that were discussed during the course of the task force's work, Appendix G holds definitions of these pathways and suggestions for implementation.

Scientific literature review

Background

Psychedelic medicine is defined in the legislation as MDMA, psilocybin, and LSD. Along with the two scientific duties outlined in the legislation, the task force voted to review the safety and risks of these medicines as treatments. In the comparison of efficacy, Dr. Caroline Johnson's review of the scientific literature was limited to randomized controlled trials (RCTs), systematic reviews, and meta-analyses. Dr. Johnson is the psychedelic medicine scientific researcher with MDH. Reports of efficacy from these sources were compared against meta-analyses of current standard treatments. Statistical results and detailed comparisons for each drug can be found in Appendix H and scientific literature review methods can be found in Appendix I.

Psychedelics are notable for their ability to elicit profound alterations in sensory perceptions, states of consciousness, and even one's sense of self. While the effects can be positive both acutely and in the long term (Preller and Vollenweider, 2018), they can be challenging as well. One outstanding concept in the evaluation of risks of psychedelic drugs, particularly psilocybin and LSD, is the notion of the "bad trip," as it has been colloquially known. However, the more appropriate term for this is "challenging experience," which describes a mentally or physically difficult drug-taking experience. When navigated well, these challenging experiences can result in profound healing. It has been suggested that challenging experiences tend to happen more frequently in response to the consumption of drugs in settings that are uncontrolled and/or by those who are inexperienced with psychedelics (Ona, 2018). It should be noted, however, that no such experiences were reported in the clinical literature evaluated here.

A common factor among these psychedelic drugs is that they readily cross into the brain (Takahashi et al., 1985) and bind with great affinity to a number of receptors, especially serotonin receptors. Classical psychedelics are agonists, or partial agonists, of serotonin 2A receptors in the brain (Green et al., 2003; Kwan et al., 2022; Nichols, 2016), as well as other serotonin (Green et al., 2003; Kim et al., 2020; Sard et al., 2005; Wacker et al., 2013, 2017;), dopamine (Green et al., 2003; Kroeze et al., 2015), and various other receptors (Green et al., 2003; Kwan et al., 2022; Marona-Lewicka et al., 2005) in myriad brain regions and networks. While the short-term behavioral and physiological effects are apparent and frequently the subject of clinical trials, psychedelics also have long-term effects, one of which appears to be structural neural plasticity found in animal studies (Jones et al., 2009; Ly et al., 2018; Shao et al., 2021). However, long-term effects are yet to be reported in the clinical literature. Given the complex nature of these substances, it is unsurprising that a unified model of psychedelic action has yet to be established (Kwan et al., 2022; Swanson, 2018). However, current research aims to understand how these substances work in the brain and body, and how they may provide new treatment options for particular health conditions, especially mental health conditions.

The review of the literature suggests that most of the health conditions that these drugs are being investigated to treat are, in fact, mental health conditions. Mental health conditions are those defined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (American Psychiatric Association [APA], 2022). Most of these psychedelic treatments have largely been administered as a part of a drug-assisted therapy model, wherein the psychedelic is administered to the patient by a facilitator in a controlled environment, with psychotherapy or psychological support occurring either concurrently or in follow-up sessions. Many of these conditions are chronic and treatment-resistant, meaning that they have not responded to the currently available standard therapies.

MDMA

An amphetamine-like compound, MDMA was first synthesized in 1912 by Merck KGaA, the German pharmaceutical company (Meyer, 2013), and resynthesized in the 1970s by Alexander “Sasha” Shulgin and used as a clinical aid to psychotherapy in the early 1980s (Benzenhöfer and Passie, 2010; Greer and Strassman, 1985; Greer and Tolbert, 1986, 1998; Shulgin and Nichols, 1978; Strassman et al., 1995). By the mid-1980s the drug had reached the public and was being used as a recreational substance, which ultimately resulted in the Drug Enforcement Agency (DEA) issuing an emergency Schedule I classification of the substance (Pentney et al., 2001). The Multidisciplinary Association for Psychedelic Studies (MAPS) was founded as a result of MDMA being put onto Schedule I and launched a series of clinical trials for post-traumatic stress disorder (PTSD) aiming to get it approved for medical use.

In 2017, MDMA-assisted psychotherapy for the treatment of PTSD was awarded Breakthrough Therapy status by the Food and Drug Administration (FDA) (Feduccia et al., 2019). Building on a number of phase II studies, two phase III studies were then submitted through the New Drug Application process by Lykos Therapeutics (Mitchell et al., 2021, 2023). In August 2024 the FDA denied approval of MDMA-assisted psychotherapy, instead requesting an additional phase III trial to gather more data, including safety data, after which the drug can be re-evaluated.

Apart from PTSD, randomized controlled clinical trials (RCTs) have investigated MDMA-assisted psychotherapy for the treatment of social anxiety disorder in individuals with autism spectrum disorder (Danforth et al., 2018), and as a way to treat anxiety in those with a life-threatening illness (Wolfson et al., 2020). For all health conditions reported, statistical information in the literature was used to evaluate the effect sizes of treatments and to compare the efficacy of MDMA-assisted psychotherapy against current standard treatments. This and other supplementary information can be found in Appendix H.

Post-traumatic stress disorder (PTSD)

Six primary RCTs investigating the use of MDMA-assisted psychotherapy as a treatment for PTSD were evaluated (Mitchell et al., 2021, 2023; Mithoefer et al., 2011, 2018; Oehen et al., 2013; Ot'alora et al., 2018). Two of these studies were phase III and four were phase II clinical trials. Participants in these trials suffered from moderate-to-severe, often treatment-resistant PTSD. Veterans and first responders were included as a specific population of interest in one trial (Mithoefer et al., 2018). All of these studies were associated with Lykos Therapeutics (founded by the Multidisciplinary Association for Psychedelic Studies (MAPS), and formerly called MAPS Public Benefit Corporation).

Phase III Trials

Because the trials were associated with the same entity (MAPS), the methods were the same between the two phase III studies. The two trials enrolled 194 participants. In each trial, participants were divided randomly into one of two groups, either MDMA-assisted psychotherapy or psychotherapy with placebo. Regardless of group, each participant received three 90-minute preparatory therapy sessions, three eight-hour treatment sessions with two therapists and an overnight stay, and three 90-minute, non-drug integrative psychotherapy sessions after each drug (or placebo) treatment session. This resulted in a total of nine non-drug integrative sessions.

Assessment of PTSD symptomology was the primary outcome in both trials and was made through the Clinician Administered PTSD Scale (CAPS), both between and within groups. In both studies, there was a statistical difference in CAPS scores at the end of the trial between those that received MDMA and those that received the placebo, in favor of MDMA. When comparing between the two groups, the effect of MDMA-assisted psychotherapy was reported to be large to moderate. When looking just at the group that received MDMA, the effect sizes of treatment from beginning to end were very large to huge. However, the effect of placebo plus psychotherapy alone also resulted in a large effect of treatment when comparing between the baseline and endpoint. At the end of each study, more participants that received MDMA than those who received the placebo were found to no longer meet diagnostic criteria for PTSD, and more who received MDMA were reported to be in remission (Mitchell et al., 2021, 2023).

Phase II Trials

All four of the phase II trials were double-blind RCTs (Mithoefer et al., 2011, 2018; Oehen et al., 2015; Ot'alora G et al., 2018). These studies enrolled 86 participants with chronic, treatment-resistant PTSD (including military personnel and first responders). Methods were similar to those described above. Participants were divided into either the experimental dose group or the control dose group. After this, each participant received preparatory

sessions, two to three eight-hour drug treatment sessions with an overnight stay, and several follow-up integrative therapy sessions after each session with the drug.

The primary outcome for each study was again the change in the CAPS score. Each of these studies found that the experimental doses of MDMA, along with psychotherapy, significantly improved CAPS scores as compared with placebo/active control groups. Furthermore, more of those who received the experimental doses exhibited a clinical response (a greater than 30 percent reduction in CAPS total severity score from baseline) than did those who received the placebo or active control doses.

Comparison of efficacy, PTSD

Current standard treatments for PTSD include various psychotherapies, including cognitive behavioral therapy (CBT), prolonged exposure therapy, cognitive processing therapy, eye movement desensitization and reprocessing (EMDR) therapy, among others, as well as certain selective serotonin reuptake inhibitors (SSRIs) and one serotonin norepinephrine reuptake inhibitor (SNRI) (APA, 2020; NIMH, 2023). The SSRIs paroxetine and sertraline are the only FDA-approved treatment options for PTSD, while the Department of Veterans Affairs and the Department of Defense PTSD guidelines also recommend fluoxetine and venlafaxine (Feduccia et al., 2019; Hoskins et al., 2015; Lee et al., 2016). However, the American Psychological Association, the Department of Veterans Affairs, and the Department of Defense specify that trauma-focused psychotherapy is preferable to pharmacotherapy (Hoskins et al., 2015).

A meta-analysis examining 112 unique studies to investigate the efficacy of all standard treatments for PTSD was analyzed and reported an overall moderate effect of treatment (Watts et al., 2013). The study also divided treatment types broadly between psychotherapies and pharmacotherapies. Psychotherapy included CBT, exposure therapy, and EMDR, and the analysis found that each of these treatments had large effects on PTSD symptomology. Pharmacological interventions alone were found to have a moderate effect of treatment (Watts et al., 2013).

In comparison, the effect of MDMA-assisted psychotherapy as calculated in the phase III trials was found to be large (Mitchell et al., 2021, 2023). However, treatment with placebo plus psychotherapy alone also resulted a large effect size of treatment; the particular type of psychotherapy employed in these studies is not considered standard treatment for PTSD and was developed by MAPS specifically for use with MDMA. This intensive form of psychotherapy appears to have some treatment effects of its own.

Overall, with these reported effect sizes, MDMA-assisted psychotherapy appears to show at least comparable efficacy to current standard treatments for PTSD. However, while the reported effect sizes from the trials on MDMA are noticeably large, the clinical trials themselves involved only a few hundred individuals, the results of which are being compared against the output of meta-analyses encompassing data from hundreds of clinical trials. Therefore, more data is needed to directly compare the efficacy of MDMA-assisted psychotherapy and current standard treatments for PTSD.

Anxiety disorders in specific populations

Two RCTs investigating the use of MDMA-assisted therapy for anxiety (outside of that which co-occurs with PTSD) were evaluated. One trial investigated its use as a treatment for social anxiety disorder in adults with autism spectrum disorder (Danforth et al., 2018), and the other evaluated its use as a treatment for anxiety associated with a life-threatening illness (Wolfson et al., 2020). Like the trials for PTSD, these studies were associated with MAPS, and therefore the methods were similar between these two studies, as well as with the methods described in the PTSD section.

In the investigation of MDMA-assisted psychotherapy as a treatment for social anxiety disorder in adults with autism spectrum disorder, a total of twelve participants were enrolled and divided into the experimental group or the placebo group. Each group received two treatment sessions, each followed by three integrative therapy sessions. The primary outcome was the change in social anxiety symptomology from baseline to the end of the study, measured by the Leibowitz Social Anxiety Scale (LSAS). MDMA-assisted therapy significantly reduced the mean LSAS score as compared with the placebo group, and more of those who received MDMA than placebo saw clinically meaningful reductions in social anxiety symptoms. The effect size of treatment was found to be large (Danforth et al., 2018).

To explore the effect of MDMA-assisted psychotherapy as a treatment for anxiety surrounding a diagnosis of a life-threatening illness, eighteen participants were enrolled and divided into two groups, MDMA or placebo. Each group received two treatment sessions, each followed by three integrative sessions. The primary outcome was the impact on anxiety, measured by the change in State-Trait Anxiety Inventory (STAI-Trait) scores from baseline to the endpoint. Results indicated that the MDMA group saw a greater mean reduction in STAI-Trait scores, indicating less anxiety compared with the placebo group. This trended toward, but did not reach, statistical significance, but it still showed a large effect of treatment (Wolfson et al., 2020).

Comparison of efficacy, anxiety disorders

Current standard treatments for anxiety disorders include psychotherapies, including CBT and acceptance and commitment therapy, among others, medication (antidepressants, anti-anxiety medications), or a combination of the two (NIMH, 2024a). Exposure CBT and group CBT are additional treatments for social anxiety disorder (NIMH, 2024b).

One meta-analysis investigated 234 RCTs, and effect sizes were calculated for standard treatments for all anxiety disorders (Bandelow et al., 2015). Looking at psychotherapies alone, including individual CBT/exposure therapy and group CBT, the effects of these treatments were found to be large. The effects of pharmacological treatments were found to be huge. Combining psychological and pharmacological treatments also resulted in huge effects of treatment (Bandelow et al., 2015). A second meta-analysis investigating twenty-five clinical trials for the use of CBT as a treatment specifically for social anxiety disorder found only a moderate effect of treatment (Kindred et al., 2022).

In both studies investigating MDMA-assisted psychotherapy for the above-noted anxiety disorders, the effects of the treatment on the respective conditions were found to be large. While the statistical measures of effect sizes reported from both trials fell within the range of those calculated for current standard treatments,

indicating at least comparable efficacy, these comparisons are again between individual RCTs and the statistical combination of a multitude of trials and do not represent a direct comparison. More research will be necessary to directly compare the efficacy of MDMA-assisted therapy and current standard treatments for anxiety.

Adverse effects of MDMA in clinical trials

In the clinical trials, nearly all participants reported some sort of adverse effect. Most were considered mild to moderate in severity. Physical effects included headache, muscle tightness, jaw clenching or tightness of jaw, decreased appetite, nausea, dizziness, hyperhidrosis (sweating), and feeling cold. Psychiatric effects included anxiety, low mood, insomnia, fatigue, and suicidal ideation (in the PTSD studies). However, given the nature of PTSD, a substantial number of the participants had a lifetime history of suicidal ideation at baseline (see Appendix H for details). Occasionally more severe adverse effects occurred, including dissociation and flashbacks. Some of the more common adverse effects (e.g., low mood, anxiety, fatigue, headache, nausea) lingered for the week following drug administration but decreased in severity during this time. The RCTs also reported transient cardiovascular symptoms in response to MDMA, including increases in blood pressure, heart rate, and body temperature. These were all considered mild and typically resolved without medical intervention. Adverse cardiovascular effects were dose-dependent (Mithoefer et al., 2018), including in trials of MDMA in healthy individuals (Vizeli and Liechti, 2017). Sex differences in adverse effects have been noted, with more negative effects occurring in females (Vizeli and Liechti, 2017). Many of the other adverse effects reported in the clinical trials have also been seen in trials in healthy individuals (Vollenweider et al., 1998).

Drug-drug interactions

MDMA modulates serotonin neurotransmission, and as such there is the potential for drug-drug interactions with other medications that also modulate this system. This includes various types of common antidepressants (Sarparast et al., 2022). Other significant interactions include between MDMA and reversible inhibitors of monoamine oxidase, pro-serotonergic drugs, and those that inhibit the enzyme CYP2D6 (Pilgrim et al., 2011). Notably, in the last category, are common antidepressants (fluoxetine, paroxetine) and antiretroviral drugs. There have been instances of fatalities in those taking antiretroviral drugs and MDMA at the same time (Harrington et al., 1999; Henry and Hill, 1998; Kuwahara et al., 2008; Papaseit et al., 2012). Finally, concomitant use of caffeine with MDMA may exacerbate changes in body temperature regulation, cardiotoxicity, and potentially lower the threshold for seizure (Vanattou-Saïfoudine et al., 2012).

Abuse potential and toxicity

MDMA is less reinforcing than many other drugs, suggesting a low potential for dependence, which may be more psychological than physical (Degenhardt et al., 2009). Tolerance and self-reported withdrawal can occur, but only a minority of users become concerned enough about their use to seek treatment (Degenhardt et al., 2009; Jensen, 1999). Studies have reported various toxic effects of MDMA, including hepatotoxicity (liver toxicity) (Antolino-Lobo et al., 2011; Brauer et al., 1997; Carvalho et al., 2010), effects on the kidneys, including hyponatremia (an abnormally low concentration of sodium in the blood) (Campbell and Rosner, 2008), and Parkinsonism (Kuniyoshi et al., 2003), as well as instances of minor memory impairment (Kloft et al., 2022; Smithies et al., 2014) and impacts on anxiety and mood (Kaplan et al., 2018; Majić et al., 2022; Montoya et al.,

2002). Fatalities following MDMA intoxication are rare; in instances of fatalities the blood concentration of MDMA has been found to be around 4,000 nanograms (ng) per one milliliter (mL) of blood (Hoorn, 2001). For reference, peak blood concentration following one of the highest clinical doses of MDMA (125 milligrams [mg]) is around 236ng/1mL (Kalant, 2001).

Another risk of MDMA-assisted psychotherapy, and indeed all psychedelic-assisted therapies, is the vulnerability of the participant. There is a power imbalance between therapist and patient in traditional psychotherapies, which can be exacerbated when psychedelic drugs are introduced (Meikle et al., 2023). Psychedelics can impair cognition (Bayne and Carter, 2018), can enhance suggestibility (Carhart-Harris et al., 2015), and may also result in a loss of the sense of self and the blurring of perceived boundaries with others (Mason et al., 2020). In particular, MDMA is known to increase plasma oxytocin as well as to increase pro-social, empathetic, and sexual arousal-like effects (Dolder et al., 2007). This may put the patient in a situation where abuse of power by a therapist could occur more readily (Meikle et al., 2023).

Limitations of MDMA trials

There were a number of specific limitations within these trials. Between the two phase III studies, a total of 40 percent of the participants had any lifetime experience with MDMA; this is a significant departure from the estimated less than 8 percent of the US population (age twelve and older) who have reported any lifetime experience with the drug (SAMHSA, 2023a). Next, the intensive psychotherapeutic process utilized in these studies was developed by MAPS and is not considered a standard therapeutic approach for any disorder, including PTSD. Furthermore, participants who received placebo along with this intervention also saw substantial improvements in PTSD symptomology, which may suggest there are effects of the psychotherapy itself, without the addition of MDMA. Each of these trials employed strict exclusion criteria, excluding individuals with certain medical conditions, including uncontrolled cardiovascular conditions. A limitation common to all studies of psychedelic drugs is the issue of functional unblinding (see Community Research section). Between the two phase III trials, 94 percent of participants in the MDMA condition correctly guessed to which condition they had been assigned, and 75 percent of those in the placebo guessed correctly. Similar limitations were encountered in the trials on anxiety.

Psilocybin

Psilocybin is found naturally in fungi throughout the world (Guzmán, 2009). While there is documented evidence of the ritualistic consumption of psilocybin-containing mushrooms from Mesoamerica dating to the early 1500s CE (Hernández Santiago et al., 2017), many pre-Columbian Mesoamerican cultures have used entheogens for millennia. Religious practices with these mushrooms have been estimated to date back at least 3,500 years and to have been used by the Mayan and Aztec cultures, among others (Carod-Artal, 2015). Despite the millennia of use among Mesoamerican cultures, it was not until the late 1950s when these mushrooms were widely introduced to a Western audience after R. Gordon Wasson traveled to Mexico to partake in a mushroom ceremony with the Mexican curandera, María Sabina (Wasson, 1957; Nichols, 2016). Psilocybin was then found to be a prodrug that is metabolized into psilocin (Horita and Weber, 1961). Psilocin is presumed to be the psychoactive component of the drug, through binding to serotonin 2A receptors, among others (Nichols, 2016).

Psilocybin was initially used as an adjunct to psychotherapy (Nichols, 2016) until its classification as a Schedule I drug in 1970 (INCB, 2003). Recently, three companies have been awarded Breakthrough Therapy status from the FDA for psilocybin in the treatment of treatment-resistant depression and major depressive disorder (COMPASS Pathways, 2018; Usona Institute, 2019; Cybin, 2024), and large, multi-site phase III trials are currently underway. Psilocybin-assisted therapy is currently being investigated as a treatment for substance use disorders as well. One RCT investigating the treatment for alcohol use disorder has been completed (Bogenschutz et al., 2022). Additionally, one RCT and a follow-up study have been completed investigating the use of the drug as a treatment for cluster headache (Schindler et al., 2022, 2024). The psilocybin used in the following RCTs is a synthetic form of the substance, and not directly from a naturally grown mushroom. For all health conditions reported, statistical information in the literature was used to evaluate the effect sizes of treatments to compare the efficacy of psilocybin-assisted therapy against current standard treatments. This and other supplementary information can be found in Appendix H.

Mood and anxiety disorders

Both major depressive disorder and bipolar type II disorder are categorized as mood disorders, and as such they will be discussed together. Similarly, because mood and anxiety disorders were considered jointly in nearly all identified trials, and because these disorders often co-occur, they are presented together as well. Nine primary phase II RCTs investigating mood and anxiety disorders were analyzed (Carhart-Harris et al., 2021; Davis et al., 2021; Goodwin et al., 2022; Griffiths et al., 2016; Grob et al., 2011; Raison et al., 2023; Rosenblat et al., 2024; Ross et al., 2016; von Rotz et al., 2023). One of these trials directly compared psilocybin-assisted therapy and the antidepressant escitalopram (Carhart-Harris et al., 2021) and will be reported separately.

Nearly 600 participants were included in the RCTs, of which 370 received the experimental dose of psilocybin. All trials utilized a therapeutic component before and after the one, two, or sometimes three doses of psilocybin, and all trials had at least one preparatory psychotherapeutic session, along with one to three integrative post-treatment psychotherapy sessions. Doses ranged from one to three mg (as an active control) to ten to thirty mg as an experimental dose. Only two of the included studies employed a true control, in which one group received only the placebo and never received psilocybin. Most either used active control doses, a wait-list control condition, or a crossover component. However, many of these studies used a primary endpoint where only one group had received the drug.

A meta-analysis of thirteen studies, including the above RCTs, investigating psilocybin-assisted therapy for mood and anxiety disorders calculated the change in depression and anxiety ratings from baseline to the primary endpoint in the psilocybin versus control groups (Haikazian et al., 2023). Results indicated a large effect of psilocybin treatment on both depression and anxiety. Those who received psilocybin-assisted therapy saw a greater improvement in depression and anxiety symptoms between baseline and the end of the study than those that were in the control groups. Response and remission rates were also assessed. The pooled response rate indicated that 57 percent of those that received psilocybin-assisted therapy saw a clinical response to the treatment, as compared with 22 percent of the control group. A similar finding was reported for remission rates, which also favored the psilocybin group over the control group. The pooled remission rate was 45 percent in the psilocybin group as compared with 14 percent in the control group (Haikazian et al., 2023).

Comparison of efficacy, psilocybin versus escitalopram

Major depressive disorder is typically treated with medications (antidepressants) and/or psychotherapy. Psychotherapy is typically cognitive behavioral therapy (CBT), but can include other forms (NIMH, 2024c). One RCT directly compared psilocybin-assisted therapy against a current standard medication for depression, escitalopram (Carhart-Harris et al., 2021). The trial consisted of two treatment sessions and four integrative sessions over six weeks. In the drug treatment sessions all participants, regardless of group, received psilocybin: the psilocybin group received the full experimental dose of twenty-five mg, while the escitalopram group received one mg of the drug, to control for the effects of psilocybin. Between sessions, all participants were given either placebo pills (psilocybin group) or escitalopram pills (escitalopram group) to take daily. The primary outcome was the change from baseline in the score on the 16-item Quick Inventory of Depressive Symptomatology–Self-Report (QIDS-SR-16). At the end of the trial, there was no significant difference in depression scores between the two groups. The lack of difference between the two treatments in a head-to-head comparison suggests that psilocybin-assisted therapy is at least as efficacious as escitalopram, over a six-week course of treatment (Carhart-Harris et al., 2021).

Results from the six-month follow-up, in which participants reported on their depressive symptoms monthly following the six-week trial, indicated that psilocybin-assisted therapy and escitalopram-assisted therapy showed similar levels of reduced symptoms at this time point (Erritzoe et al., 2024). That is, while the first study reported that the reduction in depressive symptoms seen at the six-week mark was approximately equal between the groups, this study reports that these levels remained equally low for both groups up to six months, suggesting comparable efficacy. Furthermore, those who received psilocybin reported greater work and social functioning, more social connectedness, and more meaning in life than those who received escitalopram (Erritzoe et al. 2024). However, an important caveat of the trial is that a placebo control condition was not included in the initial RCT.

Comparison of efficacy, mood, and anxiety disorders

Meta-analyses were analyzed to compare psilocybin-assisted therapy against current standard approaches for the treatment of mood and anxiety disorders. One meta-analysis evaluated 522 clinical trials covering twenty-one different antidepressants versus placebo to determine the efficacy of these drugs as a treatment for major depressive disorder. This study found that medication treatment alone had medium to low effect sizes, depending on the antidepressant (Cipriani et al., 2018). Another meta-analysis evaluated twenty-three RCTs to determine the efficacy of combined pharmacotherapy and psychotherapy in the treatment of major depressive disorder as compared with pharmacotherapy or psychotherapy alone. The effect of therapy along with medication was equal to therapy alone, and greater than medication alone (Karyotaki et al., 2016).

In comparison, the meta-analysis investigating the effect of psilocybin-assisted therapy on depression, including treatment-resistant depression, demonstrated a large effect of treatment (Hakazian et al., 2023). In the direct head-to-head comparison, psilocybin-assisted therapy was reported to be equally efficacious as a standard pharmacological treatment in decreasing symptoms of depression (Carhart-Harris et al., 2021).

A meta-analysis that evaluated 234 RCTs to determine the effect sizes of current standard treatments for anxiety was analyzed (Bandelow et al., 2015). Psychotherapies alone, including individual CBT/exposure therapy

and group CBT, resulted in a large effect size of treatment. Pharmacological treatments alone were found to have a huge effect, as did the combination of the two (Bandelow et al., 2015). A meta-analysis investigating four clinical trials for the effect size of psilocybin treatment on anxiety found a moderate effect of treatment, as compared with the control group (Goldberg et al., 2020).

Overall, the current trials of psilocybin-assisted therapy for the treatment of mood and anxiety disorders indicate large effects of treatment, and at least comparable efficacy to one standard treatment (escitalopram). However, the reported effect sizes from these trials were calculated from only a few hundred individuals and are being compared against meta-analyses encompassing data from many studies with thousands of individuals. Therefore, more clinical data is needed to directly compare the efficacy of psilocybin-assisted therapy and current standard treatments for mood and anxiety disorders.

Alcohol use disorder

One RCT investigating psilocybin-assisted therapy as a treatment for alcohol use disorder was analyzed (Bogenschutz et al., 2022). Nearly 100 participants received either psilocybin- or diphenhydramine-assisted therapy (as a control condition). All participants received four therapy sessions before treatment, two sessions with the drug, and four non-drug follow-up therapy sessions after each treatment session. Psilocybin doses were calculated by participant body weight. The study lasted thirty-eight weeks and assessed the percentage of heavy drinking days, the percentage of total drinking days, and the mean drinks per day. At the end of the study, as a group, participants who received psilocybin had a lower percentage of heavy drinking days, a lower percentage of total drinking days, and lower drinks per day than the control group. All results were statistically significant. There was a trend toward abstinence in those who received psilocybin (Bogenschutz et al., 2022).

Comparison of efficacy, alcohol use disorder

Current treatments for alcohol use disorder include three medications, naltrexone, acamprosate, and disulfiram, as well as cognitive behavioral therapy (CBT), which is often used in conjunction with the pharmacotherapies (NIAAA, 2024). One meta-analysis evaluated 118 clinical trials to assess the three pharmacotherapies for treating alcohol use disorder (McPheeters et al., 2023). In looking at the percentage of heavy drinking days, in comparing any dose of naltrexone against placebo, the analysis found that there was a mean of nearly 4 percent fewer heavy drinking days when using naltrexone, and a mean of just more than 3 percent fewer heavy drinking days when using acamprosate (McPheeters et al., 2023). The mean difference in the number of heavy drinking days between the psilocybin and control groups was nearly 14 percent (Bogenschutz et al., 2022). In looking at the percentage of any drinking days, there were 4.5 percent fewer drinking days when receiving naltrexone and just over 8 percent fewer drinking days following acamprosate (McPheeters et al., 2023). In comparison, the psilocybin group had just over 13 percent fewer drinking days than the control condition (Bogenschutz et al., 2022). Finally, evaluating the number of drinks per day, there was an average of almost one less drink per day in those receiving naltrexone as compared with placebo, while those who received acamprosate drank an average of 0.6 more drinks per day than those in the placebo group (McPheeters et al., 2023). In the comparison of psilocybin versus control, the mean difference indicated that the psilocybin group drank an average of one drink less per day than the control group (Bogenschutz et al., 2022). Overall, psilocybin-assisted therapy appears to outperform the current standard pharmacotherapies in the treatment of alcohol use disorder. However, this

comparison is between the single study on psilocybin treatment for alcohol use disorder and the statistical output of over 100 unique clinical trials. Therefore, to draw sound conclusions on the efficacy of psilocybin, more clinical trials are required.

Cluster headache

One RCT investigating the use of psilocybin as a treatment for cluster headache was found (Schindler et al., 2022), along with a follow-up to that trial (Schindler et al., 2024). A total of sixteen participants received either psilocybin, dosed by body weight, or a placebo in three separate treatment sessions. During the study participants kept track of the date, time, duration, and intensity of every cluster headache, and data was assessed three weeks after the first treatment session. While there was a reduction in the frequency of cluster headaches in the psilocybin group, this was not statistically significant. There were no differences in the duration of the attacks, or the intensity of the pain between the two groups.

Comparison of efficacy, cluster headache

Cluster headaches are difficult to successfully treat, but they are conventionally treated with triptan drugs, oxygen therapy, and non-invasive vagus nerve stimulation injections (NINDS, 2023). However, the single RCT identified found no statistical difference between psilocybin treatment and the placebo condition. Because this treatment did not show any benefit over a placebo, we cannot compare the efficacy of psilocybin against current standard treatments for cluster headache at this time.

Adverse effects in clinical trials

While there were adverse effects associated with psilocybin treatment in the RCTs, most were considered mild to moderate. The most commonly reported events during treatment were headache, nausea, dizziness, and fatigue. Occasionally there were reports of anxiety, visual perceptual effects, migraine, and gastrointestinal effects. Negative effects appeared to be dose-dependent; higher doses of psilocybin were associated with a greater number and intensity of adverse effects. Only a few participants experienced more severe effects, including panic attack and paranoia; however, a single therapeutic dose of psilocybin is not statistically associated with paranoia (Yerubandi et al., 2024). While most adverse effects occurred only during the treatment and resolved on their own, headache was reported to linger for a few days after the treatment in most studies. These effects, particularly headache, were found to occur in studies of healthy individuals as well, and again were dose-dependent (Johnson et al., 2012; Perez et al., 2023).

Psilocybin treatment was found to increase blood pressure and heart rate as compared with the control condition, but these increases were considered mild and did not require medical intervention. However, more research regarding the effects of psilocybin with serotonin receptors in the cardiovascular system is necessary. Most RCTs have excluded participants with known cardiovascular disease, and therefore the effect of psilocybin in serotonin-related cardiotoxicity is unclear. The potential for psilocybin to induce arrhythmia, as well as platelet aggregation, therefore needs further investigation (Wsół, 2023).

Drug-drug interactions

The use of psilocybin appears unlikely to result in serotonin toxicity, as psilocybin does not contain monoamine oxidase inhibitors (Malcolm and Thomas, 2021). Pre-treatment with escitalopram appears to weaken the negative drug effects of psilocybin, including anxiety and adverse cardiovascular effects, with no effect on the positive mood effects of psilocybin (Becker et al., 2021). Taking SSRIs or SNRIs concurrently, or within three months of discontinuation, with psilocybin may also weaken the overall effect of the drug (Gukaysan et al., 2023). However, an open-label, non-RCT investigated the efficacy of twenty-five mg of psilocybin (with a therapeutic component) without discontinuation of an SSRI (Goodwin et al., 2023), and found that participants reached clinically meaningful improvements in depression severity without any serious adverse effects. Certain antipsychotic medications (e.g., chlorpromazine), as well as GABAergic agents (e.g., benzodiazepines) have been shown to attenuate the drug effects of psilocybin (Johnson et al., 2008; Keeler, 1967).

Abuse potential and toxicity

Psilocybin does not appear to have great abuse potential. Reports of acute increases of anxiety in some patients, as well as a sense of contentment following taking the drug, are predictive of low abuse potential, and are not suggestive of a strong motivation for repeated and/or chronic use (Johnson et al., 2018). Physical dependence to and withdrawal from psilocybin have not been documented. Psilocybin carries a low risk of overdose toxicity, with the lethal dose of psilocybin theoretically estimated to be approximately 1,000 times an effective dose (Gable, 2004). While there are some instances of negative effects on organ systems (see Appendix H), there are only a few reported cases of fatality following ingestion of psilocybin-containing mushrooms: one case of acute overdose poisoning occurred in an individual who had previously received a heart transplant (Lim et al., 2012) and another occurred after an individual ingested a large amount of psilocybin-containing mushrooms and jumped from a two-story building (Honyiglo et al., 2019). Acute negative physiological and psychological reactions can occur (Barbee et al., 2009; Musha et al., 1986). Negative psychological reactions can occur, especially outside of a controlled environment, by those who are young, unexperienced, or unprepared, or those with, or predisposed to, psychotic disorders (Johnson et al., 2018). An incident involving a pilot for Alaska Airlines further highlights the need for awareness of the “set and setting,” referring to the mindset of the person and the physical location, in taking this substance. If a person is in a state of crisis or instability, taking psilocybin-containing mushrooms without appropriate support may further destabilize them (NYT, 2023).

Limitations of psilocybin trials

Limitations in these trials are both common to all clinical trials and specific to psychedelic trials. A limitation common to all clinical trials is that those within the trials did not have any other underlying health conditions nor were they allowed to take certain other medications, making it difficult to draw conclusions to a wider population. Specifically in these trials, the sample size of each study was relatively small compared with clinical trials for non-psychedelic drugs. Additionally, due to the psychoactive nature of psilocybin, it was difficult to create a condition in which the participant did not know they had received the drug (this is called functional unblinding). Attempts to counter this focused on giving participants a small dose of the drug, but this results in the lack of a true placebo group with which to compare results. Finally, individuals that suffered from suicidal ideation were often excluded from participation in the clinical trials.

There were additional caveats specifically in the trial comparing psilocybin and escitalopram (Erritzoe et al., 2024). Typically, escitalopram is not tested clinically with an associated therapeutic component, and therefore in this group the six-week and six-month results may show greater improvement in symptomology than if escitalopram were used on its own, as it is often prescribed. Additionally, in the six-month follow-up, 63 percent of those who received psilocybin reported seeking further treatment during this time period, while 34 percent of those in the escitalopram group reported continuation of the medication. Finally, not all participants responded to each follow-up questionnaire, and therefore missing data may slightly skew results. Therefore, more research surrounding psilocybin is necessary to draw firm conclusions about its efficacy.

LSD

LSD was first synthesized in 1938 in Switzerland (Hofmann, 1979), but it was not until 1943 that the psychoactive properties of the drug became known (Nichols, 2003). Following this discovery, the drug was explored in various clinical applications. By the 1960s, LSD was being explored for treating existential dread associated with terminal illnesses, alcohol and opioid addiction, and depression (Passie et al., 2008). However, by the mid-1960s and into the 1970s recreational use had increased substantially, and LSD was ultimately ruled to be a Schedule I substance, effectively halting medical research for decades. With renewed interest in psychedelic medicine, many of the applications for which LSD was initially being tested are once again being studied, including as a treatment for anxiety (with or without a life-threatening illness) (Gasser et al., 2014; Holze et al., 2023), as well as for alcohol use disorder (Krebs and Johansen, 2012). The drug has been tested both with and without a corresponding psychological therapy component, and it has been awarded Breakthrough Therapy status from the FDA for generalized anxiety disorder (Hopkins, 2023).

The health conditions tested by RCTs for which LSD may provide efficacious treatment include anxiety disorders and alcohol use disorder. For all health conditions reported, statistical information in the literature was used to evaluate the effect sizes of treatments to compare the efficacy of LSD as a treatment versus current standard treatments. This and other supplementary information can be found in Appendix H.

Anxiety disorders

Two RCTs investigating the use of LSD-assisted therapy for the treatment of anxiety were identified. Both explored the efficacy and safety of the treatment in patients experiencing anxiety with life-threatening illnesses (Gasser et al., 2014; Holze et al., 2023), while one of these studies also included those without a life-threatening condition (Holze et al., 2023). Both studies employed similar methods, in which one group received a full experimental dose of the drug while the other received a smaller control dose. Both studies also included one preparatory session, two treatment sessions with the drug, and one to three post-treatment therapy sessions. Each trial also measured anxiety symptoms using the State-Trait Anxiety Inventory (STAI), including both the State and Trait components separately. Ultimately, both studies reported that LSD-assisted therapy significantly reduced measurements of anxiety, as compared with the control group, with effect sizes of treatment ranging from moderate to large when looking at the STAI as a whole, and from moderate to very large on the individual State and Trait components.

Comparison of efficacy, anxiety disorders

Anxiety disorders, with or without a life-threatening illness, are typically treated with psychotherapy, pharmacotherapy, or a combination of the two (NIMH, 2024a). A meta-analysis investigating the effects of a range of psychotherapeutic interventions for generalized anxiety disorder found that the effect size of psychotherapy versus control groups was moderate on self-reported measures and large on clinician-rated instruments. Specifically, this analysis found that current standard treatments result in a moderate effect when measured by the STAI, including both components individually (Cuijpers et al., 2014). Both RCTs investigating LSD-assisted therapy found overall large effects of treatment, when measured by the STAI as a whole. When looking at individual components of the STAI, effect sizes ranged from moderate to very large (Gasser et al., 2014; Holze et al., 2023). However, the effect sizes calculated for LSD-assisted therapy come from only two studies, while those from the meta-analysis are the composite of many larger studies. More clinical trials are necessary to directly compare the efficacy of LSD-assisted therapy and current standard treatments for anxiety.

Alcohol use disorder

Five RCTs investigating the efficacy of LSD in the treatment of alcohol use disorder were analyzed, all of which were conducted in the late 1960s into the early 1970s (Bowen et al., 1970; Hollister et al., 1969; Johnson, 1970; Ludwig et al., 1969; Smart et al., 1966). The methodology, including dosages, varied widely between the studies. Most, but not all, of these studies attempted some sort of blinding, and most, but not all, employed some type of control group. When included, these control groups were not always treated the same as the LSD groups. Most of these studies found that all groups, regardless of if they received LSD or not, showed some improvements in symptoms of alcohol misuse when comparing between the beginning and end of the trial. Furthermore, the LSD groups did not tend to show significant differences when compared directly against control groups. Ultimately, the conclusions drawn by each of these studies individually indicated that treatment with LSD provided no meaningful benefit over other treatments.

A meta-analysis analyzing four of these RCTs, along with two non-RCTs, found that, when combined, the data indicated that LSD treatment resulted in a beneficial effect of improving symptoms of alcohol misuse at the first-reported follow-up session, up to six months after treatment (Krebs and Johansen, 2012). By twelve months after treatment there were no differences between groups. When looking at total abstinence, the analysis found that treatment with LSD had a greater effect than control up to three months after treatment, but by six months there was no difference (Krebs and Johansen, 2012).

Comparison of efficacy, alcohol use disorder

Alcohol use disorder is typically treated through the use of pharmacotherapy, psychotherapy, and sometimes the combination of the two. Three commonly prescribed standard medications include naltrexone, acamprosate, and disulfiram; psychotherapy is typically CBT (NIAAA, 2024). The meta-analysis by Krebs and Johansen (2012) also compared LSD against current treatments. While they reported that, as compared with placebo, daily naltrexone use provides a greater effect in treating the symptoms of alcohol misuse than acamprosate, their analysis indicated that LSD provides a greater treatment effect than either of these medications. They were unable to compare LSD against disulfiram. When analyzing abstinence from alcohol,

acamprosate was found to have an equal effect with disulfiram, and both had a greater effect than daily naltrexone use. LSD treatment was found to have a greater effect on abstinence than all three of these drugs. While the original RCTs concluded that the treatment was not any more beneficial than any other treatment, data from the recent meta-analysis suggest that LSD is more efficacious in managing the symptoms of alcohol use disorder than three of the current standard pharmacotherapies (Krebs and Johansen, 2012). However, modern clinical trials investigating the effect of LSD treatment on alcohol use disorder are necessary to draw any firm conclusions about the efficacy of the treatment.

Adverse effects in clinical trials

In general, the clinically reported adverse effects of LSD were mild to moderate, and transient. From the studies investigating anxiety, common reports were fatigue, headache, nausea, transient anxiety, illusions, feeling abnormal, and feeling cold. Most of these effects resolved when the drug treatment wore off. One patient was treated for anxiety with delusions, and another patient with a comorbid diagnosis of major depressive disorder reported transient feelings of depression, including suicidal thoughts (but no increase in suicidality) eight weeks after the last LSD treatment (Holze et al., 2023). Some participants in the RCTs, as well as in studies in healthy participants, reported flashbacks that lasted anywhere between a day to a week after treatment (Holze et al., 2022). From the trials investigating alcohol use disorder, one individual experienced a seizure (Hollister et al., 1969); this patient had a history of seizures that may have been associated with alcohol withdrawal.

Physiologically, LSD was shown to significantly increase blood pressure and heart rate during treatment as compared with the control group (Holze et al., 2023). This is consistent with clinical trials investigating LSD in healthy individuals (Holze et al., 2021a; Schmid et al., 2015). Other adverse effects reported in these trials involving healthy individuals have included headaches (including migraine), low mood, restlessness, vivid dreams, and involuntary movement of the lower extremities. These effects appear to be dose-dependent, with increased doses increasing subjective, physiological, and adverse effects (Holze et al., 2021b).

Drug-drug interactions

LSD binds to certain serotonin and dopamine receptors (Halberstadt and Geyer, 2011), among others, and is metabolized by various enzymes (Wagmann et al., 2019); therefore, any medications that interact with these enzymes will likely result in an interaction with LSD. Antipsychotics, certain antidepressants (e.g., SSRIs, MAOIs), and other agonists of serotonin receptors typically result in a dampening or lessening of LSD effects (Bonson et al., 1996; Bonson and Murphy, 1995; Grof and Dytrych, 1965; Holze et al., 2021b; Resnick et al., 1964; Straumann et al., 2023; Vizeli et al., 2021).

Abuse potential and toxicity

Exposure to LSD does not typically lead to compulsive drug-seeking behavior, nor does use result in dependence, though there may be instances of tolerance (Nichols and Grob, 2018). This suggests that the abuse potential of LSD may be low. Serious adverse reactions to LSD are more likely to occur when the drug is taken outside of a clinical setting, and in doses that are much larger than those used in the clinic. While overdose by LSD is rare, it can occur following consumption outside of a controlled environment, though the lethal oral dose for a human

is estimated to be around 100 mg. This is significantly higher than clinical doses. Presently there are only two documented cases where LSD presumably directly led to a fatality. In both cases, the post-mortem analyses indicated that each individual had ingested incredibly large quantities of LSD (Nichols and Grob, 2018). Some users of LSD outside of a clinical environment have reported impairment in color vision (Abraham, 1982), and there is at least one report of an individual with co-morbid migraine who experienced transient cortical blindness following LSD exposure (Bernhard and Ulrich, 2009). Early data suggested that schizophrenia may be a contraindication for LSD in those with a genetic disposition for the disorder (Vardy and Kay, 1983). A more recent study of adolescent twins who report psychedelic use indicated that naturalistic use of these substances may be associated with lower rates of psychotic symptoms. However, the expression of manic symptoms in response to psychedelic use may be associated with a genetic vulnerability to schizophrenia or bipolar I disorder (Simonsson et al., 2024). Finally, there have been case reports that indicate birth defects in infants born to mothers who have taken LSD, particularly during the first trimester. This includes ocular malformations, limb defects, and an elevated rate of spontaneous abortions (Chan et al., 1978; Dishotsky et al., 1971). However, there has also been a case report indicating that LSD overdose in the first trimester did not appear to have a negative outcome on the pregnancy or child (Haden and Woods, 2020).

Limitations of LSD trials

Limitations common to all clinical trials and those specific to psychedelic drugs were seen in the studies on LSD. The total sample size of participants included between the trials is relatively small and limited in who met criteria for inclusion. As with studies of other psychedelic drugs, functional unblinding was high, and some studies used a low dose of the drug in place of a true placebo, potentially limiting conclusions on efficacy. Additionally, while there were a number of studies investigating the drug as a treatment for alcohol use disorder, these studies do not meet the standards of current clinical trial rigor. Another limitation of these studies is that there have been fewer clinical studies testing LSD than there have been with either psilocybin or MDMA. With only two published RCTs in the literature, the conclusions that can be drawn regarding efficacy are extremely limited. Overall, more clinical trials in the coming years will be necessary to understand the therapeutic efficacy of LSD.

Discussion

There has been renewed clinical interest in psychedelic medicine in the last decade or so. Studies in the scientific literature focus largely on mental health conditions and investigate these drugs as part of a drug-assisted therapy model. All of the substances investigated in this review have been awarded Breakthrough Therapy designation by the FDA and are being tested in phase III clinical trials.

As part of an assisted therapy model, MDMA has been investigated in clinical trials for the treatment of PTSD, as well as social anxiety in adults with autism and general anxiety in those with a life-threatening illness. While a New Drug Application with data from two phase III clinical trials was submitted to the FDA, ultimately the agency asked for an additional phase III trial to address safety data. Psilocybin is also being investigated as part of a drug-assisted therapy model, for the treatment of mood disorders, including major depressive disorder and treatment resistant depression, anxiety disorders, alcohol use disorder, and cluster headache. Several phase III trials are underway, as are a number of phase I and phase II studies for health conditions that did not meet

inclusion criteria for this review. Finally, LSD has been investigated in two RCTs as part of a drug-assisted therapy model for the treatment of anxiety, with or without an associated life-threatening illness. A private company has also been testing LSD as a treatment for generalized anxiety disorder, without an associated therapeutic component. Phase III trials are beginning in 2025. While LSD was being tested as a treatment for alcohol use disorder in the 1960s and 1970s, no current research has been published.

The efficacy data reported in many of these clinical trials appears promising. However, the most rigorous way to compare the efficacy of two treatments is through a meta-analysis. The task force was unable to conduct its own meta-analyses due to limited resources and a directive in our task force charter to not conduct new research studies, and there are only a few meta-analyses that have been published. Therefore, it remains statistically unclear if these treatments show equal or greater efficacy than treatments that are currently available. Furthermore, the number of these trials in the scientific literature is relatively small, and there are a number of known limitations of clinical trials that restrict the generalizability of the results. In general, RCTs investigate how a drug works in a tightly controlled environment, over a limited amount of time, in a heavily curated and small subset of individuals. These trials for psychedelic drugs face additional hurdles, including functional unblinding and expectancy effects, among others. The generalizability of safety data is limited as well, and the lack of comprehensive safety data surrounding MDMA, psilocybin, and LSD is of particular concern given that long term exposure to agonists of certain serotonin receptors in the heart may lead to heart valve thickening (FDA, 2023). Though in clinical trials the drugs were generally well-tolerated, reports of adverse effects, and serious adverse effects, did occur. There has also been some concern regarding under-detection or incomplete reporting of these adverse effects (Hinkle et al., 2024).

Overall, great strides have been made in investigating psychedelic medicine as a treatment option for mental health conditions, many of which are difficult to treat with current therapies and place heavy burdens on those experiencing them. Ultimately, with more clinical trials generating data in the coming years, a more complete understanding of the efficacy of psychedelic medicine will become clear.

Community research summary

Leveraging the seven guiding principles for evaluating equitable access for all Minnesotans, the task force is called to look beyond the confines of the literature outlined in the scientific literature review section. While RCTs are the gold standard for drug approval by the FDA, they do not always reflect realities of how they will be delivered to the broader population. Furthermore, noted caveats in proper blinding have been an ongoing concern for evaluating unbiased efficacy of psychedelics in clinical trials. However, these psychedelic medicines have decades of data of use in the broader community dating back to the 1940s and have shown to be relatively safe and non-toxic for the majority of people who use them. Specifically, regarding psilocybin, there have been thousands of years of ceremonial use by Indigenous cultures. Supplementary information for certain sections can be found in Appendix H.

Limitations of clinical trials

Double-blind RCTs are considered the gold standard for the development of new medications and treatments. These types of studies are ultimately still scientific experiments, though, and have a number of known limitations. Participants in the trials often do not reflect the real-world population, since these studies frequently exclude individuals with certain conditions, both mental and physical, as well as limiting the use of certain other medications during the trial. These trials also frequently do not include a diverse group of individuals.

Clinical trials are designed to determine the efficacy of a treatment, which refers to how well it works in tightly controlled conditions. It is not until a medication is on the market and in use by the general public that measures of its effectiveness (how well it works in real-world situations) can be understood. That is, generalizability of the results of clinical trials to the wider public is often difficult. Clinical trials are often focused on a single outcome over a specific amount of time, and so any other effects of the treatment, including long-term effects, are often unable to be reported. Another limitation of clinical trials is that they are focused solely on the Western medical model, which excludes information from lived experiences, as well as other cultural interpretations.

On top of this, clinical trials of psychedelic drugs are faced with additional hurdles. One unique challenge of this class of drugs surrounds blinding, the process of keeping either or both the participants and the administrators unaware of the drug condition. Because the experiences elicited by psychedelic drugs are distinct, participants and clinicians are almost always able to correctly guess if they received the drug or the placebo; this is called functional unblinding. Another challenge with testing psychedelic drugs is the expectancy effect, which refers to how the participant's belief about the drug they may or may not receive can influence the outcome. This is a particular concern with the media attention surrounding psychedelic drugs, and the sometimes-expressed belief that these substances may act as panacea, or cure-all drugs.

Yet another effect that can influence outcomes positively is the placebo effect, or seeing an effect but not having received the drug of interest. The converse of this is the “nocebo” effect, wherein participants who expect that they will feel better after receiving a treatment may be disappointed if this is not the case, sometimes leading to worsening symptoms. While the placebo and nocebo effects can occur in standard clinical trials, given the often treatment-resistant nature of the health conditions these psychedelic drugs are being investigated to treat, these effects are of particular concern here.

Another limitation of these trials is the relatively small sample size as compared with that found in trials of current standard treatments, along with the relatively small number of trials in total. Finally, psychedelic trials, particularly regarding psilocybin, exclude Indigenous Ways of Knowing, despite thousands of years of experience with these entheogens. Because of the general limitations of clinical trials, and the specific limitations of those investigating psychedelic drugs, population-wide, community level, and other lived experiences, particularly those of Indigenous individuals and communities, are important sources of information.

Indigenous ways of knowing

Cultures around the world, and particularly those Indigenous to the Americas, have incorporated psychedelic plants and mushrooms into their practices for thousands of years. The experiences induced by these entheogens is understood to be a way of connecting with the spirit and natural world, as well as connecting internally to gain insights and wisdom, including for healing. The use of psilocybin-containing mushrooms, and related entheogens, is not taken lightly in these cultures; use occurs in rituals or ceremonies, overseen by those with experience, to ensure respect for the mushroom or plant and the powerful experiences they induce. Healing, both physical and spiritual, is a holistic endeavor in Indigenous communities, and is reflected in the use of psilocybin-containing mushrooms. Practitioners of Indigenous healing urge the use of these beings as a whole, rather than through extraction and isolation of compounds (Yeomans, 2022).

Apart from physical healing, the religious and spiritual use of psychedelics remains a vital part of many Indigenous traditions. In the current context of general prohibition, there has been a growing movement to reclaim these traditions. The Native American Church has successfully fought for legal protection of their religious practices involving peyote, and the Church of the Eagle and the Condor has recently secured its right to use ayahuasca as its sacrament (CEC, 2023). It is important to note that before 1978, practicing, or even discussing, Indigenous religious ceremonies was entirely illegal under federal law, and only further amended in 1994 with the American Indian Religious Freedom Act (AIRFA, 1994), as well as the Religious Freedom and Restoration Act (RFRA, 1993).

In light of this, the growing Western interest in psychedelics raises concerns around cultural respect, appropriation, commercialization, and exploitation of Indigenous traditions that have historically been harmed by laws surrounding these substances (George et al., 2020). In conversations regarding the present and future of psychedelics, Indigenous voices are mandatory, and adherence to responsible research—including practicing the six Rs of Indigenous research—is vital. These six Rs make up a conceptual framework of methodologies, and include: Respect, Relationship, Relevance, Reciprocity, Responsibility, and Representation (Tsosie et al., 2022), with Reverence, Reparations, and Regulation that also need to be addressed. These are grouped into 4 broad categories of Acknowledgement (Reverence, Respect), Knowledge-Translation and Education (Responsibility, Relevance), Intellectual Property (Regulation, Reparation), and Belonging (Restoration, Reconciliation) (Celidwen et al., 2022).

Unpublished data

Mind Medicine, Inc. (MindMed), a biopharmaceutical company, recently announced positive results of a completed phase IIb trial investigating LSD as a treatment for generalized anxiety disorder, following receiving Breakthrough Therapy designation for the treatment. The results of this trial are not published in peer-review literature yet, but are summarized in Appendix H. Briefly, this study compared LSD in varying dosages, including a true placebo, in the treatment of generalized anxiety disorder over the course of twelve weeks. Unlike the academic trials, participants received only a single dose of the drug with no therapeutic component. Results indicated that the highest doses of LSD significantly reduced symptoms of anxiety, as well as depression (Hopkins, 2023). The company announced in December 2024 that they have treated the first participant in their phase III trial and will continue into 2025 (Mind Medicine, Inc., 2024).

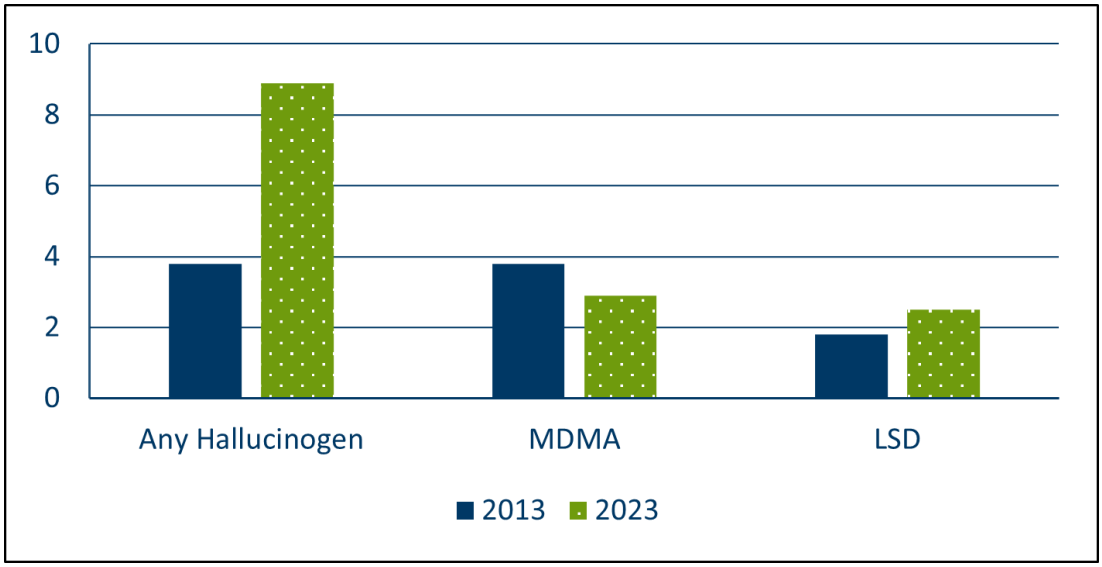
Population statistics

Population statistics are data aggregated from across a large group of individuals and are important for understanding societal trends and safety information around, in this case, psychedelic drugs. This section includes data from several national surveys on estimated and self-reported use of psychedelic drugs. Data come from several national, federal, and state institutions, national and regional poison control centers, and from various State of Minnesota agencies. Where possible, data is broken down by age group. Additional details on the population statistics can be found in Appendix H, and as a comparison, similar population statistics for both alcohol and cannabis can be found in Appendix J.

National general use statistics

The Monitoring the Future survey series produces an annual report on substance use among adults, including use of hallucinogens (Patrick et al., 2024). Hallucinogens include LSD, MDMA, psilocybin ("magic mushrooms"), mescaline, peyote, and phenylcyclohexyl piperidine (PCP) as a group. In young adults ages 19 through 30, hallucinogen use has historically been stable year after year, until 2020 when reported use began to increase, reaching an all-time high in 2023. Reported MDMA use has decreased in the 10 years between 2013 and 2023. Use of LSD has generally increased since 2012 (Figure 1). Reported use on psilocybin alone was not available.

Figure 1. Percentage of reported past year use of any hallucinogen, MDMA, and LSD in 2013 and 2023, ages 19 through 30

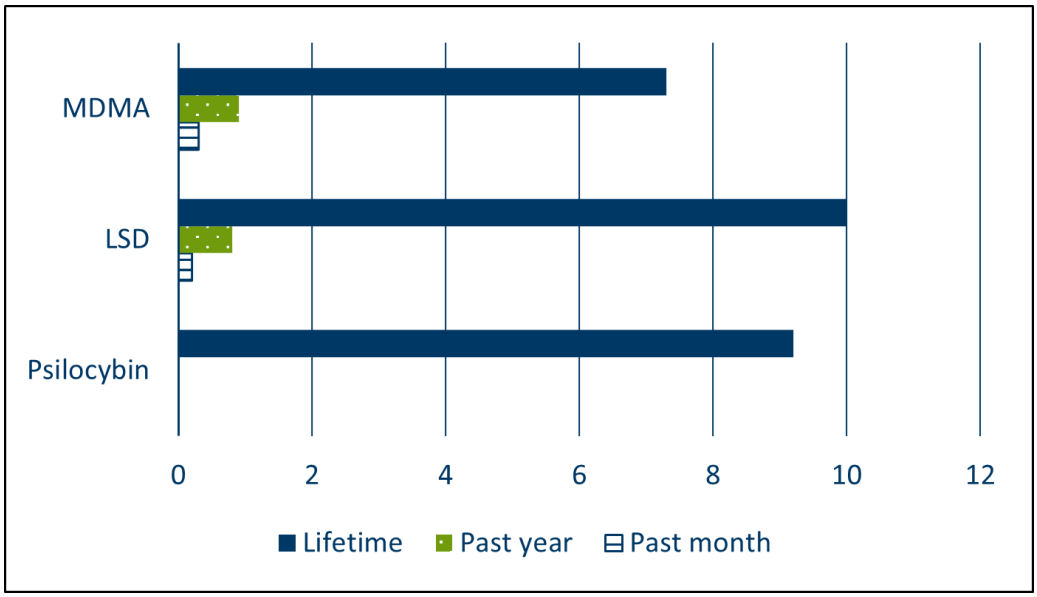


Source: Adapted from Patrick et al., 2024

The annual National Survey on Drug Use and Health sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA) reports national estimates of substance use in the United States in individuals aged twelve and above (SAMHSA 2019, 2023a). In the general population, the estimated percentage of those with any lifetime use of MDMA increased slightly between 2018 (Figure 2) and 2022 (Figure 3). Estimated past year and past month use remained stable over this time period. The estimated percentage of individuals with

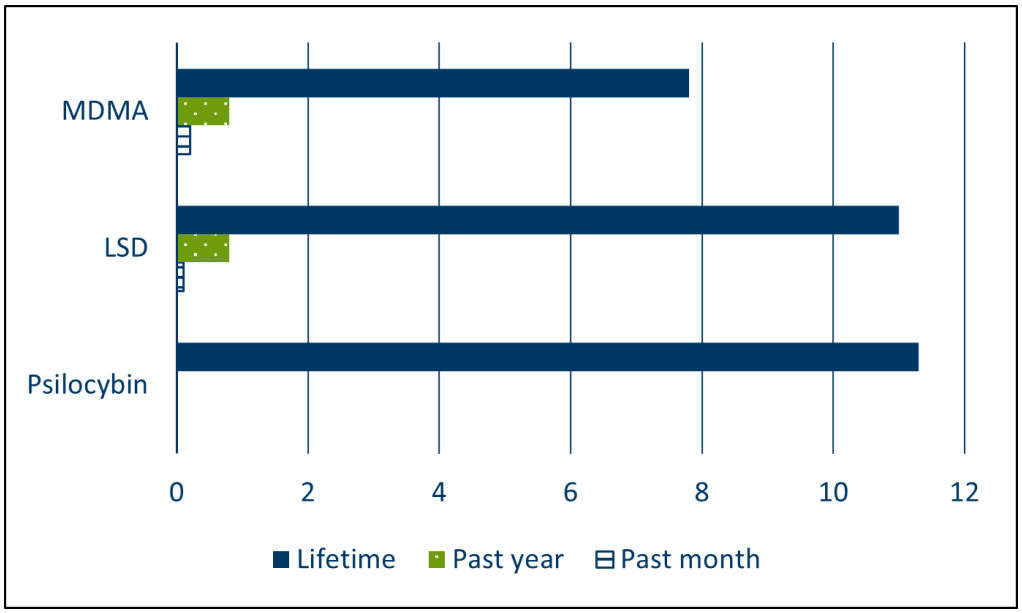
any lifetime LSD use increased between 2018 and 2022. However, in those five years, past year and past month use remained stable. Estimates of any lifetime use of psilocybin have increased noticeably between 2018 and 2022, though past year and past month data on psilocybin use were not provided (SAMHSA 2019, 2023a).

Figure 2. Estimated percentage of MDMA, LSD, and psilocybin use in 2018, ages 12 and above



Source: Adapted from SAMHSA, 2019

Figure 3. Estimated percentage of MDMA, LSD, and psilocybin use in 2022, ages 12 and above

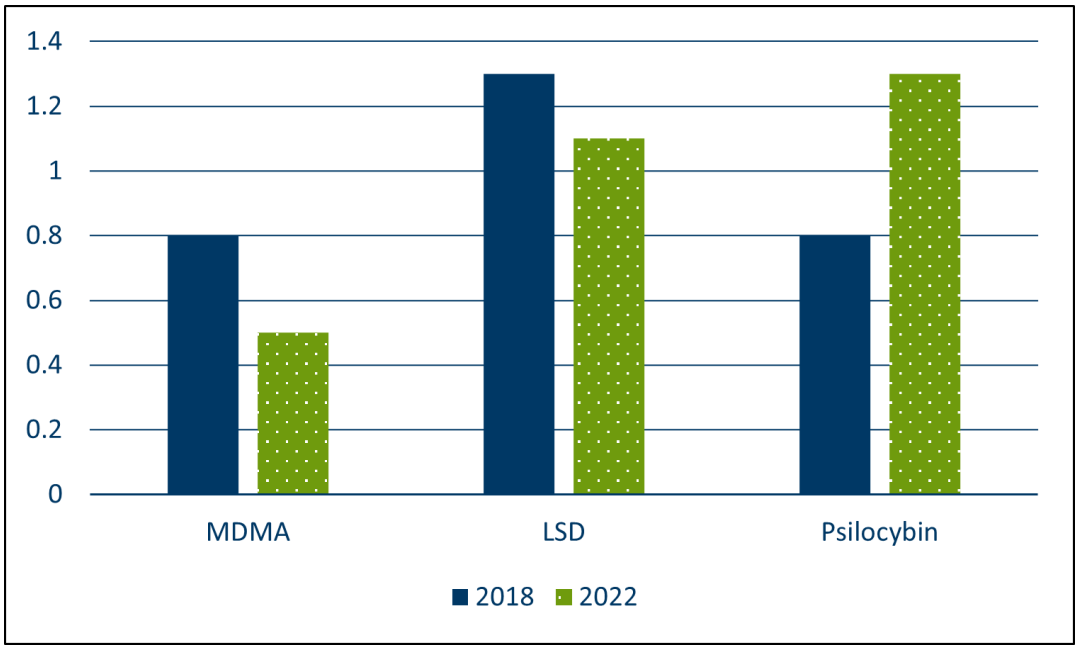


Source: Adapted from SAMHSA, 2023a

Youth Access

As of 2021, the Centers for Disease Control and Prevention (CDC) Youth Risk Behavior Surveillance System (CDC 2021) indicates that a low percentage of high school students (6.5 percent) have reported ever using hallucinogens (including LSD, mushrooms, PCP, mescaline), and even fewer (2.9 percent) have tried MDMA (including ecstasy). The National Survey on Drug Use and Health also estimated lifetime use of MDMA, psilocybin, and LSD in adolescents ages twelve through seventeen (SAMHSA, 2019, 2023a). In this age group, estimated lifetime use of MDMA decreased between 2018 and 2022. Similarly, estimated use of LSD by adolescents also dropped in the same time frame. Psilocybin use in this age group, however, was estimated to increase substantially between 2018 and 2022 (Figure 4).

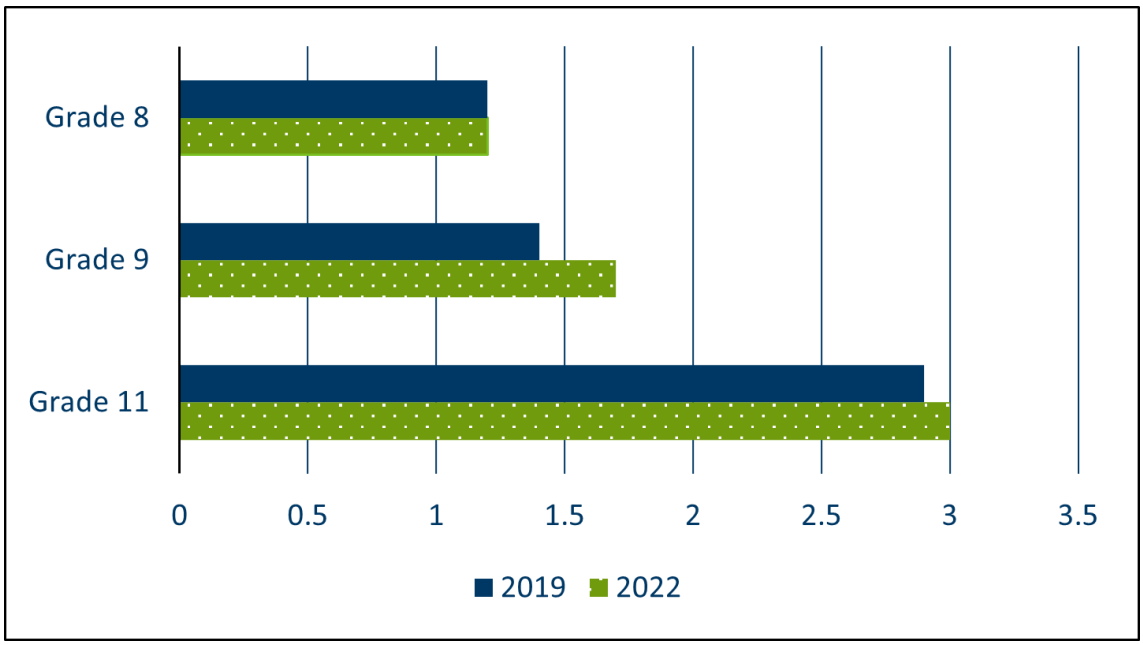
Figure 4. Estimated percentage of any lifetime use of MDMA, LSD, and psilocybin in 2018 and 2022, ages 12 through 17



Source: Adapted from SAMHSA, 2019, 2023a

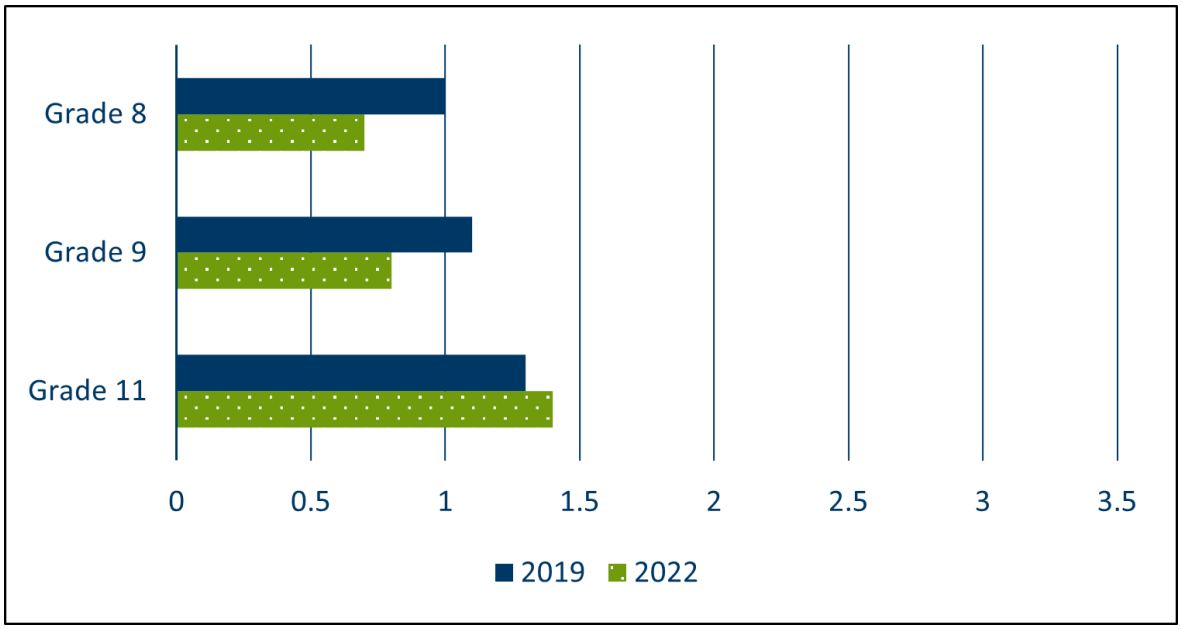
The Minnesota Student Survey includes a section on self-reported substance use (MDE, 2022). In this survey, psilocybin and LSD are grouped together, along with PCP. MDMA is grouped with gamma hydroxybutyrate (GHB) and ketamine. Therefore, use of individual psychedelic drugs is not available. The percentage of students in Minnesota who reported any past-year use of LSD, psilocybin, or PCP remained stable for grade 8, but increased in grades 9 and 11 between 2019 and 2022 (Figure 5). In this same time frame, past year use of MDMA, GHB, or ketamine dropped in grades 8 and 9, but increased in grade 11 (Figure 6).

Figure 5. Percentage of Minnesota students self-reporting past year use of LSD, psilocybin, or PCP by grade, 2019 and 2022



Source: Adapted from MDE, 2022

Figure 6. Percentage of Minnesota students self-reporting past year use of MDMA, GHB, or ketamine by grade, 2019 and 2022



Source: Adapted from MDE, 2022

Adult health data in Minnesota

For adults in Minnesota, statistics on the prevalence of diagnosed health conditions related to drug use have been compiled for the state by the Minnesota Electronic Health Records Consortium (MNEHR, 2024). See Appendix H for information on this data. Psilocybin and LSD are categorized as hallucinogens, along with peyote and PCP. The reported prevalence of health conditions related to use of these substances rose over the period between 2020 and 2023 but represents less than 1 percent of the total population. MDMA, including as ecstasy, is grouped with psychostimulants, which includes methamphetamines. While prevalence of health conditions related to the use of drugs in this category increased from 2020 to 2023, conditions resulting from use of MDMA specifically are not reported (MNEHR, 2024).

Toxicity, overdose, and drug harms

The National Center for Health Statistics includes data on drug overdose deaths but does not include data regarding psychedelic drugs (Spencer et al., 2024). Similarly, the Minnesota Drug Overdose and Substance Use Surveillance Activity from the MDH does not report data for overdose deaths attributed to psychedelic drugs (MDH, 2024). The DEA "Drug Fact Sheet on Hallucinogens" notes that deaths resulting from acute overdose of these substances on their own are extremely rare. If deaths do occur, they tend to happen as suicide, accidents, dangerous behavior, or due to an individual inadvertently ingesting poisonous plant or fungal material (DEA, 2020).

A study from the United Kingdom assessed the relative harms of drugs of abuse (Nutt et al., 2010). This study including legal drugs (e.g., alcohol and tobacco), prescription drugs (e.g., anti-anxiety medications and opiates), and illicit drugs (e.g., heroin). Psychedelics, including MDMA (as ecstasy), psilocybin (magic mushrooms), and LSD, were included in the last category. Drug harms were assessed using a weighted scale ranging from zero to 100, where zero corresponded to least dangerous in terms of harm to self or others and 100 corresponded to most dangerous. Overall, alcohol was rated as the most harmful drug (harm score = 72), followed by heroin (harm score = 55) and crack cocaine (harm score = 54). Ecstasy (MDMA), magic mushrooms, and LSD were ranked lowest, scores of nine, six, and seven, respectively (Nutt et al., 2010). In a follow up study based in New Zealand, the same type of analysis was applied and found similar results in terms of relative harms, with alcohol, methamphetamine, and synthetic cannabinoids ranking as the most harmful, with harm scores of 88, 71, and 50, respectively, whereas MDMA and other hallucinogens had the lowest overall harm scores of seven and four, respectively (Crossin et al., 2023).

Poison control data

The American Association of Poison Control Centers reports calls to poison control centers across the nation and publishes an annual report. The Minnesota Regional Poison Center (MNRPC) collects this type of data from calls throughout the state as well. See Appendix H for caveats surrounding this data.

Data from the National Poison Data System indicate that since 2018 calls regarding a single exposure to hallucinogenic amphetamines (which includes MDMA) have dropped precipitously (Table 1) (Gummin et al., 2019, 2020, 2021, 2022, 2023). In Minnesota, between 2019 and 2023, calls remained fairly stable in

adolescents, and have slightly decreased in adults in that same time period (Table 2) (MNRPC, 2024; personal communication, June 2024).

Table 1. Reported calls for a single exposure to MDMA, nationwide, 2018 through 2022

Year	Total calls	Calls, ages 20 and below
2018	810	189
2019	438	143
2020	115	31
2021	60	17
2022	52	13

Source: Gummin et al., 2019, 2020, 2021, 2022, 2023

Table 2. Reported calls for a single exposure to MDMA in Minnesota, 2019 through 2023

Year	Total calls, ages 21 and above	Total calls, ages 20 and below
2019	29	8
2020	25	13
2021	27	8
2022	19	6
2023	14	6

Source: MNRPC, 2024

Mirroring general use patterns, data from the National Poison Data System indicate a change in psilocybin use over the past decade. From 2012 to 2019, calls remained low and largely unchanged between years (data not shown). Beginning in 2020, calls related to psilocybin began to increase year after year (Table 3). Nationally, the

number of psilocybin-related calls involving those under 20 years of age increased by more than double from 2019 to 2022 (Gummin et al., 2019, 2020, 2021, 2022, 2023). This increase has been cited as "particularly alarming," because even where this substance is legal or decriminalized, use is typically prohibited for those under the age of 21 (Farah et al., 2024).

This trend was similar in Minnesota. Psilocybin-related calls involving those under twenty years of age increased by a factor of four between 2019 and 2023, and by a factor of five in those over twenty-one years of age (Table 4) (MNRPC, 2024; personal communication, June 2024). Overall, the poison control data, both nationally and within the State of Minnesota, indicate that adolescents are gaining access to psilocybin as it becomes available for adults.

Table 3. Reported calls for a single exposure to psilocybin, nationwide, 2018 through 2022

Year	Total calls	Total calls, ages 20 and below
2018	304	108
2019	387	177
2020	620	251
2021	794	353
2022	996	447

Source: Gummin et al., 2019, 2020, 2021, 2022, 2023

Table 4. Reported calls for a single exposure to psilocybin in Minnesota, 2019 through 2023

Year	Total calls, ages 21 and above	Total calls, ages 20 and below
2019	8	7
2020	22	17
2021	24	15
2022	35	17
2023	41	28

Source: MNRPC, 2024

Nationally, calls regarding LSD peaked in 2020 and dropped by a factor of around three by 2022. Calls associated with those under age twenty follow this trend (Table 5) (Gummin et al., 2019, 2020, 2021, 2022, 2023). A decrease was generally seen in Minnesota as well, in both adults and adolescents. Calls associated with those twenty years old or younger also dropped by approximately a factor of three since 2020, and in adults the number of calls dropped by a factor of at least four (Table 6) (MNRPC, 2024; personal communication, June 2024).

Table 5. Reported calls for a single exposure of LSD, nationwide, 2018 through 2022

Year	Total calls	Total calls, ages 20 and below
2018	470	289
2019	655	442
2020	885	602
2021	491	321
2022	313	194

Source: Gummin et al., 2019, 2020, 2021, 2022, 2023

Table 6. Reported calls for a single exposure of LSD in Minnesota, 2019 through 2023

Year	Total falls, ages 21 and above	Total calls, ages 20 and below
2019	25	26
2020	47	21
2021	21	19
2022	12	14
2023	17	<5

Source: MNRPC, 2024

Public safety data

The 2024 annual National Drug Threat Assessment report published by the DEA only briefly mentions both MDMA and psilocybin (in terms of definitions), and does not mention LSD (DEA, 2024). National data on drug-related emergency department visits in 2022, published by SAMHSA through the Drug Abuse Warning Network

(DAWN) categorizes hallucinogens as MDMA, psilocybin, and LSD. These drugs were not in the top ten drugs requiring emergency care (SAMHSA, 2023b). Public safety data surrounding these substances in the state of Minnesota is not available.

Recommendations

Overall, the task force voted on seven different recommendations, under four main umbrellas that represent different ways to access psychedelic medicines. This includes the removal of criminal penalties for engaging with psychedelic medicines in a variety of ways (e.g., use, possession, cultivation/sharing), creating a research program for the state with funding allocated so more clinical trials can be conducted to expand the evidence base, creating a state-regulated facilitation program as Oregon has done and state-regulated clinical program as Colorado plans to do, and creating a pathway towards adult regulated use of psilocybin-containing mushrooms.

By a two-thirds supermajority vote of its members, the task force recommends the Minnesota legislature:

1. Create a state-regulated clinical program for the therapeutic administration of psilocybin-containing mushrooms.
2. Remove criminal penalties for the personal use and possession of psilocybin-containing mushrooms.
3. Allocate funding for more research into the health benefits of MDMA, psilocybin, and LSD.

The task force considered additional proposals that did not reach a two-thirds supermajority, including:

1. The removal of criminal penalties for the personal use and possession and noncommercial (without remuneration) cultivation and sharing of psilocybin-containing mushrooms.
2. Remove criminal penalties for the personal use and possession of MDMA, synthetic psilocybin, and LSD.
3. The creation of a state-regulated program for the clinical administration of MDMA and LSD.
4. Creating a regulated, adult use market for psilocybin-containing mushrooms.

Each of these recommendations could be feasibly implemented together, depending on the views of the public, the Minnesota legislature, the governor, and state agencies. That is, these recommendations complement each other and are neither mutually exclusive nor “all or nothing” proposals. Instead, the task force considers this report to be a guide for the Minnesota legislature on how to approach and understand the subject of psychedelic medicines and anticipates its recommendations can be rolled out incrementally as scientific and medical understanding, federal and state laws, and perception by the general public develop around psychedelic medicines. Consequently, this report includes proposals that were considered but did not pass by a two-thirds majority, for reference, should the state wish to consider them in the future.

Even over the year that this task force convened (from November 2023 through December 2024), the landscape around these three psychedelic medicines has evolved rapidly. When the task force’s work started, both MDMA and psilocybin had been designated “Breakthrough Therapies” by the FDA. In March 2024, LSD also received this designation. Before the task force began work, multiple phase III clinical trials investigating MDMA had been completed, and the drug was on track to be evaluated by the FDA for treatment of PTSD by August 2024. However, the FDA ultimately rejected the application to approve MDMA as a treatment for PTSD, asking instead

for more clinical data with revised study parameters. Synthetic psilocybin had also been tested in a number of phase II trials, with phase III trials investigating the drug as a treatment for depression on track for FDA evaluation closer to 2027. Finally, LSD is currently being tested as a treatment for generalized anxiety disorder in a few small phase II studies, with phase III clinical trials anticipated to start after the publishing of this report in January 2025, though no such trial has been registered on the clinical trials registry as of report writing.

The task force met with many SMEs, discussing and integrating their expert perspectives into its recommendations. The task force grappled with the intersections between medical, spiritual, religious, and legal approaches to evaluating psychedelic medicines. The task force discussed culturally competent healthcare and health disparities, and how the term “medicine” has different meanings to different people. The task force talked about how best to regulate for equity so existing harms are not perpetuated, new harms are not being created, and innovative solutions are being explored that maximize public safety and equitable access, while mitigating harms and conflicts to the citizens and to the state.

Initial discussions about how to evaluate each of the three psychedelic medicines focused on looking at each of them separately, given different factors relating to their status in the FDA clinical trial approval process, historical uses, public acceptance, awareness of their reported risks and benefits, and logistics for how to source such psychedelic medicines legally and safely.

Differences between synthetics and naturally grown psychedelic medicines create unique limitations and opportunities for sourcing them within the state. For example, as synthetic substances, both MDMA and LSD should only be sourced through well-regulated chemistry or pharmaceutical labs, not only for Good Manufacturing Practices (GMP) standards and safety, but also because the precursors for synthesizing MDMA and LSD are heavily monitored by the federal government. Psilocybin, in contrast, may be synthesized for pharmaceutical use in clinical trials, and also may be sourced by growing the chemical in its natural mushroom form.

Therefore, many of the task force’s recommendations are specific to whether the psychedelic medicine is synthetic or naturally derived. Synthetic forms of each drug will likely only be able to be sourced through proper legal federal channels or with an intentionally designed federal-state partnership, while naturally derived medicines could be sourced within the state, similar to how Minnesota sources and regulates cannabis within the state to maintain a closed-loop system and is theoretically protected under the Tenth Amendment and the anticommandeering doctrine. However, Congress could impose financial penalties in this scenario through the Spending Clause. Natural psilocybin-containing mushrooms are fairly simple to cultivate and source, and other states have adopted programs doing just that within a state-regulated program that provides state-legalized access to this the medicine while it remains federally illegal.

However, these other state programs are, or may be, in violation of several federal laws and parameters. Certainly, these programs are in violation of federal drug laws, as all three substances are classified as Schedule I substances by the federal Controlled Substances Act (CSA). Furthermore, these states may be violating FDA parameters by advertising that psychedelic medicines may treat health conditions that have not been approved by the administration. There are also potential violations of Federal Trade Commission (FTC) laws if any interstate commerce occurs, and finally, there may be consequences from the Drug Enforcement Administration

(DEA) should pharmacies try to prescribe them. As an example of this, the DEA sent Georgia pharmacies cease and desist orders in late 2023, however at least one pharmacy has continued despite the orders (Adlin, 2024b).

The task force thoroughly discussed and researched all recommendations, though not all recommendations reached the two-thirds supermajority to be approved by the task force. The publicly appointed members endorsed nearly all of these unanimously, whereas the state agency representatives voted either "no" or "abstain" for each one, with the exception of the Attorney General's office voting "yes" for allocating funds for more research. The legislators on the task force voted more favorably for the proposed recommendations, with the most support for those that included psilocybin mushrooms, given their ease of sourcing and implied trust that natural medicines may be safer than synthetic ones. This, however, could be construed as a type of drug exceptionalism, as different communities use different drugs while being disproportionately targeted by drug enforcement and racial profiling, while people who use psychedelics are not targeted anywhere near the same extent as other drugs of abuse (Marlin, 2021).

The task force's proposed recommendations are described below, and each highlights whether the recommendation reached the two-thirds supermajority vote necessary to be approved, noted in bold text for approved recommendations. Please note that those members who abstained from voting on a recommendation did not have those votes counted towards the supermajority. Before voting on the recommendations, the task force voted to consider abstentions as non-votes that did not count toward the number of total votes. The vote log for each recommendation is provided in Appendix D.

Recommendation 1: Removing criminal penalties for psychedelic medicines

Recommendation 1A: The task force recommends the Minnesota legislature remove criminal penalties for the possession of personal use quantities of mushrooms containing psilocybin (achieved supermajority, 68 percent).

Proposed recommendation 1B: The task force recommends the Minnesota legislature remove criminal penalties for the possession of personal use quantities and non-commercial (without renumeration) cultivation and sharing of psilocybin-containing mushrooms (did not achieve supermajority, 59 percent).

Proposed recommendation 1C: The task force recommends the Minnesota legislature remove criminal penalties for the possession of personal use quantities of synthetic psilocybin, MDMA, and LSD (did not achieve supermajority, 50 percent).

The task force discussed various options for removing criminal penalties for a variety of behaviors related to psychedelic medicines, including use and possession of personal amounts of both synthetic and naturally derived medicines, and whether to recommend allowing cultivation and sharing for natural/organic psilocybin-containing mushrooms. Through a supermajority vote, the task force officially recommends removing criminal penalties for use and possession of personal amounts of psilocybin-containing mushrooms. While the task force did not officially recommend allowing cultivation and sharing (without remuneration) or for use and possession of the synthetic medicines (e.g., MDMA, synthetic psilocybin, or LSD), the task force outlined what experts in the field have recommended to the task force based on evidence-based drug policy reforms across multiple cities,

states, and countries that have various policies and practices in place around decriminalization and the impacts on public health and safety.

Context

The US is experiencing a persistent and worsening health crisis, particularly mental health, and psychedelic medicines are thought to be helpful in alleviating the suffering associated with these chronic conditions (see Scientific Literature Review and Appendix H). While the medical evidence for their uses is showing promise through clinical trials, the context with which clinical trials deliver medicines do not typically match the real-world population that would eventually use them (e.g. lacks ecological validity) with respect to how the broader population will engage with a new medicine and can take decades of testing before FDA approves (or rejects) a new medication. Of note, psychedelic medicines are currently illegal, while also experiencing wide-spread safe use in the general population with long-standing community and religious uses, some spanning thousands of years in the case of psilocybin-containing mushrooms. There is broad agreement across disciplines that decriminalization is the simplest solution to allow access, while allowing for other programs to exists that promote safety and harm reduction for users.

The Minnesota Medical Association (MMA) and American Medical Associations (AMA) have both endorsed removing criminal penalties for the possession of all drugs, including MDMA, psilocybin, and LSD. Those that are opposed to removing criminal penalties worry about higher rates of abuse and adverse events that will negatively impact public safety and diversion of dangerous drugs, but this has not been shown in evidence drawn from other cities, states, and countries that have implemented these policies to varying degrees.

- Recent headlines have circulated about recriminalization in Oregon after Measure 110 was passed by the voters in 2020. Measure 110 removed criminal penalties for use and possession of all drugs, but the measure was revoked through the Oregon legislature in 2024 after it was found that those concerns were related to the fentanyl crisis (not psychedelics) and mismanagement of funding and resources allocated for harm reduction. Similar patterns emerged in Washington (Joshi, et al., 2023).
- A peer-reviewed academic study inquiring into the Netherlands' removal of criminal penalties of psilocybin-containing truffles found no detrimental impacts on public safety or public health (van Amsterdam et al., 2011).
- The country of Portugal has had a successful program in place decriminalizing all drugs since 2001 (Drug Policy Alliance, August 2023).
- Multiple states have passed local measures to remove criminal penalties for natural psychedelic medicines under the umbrella of a movement called Decriminalize Nature (Decriminalize Nature, accessed November 11, 2024) that also allow for personal cultivation and sharing of natural medicines, while not allowing commercial sales or manufacturing, under a "grow, gather, gift" model, including in Minneapolis.
- The City of Minneapolis deprioritized entheogens in July of 2023 through an Executive Order (City of Minneapolis, July 2023) by Mayor Jacob Frey, also allowing for cultivation and sharing of natural psychedelic medicines, including psilocybin mushrooms. The Executive Order was modeled off what has been successful in other cities around the country.
- A report from Denver, Colorado (Denver Psilocybin Mushroom Policy Review Panel, November 2021) following the removal of criminal penalties for psilocybin showed nothing remarkable to report between 2019 and 2021 in changes in public safety and hospital visits post-decriminalization of psilocybin.

The rationale for the removal of criminal penalties for possession of personal use quantities of psychedelic medicines includes:

- The substances noted above have all shown promising results from clinical trials and population health data about alleviating suffering from multiple mental health and other medical conditions.
- There is minimal evidence that removing criminal penalties for possession of personal use quantities of psychedelic medicines negatively impacts public safety or public health (Monte et al., 2024).
- The policy would support health equity by allowing access to any adult who wants to use these medicines to explore their potential for healing and personal growth.
- Removal of criminal penalties would increase likelihood that users seek care for medical health effects and report abuse, assault, and other crimes to law enforcement.
- Reduces barriers to public education.
- Can create pathways for safer supply, training of facilitators, and options for access that offer safe places to use that include screening for contra indications, monitoring, facilitation, and intervention when needed.
- This policy has low to no cost for the State of Minnesota, and the lowest risk for federal involvement as it is simply not enforcing a federal law, which is within Minnesota's right as a state under the anticommandeering doctrine of the Tenth Amendment.
- Decriminalization would allow more protections for religious use and integration into ceremonies for Indigenous peoples and other communities that use psychedelic medicines, including on Tribal lands.
- Eliminates collateral consequences of criminal prosecution, which has historically impacted marginalized communities. Task force member Arielle Edelman McHenry co-authored a detailed a preliminary legislative report (McHenry and Siegler, February 2024) on the impacts of drug policing on people and communities who use drugs that is a compressive resource on this topic. A detailed table of recommendations can be found in the Appendix (A) of that report.
- Would eliminate criminal enforcement on Tribal lands through Public Law 280 from the county and state for using psychedelic medicines, ensuring that Tribes can exercise their sovereignty to work with psychedelic medicines in their communities.

Concerns surround the removal of criminal penalties for possession of personal use quantities of psychedelic medicines include:

- Any use of these medicines is a violation of the Federal Controlled Substances Act and raises the possibility of federal intervention.
- Depending on what substances exactly will have criminal penalties removed, proliferation and exploitation of starting materials may affect certain cultures and/or overall material supply chains.
- Increased use of these medicines might lead to higher levels of abuse and more incidents of impaired driving or use of emergency services, and potentially greater risk of youth gaining access to these medicines, though preliminary studies on this have not shown this to be the case.
- There would be a need for education and coordination with law enforcement and other first responders.
- This policy will require public education regarding potential risks of these medicines.

Advocates of drug policy and public health and safety reform consistently converge on the systemic benefits of decriminalizing drug use and related behaviors. Both the MMA and AMA, respectively have endorsed decriminalization of possession of all drugs, including MDMA, psilocybin, and LSD. The most successful implementation of this policy is found in Portugal, where drugs have been decriminalized since 2001 (Drug

Policy Alliance, August 2023). However, other countries, including Belgium, Estonia, Australia, Mexico, Uruguay, and the Netherlands have implemented this as well, which are described in this report (Open Society Foundations, July 2012). Arguments for decriminalization highlight issues around health equity and bodily autonomy, as well as treating problematic drug use as a health concern, not a legal or criminal one. Those against decriminalization worry it will infuse higher rates of abuse and adverse events that will negatively impact public safety and diversion of dangerous drugs.

Below are some recommended guidelines for removing criminal penalties associated with behaviors related to psychedelic medicines, including use, possession, cultivation, and sharing. Please see Appendix M for further resources, and Appendix O for cultivation considerations.

Potential statutory changes needed for this recommendation include, but are not limited to:

- Change the Minnesota Controlled Substances Act (Laws of Minnesota 2024, Chapter 152) for psychedelic medicines (MDMA, psilocybin, and LSD).
- Remove criminal and civil penalties for certain behaviors (e.g., use, possession, cultivation, sharing) and/or remove them from the state CSA entirely [i.e., descheduling, which involves redacting reference to these substances and any civil or criminal penalties related to them in (Laws of Minnesota 2024, Chapter 152)].

Other changes include deprioritizing the enforcement of aspects of the Minnesota CSA and removing criminal penalties for possession and use of psychedelic medicines (MDMA, psilocybin, and LSD), as well as allowing people to grow psilocybin-containing mushrooms for personal use and community sharing. Along with this, initiating public education campaigns to promote safe use and harm reduction will be necessary. Furthermore, allowing different stakeholders to access psychedelic medicines within culturally relevant contexts is the most equitable way to provide access to psychedelic medicines, especially ones that can be grown at home safely, like is allowed for cannabis, and is being done safely in other cities and states.

While states like Colorado are allowing people to have a noncontinuous grow space of twelve feet by twelve feet for growing personal use amounts at home under state-wide decriminalization measures, such specifics will need to be worked out by the MN legislature, per advice from task force member Representative Nolan West.

The AMA House of Delegates, the legislative and policy-making body of the association, has developed a policy regarding decriminalization of drug use and possession, and the impacts on health. Verbatim from their report (American Medical Association, 2024), they recommend that the AMA:

- Will continue to monitor the legal and public health effects of state and federal policies to reclassify criminal offenses for drug possession for personal use.
- Will support federal and state efforts to expunge, at no cost to the individual, criminal records for drug possession for personal use upon completion of a sentence or penalty.
- Will support programs that provide comprehensive substance use disorder treatment and social support to people who use or possess illicit drugs for personal use as an alternative to incarceration-based penalties for persons under parole, probation, pre-trial, or other civic, criminal, or judicial supervision.

Other regulatory and policy factors to consider for this recommendation include, but are not limited to, the following:

- Facilities: restrict use on, near, or within
  - Facilities where there might be penalties if people are possessing, using, cultivating, or sharing psychedelic medicines, similar to Minnesota public intoxication laws (Laws of Minnesota, 2023, Chapter 340A, Article 90, Section 902).
    - Federal property or otherwise utilizing other federal services (e.g., pharmacies)
    - Schools
    - Detention facilities
    - Public buildings
- Safety
    - Public surveillance for safety outcomes
  - Monitoring emergency room visits, law enforcement encounters, incident reporting from the public.
  - Provide access to harm reduction resources, including peer-support through the Fireside Chat service that has been shown to reduce harms from those who use it, even in the absence of the clinical container (Pleet et al., 2023).
  - Provide access to resources for testing drugs for adulterants
    - Literature on drug dosages
    - Ensure protections for people who use psychedelic medicines, such as shielding people from consequences that might put housing, child custody, job placement, health benefits, and other factors at risk.
- Education and training
  - Publicly accessible materials about what psychedelic medicines.
    - Pamphlets about the legal status of psychedelic medicines and what behaviors are allowed within the state, and where.
    - Peer support training for psychedelic crisis-intervention.
    - Training for specific communities that may intersect with people using psychedelic medicines (e.g., first responder, clinicians, teachers, parents) (MAPS, March 2024).
    - Youth outreach approaches, similar to how sex education is taught, with lessons learned about the failure (Wikipedia, accessed November 11, 2024) of the D.A.R.E. program (US Department of Justice, 1991).
  - Students for Sensible Drug Policy has a different outlook on this; instead of “just say no” they promote “just say know,” (Students for Sensible Drug Policy, accessed November 11, 2024) to highlight the utility of education campaigns.
- Civil systems that touch drug use: housing, immigration, child welfare, education, employment, public benefits - there are negative repercussions in each of these areas for felony drug convictions. Recommend that legislators consider removing civil sanctions as well as criminal sanctions for naturally derived mushrooms.

Recommendation 2: Creating a state-regulated clinical program

Proposed recommendation 2A: The task force recommends the Minnesota legislature create a state-regulated program for the clinical administration of synthetic MDMA, psilocybin, and LSD (did not achieve supermajority, 64 percent).

Passed recommendation 2B: The task force recommends the Minnesota legislature create a state-regulated program for the clinical administration of psilocybin-containing mushrooms (achieved supermajority, 75 percent).

The task force discussed options for two different clinical programs with psychedelic medicines, which diverged on several factors, including the feasibility of sourcing within the state, given that all three substances are currently on Schedule I of the federal CSA. Among task force members, there was overall less trust in the safety of synthetics (e.g., MDMA, psilocybin not derived from mushrooms, and LSD) compared to naturally derived psychedelic medicines (e.g., psilocybin-containing mushrooms). None of these medicines have been approved by the FDA at the time of this report writing for any health condition. However, clinical trials have shown promising evidence that give both potential patients and clinicians hope that they could be an effective alternative to currently available and federally legal options (see Scientific literature review). The state could move forward with a clinical program with psilocybin-containing mushrooms, similar to other states: Oregon (operating since August of 2023), Colorado (will be operating in 2025), and Utah (approved during the 2024 UT legislature, but notably using synthetics with unknown sourcing). Many other states have bills moving through their legislatures, including the Illinois Compassionate Use and Research of Entheogens (CURE) Act, and the Psilocybin Behavioral Health Access and Services Act in New Jersey, to name a few (see Appendix K for more details of efforts in other states). Since there is only the Oregon program to learn from in the US, and the extended rule making process for the implementation of Colorado's program, some overarching suggestions from regulators in Oregon and Colorado have cautioned about making sure to get prior authorization from licensing boards related to dual licensure for facilitators, and to keep costs down by not restricting access to facilitated services to service centers that also need to be licensed for such purposes, or requiring that the program be funded entirely by licensing fees. This has made the Oregon program extremely expensive for facilitators, service centers, cultivators, and clients wanting to access services. Because of this Oregon has had to allocate funds from tax-payer dollars to offset the costs until the program can be self-funded through licensing fees, and it would be financially more sustainable for the state to allocate funding to set up the program to get ahead of startup costs, so they don't get passed onto providers or potential clients.

The task force officially recommends a state-regulated program for the clinical administration of psilocybin-containing mushrooms, passed through a supermajority vote (75 percent). The recommendation for using synthetic psychedelic medicines was not officially approved through a supermajority vote (64 percent). The following information relates to a program with in-state or "closed-loop" sourcing of psilocybin-containing mushrooms for clinical uses. While the same principals for supportive therapy, facilitation regulations, and training apply for both natural and synthetic psychedelic medicines, sourcing synthetic medicines would not be possible outside of a number of special circumstances. This includes an FDA- or DEA-authorized clinical trial, an administrative or judicial exemption to the federal CSA granted from the DEA, or a petition of the US Attorney General to create a research program under 21 U.S.C. subsection 872(e). This is because the precursor chemicals to make these medicines are heavily monitored by the federal government and should only be sourced by pharmaceutical laboratories operating under Good Manufacturing Practices (GMP). See Appendix G for description of legal options and navigating conflicts with federal laws.

In service of creating an equitable system for clinical uses of psilocybin-containing mushrooms, efforts to remove criminal and civil penalties for their use and possession would provide further protections for Minnesotans wanting to engage in clinical programs with psilocybin-containing mushrooms, as Colorado is proposing to do. This heavily relies on the recommendation of removing criminal penalties statewide of use, possession, and cultivation of psilocybin containing mushrooms for access to the medicine. This creates a local pathway for equitable and efficient access to the psychedelic medicines for clinical uses.

Context

As the evidence base of psilocybin treatment models expand to address mental health conditions, the ethical and professional responsibility of healthcare practitioners to provide effective and advanced care currently clashes with federal DEA scheduling of psilocybin on Schedule I. Drugs on this schedule are categorized as having a high potential for abuse and with no currently accepted medical use. However, practitioners must consider the therapeutic potential of psychedelic assisted treatment options, given their ethical responsibilities. As mental health disorders and the rate of fatality of these disorders increase nationally at staggering rates, psilocybin treatment modalities are poised to alleviate the growing crisis and provide relief for other medical issues including disability related to depression, anxiety, disordered eating, and substance use disorders among others (see Scientific literature review). A state-regulated clinical program has the potential to provide guidance, increase safety, and provide mitigation of obstacles for practitioners, patients, the public, and state agencies. The development of a state-regulated program would be best supported alongside removing criminal penalties for use and possession, public education, and a working group for ongoing strategic collaboration with state agencies such as licensing boards, public health, emergency medical responders, law enforcement, and others. Additionally, such a working group can learn from other states, particularly Oregon, who have been offering psilocybin services since August 2023, and Colorado, who will be starting their program sometime in 2025.

Additionally, it needs to be stated that none of these lines of evidence taps into the long history of psychedelic medicines, including psilocybin-containing mushrooms, which have been used for thousands of years around the world, most famously in the Mazatec region of Mexico, prior to and outside of the Westernized medical framework (Chacruna, May 2021). The opinions about the status of their accepted medical use offered by organizations like the American Psychological Association and the American Psychiatric Association confines the scope of evidence for their healing potential to what can be demonstrated from clinical trials only and calls for more research (American Psychological Association June 2024; American Psychiatric Association, July 2022). Additionally, these medicines should be explored with reverence for their origins, and the traditional knowledge holders that passed down how to safely use them prior to clinicians seeing their potential, to avoid cultural appropriation and biopiracy, in alignment with the Nagoya Protocol (Mackey & Liang, 2012; Convention on Biological Diversity, accessed November 14, 2024).

Outlined below are considerations of prioritized, clinical administration requirements for psychedelic service programs. Programs are referred to broadly as psychedelic services rather than psilocybin services, holding space for the opportunity of these programs to lay the foundation for additional psychedelic medicines in the future, such as the synthetic version of psilocybin, MDMA and LSD, and other natural psychedelic medicines that could be explored (such as those legalized in Colorado). These considerations are not exhaustive or the only ways this type of program could be implemented. Any rule-making around a program that might be approved by the MN legislature would require ongoing work with a panel of subject matter experts as a working group or advisory committee. Given the rapidly changing nature of policy reform around psychedelic medicines and many new clinical trials on these medicines being developed or currently being conducted, the best practices and lessons learned from other states will continually inform this work and will need to be adapted accordingly over time. See Appendix M for a list of resources pertaining to this recommendation, and Appendix O for cultivation considerations for psilocybin-containing mushrooms.

The plan outlined below is simply a suggestion for a starting point for a clinical program with psychedelic medicines in Minnesota:

- Facilities
    - Facilities must not be:
        - On federal property
        - Near schools, in accordance with current Minnesota laws related to drug free zones (The Office of the Minnesota Attorney General, accessed November 15, 2024).
        - Near detention facilities
        - Within public buildings
            - Must have a licensed and certified psychedelic trained supervisor.
            - Facilities provide services to adults (18 years) only.
    - Accessibility:
        - Licensed facilities can have a limited number of co-locations.
        - After a year without safety issues and proven success, facilities can offer off-base services (including, but not limited to, at-home use).
            - This will be necessary as it has created some backlash in Oregon where the program was sued for violation of the Americans with Disabilities Act (Axios, July 2024) for people unable to travel to service centers due to disabilities or more severe health status. Colorado took note of this and allows for home use.
- Facilitation- age requirements, screening and background checks, and liability insurance should be in place for all facilitator types:
    - Clinical facilitators
        - Clinically licensed providers from Minnesota state boards.
        - Complete psychedelic facilitator training through an accredited program ensuring practicum experience (supervised practice) and core curriculum (history, set, and setting, etc.) of psychedelic medicine as well as national program acceptance of Indigenous members for certification.
        - Continuing education aligns with board licensing policies with the addition of annual psychedelic specific training requirements.
        - Clinical facilitators engage in peer consultation.
        - Supervision-clinical facilitators participate in psychedelic specific supervision.
    - Non-clinical facilitators
        - Facilitators for community involvement, including healers from Indigenous lineages that use psychedelic medicines. “Community members knowledgeable of psychedelics and their effects can help ensure good oversight and feedback to facilitators, provide guidance to participants seeking psychedelic care, and help report inappropriate facilitator behavior when it occurs, whether in medical or non-medical settings” (Belouin et al., 2022, page 2).
        - Must be 18 years of age and have a high school diploma or equivalent.
        - Complete psychedelic facilitator training through an accredited program ensuring practicum experience (supervised practice) and core curriculum (history, set, and setting, etc.) of psychedelic medicine as well as national program acceptance of Indigenous members for certification.
        - Continuing education and annual psychedelic specific training requirements.
        - Facilitators engage in peer consultation and engage or refer to clinical facilitators if needed.

  - State program grants civil protections around professional licensure.
    - It would be important for the state program to grant civil protections around professional licensure to not impose extra fees around compliance that may create an extra barrier to access to professional opportunities.
  - Collaborative Care-Integrative medicine
    - The psychotherapy assisted approach is an improvement in quality of care, and a view shared by many in the field, "…that the experiential component of psychedelics necessitates and facilities the development of a strong therapeutic bond between the patient and [their] guides" (Carhart-Harris et al., 2018, page 2).
    - There are various viewpoints on the appropriate types of psychological and psychotherapeutic support offered to people before, during, and after a psychedelic medicine session and thus there should be flexibility as the research continues to evolve on best practices (Cavarra et al., 2022).
    - Clearance for services from advanced practice medical professionals for medication contradiction, underlying medical conditions, and underlying disqualifying mental health conditions requires collaboration of providers within the medical field, increasing oversight and decreasing liability.
  - Access to psychedelic medicine through a medical card, similar to medical cannabis program.
    - Allows for more broad use for clients that do not do well with therapists/doctors and prefer to have their psychedelic medicine sessions to be done in isolation.
    - Same levels of prescreening as described above for contraindicated health conditions, and education and discussion with the medicine supplier about risks, and harm reduction resources if they want to seek out support during their isolated medicine session, including, but not limited to peer-support lines, available for free through Fireside Chat (Fireside Project, accessed November 11, 2024).
- Informed Consent
  - Informed consent during preparation, psychedelic medicine administration, and integration.
  - Established boundaries of touch between facilitator and patient with modifications only when client is not under the influence of medicine. Safe and supportive touch training is an integral part of training program's validity and accreditation.
  - Guidelines and procedures for reporting and record keeping (e.g., data collection) of violations of informed consent.
  - Consent must include the potential immediate risks and benefits of therapy, potential long-term risks, as well as an explanation of alternative treatments.
  - Consent may be withdrawn at any time and participation is voluntary.
  - Options to opt-in (rather than opt-out) to any data collected as part of broader public health and safety screening, and clear descriptions of what the data will be used for.
- Safety
  - As with any substance that alters an individual's state, operating a motor vehicle is prohibited on the day of a psychedelic medicine experience, invoking existing DWI laws.
  - Dietary and medication restrictions will be maintained. Dosing suggestions and restrictions.
  - Public education on adverse reactions and contradictions.
  - Psychedelic medicine supply testing, in accordance with Department of Agriculture for naturally-derived medicines.
    - The program contracts with the Minnesota Mycological Society for mushroom identification (Minnesota Mycological Society, accessed November 11, 2024).
  - Medically trained support staff for emergency situations.

    - Facilitators have the right to refuse service if there are any concerns.
    - Patients will be given resources for filing complaints.
    - Patients will be given resources in case there is a medical or psychological emergency.
    - Provide access to harm reduction resources, including peer-support through the Fireside Chat service that has been shown to reduce harms from those who use it, even in the absence of the clinical container (Pleet et al., 2023).
- Health conditions
    - Evidence based practices for specific diagnosis as supportive research is provided.
    - Clinical facilitators maintain scope of practice. Accredited training programs accept and filter practitioners within medical field, including therapists, physicians, psychiatrists, nurse practitioners, and psychologists as a strategy to cross-pollinate professional knowledge as an integrated approach.
        - Additional considerations should be made for Indigenous healers and practitioners from other cultures and their evaluations of health and contraindications.
- Record keeping
    - Confidentiality for Schedule I substance considerations, whereby a Certificate of Confidentiality from the federal government will need to be obtained to invoke HIPAA protections. Services under this program are considered treatment, therefore protecting:
        - Parents (family law)
        - Probation and parole (civil law)
        - Employees (employment law)
    - Collect general data to measure the number of patients seeking psychedelic treatment options for state funding and identification of public health needs.
    - Data practices from the Office of Medical Cannabis (Minnesota Office of Cannabis Management, accessed November 11, 2024) may be a good place to start.
        - Good data collection may help provide sufficient data for HHS to perform an evaluation of whether psilocybin has accepted medical use based on state program data, as they did recently with Cannabis being recommended to Schedule III of the CSA. This was made possible because of well collected data from two states: Maryland and Minnesota (see page 81 of this Freedom of Information Act release of the report from HHS to DEA) (US Department of Health and Human Services, August 2023).
        - Oregon, through a research study out of Oregon Health Sciences University (OHSU) has officially launched the Open Psychedelic Evaluation Nexus platform (OPEN, accessed November 11, 2024), centered on data collection from psilocybin service centers that will be protected, federally, through a Certificate of Confidentiality.
    - Maintain confidentiality for those seeking treatment; HIPAA compliance.
        - It should be noted that HIPAA does not apply when the action is not federally legal. Therefore, HIPAA best practices should be used where no-identifying information is ever collected about anyone so it cannot be linked to back to any individual, and people should be given the choice to opt-in to any data that is collected on them for using these services, rather than having to opt-out. There are ways to protect this information with federal protections under exemption requests to the DEA, access through the Right to Try Act, or conducting these programs under the umbrella of federal approved research, which are described below.
- Other considerations
    - Working group collaboration. The working group may benefit from appointing members from agencies, including, but not limited to licensing boards, public health, emergency medical

responders, law enforcement and firefighters, existing psychedelic training program leaders, Indigenous healers, natural medicine physicians, social service providers, addiction treatment providers, and others.

- Funding-insurance and state access. The development of an insurance-based model including state insurance initially supplying grants to service organizations including Veterans Affairs Community Care providers, Indigenous groups, and other marginalized groups.
- Expanded care to decentralized service options (i.e., in-home services).
- Group Facilitation centers. This has been conceptualized in Colorado's program and could be adopted for Minnesota's program and is more economically viable for delivery since the current models in clinical trials is for two therapists for one patient for an eight-hour treatment session.
- Additional psychedelic medicines and expansion of the work. It is important to consider that some service providers/organizations have trained professionals prepared to integrate additional psychedelic medicines through other legal pathways and/or alongside rescheduling of other medicines. Typically, these are existing clinics that are offering ketamine-assisted therapy in the same vein as psychedelic-assisted therapy best practices.
- As data collection grows through local and state communities, the current lack of diversity reflected in the data will decrease.
- Program advocacy. Designation of a state specific advocate for consumer reporting and provider concerns.
    - Some sort of advocate or reporting authority would need to be available for consumers if the state program allows unlicensed facilitators to provide services. Professional licenses have boards for consumer reporting, but there would need to be a state advocate or something for those that are not licensed.
- Funding and federal protections (see Appendix G for more detailed overview of legal pathways)
    - The National Institute on Drug Abuse (NIDA) has a funding mechanism (National Institute of Health, July 2023) focused on impacts to public health in states that are changing laws and policies around psychedelic medicines. This option could be explored to create a protective umbrella over the program to be branded as a research study.
    - Any state program that uses psychedelic medicines that are currently on Schedule I of the federal CSA would be in violation of federal laws, not only according to the DEA regarding violating the CSA, but also the FDA for making medical claims about what psychedelic medicines can treat.
    - Federal protections can be granted for research projects through a Certificate of Confidentiality (US Department of Health and Human Services, 2003) that ensures that data collected as part of approved research cannot be subjected to release through subpoena from law enforcement officials, including the DEA and/or DOJ.
    - The state could request an administrative exemption to the CSA by formally requesting that the DEA provide such an exemption for Minnesota's state-regulated program. If this was denied by the DEA, the state could then take them to court and request a judicial exemption to the CSA for Minnesota's state-regulated clinical program.
        - The state can request the DEA allow access to psychedelic medicines under the federal Right to Try Act (RTT), however there is an active appeals case pending a ruling in the Ninth Circuit Court of Appeals to determine if this will be allowed. Currently the federal RTT Act does not specify whether it applies to Schedule I drugs, like the three psychedelic medicines discussed in this report, however DEA has denied or delayed requests to clarify and/or allow this, to date. The Minnesota RTT act also does not say that Schedule I drugs are excluded,

however they limit the eligible patient population to those with a terminal illness (Laws of Minnesota 2024, Chapter 151, Section 151.375).
    - The Federal Right to Try Act (US Congress, 2018) states eligible patients as having a life-threatening or debilitating illness, not terminal (National Archives, March 2004).
- Attempting to comply with federal laws, exploring a state-federal partnership under the US Attorney General's research program under 21 U.S.C § 872(e) to brand the entire program as research. In doing so, the state would be afforded federal protections for data privacy and confidentiality under HIPAA, as well as working towards intentional data collection for a national database to be used for rescheduling evaluations of psychedelic medicines based on state-regulated programs.

Recommendation 3: Funding for more research

Passed recommendation 3: The task force recommends the Minnesota legislature appropriate funding for clinical research regarding the health benefits and treatment of medical conditions through the administration of psilocybin, MDMA, and LSD (achieved super majority, 100 percent).

Several states in recent years have adopted legislation to create pilot programs to get more data on safety and efficacy of psychedelic medicines in certain health conditions. Texas was the first state to do this with psilocybin for PTSD, running trials out of Baylor College of Medicine to gather more data. Washington has also allocated funding for pilot programs. This essentially taps into the existing infrastructure of federally legal research with controlled substances through the clinical trial mechanism, with oversight from FDA, DEA, and local ethics committees that approve clinical protocols (Institutional Review Boards [IRBs]). These states will allocate more funding to help institutions conduct these clinical trials, as they are expensive, and historically have been funded by either private donors or large pharmaceutical companies, rather than unbiased government agencies, such as the National Institutes of Health (NIH) or the National Science Foundation (NSF) or the Department of Veteran's Affairs (VA). While the tide is shifting at federal agencies in terms of providing funding for research for these substances, including at the National Institute of Mental Health (NIMH), the National Institute on Drug Abuse (NIDA), and the VA, the sheer volume of people interested in conducting and/or participating in clinical trials with psychedelics is not being matched by a comparable level of federal funding support (National Institute of Mental Health, November 2022; National Institute of Health, July 2023; US Department of Veterans Affairs, January 2024).

Context

While clinical trials are technically science experiments to test whether a given new treatment might work better to reduce symptoms compared to an inactive drug or placebo and/or treatment as usual, and not designed as a vehicle for the delivery of healthcare, it does give people with specific health conditions (e.g., depression, PTSD) the opportunity to access an experimental treatment in this context. While health benefits from clinical trials are not guaranteed, especially for research participants randomized to a control or placebo group, these avenues are often safer than attempting to access psychedelic medicines through illegal or underground channels, and most clinical trial participants are compensated for their time in the trial, as opposed to having to pay a provider or clinician for access. Additionally, while most trials are designed to test a placebo

group, many trials with psychedelic medicines offer an option to try the active drug after the study has collected sufficient data to test their primary hypothesis. This is called an open-label phase of a study, intended for those who were in the placebo group who would like access to the drug being tested, though that data does not typically get included other than general effectiveness outcomes. Another option that was recently used for MDMA is called Expanded Access, which is a way for eligible patients to access an investigational treatment being tested in clinical trials, however this depends on the pharmaceutical company creating this type of special clinical trial, which so far has only been done with MDMA for PTSD in a very small group of people at two clinics (Lykos Therapeutics, November 2024).

However, clinical trials are not a route for healthcare delivery or implementation of a clinical program in the state, and thus should not be viewed as such. Clinical trials are tightly controlled, do not always represent the broader patient population being studied, and typically do not generalize well to different contexts of treatment outside of what was tested in the clinical trial setting. While data from clinical trials is the current gold standard for FDA to determine whether a new drug has medical uses and should be approved to treat a health condition, it is far from a perfect system to evaluate how effective a new treatment will be, and there are many limitations related to trials with psychedelic medicines that are coming to light. Given the complications of clinical trial structure and the unique nature of psychedelic effects, the FDA recently issued guidelines on how to design and conduct clinical trials with psychedelic medicines (FDA, 2023). Please see Appendix M for more resources pertaining to this recommendation.

The rationale for funding more clinical research regarding the health benefits and treatment of medical conditions through psychedelic medicines includes:

- Clinical trials will provide safe and legal options for access to psychedelic-medicines in medical settings for those suffering from health conditions that could benefit from such treatments.
- This recommendation is fully legal under both state and federal law.
- Clinical trials will develop more data for future decisions regarding health benefits and a greater range of medicinal use.
- Funding could be obtained through federal funding mechanisms available through the NIH and the VA to help offset costs to the state.

Concerns about funding more clinical research into psychedelic medicine include:

- The State of Minnesota will incur costs for the expense of the clinical trials.
- Clinical trials alone, without other policy changes, would slow down access to patients in need of treatment, since there are strict inclusion/exclusion criteria for clinical trials that are not “ecologically valid” regarding the populations being studied.
- Clinical trials are science experiments, not treatment, and subject matter experts have cautioned the task force about trying to use the federal research infrastructure as a way to get around violating the controlled substances act to provide unapproved medical treatments masked as pilot programs.

Currently there are not any statutory changes needed to fund more research. This may change if future work with psychedelic medicines, including more research, falls under a specific state agency, or a new agency is created.

- As it currently stands, the state and organizations or institutions interested in conducting clinical trials with psychedelics can leverage the existing clinical trial infrastructure. This requires obtaining an investigational new drug (IND) approval by the FDA, getting the study protocol approved by an ethics review board (IRB), and obtaining a DEA license to administer Schedule I drugs under those specific parameters.
- These entities can also utilize the Expanded Access program, a special type of clinical trial that is created by a pharmaceutical company willing to offer their product to patients outside the context of their own clinical trials.
- It is possible to explore decentralized clinical trial designs (US Food and Drug Administration, September 2024) to get more ecological validity, which might help to generalize the findings more so than the limited design of standard randomized controlled trials. Because they're so rigid, results from these standard trials sometimes do not generalize to the population(s) they're intended to treat.

Further considerations for funding more clinical research regarding the health benefits and treatment of medical conditions through psychedelic medicines includes, but is not limited to:

- Where will the funding for clinical trials come from?
- Federal funding can currently be obtained through NIH (including NIDA, NIMH), however this is a very competitive process that depends on funding priorities of the agency and the federal budget each year, with only the top 10-20 percent of proposals submitted from all over the nation typically being approved for funding.
- The MN legislature can allocate funding to support clinical trials within the state.
- A single clinical trial with psychedelics can cost, on average, around $20,000 per research participant to implement. This cost includes study staff salary, equipment, facility costs, drug costs, participant compensation, among other factors. The cost also depends on the complexity of the study design and any advanced procedures involved (e.g., mechanistic research with brain imaging, or complex study designs to understand combination therapies of psychedelics with other evidence-based psychotherapies).
- Creating a funding mechanism within the state that interested investigators could apply for.
- Create a scientific review committee to review the proposals, similar to any other grant proposal. Certain agencies (e.g., the Department of Health and the Department of Human Services) already have existing infrastructure for creating calls for funding, reviewing proposals, and issuing and monitoring awards granted and progress reports about the conduct and outcomes. There are already existing structures for this under the umbrella of the Minnesota Department of Administration.
- Who can conduct clinical trials?
- Any credentialed researcher or clinician that is eligible to serve as a Principal Investigator on a clinical trial, according to FDA, DEA, and IRB approval. This includes doctoral level researchers, clinicians, or prescribers.
- While Minnesota allows nurses to be prescribers, they may not be eligible to lead clinical trials or receive federal funding according to the federal government, FDA, DEA, NIH, or other entities that provide funding.
- Because psychedelic medicines are Schedule I drugs and not able to be prescribed, a prescriber license is not required to be the registrant for a Schedule I researcher's license. However, research

pharmacies authorized to store and dispense controlled substances may require this for release of investigational product to the study staff and research participant.
    - Where can clinical trials be conducted?
    - Clinical facilities including, but not limited to, hospitals, therapy clinics, and research institutions.
    - These institutions are already set up to handle not only conducting clinical trials, including the medical oversight and equipment required, but also have access to a research pharmacy that is equipped to store, dispense, and restrict access to controlled substances on Schedule I (or at the very least set up to store drugs on Schedule II). The security requirements to establish this to DEA standards can be costly.
    - Community clinics in partnership with institutions that have access to a research pharmacy.
    - Clinics currently offering ketamine-assisted therapy as trial sites.
    - Other settings that may be adapted under a decentralized clinical trial structure that are implemented to incorporate digital technologies, telehealth, and home use settings to create more ecologically valid research settings.
- Who can participate in clinical trials?
    - Any patient that is eligible, according to the inclusion and exclusion criteria for the approved study. These criteria are carefully evaluated for risk by an ethics committee (e.g., IRB), and the FDA.
    - Healthy participants (those without notable health conditions) to help further the understanding of mechanistic and scientific research.
    - Patients and participants who have been deemed ineligible for other clinical trials. This includes small pilot studies or Phase I studies which can be conducted to evaluate safety parameters and feasibility for testing psychedelic medicines in new patient populations.

Recommendation 4: Adult regulated use of psilocybin-containing mushrooms

Proposed recommendation 4: The task force recommends the Minnesota legislature allow and regulate adult use of psilocybin-containing mushrooms (did not achieve super majority, 57 percent).

During the course of task force discussions on how best to regulate for equity, we discussed the option of an adult-regulated use program for psilocybin mushrooms. These discussions converged on lessons learned from an unregulated gray market with synthetic cannabinoids and public health concerns, and similar patterns emerging with adulterated mushroom edibles, notably some being recalled recently by the FDA due to a surge of bad side effects not related to psilocybin (US Food and Drug Administration, June 2024). Additionally, very few psychedelic research programs at higher educational institutions have included public health departments or consulted with Indigenous groups (Kuiper et al., 2024). While the task force did not officially approve this recommendation through a supermajority, the consensus from legal and drug policy reform and public health SMEs the task force consulted with have highlighted that this would provide the safest option for ensuring safe supply and equitable access. However, it should be noted based on conversations during our task force meetings, that while many advocates want to see an adult-regulated use model, the broader public and government acceptance of such a program is not at the same level as it is for adult-regulated cannabis programs as of Fall 2024. Conversations also emerged about honoring Indigenous lineages and practices to avoid cultural

appropriation and biopiracy, in alignment with the Nagoya Protocol (Convention on Biological Diversity, accessed November 14, 2024).

Context

According to a poll conducted by the University of California, Berkeley in June of 2023, more than six out of ten (61 percent) American registered voters support legalizing regulated therapeutic access to psychedelics, including 35 percent who report “strong” support. In addition, more than three-quarters of voters (78 percent) support making it easier for researchers to study psychedelic substances. Almost half (49 percent) support removing criminal penalties for personal use and possession (UC Berkeley, June 2023). When taken together, the combination of these approaches provides a broader social safety net for people to access psilocybin-mushrooms in more culturally relevant containers, especially in marginalized communities who have been disproportionately harmed by the western medical system of healthcare, especially here in Minnesota where health disparities are high. An adult-regulated use model would accommodate all those perspectives.

While no states in the US have yet approved adult regulated use of psilocybin-containing mushrooms, two states (Oregon and Colorado) have recently legalized its uses in a variety of contexts. In Oregon (Oregon Health Authority accessed November 11, 2024), use is allowed within strict facilitated use. In Colorado (Colorado Department of Regulatory Agencies, accessed November 11, 2024), more flexible facilitated use is allowed, as well as the personal cultivation, use, and sharing, along with decriminalization of the use, possession, cultivation, and sharing of psychedelic medicines that can be grown at home. New Mexico has allowed people to grow psilocybin-containing mushrooms in their homes since 2005, though once harvested are considered controlled substances. However, a ballot measure in Massachusetts would have allowed a similar program to be created as what Colorado has initiated but was not approved by the voters in the 2024 general election. In response to a growing mental health and addiction crisis, many states are exploring options in their legislatures to give people access to psilocybin-containing mushrooms in a variety of contexts, with the overarching goal to promote safety, equity, and culturally competent healing frameworks for safe consumption. This includes efforts in California, Washington, New Hampshire, New Jersey, and Arizona, to name a few (see Appendix K for summary of other state efforts).

Other countries allow for this to varying degrees, the most notable of which is the city of Amsterdam in the Netherlands. Amsterdam has had great success with magic mushrooms, and now psilocybin-containing truffles (which are less potent by weight). These truffles can be bought at stores called smart shops and consumed in parks around the city, and very few public safety or public health incidents have been reported. Despite their current illegal status, wide-spread use in the broader community has existed for decades, and such mushrooms have been revered as sacraments for thousands of years by Indigenous cultures, most notably to the Western world from their origins in the Mazatec traditions in Mexico.

The state could also refer to the Executive Order deprioritizing entheogens adopted in Minneapolis in July 2023. This Executive Order (City of Minneapolis, July 2023) recognized that many community members see benefits in using natural substances for health or religious purposes. As such, Mayor Jacob Frey directed the Minneapolis Police Department (with the support of Police Chief Brian O’Hara) to join agencies nationwide in continuing to deemphasize law enforcement activities related to use of entheogenic plants. Many of these substances have

been used as religious or spiritual sacraments in many Indigenous cultures around the world, including, but not limited to, ayahuasca from Central and South America, psilocybin-containing mushrooms from many countries around the world, mescaline-containing cacti from the Americas, and iboga from West Africa. While data from Minneapolis has not been adequately collected to understand the broader impact to public safety, Denver initiated a similar ordinance in 2019, and a two-year report published in 2021 found no significant impacts to public health and safety (Psilocybin Mushroom Policy Review Panel, November 2021). Having broader access allows for people to engage with psilocybin mushrooms on their own terms to promote healing, whether it be through personal, spiritual, or clinical options.

In addition, regulated use would help prevent adulterated products from hitting the market by companies trying to get around violating the CSA and selling products with untested and unregulated, though technically legal, research chemicals. The harms of this were seen with cannabis prohibition where several synthetic cannabinoids became more available and accessible in stores, and children and adolescents were able access them, leading to public health and safety concerns (Burgess et al., 2024; Castellanos and Gralnik, 2016). Untested research chemicals being sold as mushroom chocolates or gummies have the potential to follow a similar path, as seen with the recent recall of Diamond Shruumz products (US Food and Drug Administration, June 2024). In June 2024, the FDA recalled many of these products that were being sold as mushroom chocolates following multiple reports of serious side effects and health concerns from several states. These included seizures, central nervous system depression, loss of consciousness, confusion, agitation, abnormal heart rates, hyper- and hypotension, nausea, and vomiting. Analysis of these products revealed they contained several unknown and untested, though still legal, substances, and testing labs in the space have been evaluating these products and their contents, such as this analytical report put together by Tryptomics (Tryptomics, May 2024). These side effects, however, were not attributed to psilocybin.

The cannabis industry is an example of both government and the publics willingness to pursue legalization and state-regulated programs despite being in violation of federal law. A similar approach can be used for psilocybin-containing mushrooms. The benefits of a regulated program are significant. The supply is controlled, people know what they are consuming, individuals are educated about risk and safety considerations, and people could have access to trained facilitators to monitor and assist as needed. At present, the market for psychedelics is significantly smaller than the cannabis industry. According to a recent RAND report (RAND, June 2024), of those who reported cannabis use in the past month, almost 50 percent reported using it daily or nearly daily. For those who use psychedelics, only 2 percent reported this same pattern of use. When looking nationally at the number of days of past-month cannabis use, cannabis was used nearly 650 million days in 2022. The comparable number for hallucinogen use was 7 million days. When looking just at those who reported hallucinogen use, 50 percent indicated that they microdosed, or used just a small amount of the drug to minimize the overt effects.

Though the recommendation was not approved by the task force, from the group's discussions the rationale for allowing and regulating adult use of psilocybin-containing mushrooms includes:

- Broad access for adults that offers a safe supply that are unadulterated, with known dosage.
- Would allow for facilitators to be trained to offer services to promote safety for those that choose to use psilocybin-containing mushrooms.
- Would create a format for screening of contraindications and individual education and training regarding low-risk use, potentially allowing for state dual-licensure for clinicians that may want to

pursue offering psilocybin services to clients without the risk of losing their current license to practice their profession.

- Psilocybin-containing mushrooms are non-toxic, and the lethal dose of psilocybin-containing mushrooms is estimated to be around 1000 grams, an amount that would be exceedingly difficult to consume.
- Respects the bodily autonomy of adults to engage in healing practices that best suit their needs.
- Psychological safety would be increased if also combined with removal of criminal penalties around use, possession, growing, and sharing.
- Allows for access outside of research or medical options, which helps promote equity.
- Could generate a large pool of safety data for future decision making.
- Adult regulated use could be a revenue source for the state of Minnesota.
- The Netherlands has had an adult regulated use system for psilocybin truffles for many years, and peer-reviewed academic research shows few negative health issues or public safety issues (van Amsterdam et al., 2011).

Concerns about allowing and regulating adult use of psilocybin-containing mushrooms include:

- Psilocybin-containing mushrooms are Schedule I drugs under the federal controlled substances act (CSA), and illegal for use outside of approved research settings (e.g., clinical trials).
- Manufacturing a regulated supply creates a risk of commercialization and biopiracy.
- Broad access increases public safety concerns, and there would need to be public education and systems to support those with adverse reactions.

Statutory changes that would be necessary for the adoption of this recommendation, were it to pass in the future, include:

- Change the state Controlled Substances statute (Laws of Minnesota 2024, Chapter 152) to legalize psilocybin-containing mushrooms.
- Explore adopting statutory language from the creation of the Office of Cannabis Management (Laws of Minnesota 2024, Chapter 342), which would also require referencing or modifying language in Minnesota Statute 15.039 (Laws of Minnesota 2024, Chapter 15, Section 15.309).
- Include psilocybin-containing mushrooms in Minnesota Statue Ch. 27, Farm Products Dealers (Laws of Minnesota 2024, Chapter 27).

Outlined below are some considerations for a regulated program for adult use of psilocybin-containing mushrooms. These considerations are not exhaustive and would require refining given the rapidly changing nature of policy reform around psychedelics. Please see Appendix M for further resources, and Appendix O for cultivation considerations.

- Options for sourcing and testing psilocybin-containing mushrooms
    - Because, psilocybin and psilocin, both of which are in magic mushrooms, are on Schedule I of the federal CSA, these mushrooms will need to be sourced and cultivated within the state to avoid federal conflicts (e.g., complying with interstate commerce regulations). Existing statutes could be adopted and state agencies and partners could be tapped to help regulate this market.
    - Existing local (in-state) cultivators should be given priority access to licenses.

    - Create equity licenses for marginalized communities, similar to what is being implement for cannabis.
    - Create more opportunities for cultivators to move from the gray market into a regulated market, to prevent big corporations from creating monopolies on supply.
    - Implement known testing procedures for quantifying dosing of different strains and quantities of psilocybin-containing mushrooms so people understand how much of the drug they are taking.
    - Anecdotes about dosing often refer to both "microdoses" and "heroic doses." The latter is often described as five or more grams of dried *Psilocybe cubensis* mushrooms. However, the effects of any dose are dependent on individual metabolism and genetic predisposition (Alchakee et al., 2022). Furthermore, there are over 100 different types of psilocybin-containing mushrooms (Strauss et al., 2022), which have different potencies of the substance within them. For example, one gram of a mushroom within the *Panaeolus* genus may elicit the same effects as five grams of a mushroom from the *Psilocybe* genus (Busby, 2024).
    - Utilize programs already in place within the Department of Agriculture (MDA) for identifying, testing, and regulating natural products such as mushrooms. The Minnesota Mycological Society assists with identification of mushrooms of all varieties, including assisting the poison control centers. The MDA maintains the Certified Wild Mushroom Harvester Database (Minnesota Department of Agriculture, accessed November 11, 2024).
- Create infrastructure for safe use and distribution.
    - Provide public and point-of-contact individual education materials regarding both risks and benefits.
    - Build on lessons learned from industries of other controlled substances, both within the state and the nation, as well as internationally.
    - Both Spain and Malta have implemented "social clubs" for cannabis use. These social clubs are non-profit operations that cultivate their own cannabis, and memberships to them can be purchased to further allow purchase and consumption. A similar model could be used as a reference in Minnesota (International Cannabis Business Club, February 2022; International Cannabis Business Club, March 2024).
        - Colorado is allowing people to have a noncontinuous grow space of twelve feet by twelve feet for growing personal use amounts of psilocybin-containing mushrooms at home, under state-wide decriminalization measures.
        - Provide access to harm reduction resources, including peer-support through the Fireside Chat service that has been shown to reduce harms from those who use it, even in the absence of the clinical container (Pleet et al., 2023).
- Create a certification or licensing process that trains individuals to help monitor people who consume psilocybin-containing mushrooms.
    - Offer trained facilitators to assist people seeking monitoring and support, as is being done in Colorado, and proposed in other states, where decriminalization allows for more community use accompanied with harm reduction approaches that support users outside of clinical settings.

Tribal nation sovereignty

Pursuant to Minnesota Statute 10.65 (Laws of Minnesota 2024, Chapter 10, Section 10.65), the state of Minnesota acknowledges and supports the unique status of the Minnesota tribes and their absolute right to existence, self-governance, and self-determination. In considering any decision that will have impact on Tribal nations, timely and meaningful consultation between the state of Minnesota and Minnesota Tribal governments

is both important and mandated. The Dakota and Ojibwe Tribal representatives have stressed the importance of not allowing Minnesota policies to infringe upon the inherent rights to govern their own Tribal Nations.

Per suggestion, the task force looked at what kind of language was shared from the Office of Cannabis Management about tribes and sovereignty, as they drafted policies for the medicine. Reference to statutes about creating compacts between tribes and the state for adult-use cannabis sales (Laws of Minnesota 2024, Chapter 3, Section 3.9228) and for the medical cannabis program (Laws of Minnesota 2024, Chapter 3, Section 3.9224) can be found on page 111 of first draft of the rulemaking document (Minnesota Office of Cannabis Management, July 2024), released in July 2024. There is not much about this in Minnesota Statute Chapter 342 (Laws of Minnesota 2024, Chapter 342)) of the new adult-use cannabis statute, though the Office of Cannabis Management has a brief description and links to resources (Minnesota Office of Cannabis Management, accessed November 11, 2024), including training for state agencies on government-to-government relations, and a link to the Minnesota Indian Affairs Councils website.

In addition to member feedback from Tribal representatives on the task force, the task force consulted with Indigenous lawyers Tadd Johnson, JD and Brandon Alkire, JD on this subject and Public Law 280 (PL280). Details of what they shared with the task force are in Appendix E.

In discussions on the potential legalization of psychedelic medicines, the following points are imperative for moving forward.

Recognize Tribal sovereignty

Tribal Nations have the inherent authority to govern themselves, make their own laws, and manage their own affairs without external interference, particularly from federal and state governments.

Recognize that tribes have the ability to forge their own paths

Tribal Nations possess the autonomy to determine their own governance, cultural practices, economic development, and social services, allowing them to develop in ways that align with their unique traditions and aspirations.

Highlight the areas that were voted on

It is likely the recommendation for the removal of criminal penalties will help prevent criminal prosecution on tribal lands via Public Law 280 for any psychedelic medicine programs created and implemented on tribal lands/reservations.

Discuss Tribal consultation related to the recommendations

The Dakota and Ojibwe Tribal representatives engaged with Tribal Nations, the people, programs, and spiritual leaders in meaningful dialogue and consultation regarding knowledge on topic, interest and understanding how this medicine can serve as a healing potential option in the future, ensuring their voices and perspectives are heard and taken into account.

Tribes can move forward with their own processes and the state shall not intervene

Tribal Nations have the right to implement their own systems, procedures, and decision-making processes without interference or oversight from state authorities, reinforcing their sovereignty and self-determination. We, as Tribal Nations, are entering into an agreement with the federal government through treaties, which serve as the supreme law of the land. The capacity to govern Tribal Nations empowers those nations to protect and serve their communities according to their values and needs.

Veterans Affairs

Recent studies have shown the actual numbers of veterans committing suicide and dying from deaths of despair, such as drug overdoses and alcohol related deaths, are grossly underestimated. In Operation Deep Dive (see Appendix M) it was discovered that reporting errors resulted in undercounting these deaths and when incorporating self-injury mortality, the rate of premature and unnatural death is closer to 44 per day as opposed to the 17.7 reported by the US Department of Veterans Affairs (VA). Crime scene investigators report that when there is any doubt of cause of death as a possible veteran suicide, they will almost always report the deaths as accidental because life insurance companies will not pay beneficiaries and other benefits will not continue for the families in cases of suicide (Willink & Charles, 2015—present). These factors indicate that the veteran suicide rates and deaths from despair are far greater than previously believed.

Veterans and first responders are uniquely qualified for psychedelic medicine for many reasons. Primarily they are more likely to have suffered from post-traumatic stress due to the nature of their work. Upon entering the military or academies, they will have been given psychological evaluations, so they are prescreened for the mental illnesses and psychotic disorders which might disqualify them from treatment. Former service members and first responders are equipped to handle stressful situations, a skill they have trained for and learned in their occupational or wartime experience. More generally, they are adaptable, have less fear of death, and do not lack courage, beneficial characteristics for psychedelic journeying. Being receptive to training and an ability to follow orders is also helpful during the preparation and integration stages of the process. Most veterans have access to mental health professionals and excellent health care facilities as well as comprehensive records. Not only do veterans and first responders warrant a greater need for psychedelic medicine, but they make exceptional candidates for this therapy and excellent cohorts for clinical trials.

While the VA is conducting and funding trials of psychedelic medicines for PTSD, clinical trials are not designed to scale as a widespread treatment option. The recent rejection of MDMA by the FDA and the continued suppression of psychedelics by the federal government leaves veterans few options for access and most come with considerable risks. However, in the last few years there have been several non-profit organizations started in order to get help to those most in need. The waiting lists are long and they are only able to assist a small percentage of applicants. Recently a few distinguished veterans shared their stories raising awareness and demonstrated the desperate need for more access to psychedelic medicine. US Congressman Morgan Luttrell credited psychedelic medicine with “being like twenty years of therapy in three days.” Marcus Capone

attributed psychedelics for saving his marriage and his life and later went on to start Veterans Exploring Treatment Solutions (VETS; accessed November 11, 2024), a foundation providing grants to end the veteran suicide epidemic by providing resources, research, and advocacy for US military veterans seeking psychedelic-assisted therapies.

The US Congress has already acted passing several bills to increase access, funding, and research for psychedelic medicine in the Department of Defense and the VA. Dan Crenshaw introduced the Douglas Mike Day Psychedelic Therapy to Save Lives Act of 2023 (H.R. 3684) to the US House (05/25/2023), which was written to direct the Secretary of Defense to establish a grant program for using psychedelic substances to treat certain conditions, and for other purposes. In January, the VA announced a request for applications for research proposals (see Appendix M) to study the use of certain psychedelic compounds in treating post-traumatic stress disorder and depression. The VA intends to collect definitive scientific evidence on the potential efficacy and safety of psychedelic compounds such as MDMA and psilocybin when used in conjunction with psychotherapy to treat mental health conditions. Without the VA's involvement, veterans must rely on grassroots organizations working to help bring healing, including, but not limited to Heroic Hearts Project (HHP, 2024), VETS, Reason for Hope (RFH, 2024), and other organizations which can be found on the Veteran Mental Health Leadership Coalition (VMHC) website (see Appendix M). While there are some programs which are legal at the state level, they are in conflict with the federal prohibition, and integrating such programs with current VA healthcare is only possible through clinical trials. While this development provides some access for veterans it is not the environment most likely to promote the healing response.

The lack of access to psychedelic medicine for veterans is concerning considering the positive outcomes for those with PTSD and the possibility of significantly reducing the number of veteran suicides in the state. The overwhelming recommendation of the task force has been to remove barriers to access and increase funding for treatment and research. However, even if a clinical program is created within the state, the high cost of this therapy still produces a significant barrier for most veterans. An adult regulated use model for psilocybin would be the most beneficial statutory outcome for veterans who need access to psychedelic medicine. Most members of the task force agreed that after one or more guided medicine sessions, veterans could safely use organic mushrooms within the privacy of their own homes (or other safe and secure settings) without serious risk to the veteran or society in general. As access to this treatment is a pressing matter, in the interim, grants provided by MDVA for interstate and international programs would be instrumental in combating veteran suicide. If certain psychedelics were to be rescheduled at the federal level, it is a possibility that established Minnesota state facilitators could participate in The Veterans Choice Program (VCP, 2024). The program, which allows eligible veterans to receive care from non-VA medical facilities was embraced by President Donald J. Trump, who signed the Veterans Choice Program Extension and Improvement Act in 2017 (Cronk, 2017). This could create a pathway to services and funding which would be the best-case scenario, making Minnesota an elite state for these innovations in healing, treatment methods, and approaches to suicide prevention.

This report has demonstrated the effectiveness of psychedelic medicine in treating addiction, one of the most problematic issues for veterans struggling with PTSD, anxiety, and depression. Whether intentionally or spontaneously, many veterans who have completed this type of therapy report that they often quit abusing alcohol, drugs, and prescription medications because they do not feel the need for them anymore. Famous podcaster and former Navy Seal Shawn Ryan has said "I did psychedelics in Mexico and it changed my life in so

many different ways…I haven't had a drop of booze in two and half years and I didn't even go down there for that (and I'm) way more in the moment with my family" (Ryan, S., 2019—present). Changing one's relationship with alcohol has been widely reported as one of the benefits of psychedelic therapy and after the experience, many veterans have stopped abusing alcohol or abstain completely with little to no effort.

Treating the root causes of veteran mental health and wellness issues, particularly for PTSD, would likely be more cost effective than appropriations for housing, disability, addiction treatment, and many other expenses. A significant number of veterans who were previously 100 percent disabled by conditions like depression and PTSD have been known to make complete and total recoveries using psychedelic medicine which has made them more self-sufficient and employable. Most veterans would rather work than receive benefits due to unemployability, but their conditions are often too severe to maintain extensive periods of productivity. State funded grants for psychedelic therapy and various facilitator incentives such as tax rebates for pro bono services for veteran clients, would likely be less expensive. Rather than paying for the damage that results from these conditions, money might better be spent in prevention and saving veterans and their families from lifetimes of unnecessary suffering. Any proposed legislation should prioritize veterans access to this medicine and consider the funding, waivers, and exemptions that could be employed to remove the barriers preventing access to this life saving therapy.

For resources on psychedelic medicine for veterans from this section, as well as additional resources, please see Appendix M.

Public education

The final directive in the authorizing legislation was to develop an education plan for the MN legislature, and the public, surrounding the recommendations of the task force, and other aspects related to the legalization of psychedelic medicine in the state. Through discussions at task force and work group meetings, a number of priorities for a public education plan were identified and recommended to be delegated to MDH for widespread distribution. MDH has the option to reach out to task force members, community organizations for educational information and guidance.

- Government/state agency intersection and collaboration to inform the general public
- Task Force on Illicit Drug use
- Task Force on SUD and Pregnancy
- Alcohol and Other Drug Abuse Advisory Council
- Drug Formulary Committee
- Drug Utilization Review Board
- Department of Corrections
- Governor's Task Force on Mental Health
- Health Services Advisory Council (access through evidence-based coverage policy)
- Medicaid Services Advisory Committee (payment for services)
- State Advisory Council on Mental Health
- State Innovation Model (SIM) Community Advisory Task Force

- State Innovation Model (SIM) Multi-Payer Alignment Task Force
- DHS Licensing Boards (all providers i.e. mental health, physicians, physiatry, pharmacists, nurses, treatment facilities, etc.)
- Minnesota Commander's Task Force (veteran organizations)
- Department of Children, Youth and Families
- Center of Excellence on Public Health and Homelessness (unsheltered)
- Minnesota Chiefs of Police Association
- Minnesota Sheriffs' Association
- Minnesota State Fire Chiefs Association
- Minnesota Ambulance Association
- Promote and list existing peer-run education, safe use, and harm reduction resources
- Fireside Project crisis line
- Psychedelic Society of Minnesota
- DanceSafe
- Drug testing kits
- Community outreach, media, reporters, and journalists
- Testimony at the MN legislature, Interviews with print, television, radio, and digital media
- Speaking to community organizations, such as Rotary Clubs
- Generalized adult use will be perceived very differently than medical and health initiatives and will have unique issues associated with that.

Religious uses

Psychedelic medicines have been revered as sacraments by Indigenous cultures for hundreds, if not thousands of years. While this has been acknowledged recently in the efforts to legalize psychedelic medicines, such acknowledgements do not address the historical harms that have been done to religious uses of psychedelic medicines, many of which that have been perpetuated by ongoing colonization of Indigenous resources and practices. For a detailed history of how this unfolded in the United States with the Native American Tribes who used peyote (containing the Schedule I drug mescaline) and how they were subjected to cultural genocide at the hands of both the US government and the Catholic church, please refer to SME Christine Diindiisi McCleave's presentation on this from the task force's March meeting (see Appendix E), as well as an educational lecture she delivered to the Minnesota psychedelic community on how that is impacting legislation around psychedelic medicines in other states (Psychedelic Society of Minnesota, March 2024).

Religious uses of psychedelic medicines have only recently been legally protected in the US, despite the long history of religious use around the world, and one of the founding principles of the US being religious freedom (1st amendment of the US Constitution). The first exemption for use of a Schedule I drug for religious purposes, peyote, was obtained by the Native American Church, an award won over the reluctance of DEA and only by force of the Supreme Court. Three other exemptions for religious use have been granted in the US for psychedelic medicines, all for ayahuasca (containing the Schedule I drug dimethyltryptamine (DMT)), two of which that are religions protected by the Brazilian government (Santo Daime and União do Vegetal), and one formed in Arizona by a group with various Indigenous backgrounds (Church of the Eagle and Condor). However, other churches using this sacrament have been denied such exemptions either for not properly filing as a church

with the Internal Revenue Service (IRS) (Thomson Reuters, October 2024), or because they were viewed as a healing center, not a church (Chacruna, June 2021). No religious groups in the US have been granted exemptions for religious use with psilocybin mushrooms, however there is a long-standing documented history for spiritual uses from the Mazatec regions of Mexico, as the most notable example.

Additionally, outside of Indigenous contexts, people who engage with psychedelic medicines have consistent experiences that contain religious or spiritual elements that are often associated with their underlying beliefs, and such experiences consistently predict improvements in therapeutic outcomes in clinical trials (Ko et al., 2022; Roseman et al., 2018). Chaplains are often brought in to help with such experiences, as they are well-equipped to manage the spiritual nature of psychedelic medicines, particularly for people at end of life (California Institute of Integral Studies, October 2023). A landmark study in the 1990s by Dr. Rick Strassman studied the experiences of people taking DMT (the psychedelic ingredient in ayahuasca), and dubbed it “The Spirit Molecule,” which has been further validated given that scientific research on near death experiences (Timmermann et al., 2018) and animal and human autopsy reports have found that this same molecule, which is also produced by the human brain, is released at the moment of death/cardiac arrest (Dean et al, 2019). From an evolutionary standpoint, it’s unclear why humans have this in their brains, and what its purpose is. DMT exists in many plant species potentially to help ward off predators/insects, yet we do not fully understand it’s purpose for human biology, beyond its ability to induce such profound spiritual experiences, with similar chemical properties as psilocybin.

Appendix A: Legislation

Laws of Minnesota, 2023, chapter 70, article 4, section 99

Sec. 99**.** Psychedelic Medicine Task Force.

Subdivision 1. Establishment; purpose.

The Psychedelic Medicine Task Force is established to advise the legislature on the legal, medical, and policy issues associated with the legalization of psychedelic medicine in the state. For purposes of this section, "psychedelic medicine" means 3,4-methylenedioxymethamphetamine (MDMA), psilocybin, and LSD.

Subd. 2. Membership; compensation.

(a) The Psychedelic Medicine Task Force shall consist of:

(1) the governor or a designee;

(2) two members of the house of representatives, one appointed by the speaker of the house and one appointed by the minority leader of the house of representatives, and two members of the senate, one appointed by the senate majority leader and one appointed by the senate minority leader;

(3) the commissioner of health or a designee;

(4) the commissioner of public safety or a designee;

(5) the commissioner of human services or a designee;

(6) the attorney general or a designee;

(7) the executive director of the Board of Pharmacy or a designee;

(8) the commissioner of commerce or a designee; and

(9) members of the public, appointed by the governor, who have relevant knowledge and expertise, including:

(i) two members representing Indian tribes within the boundaries of Minnesota, one representing the Ojibwe tribes and one representing the Dakota tribes;

(ii) one member with expertise in the treatment of substance use disorders;

(iii) one member with experience working in public health policy;

(iv) two veterans with treatment-resistant mental health conditions;

(v) two patients with treatment-resistant mental health conditions;

(vi) one psychiatrist with experience treating treatment-resistant mental health conditions, including post-traumatic stress disorder;

(vii) one health care practitioner with experience in integrative medicine;

(viii) one psychologist with experience treating treatment-resistant mental health conditions, including post-traumatic stress disorder; and

(ix) one member with demonstrable experience in the medical use of psychedelic medicine.

(b) Members listed in paragraph (a), clauses (1) and (3) to (8), and members appointed under paragraph (a), clause (9), may be reimbursed for expenses under Minnesota Statutes, section 15.059, subdivision 6. Members appointed under paragraph (a), clause (2), may receive per diem compensation from their respective bodies according to the rules of their respective bodies.

(c) Members shall be designated or appointed to the task force by July 15, 2023.

Subd. 3. Organization.

(a) The commissioner of health or the commissioner's designee shall convene the first meeting of the task force.

(b) At the first meeting, the members of the task force shall elect a chairperson and other officers as the members deem necessary.

(c) The first meeting of the task force shall occur by August 1, 2023. The task force shall meet monthly or as determined by the chairperson.

Subd. 4. Staff.

The commissioner of health shall provide support staff, office and meeting space, and administrative services for the task force.

Subd. 5. Duties.

The task force shall:

(1) survey existing studies in the scientific literature on the therapeutic efficacy of psychedelic medicine in the treatment of mental health conditions, including depression, anxiety, post-traumatic stress disorder, bipolar disorder, and any other mental health conditions and medical conditions for which a psychedelic medicine may provide an effective treatment option;

(2) compare the efficacy of psychedelic medicine in treating the conditions described in clause (1) with the efficacy of treatments currently used for these conditions; and

(3) develop a comprehensive plan that covers:

(i) statutory changes necessary for the legalization of psychedelic medicine;

(ii) state and local regulation of psychedelic medicine;

(iii) federal law, policy, and regulation of psychedelic medicine, with a focus on retaining state autonomy to act without conflicting with federal law, including methods to resolve conflicts such as seeking an administrative exemption to the federal Controlled Substances Act under United States Code, title 21, section 822(d), and Code of Federal Regulations, title 21, part 1307.03; seeking a judicially created exemption to the federal Controlled Substances Act; petitioning the United States Attorney General to establish a research program under United States Code, title 21, section 872(e); using the Food and Drug Administration's expanded access program; and using authority under the federal Right to Try Act; and

(iv) education of the public on recommendations made to the legislature and others about necessary and appropriate actions related to the legalization of psychedelic medicine in the state.

Subd. 6. Reports.

The task force shall submit two reports to the chairs and ranking minority members of the legislative committees with jurisdiction over health and human services that detail the task force's findings regarding the legalization of psychedelic medicine in the state, including the comprehensive plan developed under subdivision 5. The first report must be submitted by February 1, 2024, and the second report must be submitted by January 1, 2025.

Appendix B: Task force membership

Members included: representatives from the Dakota and Ojibwe tribes (2), veterans with treatment-resistant mental health conditions (2), a psychologist and psychiatrist with experience treating treatment-resistant mental health conditions (2), patients with treatment-resistant mental health conditions (2), members with expertise in the treatment of substance use disorders (1), with experience in public health policy (1), a healthcare practitioner with experience in integrative medicine (1), a member with demonstratable experience in the medical use of psychedelic medicine (1), Senate members of both the Majority and Minority (2), members of the House of Representatives (2), a governor designee, the executive director of the Board of Pharmacy, as well as members designated by the Commissioner of Human Services, Commissioner of Health, Commissioner of Commerce, and the Attorney General.

Dr. Jessica Nielson was elected to fulfill the role of chairperson by majority vote during the December 2023 task force meeting. Bennett Hartz was elected as the vice chair, and Paula DeSanto was elected as the work group chair at the task force's May 2024 meeting. The role of the elected leaders was to work in conjunction with Minnesota Department of Health (MDH) Psychedelic Medicine Program Staff and Management Analysis and Development (MAD) consultants to help create and maintain the processes, structure, annual work plan, and meeting agendas to keep the task force effective and efficient.

Unless otherwise noted, all members served in their position for the duration of the task force.

Symbols: *Chair, ^Vice-Chair, #Work group Chair.

Task force seat	Name
Governor's designee	Jeremy Drucker
House of Representatives, Speaker designee	Rep. Andy Smith
House of Representatives, Minority leader designee	Rep. Nolan West
Senate, Majority leader designee	Sen. Kelly Morrison (August 2023—June 2024) Sen. Scott Dibble (August 2024—September 2024)
Senate, Minority leader designee	Sen. Julia Coleman (August 2023—June 2024) Sen. Mark Koran (September 2024—January 2025)

Task force seat	Name
Commissioner of Health designee	Chris Tholkes (August 2023—December 2023) Dr. Nick Lehnertz (December 2023—January 2025)
Commissioner of Public Safety designee	Kenneth Sass
Commissioner of Human Services designee	Dave Hoang (August 2023—September 2024) John Connolly (September 2024—January 2025)
Attorney General designee	Bennett Hartz^
Executive Director of the Board of Pharmacy	Jill Phillips
Commissioner of Commerce designee	Helen Bassett
Dakota Representative	Guthrie Capossela
Ojibwe Representative	Donovan Sather (March 2024—January 2025)
Member with expertise in the treatment of substance use disorders	Paula DeSanto#
Member with experience working in public health policy	Arielle McHenry
Veteran with treatment-resistant mental health	Michael Tabor
Veteran with treatment-resistant mental health	Stefan Egan

Task force seat	Name
Patient with treatment-resistant mental health condition(s), including post-traumatic stress disorder	Kit O'Neill
Patient with treatment-resistant mental health condition(s), including post-traumatic stress disorder	Adam Tomczik
Psychiatrist with experience treating treatment-resistant mental health conditions, including post-traumatic stress disorder	Dr. Ranji Varghese
Healthcare practitioner with experience in integrative medicine	Cortney Amundson
Psychologist with experience treating treatment-resistant mental health conditions, including post-traumatic stress disorder	Dr. Margaret Gavian
Member with demonstrable experience in the medical use of psychedelic medicine	Dr. Jessica Nielson*

The task force encountered delays in appointment of members from Tribal nations. For example, while the deadline for the Governor's Office to appoint two tribal nation representatives was July 2023, not until October 2023 did the governor's office appoint the Dakota representative, and not until February 2024 did it appoint the Ojibwe representative, by which point the task force had already met several times. The task force recommends direct appointments, from an appointing authority like MIAC, to reduce any future delays.

Appendix C: Report development process

The task force followed a number of processes, decided upon at the first two meetings in November and December 2023, to guide the work. The following are elements of the Psychedelic Medicine Task Force Charter.

Guiding principles

Scientific and research rigor: Use the best scientific data and evidence-based methods available to guide research and final policy recommendations. Include research beyond clinical trials, including population studies and gray literature given the complexity of mental health treatment and realities of policy change. Operate with safety of people's medical, psychological, and spiritual health as the primary objective.

Collaboration and inclusivity: Diversity in perspectives and experiences foster innovative solutions and strengthens the capacity to deliver results. Some perspectives have historically, at times intentionally, been excluded. Be intentional in creating space for these voices.

Accountability and integrity: Act as effective and efficient managers of the public trust and public health, operating with open communication, transparency, honesty, and timeliness to ensure appropriate high standards.

Awareness in evaluation: Recognize limitations of existing research in the field and benefits of emerging or promising practices generated in community. Continually address contradiction, disagreement, possible risks of bias, and any unknowns throughout the decision-making process. Consider member positionality and reality of capacity throughout this work. Utilize opportunities and support where possible to ensure these biases are addressed and highlighted where needed. Strive for the highest level of consensus throughout the evaluation process, to further likelihood of plan's success and potential impact.

Strive for practicality of recommendations: Aim to address the reality of implementing recommendations throughout the development process and creation of the final comprehensive plan. Consider possible barriers (e.g., funding and regulatory needs) to ensure final recommendations are feasible and capable of being adopted into existing infrastructure to ensure sustainable, long-term success.

Social equity: Psychedelic medicine has a complex past rooted in culturally diverse histories, particularly within Indigenous communities. This, in conjunction with the impact of past drug policies, provides a need to continually consider the future impact of recommendations while acknowledging past mistakes. Prioritize health equity (including culturally appropriate treatment options) and identify possible unintended harms or injustices prior to submitting recommendations.

Engage the public whenever possible: Continually engage in opportunities to center the voices of those most impacted by policy decisions.

Working agreements

The task force decided upon a number of expectations, both for individuals and for the group, to drive the task force's work. The working agreements are as follows.

Individual expectations

- Come to meetings prepared. Review the agenda and read required materials sent ahead of the meeting.
- Seek to understand the opinions, viewpoints and lived experiences of others.
- When sharing information or expertise, use plain language and avoid unnecessary acronyms.
- Be present. Minimize the use of cell phones, email, and side conversations.
- Keep discussion focused on directly relevant topics.
- Step up/step back.
    - If you're more likely to remain quiet during meetings, step up a bit more and share your ideas and suggestions.
    - If you're more likely to do most of the talking in meetings, step back a bit and let others contribute as well.
- Refrain from writing letters or engaging in other kinds of communication in the name of the task force unless the chairperson specifically authorized such communication.
- Be mindful of the risks of a dominant culture's ways of thinking. Hold space for alternative ways of working together.

Expectations for participating in remote meetings

- Participate with video on as much as you are able so everyone feels your presence throughout the meeting.
- Mute yourself when not speaking.
- Use the "raise hand" feature when you want to speak.
- Refrain from using chat as a means of making comment or participating in a conversation.
- Help facilitator encourage remote participation and check in with members to assure all are heard.
- Do your part to assure functioning technology by joining early to check connection and joining meeting from stable environment.

Expectations during challenging moments

- Sometimes words land on other ears or come out wrong. Offer or ask for "do-overs".
- Lean into discomfort with respect and to seek understanding.
- Assume good intent but acknowledge harm.
- Ask for a break or a few moments for quiet reflection if discussion becomes re-traumatizing or stress inducing.
- Focus on the issue, not the people.
- Be objective, respectful, and solution-driven when sharing amongst a group of passionate professionals.
- Be open-minded and curious about others' experiences.

- Seek to address issues during a meeting.

Decision making tools

A broad complement of decision-making tools was explored by the task force with the goal of creating more nuanced understandings, building consensus where possible, and abiding with open meeting laws. Decisions on the scientific research summary, about which legal pathways to pursue, as well as regulations and policies needed, were all decided on by a simple majority through Mural. The general direction for the recommendations was also decided upon by a simple majority. As the recommendations were parsed out, decisions were made through SWOT analysis and through gradients of agreement. A SWOT analysis is a framework based on Strengths, Weaknesses, Opportunities, and Threats. This method is used to assess these factors both internally and externally. Task force members expressed their opinions in one or more of the four categories in Mural. Gradients of agreement were used after the SWOT analysis; this framework allows for opinions to be heard along a continuum of responses. This continuum consisted of: Love it, Like it, Live with it, Leery of it, and Loathe it. The first three responses indicate acceptance, while the remaining two indicate rejection. If members voiced that they fell in the final two categories, they were asked to provide input on why, along with what would need to change for them to accept the decision, in Mural. After deciding upon the recommendations, a simple majority vote decided on if abstentions counted in the denominator of the vote. Finally, final votes on which recommendations would be included required a two-thirds supermajority to pass.

Meeting schedule and work cadence

All meetings occurred on the first Monday of each month from 9:30 a.m. to 12:30 p.m. If the proposed time was a holiday, the meeting occurred the following Monday at the same time.

Date	Activities
November 6, 2023	Establish guiding principles, decision making tools, and other grounding documents.
December 4, 2023	Identify benefits and challenges of legalization, and policy areas for work groups to focus on, discuss literature review methods.
January 8, 2024	Overview of legal issues, finalize literature review methodology.
February 5, 2024	Plan development and recommendations. Continual review through work group updates, subject matter expert presentations, and collaborative decision-making.

Date	Activities
March 4, 2024	Education, research, subject matter expert presentations, and plan development. Work group meetings.
April 1, 2024	Education, research, subject matter expert presentations, and plan development. Work group meetings.
May 6, 2024	Education, research, subject matter expert presentations, and plan development. Work group meetings.
June 3, 2024	Education, research, subject matter expert presentations, and plan development. Work group meetings.
July 1, 2024	Information synthesis, narrowing, and prioritization of report. Work group meetings.
August 5, 2024	Drafting of recommendations. Work group meetings.
September 9, 2024	Voting on recommendations. Work group meetings.
October 7, 2024	Voting on revised recommendations. Drafting report. Work group meetings focusing on writing.
November 4, 2024	Reviewing draft of report. Editing report.
December 2, 2024	Editing report.
January 1, 2025	Submit report to the Minnesota legislature.

For a list of topics covered at each full task force meeting, and links to meeting recordings on YouTube (thanks to a volunteer from the community who captured the meetings), please see Appendix E.

Appendix D: Voting logs

During the course of the task force work, the task force workshopped some decision-making tools for how members would decide on the task force's final recommendations. The task force discussed different tools, such as giving a thumbs up, doing a "gradients of agreement," or voting based on a simple or supermajority. The task force decided that official recommendations will be decided by a two-thirds supermajority vote. Voting for general decisions occurred through activities on Mural, while voting for the recommendations occurred through a roll call. Prior to voting on final recommendations, the task force held a vote about whether abstentions would be counted towards the total needed for a supermajority. The task force voted through a simple majority that abstentions were not considered votes, and thus did not count towards the total. Records of voting logs are included to highlight how each member voted for each recommendation (yes, no, or abstain).

Following the vote at the September 2024 meeting, it was raised that recommendations one and two may have been unclear. Because of this the language was updated and these revised recommendations were voted on in the October 2024 meeting, to supersede the initial vote.

Name	Rec. 1 (original) Remove criminal penalties for possession of personal use quantities of MDMA, psilocybin, LSD	Rec. 1 (updated) Remove criminal penalties for the possession of personal use quantities of mushrooms containing psilocybin	Rec. 2 (original) Remove criminal penalties for non-commercial cultivation of psilocybin-containing mushrooms	Rec. 2 (updated) Remove criminal penalties for the possession of personal use quantities and non-commercial cultivation and sharing of psilocybin-containing mushrooms.
Jeremy Drucker	No	No	No	No
Rep. Andy Smith	Yes	Yes	Yes	Yes

Name	Rec. 1 (original) Remove criminal penalties for possession of personal use quantities of MDMA, psilocybin, LSD	Rec. 1 (updated) Remove criminal penalties for the possession of personal use quantities of mushrooms containing psilocybin	Rec. 2 (original) Remove criminal penalties for non-commercial cultivation of psilocybin-containing mushrooms	Rec. 2 (updated) Remove criminal penalties for the possession of personal use quantities and non-commercial cultivation and sharing of psilocybin-containing mushrooms.
Rep. Nolan West	Yes	Yes	No	No
Sen. Mark Koran	No	Yes	No	No
Dr. Nick Lehnertz	No	No	No	No
Kenneth Sass	No	No	No	No
John Connolly	absent	No	absent	No
Bennett Hartz	No	No	No	No

Name	Rec. 1 (original) Remove criminal penalties for possession of personal use quantities of MDMA, psilocybin, LSD	Rec. 1 (updated) Remove criminal penalties for the possession of personal use quantities of mushrooms containing psilocybin	Rec. 2 (original) Remove criminal penalties for non-commercial cultivation of psilocybin-containing mushrooms	Rec. 2 (updated) Remove criminal penalties for the possession of personal use quantities and non-commercial cultivation and sharing of psilocybin-containing mushrooms.
Jill Phillips	No	No	No	No
Helen Bassett	No	No	No	No
Guthrie Capossela	Yes	Yes	Yes	Yes
Donovan Sather	Yes	Yes	Yes	Yes
Paula DeSanto	Yes	Yes	Yes	Yes
Arielle McHenry	No	Yes	Yes	Yes

Name	Rec. 1 (original) Remove criminal penalties for possession of personal use quantities of MDMA, psilocybin, LSD	Rec. 1 (updated) Remove criminal penalties for the possession of personal use quantities of mushrooms containing psilocybin	Rec. 2 (original) Remove criminal penalties for non-commercial cultivation of psilocybin-containing mushrooms	Rec. 2 (updated) Remove criminal penalties for the possession of personal use quantities and non-commercial cultivation and sharing of psilocybin-containing mushrooms.
Michael Tabor	Yes	Yes	Yes	Yes
Stefan Egan	No	Yes	Yes	Yes
Kit O'Neill	Yes	Yes	Yes	Yes
Adam Tomczik	Yes	Yes	Yes	Yes
Dr. Ranji Varghese	No	Yes	Yes	Yes
Cortney Amundson	Yes	Yes	Yes	Yes

Name	Rec. 1 (original) Remove criminal penalties for possession of personal use quantities of MDMA, psilocybin, LSD	Rec. 1 (updated) Remove criminal penalties for the possession of personal use quantities of mushrooms containing psilocybin	Rec. 2 (original) Remove criminal penalties for non-commercial cultivation of psilocybin-containing mushrooms	Rec. 2 (updated) Remove criminal penalties for the possession of personal use quantities and non-commercial cultivation and sharing of psilocybin-containing mushrooms.
Dr. Margaret Gavian	Yes	Yes	Yes	Yes
Dr. Jessica Nielson	Yes	Yes	Yes	Yes

Table 2: Recommendations three through six

Name	Rec. 3 Create a state-regulated program for clinical administration of MDMA, psilocybin, LSD	Rec. 4 Create a state-regulated program for clinical administration of psilocybin-containing mushrooms	Rec. 5 Appropriate funding for research	Rec. 6 Allow and regulate adult use of psilocybin-containing mushrooms
Jeremy Drucker	No	Abstain	Abstain	No
Rep. Andy Smith	Yes	Yes	Yes	Yes

Name	Rec. 3 Create a state-regulated program for clinical administration of MDMA, psilocybin, LSD	Rec. 4 Create a state-regulated program for clinical administration of psilocybin-containing mushrooms	Rec. 5 Appropriate funding for research	Rec. 6 Allow and regulate adult use of psilocybin-containing mushrooms
Rep. Nolan West	Yes	Yes	Yes	No
Sen. Mark Koran	No	Yes	Yes	No
Dr. Nick Lehnertz	No	No	Abstain	No
Kenneth Sass	No	No	Abstain	No
John Connolly	No	No	Abstain	No
Bennett Hartz	No	No	Yes	No
Jill Phillips	No	No	Abstain	No
Helen Bassett	No	Abstain	Abstain	Abstain
Guthrie Capossela	Yes	Yes	Yes	Yes
Donovan Sather	Yes	Yes	Yes	Yes
Paula DeSanto	Yes	Yes	Yes	Yes
Arielle McHenry	Yes	Yes	Yes	Yes

Name	Rec. 3 Create a state-regulated program for clinical administration of MDMA, psilocybin, LSD	Rec. 4 Create a state-regulated program for clinical administration of psilocybin-containing mushrooms	Rec. 5 Appropriate funding for research	Rec. 6 Allow and regulate adult use of psilocybin-containing mushrooms
Michael Tabor	Yes	Yes	Yes	Yes
Stefan Egan	Yes	Yes	Yes	No
Kit O'Neill	Yes	Yes	Yes	Yes
Adam Tomczik	Yes	Yes	Yes	Yes
Dr. Ranji Varghese	Yes	Yes	Yes	Yes
Cortney Amundson	Yes	Yes	Yes	Yes
Dr. Margaret Gavian	Yes	Yes	Yes	Yes
Dr. Jessica Nielson	Yes	Yes	Yes	Yes

Appendix E: Subject matter experts

A number of subject matter experts (SMEs) provided valuable information to the task force. The Psychedelic Medicine Task Force would like to extend grateful acknowledgement to each of them for their contributions, without which this report would not be possible. While the full task force meetings were not recorded in an official capacity, a member of the public recorded the meetings and made them available. Thus, a summary of the SMEs, the content they provided, and relevant video recordings, in the order that they were consulted for the task force's work, follows.

Robert Rush, Esq and Ismail Ali, JD discussed the history of drug prohibition, the creation of the Controlled Substances Act, and the concept of closed-loop systems for state-regulated programs, where new programs and policies are being implemented that are alternatives to federal drug policies, a term called "states as labs." This was presented to at the January 2024 full task force meeting, starting at 2:09:13 of the January video recording (Psychedelic Medicine Task Force, January 2024).

Dr. Mason Marks, MD, JD provided an extensive legal overview of psychedelic drugs in the United States, including frameworks used in Oregon and Colorado, challenges and legal issues, and provided ongoing consultation throughout the task force's work to keep members grounded in the realities of federal laws. This was presented at the February 2024 full task force meeting, starting at 48:56 of the February video recording (Psychedelic Medicine Task Force, February 2024).

Shannon Geshick, MTAG, citizen of the Bois Forte Band of Chippewa, is the Executive Director for the Minnesota Indian Affairs Council (MIAC). In this capacity, she works to protect tribal sovereignty and promote the wellbeing of American Indians citizens in the state. Task force member Guthrie Capossela and Chairperson Nielson met with Ms. Geshick to discuss tribal consultation, MIAC's process for providing recommendations for appointments to state task forces, and some background on government-to-government relations in Minnesota. This meeting was held on February 9, 2024, but was not recorded.

March speakers related to regulating businesses, equity considerations, Tribal consultation, and the history of cultural genocide on Native Americans, including of their sacramental use of peyote. Ariel Clark, JD, cofounder of the Psychedelics Bar Association, gave a presentation on regulatory, legal, and business considerations and lessons learned from the cannabis industry, and the importance of Tribal consultation. Christine Diindiisi McCleave, MA, PhD(c) (Turtle Mountain Anishinaabe) is the Moderator/Project Manager for the Colorado Federally Recognized American Tribes and Indigenous Community Working Group contracted through Project Mosaic for the Department of Regulatory Agencies (DORA). McCleave is the former CEO of The National Native American Boarding School Healing Coalition and is currently a doctoral candidate pursuing her Ph.D. in Indigenous Studies at University of Alaska Fairbanks. Her research focuses on healing historical trauma with traditional plant medicines in an Indigenous context. She gave a presentation on psychedelic medicine within an Indigenous context, discussing the historical context of the "psychedelic boom" and its roots in the colonization of Indigenous resources, culture, and knowledge. This section was presented starting around 1:22:29 of the March video recording (Psychedelic Medicine Task Force, March 2024).

Brett Waters, JD. Founder and Executive Director, Reason for Hope; consulted with the task force's legal working group on March 25, 2024, about the Breakthrough Therapies Act, the Right to Try Clarification Act (both have been introduced into Congress, but have not moved beyond that), and efforts to support veterans and access to psychedelic medicines.

In April, Shane Pennington, JD, partner at Porter Wright Morris and Arthur LLP, gave a presentation on the federal Right to Try Act and other federal exemptions to the Controlled Substances Act. Shane discussed the Food and Drug Administration (FDA) drug approval process, the difficulties and risks associated with collecting acceptable data, and safe documentation procedures. This was presented to at the April 2024 full task force meeting, starting at 2:02:54 of the April video recording (Psychedelic Medicine Task Force, April 2024).

In May, the task force convened a panel to present, including a returning SME, Mason Marks, MD, JD, and the panelists below. The other panelists were Dominique Mendiola, JD, Senior Director, Marijuana Enforcement Division and Natural Medicine Division (CO); Emma Knighton, MA, LMHC, somatic trauma and psychedelic integration therapist, member of the Washington Psilocybin Task Force and involved in the implementation of Oregon Measure 109 program as facilitator trainer and service center director; and Jason Ortiz, Director of Strategic Initiatives for the Last Prisoner Project. The recording of this panel can be found starting around 44:25 of the May video recording (Psychedelic Medicine Task Force, May 2024).

Angela Allbee, MPA, manager of Oregon Psilocybin Services Section at Oregon Health Authority met with Dr. Johnson and Chrissie Deutsch in February 2024 to discuss the program in Oregon, and she also met and presented to the work group. The following is a summary of the work group meeting.

- Oregon has compiled everything into their Guidance document, and highly suggested reading though it, as well as the other parts of the website containing forms and the administrative rules (Oregon Health Authority, accessed November 11, 2024) for the task force's own guidance.
- Since the initial eleven recommendations put forward in the review, they've implemented over 100 rules/recommendations.
- Every year they will amend rules after meeting with the board, community, etc.
    - Every summer they host three listening sessions.
- Every autumn they compile the potential rule changes and present updates to the public.
    - By the end of the year they formalize new rules, to take effect starting Jan. 1 of the following year.
    - The rulemaking process is trial and error.
- For the initial scientific research and recommendations, the scientific results were presented to the full board to inform decision making.
    - They also had pushback regarding scientific focus because of lack of equity in this space, this is what prompted them to create a separate cultural and anthropological review.
    - Acknowledging this gap was an important step.
- The Oregon government used their government-to-government relationship with their nine sovereign Tribal Nations to address the considerations around Indigenous peoples.
    - Were receptive to outreach, presentations, community conversations.
- Their public health department has contracted with community groups regarding education, outreach, training.
- Statistics/data since rollout:

    - Collection and reporting of aggregate data begins in 2025 (rulemaking occurred in 2024 on the specific requirements, data available after the first quarter of 2025).
- The only data they've collected so far is if emergency services have been contacted during an administration session.
- Indigenous feedback: Keep the medicine natural, do not isolate compounds.
    - Oregon using whole mushroom.
    - They do not allow standardization, based on Indigenous feedback, but they do test every mushroom/product before packaging.
    - Tests are for the content of psilocybin analyte (milligrams (mg) of analyte per gram of whole mushroom), this is put on the label of the individually-packaged product. (Individual serving not to exceed 25mg).
    - Dosage is determined by facilitator in a client-centered way (i.e., with client input). There is no minimum dosage, but the maximum dosage is 50 mg/session.
    - Oregon created a dosage and duration schedule indicating the minimum amount of time a client must stay at the center for a particular dose (can be longer, but no less). Also created guidance around client/facilitator ratio per dose.
    - These are all public health and safety minimums, not best practices per se.
- Stressed to make clear that regulations are necessary not from a drug enforcement perspective, but from a public safety perspective (e.g., potential for abuse in a vulnerable state, regulated sourcing of mushrooms ensures no adulterants, protections for facilitators as well).
- Check the Oregon Health Improvement Plan (Oregon Health Authority, accessed November 11, 2024) for more on steps toward equity.

Ben Everett, Senior Director of Medical Science and Health Outcomes, and Gretchen Shaub, Associate Director of State Government Affairs and Public Policy at Lykos Therapeutics, provided an overview of Lykos' efforts to gain MDMA approval from the U.S. Food and Drug Administration (FDA). Lykos has since let go of 75 percent of their staff since the US Food and Drug Administration (FDA) did not approve their New Drug Application for MDMA-assisted therapy for post-traumatic stress disorder (PTSD). This was presented to the task force at the June meeting, starting around 1:47:20 of the June video recording (Psychedelic Medicine Task Force, June 2024).

Tadd Johnson, JD, Professor Emeritus of the Department of American Indian Studies at the University of Minnesota Duluth, tribal attorney specializing in Native American policy and law, first Senior Director of American Indian Tribal Nations Relations at the University of Minnesota, Director of the Tribal Sovereignty Institute, and member of the Board of Trustees of the Udall Foundation presented to the working group on July 26, 2024. The following is a transcript of his presentation to the working group, lightly edited for clarity:

- Criminal scheme in the US was pretty much the fact pattern of Indian kills Indian in Indian Country was left to the tribes. In the 1980s, a murder case went to the Supreme Court of the United States (SCOTUS), and they gave jurisdiction to the tribes. Congress passed the Major Crimes Act; there are seven crimes that are prosecuted by the federal government, while misdemeanors are prosecuted by the tribes (Red Lake and Bois Forte). Until 1953 there was a movement afoot in the federal government called the Termination Policy, and 109 tribes were terminated. The members of these tribes lost Indian Health Services (HIS), access to the Bureau of Indian Affairs (BIA), and all the treaty promises were taken away. Public Law 8230 that took five states (MN, WI, OR, NE, and CA) and changed the criminal jurisdiction scheme from the way it was (Red Lake was the exception in Minnesota, with major crimes going to the federal government). The states were always excluded

from federal-tribal relations, but then state criminal laws were suddenly changed. Next, the Nelson Act in Minnesota wanted to get inside the Tribal nations to get timber. Some tribal members took allotments and would declare the rest of the reservation surplus land. Most tribal nations in Minnesota were under this Act, with the exception of Red Lake, which is one big solid chunk of Indian land. Timber companies came in and took all the timber and then sold the land to white folks. Counties took over parts, the federal government also took parts of the land, resulting in a patchwork quilt of ownership. Non-Indians in these areas wanted the protections of the state, so the way that Public Law 280 reads, tribes can claim concurrent jurisdiction with the state. The other nine tribes (outside of Red Lake and Bois Forte) are still done by the counties. There is also a civil part that confused a lot of people. What the state thought it meant in the late 1970s was that the state could regulate civil members on tribal lands. However, SCOTUS said that tribes had civil regulatory matters, which is how gaming started. When it comes to regulating this stuff, Public Law 280 says tribes have the right to regulate matters on their reservation. I don't know how this [psychedelic medicine] is going to be done in the state. There will be compacts (similar to the gaming compacts that have existed since the 1990s), probably.

- The task force member with experience working in public health policy asked if people could go into a shop and buy legal cannabis on the White Earth reservation and that falls under Public Law 280. Tadd's response was that that would be the argument of the tribes, because they have civil regulatory authority on their lands. This has worked out in other areas, like Indian gaming, where the tribes worked out sales tax agreements with the state. It's easier to have an agreement than go to court. I think you could probably get assistance from the BIA, potentially the US attorney's office from their folks who specialize in Indian law.
- The Attorney General's designee asked about another specific aspect of tribal law, which is religious use. He noted that Minnesota is dealing with potential legal challenges around Schedule I drugs. Under RFRA, SCOTUS has said that organizations like the Native American Church can use some drugs completely outside the normal legal boundaries. Tadd's response was that it had to do with the sacramental use of peyote. Went to SCOTUS. Had to be a compelling government interest test if you wanted to take away religious freedom. SCOTUS made it very difficult to take away religious freedom rights. Used the rational basis test for this, so a state/the federal government can take away religious freedom rights without showing compelling government interest. RFRA tried to make it more difficult to take away those rights. Decided each state could look at a religious freedom right and decide whether to impose strict scrutiny or rational basis. There's a very strong religious freedom clause in the state constitution, which means Minnesota has a strict scrutiny test, similar to the federal one. Other states do not necessarily have that. Hard to judge when something falls into the religious freedom category if you are not familiar with the religion.

Brandon Alkire, JD, tribal lawyer from MIAC provided further support on questions surrounding Tribal Law. Chairperson Nielson and Dakota Tribe representative Guthrie Capossela met with Brandon Alkire to discuss additional legal questions around Public Law 280 (PL 280) and Tribal Sovereignty with respect to the task force's legislative charge. The following are portions of an email that was sent as a follow up to this meeting, with some suggestions for the task force:

- "I have also included the relevant federal law(s) language that are referenced in both the statute and identified by your team (i.e. Native American Freedom of Religion Act [American Indian Religious Freedom Act; AIRFA]). I believe that the language is crucial to both creating the lens your team could use and for the justification for any recommendations. I also believe that this could guide your team in addressing any federal-state law conflicts, which is one of your duties.

- Federal law, policy, and regulation of psychedelic medicine
    - Focus
        - Retaining state autonomy without federal law conflict
        - Methods for resolving conflicts including.
            - Seeking administrative exception(s) to Federal Controlled Substance Act
            - Seeking a Judicial exemption
            - Petitioning US Attorney General to establish a research program
            - Using FDA expanded access program
            - Using the federal Right to [Try] Act
- "The Lens that could guide your team when making recommendations is pretty straight forward and fairly simple. Here are some guided questions that I would ask:
    - 1. Does this meet any Native American Religious Freedom Act [American Indian Religious Freedom Act; AIRFA] elements?
        - If so, justification for your recommendations should be stated clearly on how they would meet this recommendation(s). I.e., showing a long-standing (both historic and current) practice(s) both national and regional.
        - 2. Does your recommendation for decriminalization of psychedelic medication include use for people suffering from terminal illness to which no other treatment has been identified (Federal Right to Try Act)?
        - 3. Does your recommendation for psychedelic medication or use address a public health or safety need (21 U.S.C. § 822(d)?
        - 4. Does your recommendation for decriminalization of psychedelic medication include a research component (21 U.S.C. § 872(e)?
            - If so, I am certain that an IRB or other documentation would be required."
- "It would appear that your question on PL 280 would and any other potential state-federal law conflict could be address by simply requesting a waiver from the US Attorney General. The purpose for the waiver, and the applicability of law, would hinge on the basis for your request for waiver (see items 1-4 above)."

Chairperson Nielson met with a consultant familiar with data collection and public health policy that asked to remain anonymous, based on where they work, to discuss data collection options and mitigating risks to privacy while allowing for intentional data collection that helps track outcomes and public safety. They mentioned a project that researchers in Oregon will be conducting through Oregon Health and Sciences University (OHSU), called the Open Psychedelic Evaluation Nexis (OPEN, accessed November 11, 2024). Also highlighted a recent report released by the National Academies about the public health impacts of cannabis regulations over the years (National Academies of Science, Engineering, and Medicine, 2024), as a comprehensive report on mistakes made and lesson learned, hopefully not to be repeated with psychedelic medicines.

Chairperson Nielson consulted with a cannabis and Schedule I drug policy expert that asked to remain anonymous, based on where they work. A summary of their discussion follows.

- Consulted about federal oversight and lessons learned from state-level data collection for medical programs with Schedule I drugs, like cannabis. Referenced the US Department of Health and Human Services (HHS) recommendation to the Drug Enforcement Agency (DEA) to reschedule cannabis to Schedule III. That recommendation was informed by data from states, but complete epidemiological reports/surveys from only two states were cited: Maryland and Minnesota. Thus, those data

collection plans appear to be a good template for being useful to inform future federal policy considerations in the longer term. Discussed that states can decide and write into law what level of data they will allow to be shared to outside entities, with the exception that a federal subpoena likely needs to be complied with.

- Also discussed risk to prescribers who engage with psychedelic medicine services, and some parameters about which federal agency has jurisdiction over what, such as state regulated supplies, supplies from the gray market being sold as food, supplies being marketed for unapproved medical uses, and what would cross a threshold for prescribers losing a state or federal registration or license under a state program, based on lessons learned from medical cannabis. Prescribers and physicians only had their DEA registrations revoked, or state licenses lost due to other issues where a crime or malpractice was being committed, but otherwise if operating under state law and not prescribing, recommendations should not put prescribers at risk, based on current federal policies. However, a lot of this was outlined for cannabis initially with the Cole Memorandum, in effect from 2013 through 2018 (and adhered to thereafter), and through the Rohrabacher - Farr appropriations amendment which prevented the US Department of Justice (DOJ) from prosecuting violations of federal law which comply with state medical cannabis programs. A similar type of memorandum or appropriations amendment has not been created for psychedelic medicines.

Charlene Briner, Interim Director, Office of Cannabis Management (OCM), and Sophie Leininger, Director of Government Relations, OCM. Chairperson Nielson met with the OCM staff regarding whether they would be able to house such a division under their department. A summary of the discussion follows.

- The task force has discussed whether OCM would be an appropriate home for future work for psychedelic medicines, whether it be research, a clinical program, or adult-regulated use, based on the fact that Colorado combined their efforts under the Natural Medicine division, however the staff at OCM cautioned that the Colorado program has been up and running with the appropriate infrastructure for well over a decade, and the Minnesota program is simply not sufficiently resourced to take on another division under their office.
- OCM is not necessarily opposed to further discussions about what the task force is talking about or programs that might come out of the report and/or future legislation but would need more details and specifics before making any definite policy recommendations on behalf of the office. They did emphasize that the office as it stands does not have the capacity or resources to take on the additional project in the foreseeable future.

Lieutenant Diane M. Goldstein (Ret.), Executive Director, Law Enforcement Action Partnership (Law Enforcement Action Partnership, accessed November 11, 2024) was consulted with by Chairperson Nielson to discuss the position of law enforcement on psychedelic medicines. This group should be consulted in connecting resources for law enforcement, not only for first responder training in cities and states that broaden access to psychedelic medicines, but also to connect around opportunities for healing job-related PTSD for first responders. She shared a video of Sarko Gergerian, a lieutenant and psychotherapist in the Winthrop, Massachusetts Police Department, who believes MDMA and other psychedelics could be game-changing tools for treatment-resistant PTSD (World Science Festival, September 2022). She also recommended the recent RAND report, mentioned in other sections of this report, for best practices moving forward to regulate psychedelic medicines and alternatives to drug prohibition (RAND, June 2024). This meeting happened on April 25, 2024, and was not recorded.

Allison Hoots, Esq, is the founder and principal attorney of Hoots Law Practice PLLC and has been an attorney since 2011. She is licensed to practice law in: New York, District of Columbia, and Pennsylvania. Chairperson Jessica Nielson, Vice Chairperson Bennett Hartz, and Working Group Chair Paula DeSanto met with Ms. Hoots on August 8, 2024, to discuss psychedelic medicine churches trying to operate under the Religious Freedom and Registration Act (RFRA). Ms. Hoots has developed a comprehensive set of legal guidelines for churches that use psychedelic medicines as their sacraments, and best practices to ensure legal protections under RFRA (Chacruna and Hoots, 2021), and how Minnesota religious protection laws intersect with federal laws under RFRA. This meeting was not recorded.

Appendix F: Personal anecdotes

Anecdotes from task force members

Chairperson and member with demonstrated experience in the medical administration of psychedelic medicine: Jessica L. Nielson, PhD.

My relationship with psychedelic medicines spans multiple decades, and multiple domains. From my early days in high school and college experimenting recreationally with psychedelic medicines, to developing a transformative spiritual practice with psilocybin mushrooms during the tail end of my first marriage and PhD training in neuroscience. As my experiential knowledge of psychedelics began to mature, so did my scientific understanding of how our brains process trauma and disconnection. My path converged with the experiential, spiritual, and scientific knowledge necessary to dive into the world of psychedelic advocacy.

My first experience was with LSD when I was 15 years old. I wasn't yet old enough to truly understand this experience, beyond the "trippy" visuals, yet I do recall having pretty intense emotional experiences that I can still recall with a deeply felt sense, even 29 years later. When I went to college, I was introduced to MDMA and "magic mushrooms" (also known as psilocybin) through being a part of the rave culture, experimenting with music, mind-altering drugs, and ecstatic dancing. While these experiences were predominantly recreational in nature, they were transformative to my social development. As I started to focus more on my education mid-way through college, I stepped away from doing psychedelic medicines. Partly to focus on school, partly due to a no-drug policy from my first husband. I won't go into the details of my failed first marriage, suffice it to say psychedelic medicines pulled me out of bad situation and gave me the courage and strength to step out onto my own and become the person I am today. Following a journey to Peru in 2010, taking ayahuasca with a group of US war veterans and other people seeking alternative forms of healing, I became connected with the Multidisciplinary Association of Psychedelic Studies (MAPS) and began an academic study to confirm what I witnessed in Peru; that experiences like ayahuasca could help people suffering from PTSD. Two relevant peer-reviewed academic publications include Nielson & Megler, 2014 and Nielson et al., 2021. More recently I conducted a pilot clinical trial with psilocybin (National Library of Medicine, June 2024) at the University of Minnesota to try and dive deeper into the science of psychedelics and contribute to our understanding (Swanson, et. al., 2024) of how they induce such profound experiences in our brains (MAPS, 2023). As a neuroscientist, I recognize their profound impact on how the brain functions, making them powerful tools for understanding how much potential our brains have. The fact that we now know that psychedelic medicines open up functions in the brain that makes it easier to change (e.g., neuroplasticity), there is real promise that they can help people heal and move towards wellness and a better quality of life. I discuss this all in more detail in a three-part educational video (Psychedelic Society of Minnesota, October 2024) I put together through the Psychedelic Society of Minnesota.

It has been a deep honor and privilege to chair this Task Force, as psychedelic medicines have been an integral part of not only my personal and spiritual development, but also my professional career. I hope that this report can contribute to our government helping to foster more ways to access healing through psychedelic medicines. Trusting in the ancient wisdom these medicines hold, respecting and honoring the cultures that have stewarded that knowledge and practices for millennia, and supporting the modern and ongoing efforts to integrate them

respectfully and purposefully with healthcare systems that aim to help patients with deep suffering finally find relief.

Representative for patients with treatment-resistant mental health condition(s), including post-traumatic stress disorder: Kit D. O'Neill

To preface, I'm extremely thankful to be involved in this task force, and I'm incredibly amazed by the expertise and volume of work performed by my fellow members on this force. While I may not have professional expertise in this field, I hope that my lived experiences can help shed some light on the current state of treatment available to other Minnesotans with treatment-resistant depression or other mental health conditions and what it means to us have a new avenue of treatment opening up.

My experience with mental health has always been a challenging one. I have dealt with depression since I was quite young. In fact, I remember having my first suicidal thoughts at age 11. I was lucky enough to have a supportive family, and I was able to get medical help within the first couple years of symptoms emerging. I started therapy and saw a psychiatrist as a young teen. I've been on various classes of medications and tried several different therapies over the years. I've had several periods of severe depression requiring hospitalization for my own safety. I've been lucky enough to still finish high school with honors, though it was extremely challenging. Overall, the various therapies and over a dozen medication trials have led me to reach a state of being just functional enough to keep going. I shelved so many of my passions and hobbies in favor of sleeping and trying to avoid my dark thinking patterns. I can't remember a time I haven't had intrusive suicidal thoughts every couple of hours, or felt exhausted at the idea of waking up another day. I've since been involved with several doctors trying various cocktails of medications off-label, involved in studies on novel drugs, and most recently I've received regular applications of electroconvulsive therapy (ETC) as a last-resort option for my depression. For the first time in 15 years, I felt relief from the depression, and started to feel like a lighter, more positive and energetic version of myself. I felt a bit more excited for the world again. Stressors that previously triggered depressive episodes or panic attacks seemed manageable, and I felt I could speak more openly about my emotions. ETC is a last-resort option for a reason; each procedure itself is extremely expensive, requires full anesthesia, entire days of recovery, and numerous sessions to produce symptom improvement. For myself, it also results in episodic memory loss. I've forgotten reading entire books just a month after reading them, and I've forgotten meeting several people and places I've visited. Unfortunately, the positive effects of ECT have shown to only be temporary for me and tends to wear off just a couple weeks after each burst of treatments. I felt like I was allowed to touch wellness, only to have it torn away again. Eventually, it simply became too expensive of a procedure for me to justify the temporary relief from my depression.

I've been interested in new medications and studies regarding depression, particularly treatments that go beyond the traditional model of treatment I've already experienced. I want to preface that I've never been interested in psychedelics or state-altering drugs before I read about their use in treatment-resistant depression. It was Dr. Jessica Nielson's work with the University of Minnesota and their calls for volunteer recruitment that introduced me to the concept of psilocybin as a potential treatment option. I reached out to my community and discussed the concept with my psychiatrist; I wanted to see if trying natural psilocybin-containing mushrooms might help me with my depression. I read several studies and books on the subject and found that growing my own supply would be the easiest, most affordable and safest route of obtaining the mushrooms. With guidance from peers and use of the Fireside app (an app offering live support and integration for those undergoing a

psychedelic experience) I was able to experience my first dose. I took a small amount, and I was soon able to feel the same effects as when I had symptom relief after ECT. I felt light, like a fog had lifted and I could think clearly and see the world for what it was, not seeing the world as a threat or impending gloom. I didn't feel the chronic shame anymore, and I felt I could fully appreciate my surroundings and see the soul of the world. I felt hope and interconnection, and that I could be present with my whole self. Even after the effects had worn off, for several days I felt like I did as a kid again, and felt stressors could roll off of me and that my life was worth living, and I didn't dread waking up the next day. While I can't consider myself fully recovered, I've found that the combination of low-dose psychedelic mushrooms with integrative therapy to have been one of the biggest sources of relief from my depression. I've found in subsequent doses that I've been experiencing far less suicidal thinking and more motivation to explore my interests, and I feel more confident with my life. I've felt relief lasting longer than I've felt with any medication or ECT thus far, and it's been affordable to boot.

While I am young, my story of fighting against my depression and facing poor results for years isn't unique. I've heard similar accounts from dozens of others, young and old who feel stuck with their current options. Depression is a challenging disease with many unique facets for each individual, but the feeling of helplessness after trying treatment after treatment is far from rare. I hope that others get to experience the same level of relief and hope by being able to try these medicines in safe and supportive settings. Minnesota has a proud history of uplifting those who are struggling with their health, and it would be unfair to overlook those with conditions of the mind just because they are less visible. I hear the struggles of those who've tried everything and have nowhere else to look. Even if the use of these medicines become just a new tool, any advancement in today's treatments for mental health conditions will save numerous lives and lead to further advancements. I hope my experience sheds some light for those distanced from the current reality of those with mental health conditions, and that others can see themselves in my story. I hope you will support this legislation and help uplift those with nowhere else to turn.

Representative for patients with treatment-resistant mental health condition(s), including post-traumatic stress disorder: Adam Tomczik

I am Adam Tomczik, Governor Tim Walz appointed me to serve on the Psychedelic Medicine Task Force as a representative for patients with treatment-resistant mental health conditions. My diagnoses are complex post-traumatic stress disorder, major depression, and generalized anxiety disorder. I came to ketamine-assisted psychotherapy in early 2023 as the final option before suicide. I was drinking alcohol daily and I suffered from intrusive and near-constat suicidal thoughts. Thankfully, ketamine-assisted psychotherapy gave me short-term reprieve from major depression and from suicidal ideation. But more importantly, ketamine and the attendant psychotherapy granted my brain more neuroplasticity to end unhealthy habits and to start healthy habits. After six ketamine sessions, I quit alcohol completely. After a year of treatment, I was finally able to successfully address the complex childhood trauma that led to many dangerously maladaptive modes of thinking and acting. Now, I am finally out of that bottomless pit of depression, never-ending anxiety, and suicidal thoughts.

The doctor who prescribed my ketamine trained with other psychedelic medicines in the United States and the Netherlands, and she has repeatedly explained that scientific literature suggests that psilocybin likely would have been a more powerful tool for personal change due to the combination of major depression and substance abuse. The Psychedelic Medicine Task Force studied psilocybin, MDMA, and LSD for more than a year. The scientific data shows that psilocybin, MDMA, and LSD are some of the most effective tools available to help

people with major depression, post-traumatic stress disorder, generalized anxiety disorder, and substance abuse. The task force learned that psilocybin, MDMA, and LSD are remarkably safe for individual patients and their families, and these medicines pose little threat of harm to public safety. In my personal recovery efforts, I don't want to pull up the ladder behind me; I want to reach out my hand to help other Minnesotans climb from their own pits of depression, trauma disorders, anxiety, and substance abuse. Psychedelic-assisted therapy has changed my life for the better, and I will do everything I can to help make these tools available for other Minnesotans.

Representative for veterans with treatment-resistant mental health condition(s): Michael Tabor

I served as Marine for ten years including a combat deployment to Iraq. Upon returning to civilian life, I had some difficulty adjusting and began suffering from symptoms of post-traumatic stress and a sleep disorder. I was engaged in psychotherapy for many years but after some time I felt it wasn't helpful for managing the symptoms. Hypervigilance and insomnia were conditions that dominated everyday life. I started to become reclusive and stopped going places because of unpredictable anxiety attacks. I lived in constant worry and self-loathing that was clearly being driven by past trauma. Perhaps the worst of these conditions was anhedonia, an inability to experience joy and feelings of happiness. It was a miserable existence and although I had found some success with different therapies, I began to feel as if I were running out of solutions.

After several years of consideration, I decided to try ketamine assisted therapy (KAT). I was afraid it might provoke an anxious situation too severe to manage, but I had no other options. Eventually, I connected with a highly experienced psychedelic therapist and after building a solid sense of trust with her, I went through several medicine sessions. Although it was intense at times, it didn't provoke the anxiety I thought it might. I felt the KAT was helpful, but it didn't provide the total relief I was hoping for. It did, however, give me the confidence to attempt other more powerful psychedelic medicines. Months later, while listening to a podcast, I heard the story a veteran whose symptoms were identical to mine. After just one medicine session with psilocybin, he noticed a drastic improvement of his symptoms and I wondered if I might experience similar relief. I was gifted a small amount of mushrooms from a firefighter who used the medicine for his own past trauma. In the privacy of my own home, I created a safe and comfortable environment with a trustworthy companion to sit with me. I set intentions and engaged with the preparation and integration as I had for my previous sessions. It felt like a more natural experience, inducing radiant and colorful hallucinations. It was significantly more impactful than the ketamine and I was able to find the relief I was seeking.

Since then, I have stopped suffering from the anxiety attacks that plagued me almost daily. I have a renewed ability to experience happiness. I feel more motivated and purpose driven which has made me a better father and husband. In general, it has given me a more positive outlook and better quality of life. I would call it a life changing event, but I also put in the work and preparation needed to enable my recovery. I went from someone overwhelmed by post-traumatic stress to living in a state of well-being in a remarkably short amount of time. I've been able to maintain this for almost three years. I urge other veterans, first responders, and anyone suffering from past trauma to look into psychedelic medicine as a potential pathway to their own recovery.

Anecdotes and submitted testimonials from the public

Members of the task force surveyed their communities to bring the voice of the public to this report. Any analysis conducted on the responses to these surveys was done by the task force member conducting the survey. The following surveys and personal anecdotes begin to represent the wide range of public opinion surrounding psychedelic medicine.

Survey of licensed medical providers in Minnesota

A survey was sent to licensed medical providers in Minnesota to gauge opinions on the use of psilocybin by residents of Minnesota. Participants included professionals in both psychiatric and nonpsychiatric fields, encompassing a range of roles from MDs and DOs to nurse practitioners and physician assistants. Responders were anonymous.

Total responses:

- 43 surveys were returned in total.
- 31 respondents were from psychiatric providers.
- 12 respondents were from nonpsychiatric providers.

Responses from psychiatric providers:

- General sentiment: There was a blend of skepticism and cautious optimism regarding the effectiveness of psilocybin for patients unresponsive to conventional treatments for mental health conditions, including depression.
- Majority opinion: A strong preference for administering psilocybin under strict medical supervision rather than allowing adult regulated use.
- Reasons for medical oversight: Ensuring appropriate screening for medical conditions, potential drug interactions and intervening in case of emergency. Identifying patients with psychiatric diagnoses that could exacerbate under the influence of hallucinogens.
- Concerns: Several providers recounted instances where patients experienced negative effects from psychedelic trips, including temporary psychosis and increased anxiety.

Responses from nonpsychiatric providers:

- General sentiment: A mix of skepticism and cautious optimism, similar to their psychiatric counterparts, but with less direct experience of a patient who has used hallucinogens. The views of responders who have had limited experience in working with patients with psychiatric conditions were shaped by media reports and outcomes from clinical trials conducted by academic institutions.
- Majority opinion: Support for a medical model to protect patients from potential harms, emphasizing safety and oversight.

Conclusion:

Both groups showed a predilection towards a medical model for psilocybin use, underlining appropriate patient screening and oversight to mitigate risks.

Testimonial 1

I have a strong personal/professional commitment to harm reduction approaches to the care of individuals dealing with substance use disorders because I believe strongly in the importance of respect and autonomy in the development of healthy individuals and communities. The pervasive and systemic harms that individuals and communities experience due to the criminalization of substance use are significant issues that I would love to see addressed in a realistic way, which to my way of thinking must start from the creation of a safe legal supply of these substances for recreational and clinical use. I believe there is good clinical evidence that a focus on quality of life over abstinence in the treatment of substance use disorders is an approach that will better serve the well-being of individuals dealing with substance use disorders. I believe that communities have been harmed from the myopic focus on the black and grey market for (currently) illicit substances that would be better directed to attempting to address more serious crimes. Most vitally, I think that we have missed out on decades of research and treatment using these medications. I absolutely believe that there are people who have suffered and even died sooner than they should have because we did not allow for a study of and use of these medications sooner.

If I take the question very literally, and very personally, the answer is that it makes me angry. It makes me angry that this conversation has taken this long to get here, it makes me angry that we don't simply adopt the same way of thinking as we do about alcohol, it makes me angry that the broader tone of the conversation validates and encourages biases against people – including me.

For all intents and purposes, I'm a second-generation hippy. I have family who were Deadheads. They funded their lifestyle between a combination of working and growing and selling cannabis (and other substances) in the 70s. For over a decade the use of psilocybin, LSD, and MDMA (and other psychedelics) was a normal part of my life, much like some family members at that age. What strikes me about this is that these family members have always held jobs, made good money my whole life, were present part of my life, maintained their marriages to this day, and never experienced any legal issues.

We are productive, peaceful members of our communities and yet we would be judged very harshly by many should we be open about our relationship with/history of/preference for substance use. Yet the times that I've been able to access these substances have been very positive experiences for me without any known medical, legal, or interpersonal complications worthy of deep concern. When I got older and realized that I was no longer comfortable assuming the risks of psychedelic use, I stopped. The risks I am concerned about are not related to substance use itself, but the legal and personal risks that come from accessing the grey and black markets. So, despite knowing that pain management, interpersonal relationships, and quality of life would all be better if I could access psychedelics, I stepped away from them around 2012.

These substances are used by thousands of people daily. I don't want to ignore or minimize the fact that some have been harmed by their use of these substances. Even more have been harmed because of the criminalization of these substances, including people that were close to me. I've known people who have been assaulted, very seriously, while attempting to access an unsafe, illegal supply of psychedelics. I've known people who have lost relationships, time with family, and dreams because of their entanglement with the legal system due to their psychedelic use. I can only assume that you've worked with many clients who have experienced more harm from the criminal justice system than their substance use. I know I have, and even before I started

my graduate program, I knew that I had to remove that kind of risk from my life. That makes me angry. I'm given permission to go to a liquor store or recreational cannabis store, so why not let me decide if I want to use psilocybin or LSD or MDMA or anything else? Why not let my healthcare provider provide these medications and interventions if it is appropriate to my care? Haven't we shown over the last 50 years that prohibition of these substances is no more helpful or necessary than the prohibition of alcohol?

How do I feel about the legalization or clinical use of psilocybin, LSD, MDMA? I feel like it is 50 plus years overdue. I feel like people are suffering and dying because of prohibition and the government should care more about that then they seem to. I feel like the funding and human capitol that has been invested in policing the black and grey markets has been a criminal waste of resources that has done far more harm than good.

Testimonial 2

American military veterans are experienced at looking after each other, especially in the face of destructive U.S. government (and profit-maximizing contractors) failure to keeping faith with our warriors who sacrifice so much. We veterans pay attention to detail, adapt, overcome, and never leave a shipmate behind. Prohibiting veterans from cultivating mushrooms will not stop grown-ass adult veterans from being who we are.

Support us, don't criminalize us. Otherwise, stop using us as a prop in your manipulative political campaigns because we won't be your allies.

-Anonymous veteran, Rochester, MN

Testimonials gathered from psychedelic community members

Chairperson Nielson also is the president of a community organization and 501(c)(3) nonprofit, the Psychedelic Society of Minnesota. A call for testimonials was sent out to the community through newsletters and social media between October 9, 2024, until November 17, 2024:

In this form, according to Minnesota Data Practices Act around informed consent for data collection and use, we have explicitly described that submitted testimonials will be included in the final report that will be accessible to the public, with options to consent to a full quote, a summary/theme aggregated with other responses, or to share only and not include in the report. Survey takers also had the option to include identifying information (e.g., name, voting district) that they wished to provide, however such identifying information for name and voting district are not included with each quote is not shared in this report. Voting districts mentioned include Minnesota's Second, Fifth, and Sixth congressional districts, District 63, the cities of Minneapolis and St. Paul, and Hennepin, Ramsey, and Dakota counties.

The quotes below are those where survey respondents provided explicit consent to be quoted:

Psychedelic community member #1

"Microdosing magic mushrooms has done more for my depression, anxiety, and PTSD, than all other medications I've tried combined, not to mention they all had side effects and the mushrooms do not. They've allowed me to function and even feel like I'm starting to thrive after 25 years of debilitating mental health

struggle. I don't feel drugged at all when on a tiny dose- I just feel like my true self without all the "noise". People deserve to not only feel better but heal, In the least invasive ways possible."

Psychedelic community member #2

"LSD, psilocybin, and MDMA have all played a tremendous role in my development as a person and willingness to survive. I'll primarily speak to LSD and psilocybin though as those two have had the greatest and lasting impact. I credit LSD to my personal development as a youth and aiding me into adulthood, helping me make sense of the world around me and where I fit into it. LSD challenged my beliefs about myself and allowed me space to really dive into who I was and wanted to be in this world, something I did not receive elsewhere. There existed an absence of personal responsibility and internal power, both of which LSD aided me in discovering in myself, truly long walks at night on LSD have not only been some of the most fun experiences but also transformative in my coming of age. Psilocybin holds closest to my heart, in part by what they represent; nature, community, generosity, and curiosity but also by the vibrant personality they bring into my life. At times I would consider them my second parents, my closest friends, or even my partner. Being a living being they have also impacted my life outside of taking them, rather helping me in my journey through their outward expression of life. In honesty taking psilocybin mushrooms doesn't even come close to the impact of cultivating and sharing them, that is where the true elegance of their impact shines for me. I could go the rest of my life without eating mushrooms, I could not without cultivating and sharing my relationship with them. The benefits of mushrooms extends beyond the chemical, it exists in between the lines of drug and friend, their impact for me can only be seen through the colors and expressions of their movements in life, their smells and tastes, their responsiveness to conversation, and their challenges of learning to speak with them. Eating them is but a tiny sliver in what they have to offer me, their connection requires communal gathering, it requires getting your hand dirty in the soil they reside in, it requires conversation and attentive ears. I would not be alive if was not for cultivating these very extraordinary fungi. Caging them in a system that doesn't even take them time to get to know them on an interpersonal level is not only disrespectful to them but disrespectful to world in which they come from, consider if you care about their wellbeing, I know I do."

Psychedelic community member #3

"I was in the midst of constant depression and anxiety, constantly self-medicating with alcohol. This began at a relatively young age, and continued to build throughout my 20's and early 30's to the point where it was costing me any meaningful relationship and having detrimental effects on my physical and mental health. The Covid lockdowns led to me being furloughed from my job, exacerbating the disconnection from meaningful connections, and once George Floyd was murdered, I was nearing a full-blown existential meltdown. Two days after that happened, I was asked by a close friend to join him and another to take a psychedelic trip together. I had never taken a high dose of psychedelics, only trying a small dose a few times while in nature. One of the gentlemen had experience and been receiving coaching via the underground, and setup the evening with consideration to what we were doing that night. He provided 3g of psilocybin and a 125mg MDMA pill, gave basic instructions as to how to work with what comes up, and what to expect would happen. All three of us went into it together around 9pm. To this day I cannot explain what happened, but I know something in my heart, mind, and soul was changed. I had a transformative experience, felt immediately the next day and have been experiencing it ever since. It has been like a light switch, which I had forgotten about at sometime in my youth due to a series of traumatic abuses and experiences, was flipped back on. I felt connected to myself, my

life, and the people around me again for the first time in my adult life. Since that evening, I have stopped drinking to cope, changed careers, returned to grad school where I am about to graduate with a 4.0GPA to become a therapist, and engaged in a long term relationship with a wonderful partner in a way that I never imagined before. Without that evening, I cannot imagine where I would be today, but I'm confident that my trajectory towards rock bottom would have continued until I was hurt, or potentially worse. Working with those medicines saved my life that night."

Psychedelic community member #4

"Psilocybin has changed my life after only one session. I had been a moderate drinker for most of my life and now I rarely choose to have a drink. This was not my intention for the session but a happy outcome for me and the health of my body."

Psychedelic community member #5

"My journey with psychedelic medicines began 8 years ago when I was 26 years old, starting with psilocybin and within 2 years of identifying the powerful healing qualities of mushrooms, I decided to also explore with LSD and MDMA. Thankfully all of my experiences with psychedelics have felt protected and contained within community, twice in the form of traditional fire ceremonies, and otherwise mostly what would be considered "recreational" communions with these medicines. Fast forward to present day, I have worked as a psychedelic assisted psychotherapist in St. Paul for the past 5 years with Ketamine, which I have also recognized as a potent tool enhancing trauma resolution work where I have specialized in supporting survivors of religious trauma and spiritual abuse. With all of my years of clinical practice working with Ketamine in a clinical container, all of which I have truly cherished, I cannot deny my profound gratitude that I have been able to access safe medicines and transcend in protected, intentional settings outside of the clinical container for my personal healing trajectory. ~ I will forever recall one sacred communion with magic mushrooms surrounded by girlfriends at a cabin when I experienced a mystical vision of receiving my "calling." Lake Mille Lacs literally called me towards her and with each step I took more messages and downloads came for what I understood would be my life's work, or at least my next steps to align with my life's purpose. I share this testimony as an LICSW in the state of Minnesota to bring light to the reality that these medicines hold potential to save lives and align spirits and heal emotional, relational, and spiritual pain in way that trauma resolution modalities within the clinical sphere of mental health care simply cannot compete. Better is possible and creating protected pathways for humans to access psychedelic medicines such as psilocybin, LSD, and MDMA has the potential to heal in ways our clinical systems and medical industries have historically and at present fallen short."

Psychedelic Community Member #6

"I am 69 years old. I have had chronic treatment resistant depression my whole adult life, and quite possibly as a child. After 25 years of medications that provided no results and awful side effects, I stopped taking antidepressants all together. In 2018, at the age of 63, psilocybin provided the first medicinal relief from my depression. The neuroplasticity that I experienced gave me the ability to begin healing. In 2020 I tried an antidepressant again, and I finally received the expected benefit of that medication. I credit that surprising outcome to the neuroplasticity which the psilocybin had provided. I am currently taking a standard

antidepressant and occasional ketamine infusions. But it was the psilocybin that first made healing possible for me."

Psychedelic community member # 7

"As a mother, addiction counselor, and wellness consultant who has a high ACE score and history of traumatic abuse as a child, I have been blessed to have found psilocybin. Following the COVID lockdown period I was triggered to have a recurrence of CPTSD symptoms due to isolation, abandonment, and the negative, hopeless outlook that many portrayed during the crisis. I had sought traditional talk therapy and medications for depression and anxiety but had little improvement in my daily symptoms. In 2022, I came across information about psilocybin being effective for CPTSD and wanted to combat a growing habit of cannabis use. I studied the process and its effects and sought guidance for a psilocybin journey. I planned my intentions when I found a reputable source and trustworthy guide. I found the experience to be effective in helping me stop using cannabis and had a dramatic reduction in depression/anxiety symptoms. The effects were profoundly healing, allowing me to develop a sense of trust in my capabilities as a mother, wife, and professional that I was not able to attain throughout a lifetime of therapy and educating myself on mental health due to CPTSD. I had long believed I would always suffer from the abuse of my parents, having had my father attempt to end my life when I was three being raised by alcoholics and sex abusers, and having to raise my children without a healthy family unit. Having had psilocybin available I am more confident in my ability to overcome challenges in the future and grateful to have an effective way of rebuilding hope and faith in my ability to be resilient throughout the rest of my life. I have had 2 guided journeys to go deep into my feelings and beliefs about myself that have been most challenging for me to live a happy life and have addressed my fears of being abandoned. I have found improvements in vocalizing my feelings without being overwhelmed, a reduction in fear of abandonment, and ability to speak for myself without worrying about being rejected by others. I am a strong advocate for others who suffer from having a high ACE score, CPTSD and PTSD to discuss the benefits of magic mushrooms on a microdose schedule or experiencing a medium-high dose journey with guidance and support."

Psychedelic Community Member #8:

"My experiences are strictly psilocybin. I have been an addict my whole life and had always had questions about my faith in life. When I was younger I had taken them a handful of times but the experiences were only goofy colorful, but also mixed with alcohol and others at times. 3+ years ago I tried them again but only used mushrooms no other drugs or prescriptions involved. At one point I ended up laying back and just let it do it's course. My eyes weeping for minutes! Afterwards I was opened up to what I understand to be was my own cross. All the sudden I got this surge of knowledge of why Jesus died on the cross and an understanding that we go on after death! It put love into my heart that can never be broken by anyone. Being the addict I am I continued to try to get back to what it showed me that night. Had a few amazing experiences and then ate some powerful mushrooms that was probably twice the dosage of my usual. God showed up that night and I had an ego death that it felt like I truly died for a second and was chained up stretched out into a hole of nothingness. I had to give up everything that I ever cared about at that moment and I had to give my life up. Now this happened a couple times and then I had a handful of other trips that taught me moderation, the understanding to all life and all connected as one. It has been the backbone to my faith in God and Jesus."

Psychedelic Community Member #9:

“I’ll keep this short and sweet. I got diagnosed with depression at the age of 12 and from the ages of 12 to 29 I struggled with very severe suicidal depression which resulted in opiate addiction with the end goal of not being alive. I dabbled with mushrooms through those years but it was at the age of about 24 that I started using them as a medicine to learn about myself and how I perceive the world. Fast forward to age 28 I had some experiences with psychedelic mushrooms that really opened my mind to loving and caring about myself and I remember one exact moment when the real work felt “complete”. During my trips I would get very concerned that my friends were going to kill themselves when they went to the bathroom or left the room during a trip. What I learned was the amount of care I have for them is the same amount of care I should have for myself which didn’t cure my suicidal ideation and depression, but it planted the seed of how I should be thinking about myself in this world. Since then, I do not ever dream of taking myself away from this planet and it’s such a relief. I am now a business owner, a homeowner, and a loving member of society. I do not think I would be who I am today without the equation of psychedelics assisting my thoughts my thoughts. Psychedelics are not a miracle drug because the individual must put in work to achieve results but 100% believe that they can positively affect people’s lives for the betterment of themselves and society.”

Psychedelic Community Member #10:

“Psilocybin mushrooms directly led to me understanding my differences from normal humans and motivated me to obtain an Autism diagnosis. Continued microdosing helps to manage the depression. I remember snapping to a state where I felt content and I thought, "if this is all it took not to feel depressed anymore, why did I wait so long?" It is because it is illegal. It is because the best source I have is a [redacted] felon [redacted], who is someone I might not otherwise associate with.”

Psychedelic Community Member #11:

“As a licensed clinical social worker, I serve adults with severe mental health and substance use disorders linking Minnesotan residents to conventional forms of community mental health care and support. Moreover, I too have experienced persistent mental illness and addiction to alcohol and methamphetamine across my lifespan. Despite my personal engagement in behavioral healthcare and treatment, trials of prescription psychotropic medication, and exploring evidence-based interventions, I continued to struggle for years. Fortunately, psilocybin brought me relief from intractable substance use disorder, healing from the trauma associated with devastating loss, chronic illness, and profound hopelessness. This transformative experience with psilocybin as medicine has removed cravings, alleviated symptoms of depression and anxiety, enhanced cognitive functioning, leading to optimal health and well-being. As a result, my personal and professional ambition is to advance psychedelic medicine in the healing of mental health disorders with access and application to community mental health, harm reduction, and addiction recovery.”

Psychedelic Community Member #12:

“As a holistic psychologist I have seen personally and heard anecdotally from others about the beneficial impact of mushrooms, ayahuasca, DMT and MDMA. They are extremely powerful to help people get to deeper subconscious issues that keep them stuck in reactive patterns and help them release stuck beliefs from the "Default Mode Network" in the brain. Applied with intention, these psychedelic substances are truly medicine

and can expedite the therapeutic process and access realizations and insights that might otherwise not be recognized. I have seen people be helped with addiction, depression, anxiety, ADHD, and relational traumas."

Psychedelic Community Member #13:

"I have been quite experienced with psychedelics, over the past 4 decades. I find it interesting to note that I have attended three different Ayahuasca ceremonies, in three different countries, and it has ZERO effect on me. Same with 5-MeO-DMT. Wasn't on any pharma the years I tried those substances. My older sister has had similar ineffective experiences, including on DMT. So maybe a chemical/brain difference? However, the meds do seem to be helping with her ongoing mental health issues, despite not having, 'An experience.'"

Psychedelic Community Member #14:

"I've never abused drugs recreationally, not even in college. I was athletic, allegedly handsome, social, and exited the closet in my mid 20s. My endorphins and spirits were always naturally high. It seemed I'd left my childhood traumas behind. But that's not how life works, is it? [Section redacted due to highly detailed trauma history that could be identifiable.] I tried Prozac, but the doctors played dosage roulette as my emotions rode a rollercoaster of ups and downs. I quit that poison cold turkey, preferring my unaltered sadness to whatever Prozac offered. Coming down from Prozac was so excruciating I once searched my apartment for a gun to shoot myself though I've never owned one. I was hoping one was left behind by a previous tenant. That's what Prozac did to me. I tried St Johns Wort. I tried Sam-E. Nothing worked the way I wanted it to work and so I put on a happy face at the office and in public, but was the picture of depression at home alone. Finally in my early 60s, I learned about microdosing psilocybin. I started on low doses to figure out what worked best for me. I've been taking 20mg every third day for more than a year. That dosage was exactly what I was hoping for after the Prozac nightmare. My mood stabilized. Microdosing didn't cure my depression, but it made it so much easier to live with. I can't remember the last crying spell I had, but they used to be almost daily before microdosing. Psilocybin should be a legal substance and there should be a lot of research on it. It's ethically criminal that we who suffer with depression are left to figure this out on our own. It's time for our elected leaders to do something positive on this front despite big pharma's objections."

Psychedelic Community Member #15:

"It is truly impossible to express how profoundly psilocybin has changed my life. Having experienced my own versions of rock bottom mentally, emotionally, physically, and spiritually, psilocybin has held me in being guided back to myself. It wasn't until my introduction to psychedelic medicines that all of the other work I had done and healing modalities I had opened myself up to over my life clicked into place. Suddenly, I felt the tides of my life shift in a way that I knew would be impossible to go back from. If all the other modalities had worked to turn the handle and creak the door open, psilocybin brought me right to the threshold and urged me to step through. I struggled with GI issues my entire life, visiting my first specialist when I was 8 years old. Over the course of almost 20 years, I was on a quest to find the answers to what was wrong. I suffered from debilitating symptoms, including chronic constipation that at its worst lasted 16 days at a time without medical intervention. My system's dysfunction led to a full rectal prolapse when I was 20 years old, and many cases of hospitalization and evaluations for surgical intervention. My experience with Western medicine showed it to be extremely lacking in that it doesn't offer a holistic view to healing. It puts everything in boxes and separates our body from our mind, and leaves our spirit out entirely. I know how desperate I felt for healing, and every time I went to another specialist, it felt like a knife in my heart to hear that there was something wrong with me, my system didn't work, but they didn't know why. That only further contributed to the pain I was feeling physically, emotionally,

and mentally. Over so many years, to continue hearing invalidating things like “just take these medications daily for the rest of your life” or “it’s just the way your body works” or “we don’t know why” took an extreme toll. Nothing worked for my body that “didn’t work.” Psilocybin reconnected me to my body, and allowed me to start getting to the root causes of my physical symptoms. There is of course so much complexity to the way our experiences, environment, etc. impact our health. As one example, I came to understand how unprocessed and repressed trauma from multiple sexual assaults were manifesting in my GI issues. The toll trauma takes on all of our systems is immense - especially when it isn’t addressed. With psilocybin, so much that was once stuck finally started to move through me. Psychedelic medicines are woven into the shared tapestry of humanity, with different types having been utilized and revered since time immemorial. We cannot lose our reverence for what these allies have to offer us, not only individually, but at the collective level that extends past the present. Indigenous stewardship and guidance is essential to avoiding the commoditization and misuse of these medicines.”

Appendix G: Legal pathway definitions

Administrative exemption to the Controlled Substances Act

This is a pathway where a request is made to the Drug Enforcement Agency (DEA) for exemption to use a controlled substance for a specific use case. Several churches that use plant medicines as sacraments have been granted this under RFRA, including the Native American Church for peyote, two Brazilian based churches: Santo Daime and União do Vegetal (UDV) for ayahuasca, and more recently the Church of the Eagle and the Condor (CEC) based out of Arizona to use ayahuasca (technically a settlement after filing a case to sue the DEA and other federal agencies after sacraments were confiscated). CEC was the first exemption granted without having to go to trial with the DEA (as opposed to getting busted and needing to defend their religious protections, which is more a judicially created exemption), and the first Indigenous based church to be granted this exemption where the religious infrastructure was not based on syncretic Christians churches, as the other ones are. This has now set a precedent for other Indigenous groups in the US to request exemption (e.g., AIRFA for psilocybin on reservations for use in existing ceremonial contexts, however would likely be creating new ceremonies that use a broader range of plant medicines, such as psilocybin-containing mushrooms, as those are traditionally used in Mazatec cultures in Mexico and all around the world actually, but they were introduced to the foreigners from the United States through the Curandera Maria Sabina, from Oaxaca, Mexico). It should be noted that mushrooms are not part of the plant kingdom, and thus lumping them into the term “plant medicine” is not accurate, from a biological/botanical perspective. In fact, fungi are genetically closer to humans than they are to plants (Baldauf and Palmer, 1993).

1. Definition
    - Formally submitting a request to the DEA to reschedule/deschedule these three drugs or to be granted an exemption from the CSA to use them for a compelling reason.
2. Legality
    - Federally legal, if granted
3. Implementation options
    - Requesting formally that the DEA grant the state of Minnesota an exemption to the CSA to use psychedelic medicines for a state-regulated programs.
        - DEA is notorious for taking a long time to respond to such requests, as has been seen with churches requesting exemptions to use psychedelics for religious purposes, and some waiting up to eight years for a response.
            - Under Presidential Executive Order 13132 (Federal Register, August 1999) related to federalism (Clinton), federal agencies have to respond to requests from states within 120 days.
    - To the best of the task force’s knowledge (more legal research is needed), this has never been granted to a state, and mostly, if not solely, has only ever been granted for specific churches that use peyote (Native American Church) and ayahuasca (Santo Daime, UDV, CEC) as sacraments under religious freedom (AIRFA, RFRA, First Amendment to US and Minnesota Constitutions)
4. Regulatory frameworks/agencies

- Exemption requests may need to come from the Governor, the Commissioner of Health, the Attorney General, the Board of Pharmacy, Department of Agriculture, or another agency, depending on what it is being requested for.

- Could ask for an exemption to allow the use of specific Schedule I drugs to be allowed in state-regulated programs (under the 10th Amendment and anticommandeering doctrine, the state should have sovereignty to govern itself).
- Doing this is not likely to be successful, however it would be an important addition to the official legal record if the DEA denies the request.
    - This would give us standing to bring a case against the DEA and argue it before a judge (post-*Chevron* test), through a judicial exemption described in the next section.
    - Previous attempts have been used by Governor Ventura in Minnesota in 1999 related to growing hemp, reported in a *Star Tribune* article from 09/30/1990. The DEA ultimately rejected this request.
        - Additionally, several attempts explored in the state of Iowa (Drug Enforcement Administration, April 2024) for a variety of reasons related to medical cannabis.
        - More recently this was suggested from a bill (Minn. S.F. 1540 (2023) (Office of the Revisor of Statutes, February 14, 2023) introduced by task force member Senator Koran, related to medical cannabis, and also on the floor in this past 2024 legislative session relating to getting an exemption to the CSA for cannabis to protect the 2nd amendment rights of people using cannabis legally in the state (Minnesota Senate Media Services, May 2024).
            - Vice Chair Hartz has requested this information to see if a request has been made by the AG's office, and can confirm they have not, and any requests dating back to 1999 will not be obtainable due to statutes of limitation on state record keeping.
- Equity/access and justice considerations
- This could present conflicts related to people's engagement with state-regulated programs, related to federal benefits/employment, parental/custody issues.
- A path towards expunging drug records related to psychedelic medicines,
- Prioritizing the legacy market to become involved
- Priority access to services and licensing for Tribal nations (like they did with cannabis)
- Not restricting access to psychedelic medicines that may pose ADA issues related to age and disability discriminations.

5. Tribal consultation

- Federal exemptions that are statewide would protect against federal drug related enforcement on reservations for any programs they (Tribes) want to develop independently of the state, as is their sovereign right. Would also protect from enforcement under Public Law 280.

6. Veteran consultation
    - Partnering with VA for delivery and safety monitoring
7. Patient consultation
    - Partnering with community advocacy and patient groups
8. Drug supply

- With an exemption, there are more options. Pharmaceutical companies might be willing to supply if that was granted and the data collected could be used towards their new drug application to the FDA (usually a requirement when using someone's investigational product outside their own trials).
- Minnesota might also be able to source more psychedelic medicines within the state with such an exemption.

9. Data collection/monitoring
    - Standard rules around HIPAA should apply with a federal exemption. Best practices for confidentiality of identifiable data.
    - Tracking outcomes on public safety, diversion, public perception, manufacturing standards and quality control for psychedelic medicines made/used in state (detailed data collection and data sharing needed if using a pharmaceutical investigational product)

- Informed consent needed from people interacting with any system that is collecting data about people engaging with psychedelic medicines.

10. Consequences if law is violated

- Consequences for diversion if monitoring is required, with similar oversight as clinical trials. For example, churches using sacraments still have to keep thorough records of their supply chain of custody, and consequences could include:
    - Revocation of the exemption
    - Fines
    - Federal criminal prosecution
    - Revocation of other licenses if convicted of a crime.
- Consequences related to invoking the Anti-Commandeering Doctrine could result in extra financial burdens imposed by the federal government, such as the Spending Clause (Constitution Annotated, accessed November 11, 2024).

11. Medical and psychological safety/screening
    - Informed consent
    - Adverse event reporting
    - Mechanisms for handling unethical practices
12. Cost to implement
    - To be determined by the MN legislature
13. Minnesota state agencies with existing infrastructure/authority

- Attorney General (AG) or Governor's Office (GO) – needed to request the exemption
- Minnesota Department of Health (MDH)
    - Board of Pharmacy
    - Department of Human Services (DHS)

Judicial exemption to the Controlled Substances Act

When an exemption is granted through trial/litigation (see above about Santo Daime, UDV). Much of this is similar to the administrative exemption, except this step is only possible after first having the administrative request denied, thus giving the state standing to sue the federal agency that denied the request (e.g. the DEA). This is how advocates are trying to gain access to psilocybin for the terminally ill, under the Right to Try (RTT) Act and litigation against the DEA. See RTT section below for more details.

United States Attorney General creates national research program

As of report writing, to the best of our knowledge, only one program has been implemented under this legal pathway to establish methadone clinics in the US. This pathway was proposed by Shane Pennington, who has authored a white paper detailing how this could be implemented with psilocybin and creating state-federal partnerships. This is an interesting theory that has not yet been tested for psychedelic medicines (Pennington et al., 2024). There are some known issues related to barriers to access with how methadone came to become what it is today through this program (Yarmolinsky and Rettig, 1995), however this might be challenging to get the public to engage with, given the history of mistrust with the DOJ/DEA. These institutions would have final authority over this, rather than agencies responsible for monitoring health and safety (e.g., HHS or CDC), and the barriers to access that were created with this program for methadone (Yarmolinsky and Rettig, 1995). This would be a larger state-federal partnership, and a somewhat similar program was launched in Canada, specifically for British Columbia (Government of British Columbia, 2023), where certain drugs and amounts were decriminalized. This includes locations for use and plans for education and harm reduction, with an intentional data collection plan to monitor safety and outcomes (mostly for amphetamines and opiates, but also includes MDMA).

Chairperson Nielson consulted with several lawyers in the Policy and Advocacy division at the Multidisciplinary Association for Psychedelic Studies (MAPS), who provided us with an overview of this type of program. Several questions about this program were posed to the team at MAPS, and their analysis of this program and what could be possible are summarized below.

USC 21 872(3/e) allows the US AG to authorize a number of studies, mostly within its mandate to study drugs for a number of reasons, mostly in service to its enforcement/policing powers. If a state wanted to conduct research in this way, then the relevant state agencies would seek approval from the US AG. HHS can provide input/influence into the process, but likely could not stop it. Working with SAMHSA to collect data would require strict data privacy requirements for any research they were involved with, but would provide federal protections over data privacy, and is currently being explored to help Oregon's program through the Open Psychedelic Evaluation Nexus once data collection becomes mandatory in 2025 under SB303 (Oregon Health Authority, July 2024). The task force agrees that a federal partner other than DEA would be best to try and implement this program in Minnesota, however this may not be sufficient to convince pharmaceutical companies like Lykos or COMPASS to supply states with their investigational products for clinical/medical programs and might be more appropriate to seek out suppliers not based in the US. Below are detailed some relevant points to consider about the history and potential of utilizing this approach to petition the US AG to set up a research program under 21 U.S.C. § 872(e):

- Summary of the scope and limitation of 21 U.S.C. § 872(3)
    - A fairly broad scope. Under 872(a) there are a handful of defined categories of drug studies that the AG can authorize, most of them related to police/law enforcement (i.e., studies about how to measure the amount of drugs in a person’s system, how to prevent drug use, studies on where drugs originate, etc.). However, 872(e) opens the door to drug research, limited only by the AG’s discretion. If it is for research, the AG can essentially opt any person or entity out of drug laws.

- Based on the above description of this program, does this allow for a state-federal partnership for research/pilot studies, or treatment with a Schedule I drug?
- Mostly yes. 872(e) does not appear to make distinctions between Schedule I drugs and other drugs; the AG has the power to allow research of "a controlled substance" which likely captures every schedule of drug. While the statute does not specify about partnerships, the power to allow research would imply that any entity that wants to participate in research could, provided that the AG gives approval. Using it in the context of treatment would be a different legal analysis. A quick review of the statutes did not indicate that the AG can waive drug laws for treatment, only for research and studies and the specific areas described above related to police/law enforcement.
- Can HHS modify the policy (i.e. via rule making)?
- HHS does not appear to be able to restrict the AG's power to allow research on drugs. The agency can/does conduct its own research (largely through the FDA) but there doesn't appear to be an ability for them to limit other drug research that the AG allows pursuant to 872 (e). This tracks with what has been seen in drug scheduling, where HHS gives input but ultimately does not have the final say. The AG's authority overrides.
- Is there any federal legislation from the last approximately 10 years that has touched on this topic?
- Another use case of this program was not found, however that does not mean it has not simply because it could not be tracked down with the current report research and resources allotted. HHS has given drug-related input through the new two-part test for "currently accepted medical use," however it appears the courts have not been involved in this and the task force could not find any examples that HHS has disputed the AG's ability to authorize research pursuant to 872 (e).
- Interestingly, the cases that do exist seem to be related to data privacy. Texas sued about data collection overreaching HIPAA's requirement (Fierce Healthcare, September 2024). However, this is a slightly different situation where a state is trying to access data about state-specific crimes that federal law prohibits (breaching patient confidentiality), whereas in the situation related to accessing psychedelic medicines, a state would want to invoke federal protections of patient confidentiality for legal state activity (e.g. a state-regulated clinical program with Schedule I drugs) that is a federal crime.
- Definition. A formal request made to the US Attorney General to initiate a research program to study access and use of controlled substances.
- Legality
- Fully legal, however has only been implemented once for methadone in the 1970s.
- At the time of report writing, no other program besides for methadone could be found using this federal pathway.
- Implementation options. If granted by the US AG, this could be implemented at state-approved clinics to allow psychedelic medicine to be administered to patients.
- Regulatory frameworks/agencies
- Any clinic or facility that can store and dispense controlled substances, such as hospitals that have research pharmacies or any institution equipped to securely store Schedule I and II drugs, according to DEA parameters
- Clinics with appropriate medical equipment to monitor safety and adverse events
- Equity/access and justice considerations. Broaden inclusion criteria and settings for treatment.
- Tribal consultation
- If conducted through healthcare facilities, such as IHS, would be similar regulations for other federal research programs, like clinical trials.

- Other treatment settings that can be decided and regulated by Tribes.
- Veteran consultation. Ensuring veterans have access through the VA and negotiating with local VA hospitals about willingness to partake in this type of research program, which may have similar parameters as a federally approved clinical trial.
- Patient consultation. Engage with patient advocacy groups on priorities for access under this program.
- Drug supply. Unclear whether this supply would need to come from a pharmaceutical company with an IND (investigational new drug) from the FDA for their product, or if local resources could be used to grow or manufacture psychedelic medicines under this program.
- Data collection/monitoring. Would be protected under HIPAA and federal protections could be ensured with a certificate of confidentiality and data sharing agreements with the drug supplier.
- Consequences if law is violated
- Same risks for medical malpractice or drug diversion if rules and procedures are not followed.
- Fines if HIPAA is violated
- Medical and psychological safety/screening
- Informed consent
- Adverse event reporting
- Mechanisms for handling unethical practices
- Screening patients for contraindicated medications and health conditions
- Cost to implement. This depends on the clinical setting and whether the manufacturer of the investigational drug to be used has a purchase cost, or cultivation and/or manufacturing and testing costs if sourced locally within the state.
- Minnesota state agencies with existing infrastructure. MDH, DHS, Board of Pharmacy, AG.

Expanded access

- Definition. A special type of clinical trial (US Food and Drug Administration, accessed November 11, 2024) created by a pharmaceutical company that is authorized to grant access to their investigational product to be used for specific patients.
- Legality. Fully legal, if created through FDA channels and registered on the registry of clinical trials. The EA trial is created by the pharmaceutical company, and then physicians can request access to the investigational product.
- Implementation options
- This is achieved on a case-by-case basis, depending on physicians' approval, patient eligibility, and pharmaceutical companies’ willingness to supply their investigational product.
- Lykos Therapeutics are the only company that has offered expanded access to date (Lykos Therapeutics, May 2024).
- Regulatory frameworks/agencies
- Any clinic or facility that can be authorized as a site for a clinical trial can be a site for Expanded Access, which usually involves having a DEA approved storage facility for the controlled substances (e.g. research pharmacy), such as hospitals or any institution equipped to securely store Schedule I and II drugs, according to DEA parameters.
- Clinics with appropriate medical equipment to monitor safety and adverse events.
- Equity/access and justice considerations. Broaden inclusion criteria and settings for treatment.
- Tribal consultation

- If conducted through healthcare facilities, such as IHS, would be similar regulations for other clinical trials approved by the federal government.
- Other treatment settings that can be decided and regulated by Tribes, with prior authorization from the FDA and the DEA.
- Veteran consultation. Working to create more opportunities for exploring expanded access within the VA, which would be similar to other clinical trials being conducted there and would not be breaking any federal laws.
- Patient consultation. Engage with patient advocacy groups on priorities for access under this program.
- Drug supply. Typically for drugs with promising phase II and/or phase III trials, however access is contingent on whether a drug company has created an expanded access trial, and whether the patient is eligible. This up to the discretion of the pharmaceutical company and is not a guarantee for access.
- Data collection/monitoring. Would be protected under HIPAA and federal protections could be ensured with a certificate of confidentiality and data sharing agreements with the drug supplier.
- Consequences if law is violated
- Same risks for medical malpractice or drug diversion if rules and procedures are not followed.
- Fines if HIPAA is violated
- Medical and psychological safety/screening
- Informed consent
- Adverse event reporting
- Mechanisms for handling unethical practices
- Screening patients for contraindicated medications and health conditions
- Cost to implement. This depends on the clinical setting and whether the manufacturer of the investigational drug to be used has a purchase cost.
- Minnesota state agencies with existing infrastructure. MDH, DHS, Board of Pharmacy, AG.

The Right to Try Act

1. Definition
    a. A federal right (US Food and Drug Administration, accessed November 11, 2024) to allow a physician to use an investigational product that has completed a Phase I clinical trial, is showing promising results in phase II and/or III clinical trials for the condition to be treated, but is not yet FDA approved, and the patient has a life-threatening or debilitating illness that has not responded to currently available treatments or they are not eligible for access through a clinical trial due to limited inclusion criteria.
2. Legality
    a. Technically this is a right, and physicians should not have to ask the government (e.g. DEA or FDA) for permission. They only need to get approval from the pharmaceutical company to supply the experimental drug.
    b. The federal statute does not explicitly state that drugs on Schedule I are not considered eligible investigational drugs, however the DEA has not allowed anyone to use a Schedule I drug, even those meeting the criteria for what an eligible drugs under this statute by, leveraging their administrative authority under the Administrative Procedures Act (US Department of Justice, accessed November 11, 2024) and the *Chevron* Deference (Cornell Law School, accessed November 11, 2024).

- A case challenging this in 9th Circuit Court of Appeals is currently pending a ruling between a physician wanting to give his terminal patients psilocybin, and the DEA not providing definitive guidance on this (Adlin, 2024a). An Amicus brief was submitted during an earlier iteration of this case, where 10 separate state AGs signed on in support, including Keith Ellison for Minnesota (US Court of Appeals for the Ninth Circuit, accessed November 11, 2024).
- Since the overturning of the Chevron Accord in June of 2024 by SCOTUS, the authority granted to the DEA has now been limited and this decision must be decided by a judge (or panel of judges), and the *AIMS vs DEA* case pending in the 9th Circuit is the first test of this for accessing psilocybin for end-of-life care under RTT.

3. Implementation options
    a. Minnesota has its own RTT Act (Laws of Minnesota 2024, Chapter 151, Section 151.375) which closely mirrors the federal version, however it has additional restrictions to only allow terminal patients (e.g. only having a limited time to live and nothing they can do will reverse that course, such as hospice care) to access eligible investigational drugs. If Minnesota wants to explore this option, it might make sense to amend the state RTT to allow for a broader definition of eligible patients to include those with life-threatening or severely debilitating conditions National Archives, March 2004) that could be helped by an experimental drug, as the state law is far more restrictive than what the federal law allows.

- The state could also use the federal RTT act, if not superseded by the state version of this program and limitations on eligible patients, as the statute does not explicitly say that Schedule I drugs like the three psychedelic medicines the task force is reviewing are not eligible treatments.

4. Equity/access and justice considerations
    a. Given that this program can only be adopted on a case-by-case basis, at the discretion of a physician and the pharmaceutical company producing the experimental treatment, this would not be the most equitable way to provide access, and the costs are not known as it has not been used thus far for psychedelic medicines
    b. Given that this would fall under federally protected channels (a federal right and given it is part of the supply from a DEA and FDA approved drug sponsor, may help with legal protections such as those gaining access through the structure of a clinical trial), patients would not be put at extra-legal risk for trying such treatments, and their information could be protected from subpoena to be used against them for child custody or other benefits that might be at risk for using illegal drugs through a Certificate of Confidentiality
5. Tribal consultation
    a. If conducted through healthcare facilities, such as IHS, given it is part of the supply from a DEA and FDA approved drug sponsor, may help with legal protections such as those gaining access through the structure of a clinical trial within Indian country.
    b. Other treatment settings that can be decided and regulated by tribes.
6. Veteran consultation
    a. Working to create more opportunities for exploring RTT access within the VA, which would be similar to gaining access given it is part of the supply from a DEA and FDA approved drug sponsor, may help with legal protections such as those gaining access through the structure of a clinical trial would not be breaking any federal laws.
7. Patient consultation
    a. Engage with patient advocacy groups on priorities for access under this program.
8. Drug supply

   a. Whether the drug will be granted access to the patient from the pharmaceutical company is up to the discretion of that company, and not something that can be mandated by this law.
9. Data collection/monitoring
   a. Would be protected under HIPAA and federal protections could be ensured with a certificate of confidentiality and data sharing agreements with the drug supplier.
10. Consequences if law is violated
   a. Same risks for medical malpractice or drug diversion if rules and procedures are not followed.
   b. Fines if HIPAA is violated
11. Medical and psychological safety/screening
   a. Informed consent
   b. Adverse event reporting
   c. Mechanisms for handling unethical practices
   d. Screening patients for contraindicated medications and health conditions
12. Cost to implement
   a. This depends on the clinical setting and whether the manufacturer of the investigational drug to be used has a purchase cost.
13. Minnesota State agencies with existing infrastructure
   a. MDH, DHS, Board of Pharmacy, AG

Adult regulated use (medical or non-medical)

1. Definition
   a. A state-approved program, such as what is happening in Oregon, and about to get started in Colorado, where access to psychedelic medicines is being regulated either for facilitated use without claims of medical benefits, or by merging services with health care systems to provide treatment to patients under the supervision of trained healthcare providers.
2. Legality
   a. Would be federally illegal, given that psychedelic medicines are on Schedule I of the CSA
   b. State legal programs could offer some protections, depending on the degree of conflicts with federal laws and the government policies and resources for enforcing federal laws for these state programs.
      i. There is a spectrum that can be adopted that aims to conflict as little as possible, while acknowledging that it will inherently conflict with federal laws.
3. Implementation options
   a. Oregon only allows psilocybin to be offered within licensed service centers, with supplies from state-licensed facilities, and only allowed to be consumed with a licensed facilitator. They are not allowed to blend any of this with traditional healthcare settings and practitioners are not allowed to diagnose or use any of their clinical tools while providing psilocybin facilitation.
   b. Colorado will allow more psychedelic medicines to be available, with initial adoption and regulations for psilocybin mushrooms, and additional plant medicines to be folded into the program in subsequent years. They allow services to be blended with healthcare practitioners and settings, as well as options for nonclinical facilitation and decriminalization that allows for people to “grow, gather, gift” psychedelic medicines for personal and community use.

   c. A program similar to how medical cannabis was regulated in Minnesota could be explored, with notable differences in the extra regulations around facilitation for people wanting to use psychedelic medicines.
4. Equity/access and justice considerations
   a. Creating a state-regulated supply will help with consumer protections around adulterated products, as was seen with unregulated cannabis products and the public health risk that posed.
   b. Allowing for home use will prevent ADA violations regarding medical or other disabilities that may limit options for certain patients.
   c. Allowing for options for access to trained facilitators outside of the medical system will allow for more culturally competent care, especially given the current health disparities in Westernized healthcare settings for marginalized communities.
   d. Removing criminal and civil penalties will prevent disproportionate enforcement on communities already marginalized and harmed by drug laws, and will protect patients and citizens engaging with psychedelic medicine programs from experiencing other consequences that could impact housing, employment, parental rights, etc.
   e. Allow for personal cultivation of psychedelic medicines to ensure costs for access are not a limiting factor.
   f. Carefully screening for vulnerable populations who may have a higher rate of adverse events with psychedelics, including but not limited to, patients with severe mental illness (e.g. psychosis), or with cardiovascular diseases that may be made worse while consuming psychedelic medicines, and for those that still want to engage, providing adequate medical support.
   g. Grant or funding programs to help offset costs to receive treatments under state-regulated programs.
   h. Find a way for state insurance to cover costs for patients with limited financial means
   i. Expungement/sentence commutation (AG or DOC)
   j. Are there racial disparities in drug enforcement of these 3 drugs?
   k. Equity Programs
5. Tribal consultation
   a. Tribes should be allowed to create and regulate their own programs through compacts and treaties with state and federal governments.
   b. Decriminalization of psychedelic medicines would prevent criminal prosecution under Public Law 280 so tribes could implement a program that works best for them.
6. Veteran consultation
   a. Continually discuss access options for veterans who receive most of their healthcare through the VA, however since that is a federal institution, they will likely not allow access to psychedelic medicines outside the context of clinical trials.
   b. Working with community advocacy groups to help provide funding specific for veterans to gain access and pay for psychedelic medicine treatments.
7. Patient consultation
   a. Engage with patient advocacy groups on priorities for access under this program
8. Drug supply
   a. Psilocybin can be sourced by allowing people to grow mushrooms, while also having state-licensed cultivation for supplying state programs
   b. MDMA and LSD (and synthetic psilocybin) - likely not able to source within the state, given the complexities of synthesize pharmaceutical grade drug products. The precursors are heavily monitored and either an exemption to the CSA, or a research program in

collaboration with the federal government (e.g. HHS or SAMHSA) would be needed. Otherwise, the state waits for FDA-approved products to hit the market (if/when that happens), and decriminalize possession and use of these psychedelic medicines, but not allow manufacturing.

9. Data collection/monitoring
    a. HIPAA does not apply in data collection programs being implemented for state programs (HIPAA is federal and does not cover programs that violate federal laws)
    b. Oregon - collecting aggregated to monitor adverse events/public health outcomes (with some individual data flowing to research organizations/OHSU - at medium risk of re-identification by federal agencies)
    c. Colorado - proposing to collect individual level data through Healing Advocacy Fund (HAF) and Rocky Mountain Poison and Drug Center - at high risk of being re-identified by federal agencies).
10. Consequences if law is violated
    a. Violation: When it comes to the FDA, the considerations are a bit different. Making medical claims, undermining the FDA's authority to regulate medical drug products, and operating medical clinics that use unapproved treatments are likely to provoke the FDA.
    b. Consequence: The most common response from FDA is to issue warning letters, but it does have the power to shut down clinics. There is also potential for Medicare and Medicaid fraud and violations of the federal False Claims Act, which can carry criminal penalties. According to SME Mason Marks, these are going to be big issues in Colorado, where they are blending conventional healthcare with psychedelics, which may cause conflicts with the FDA (Marks, 2023).
11. Medical and psychological safety/screening
    a. Informed consent
    b. Adverse event reporting
    c. Mechanisms for handling unethical practices
    d. Screening patients for contraindicated medications and health conditions
12. Cost to implement
    a. Oregon has hundreds of cannabis dispensaries and only a few dozen psilocybin service centers, so the program does not generate enough revenue to sustain Itself, resulting in high costs for licenses and thus high cost for services. Taxpayers have had to bail out the state program until it can pay for itself through licensing fees, a strategy that we've been warned not to implement as it's likely not sustainable.
    b. Colorado's program has yet to begin and costs are unknown, however similar issues are arising with hoping the program fees will pay for itself, however they are allowing alternative options through community use, decriminalization, not restricting the locations where facilitated sessions can occur, and allowing for people to grow and source their own psychedelic medicines.
13. Minnesota state agencies with existing infrastructure
    a. Department of Agriculture, MDH, DHS, Board of Pharmacy, AG

Decriminalization

This is technically not legal or illegal, but rather not enforcing a specific law. In this case, the state would not enforce the federal CSA and would be protected under the anticommandeering doctrine of the 10th amendment of the US Constitution.

1. Definition
    a. Removing criminal penalties and not allowing enforcement of the federal and state controlled substances act
2. Legality
    a. Not legal or illegal, as it's simply not enforcing a federal law, which is a right that states can exercise under the anticommandeering act of the 10th amendment of the US Constitution
3. Implementation options
    a. Removing criminal and civil penalties for certain behaviors related to use, possession, and sourcing of psychedelic medicines.
4. Equity/access and justice considerations
    a. Expungement/sentence commutation (AG or DOC)
    b. Are there racial disparities in drug enforcement of these 3 drugs?
    c. Equity Programs
    d. Removing civil fines and penalties for behaviors related to engagement with psychedelic medicines.
5. Tribal consultation
    a. Tribes should be allowed to create and regulate their own programs through compacts and treaties with state and federal governments.
    b. Decriminalization of psychedelic medicines would prevent criminal prosecution under Public Law 280 so tribes could implement a program that works best for them.
6. Veteran consultation
    a. Continually discuss access options for veterans who receive most of their healthcare through the VA, however since that is a federal institution, they will likely not allow access to psychedelic medicines outside the context of clinical trials.
    b. Working with community advocacy groups to help provide funding specific for veterans to gain access and pay for psychedelic medicine treatments.
7. Patient consultation
    a. Engage with patient advocacy groups on priorities for access under this program
8. Drug supply
    a. Psilocybin can be sourced by allowing people to grow mushrooms
    b. MDMA: FDA-approved product (if/when that happens), decriminalize possession and use of non-prescription, but not allow manufacturing.
    c. LSD: FDA-approved product (if/when that happens), decriminalize possession and use of non-prescription, but not allow manufacturing.
9. Data collection/monitoring
    a. General population health monitoring, like what was done for Denver to report on the impact of two years of decriminalization of psilocybin (Psilocybin Mushroom Policy Review Panel, November 2021).
    b. Intentional collection for public health and safety surveillance, akin to what Oregon is implementing (OPEN, accessed November 11, 2024).
10. Consequences if law is violated

    a. At the state level, descheduling would be one possible means of removing all criminal penalties. Deprioritization is another option where they are still illegal, but law enforcement are directed to not prioritize enforcement of drug laws. Either way, the substance remains federally illegal. Regarding conflicts with federal law, decriminalization is the least offensive. As SME Mason Marks discussed with us, the state would just be saying "we're not enforcing the federal CSA." Due to the anticommandeering principal under the 10th amendment, there's arguably nothing the federal government can do about that. Congress cannot force states to enforce federal laws, but they could impose financial penalties under the Spending Clause.

11. Medical and psychological safety/screening
    a. Informed consent
    b. Adverse event reporting
    c. Mechanisms for handling unethical practices
12. Cost to implement
    a. Not enforcing a law will not incur additional costs or needs for funding, however funding could be allocated to support organizations and efforts that provide services related to harm reduction, education, community outreach, and training for first responders and the public. This will help create a social safety net around potential increases in usage by the public, which were not allocated properly in Oregon following the passage of Measure 110.

Appendix H: Detailed scientific data

Effect sizes are a statistical measure of the magnitude of differences between two populations. Effect sizes are typically considered small if they are 0.2 or less, medium if they are around 0.5, large if they are 0.8, very large if they are 1.2, and huge if they are 2.0 and above. Values can be negative, with the magnitude ranges being the same (i.e., the further away from 0, the greater the effect).

MDMA

MDMA has a chemical structure somewhat similar to both mescaline and amphetamine (Green et al., 2003; Vollenweider et al., 1998). This drug readily diffuses across the cell membrane (Parrott, 2001) and binds to serotonin, dopamine, and norepinephrine transporter proteins, ultimately blocking the reuptake, while stimulating the release, of each respective neurotransmitter (Han et al., 2006; Verrico et al., 2007). MDMA may induce perceptual disturbances through the 5-HT2A receptor (Hasler et al., 2009; Liechti et al., 2001; van Wel et al., 2012), and activity of serotonin and oxytocin receptors may be associated with the noted pro-social empathetic effects of the drug (Nichols, 1986; Tancer & Johansen, 2007; Thompson et al., 2007). There is also preliminary research indicating that this treatment may provide relief from tinnitus (Searchfield et al., 2020).

PTSD

Phase III Trials

In these trials, participants in the MDMA group received 80 milligrams (mg) of the drug at the beginning of the first treatment session, with an optional half-dose administered approximately two hours into the session. During the second and third treatment sessions, the dose was 120 mg, again with an optional half-dose. Each escalation was at the discretion of both the participant and the therapists. Participants in the control group received a placebo in place of the MDMA, but otherwise went through the same protocol.

Investigators also assessed clinically meaningful responses (defined as a greater than or equal to 10-point reduction in CAPS total severity score), loss of PTSD diagnosis, and remission from the disorder (defined as the loss of the diagnosis along with a total CAPS score of less than or equal to 11). Effect sizes, a statistical measure of the magnitude of differences between two treatments (in this case, between drug and placebo) were reported using Cohen's d. The further from zero, the larger the effect of the experimental treatment. When comparing between the two groups, effect sizes of MDMA-assisted psychotherapy were reported to be large to moderate, using the Cohen's d statistic (d=0.91 and d=0.70). When looking just at the group that received MDMA, the effect sizes of treatment from beginning to end were huge to very large (d=2.10 and d=1.95). However, the effect of placebo plus psychotherapy alone also resulted in large effect sizes of d=1.20 and d=1.25 when comparing between the baseline and endpoint. At the primary study endpoint, the first phase III trial reported that 67 percent of the participants in the MDMA group no longer met the diagnostic criteria for PTSD, compared with 32 percent of those in the placebo group. Furthermore 33 percent of the MDMA group met the criteria for remission, as compared with 5 percent of the placebo group (Mitchell et al., 2021). In the second phase III trial, 87 percent of participants of those that received MDMA saw a clinically meaningful response,

compared with 69 percent of the placebo group. In this study, 71 percent of the participants in the MDMA group no longer met the criteria for a PTSD diagnosis, as compared with 48 percent of the placebo group. Finally, 46 percent of those who received MDMA met remission criteria, as opposed to 21 percent of the placebo group (Mitchell et al., 2023).

These studies also investigated functional impairment as a secondary outcome, measured by the Sheehan Disability Scale (SDS). Like the primary outcome, these studies found that MDMA-assisted psychotherapy significantly reduced SDS scores both within and between the two groups. Effect sizes of the treatment were moderate, at d=0.42 in the first trial and d=0.40 in the second trial. One of these trials investigated the effect of treatment on symptoms of depression, using the Beck's Depression Inventory-II (BDI-II). MDMA-assisted psychotherapy was found to be significantly more effective than placebo in reducing symptoms of depression over 18 weeks.

Phase II Trials

In the phase II trials, endpoints ranged from three weeks to two months after the last treatment session. Doses ranged from 0 mg to 125 mg; 0 mg was a true placebo, while 25 mg, 30 mg, and 40 mg were typically considered active control doses, and 75 mg, 100 mg, and 125 mg were considered full experimental doses. Secondary outcomes included other measures of PTSD symptoms, depression, sleep quality, perceived growth, personality factors, dissociation, and psychological function. One of these trials reported that the rate of clinical response was 83 percent in the MDMA group, as compared with 25 percent in the placebo group (Mithoefer et al., 2011). In a trial investigating an active control dose of the drug (40 mg) versus experimental doses (100 mg and 125 mg), results indicated that more participants in the experimental dose groups attained a clinical response than did those in the active control group (16.7 percent (40 mg), 55.6 percent (100 mg), and 50.0 percent (125 mg)) (Ot'alora G et al., 2018). Additionally, secondary outcomes also generally showed greater improvement in response to higher doses of MDMA as compared with placebo/active control.

Comparison of efficacy, PTSD

Overall, the effect size (using Hedge's g) for all comparisons combined was 0.81, indicating a moderate effect (Watts et al., 2013). Evaluating each psychotherapy individually, the study found an effect size of 1.26 for CBT, 1.08 for exposure therapy, and 1.01 for EMDR. When combining all types of psychotherapies, the effect size was 1.14. Effect sizes of pharmacological treatments were found to be moderate. Among the SSRIs paroxetine, sertraline, and fluoxetine, the effect sizes were found to be g=0.74, g=0.41, and g=0.43, respectively. The effect size of venlafaxine (an SNRI) was g=0.48 (Watts et al., 2013).

In comparison, the Cohen's d effect sizes of MDMA-assisted psychotherapy versus placebo with psychotherapy were d=0.91 (Mitchell et al., 2021) and d=0.80 (Mitchell et al., 2023). Just within those who received the drug, there was a large treatment effect between baseline and the endpoint, with effect sizes of d=2.10 (Mitchell et al., 2021) and d=1.95 (Mitchell et al., 2023). However, the particular type of psychotherapy employed in these studies appears to have some treatment effects on its own, demonstrated by the large effect sizes (d=1.20 (Mitchell et al., 2021) and d=1.25 (Mitchell et al., 2023)) in the placebo groups.

Anxiety disorders

In the study investigating MDMA-assisted psychotherapy on social anxiety in adults with autism spectrum disorder, participants in the experimental group received doses of MDMA that ranged from 75 mg to 125 mg. Those in the control group received a placebo (0 mg of MDMA). MDMA significantly reduced the mean LSAS score (-44.4-point reduction) as compared with the placebo group (-19.3-point reduction). The placebo-subtracted Cohen's d effect size was 1.40. The rate of clinically significant changes in social anxiety disorder symptoms from baseline was 75 percent following MDMA-assisted therapy versus 50 percent in response to the placebo (Danforth et al., 2018).

In the study investigating MDMA-assisted psychotherapy as a treatment for anxiety surrounding a diagnosis of a life-threatening illness, the experimental group received 125 mg of the drug, with an optional half dose approximately two hours later. The control group received 0 mg (a true placebo). Results indicated that the MDMA group saw a greater mean reduction in STAI-Trait scores (−23.5 points), indicating less anxiety, compared to placebo group (− 8.8 points). This trended toward, but did not reach, significance. One individual in the placebo group saw substantial improvements in symptomology, potentially acting as an outlier. If this individual was removed, the difference between groups became statistically significant. The Hedge's g between-group effect size was 1.03, which is large. This study investigated a number of secondary outcomes, including post-traumatic growth, depression symptomology, sleep quality, and global functioning. All of these followed the same trajectory of improvement as seen with the primary outcome in those that received MDMA (Wolfson et al., 2020).

Comparison of efficacy, anxiety disorders

Effect sizes for psychotherapies, including individual CBT/exposure therapy and group CBT, were 1.30 and 1.22, respectively (Bandelow et al., 2015). Combining all types of psychotherapies, the effect size was 1.22, representing a large effect of treatment. For pharmacological treatments, effect sizes were 2.25 for SNRIs, 2.15 for benzodiazepines, and 2.09 for SSRIs. Combined, all medications resulted in an effect size of 2.02. These are all huge effect sizes. The combination of medication and CBT specifically resulted in an effect size of 2.10 (Bandelow et al., 2015). A second meta-analysis investigating the use of CBT as a treatment specifically for social anxiety disorder found a moderate Hedge's g effect size of 0.74 (Kindred et al., 2022). In the study investigating MDMA-assisted psychotherapy as a treatment for social anxiety in individuals with autism spectrum disorder, the immediate Cohen's d effect size of treatment was 1.40, and six months after the end of treatment was 1.10, both large effect sizes (Danforth et al., 2018). In the study evaluating MDMA as a treatment for anxiety in response to a life-threatening illness, the Cohen's d effect size after treatment was calculated to be 1.03 (Wolfson et al., 2020), considered a large effect of treatment.

Adverse effects

Although the number of participants who reported suicidal ideation in the phase III trials varied throughout the visits, prevalence never exceeded baseline and was not exacerbated in response to MDMA. In one phase II trial suicidal ideation was elevated in all groups that received MDMA during the treatment period (Mithoefer et al.,

2018), and in another there were a greater number of reports of suicidal ideation in active dose (as compared with control dose) groups (Ot'alora G et al., 2018).

There have been reports that adverse effects of MDMA vary by sex. In trials of healthy individuals, negative drug effects, including subjective effects, were significantly more common in women (Vizeli and Liecthi, 2017). Notably, hyponatremia (a low concentration of sodium in the blood) occurs more often in females than in males (Campbell & Rosner, 2008; Simmler et al., 2011). The greater negative effects of the drug may be due, in part, to lower body weight and correspondingly higher drug dose per body weight in women (Studerus et al., 2021). Finally, infants born to mothers who had used MDMA during pregnancy had worse motor quality development and lower milestone attainment at four and 12 months of age, in a dose-dependent manner, as compared with infants not exposed to MDMA (Singer et al., 2012a, 2012b).

Psilocybin

Psilocybin, and psilocin, are classical psychedelics of the tryptamine family (Kwan et al., 2022). Psilocin readily crosses the blood-brain barrier (Migliaccio et al., 1981), and is an agonist of a number of serotonin receptors, including notably the 2A receptor (Klein et al., 2020), among others. Following the ingestion of psilocybin, it has been shown that there are noticeable changes in the functional connectivity between particular brain regions. There is a decrease in functional connectivity between the anterior hippocampus, a region implicated in the sense of self, space, and time, and the default mode network, active during wakeful rest (such as daydreaming) and during self-directed thought, thoughts of others, or the future (Siegel et al., 2024). Increases in functional connectivity between the hippocampus and the default mode network have been associated with symptoms of depression (Colasanti et al., 2016), while decreases are associated with symptom relief (Siegel et al., 2021; Yan et al., 2019).

Psilocin has also been shown to upregulate brain-derived neurotrophic factor in certain brain regions, suggestive of an increase in neural plasticity (Vaidya et al., 1997). A recent study found that, in male mice, whole mushroom extract resulted in greater changes in markers of neuronal synaptic plasticity than did synthetic psilocybin (Shahar et al., 2024), suggestive of the "entourage effect." This theory describes the idea that different compounds within a plant or fungus work synergistically to modulate the outcome, or said another way, that the whole is greater than sum of its parts. While only recently being discussed in Western medicine, particularly in regard to cannabis (Ben-Shabat et al., 1998; Chen, 2017), this effect has a long-standing history in Indigenous medicinal and spiritual practices. In Indigenous ontology, mushrooms containing psilocybin are not considered drugs, but rather sacred beings with whom we share reciprocal relationships (Estrada, 1989; Williams et al., 2022). Indigenous cultures who use entheogens, or psychoactive plants and fungi, for healing urge a holistic approach, treating not just the symptom of an illness, but aiming to restore balance to the individual as whole (Yeomans, 2022).

Mood and anxiety disorders

Trials for the use of psilocybin-assisted therapy in the treatment of tobacco use disorder have also provided promising results, though these are not RCTs (Johnson et al., 2014, 2017). Additionally, a number of non-RCTs

have begun exploring psilocybin-assisted therapy for the treatment of obsessive-compulsive disorder (Moreno et al., 2006) and anorexia nervosa (Peck et al., 2023).

In the meta-analysis conducted by Hakazian et al. (2023), the standardized mean difference (SMD) between the groups was -0.78, approaching a large effect size of treatment. This was true for both major depressive disorder and depression and anxiety symptoms associated with life-threatening illnesses, reporting SMDs of -0.75 (moderate effect size) and 0.96 (large effect size), respectively. In this study, a clinical response was defined as a reduction of >50 percent in the primary depression rating at the primary endpoint, as compared with baseline, while remission was defined as a participant scoring being a certain pre-defined threshold on each of the depression scales (less than or equal to seven on the Hamilton Depression Rating Scale, less than or equal to ten on the Montgomery-Asberg Depression Rating Scale, and less than or equal to five on the Quick Inventory of Depressive Symptomatology) (Haikazian et al., 2023).

Another meta-analysis evaluated four clinical trials and indicated that psilocybin-assisted therapy resulted in larger reductions in both anxiety and depression symptoms between baseline and the endpoint of a trial, as compared with the control condition. Comparing between the two groups, the Hedge's g effect size of psilocybin-assisted therapy on anxiety was 0.82, indicating a moderate effect of psilocybin treatment. Data from this analysis confirmed that psilocybin produced a moderate effect on depression, as well (g=0.83). When comparing between the beginning and endpoints in the experimental groups, these effects of treatment were found to be very large (g=1.38 for anxiety, g =1.47 for depression). At the follow-up point (often six to twelve months after the conclusion of the study), the effect of psilocybin treatment was still found to be large for both anxiety and depression (g=1.16 and g=1.17, respectively) (Goldberg et al., 2020).

Comparison of efficacy, psilocybin versus escitalopram

A total of 59 participants with major depressive disorder were assigned to either the psilocybin treatment group (n=30) or the escitalopram treatment group (n=29). Treatment sessions were separated by approximately three weeks. After the first session, all participants took one pill (placebo or 10 mg escitalopram) per day, while after the second session they were instructed to take two pills per day. Key secondary outcomes included response to the drug (as a reduction in score of more than 50 percent on the QIDS-SR-16) and remission from the disorder (a score of less than or equal to five on the QIDS-SR-16). At six weeks, 70 percent of those in the psilocybin group met the criteria for a response, as compared with 48 percent in the escitalopram group. Remission occurred in 57 percent of those who received psilocybin and 28 percent of those who received escitalopram. Again, there were no statistical differences between the groups on these measures (Carhart-Harris et al., 2021).

The six-month follow-up to the above study reported data from 25 participants in the psilocybin group and 21 participants in the escitalopram group. Assessments occurred via online questionnaires at monthly intervals for six months after the end of the six-week trial. Participants received no additional treatment from the study team but had no restrictions on their psychiatric care. Depressive symptoms were assessed again using the QIDS-SR-16. At the one-month mark there was a significant time x condition interaction between the two groups when comparing with baseline scores ($p = 0.011$, pFDR = 0.021). At the end of the follow-up, both groups showed sustained improvements in depressive symptom severity, without difference, with the mean between-condition difference in QIDS-SR-16 found to be 1.51 (95 percent CI: -1.35, 4.38; $p = 0.311$). As compared with the

escitalopram group, those who received psilocybin reported greater mean between-condition differences in functioning (WSAS: −7.46; 95 percent CI [−12.4, −2.47]; p < 0.001), psychological connectedness (WCS: 11.02; 95 percent CI [1.25, 20.83]; p = 0.033), and meaning in life (MLQ: 4.86; 95 percent CI [0.67, 9.05]; p = 0.021) (Erritzoe et al., 2024).

Comparison of efficacy, mood, and anxiety disorders

The meta-analysis by Cipriani et al. (2018) estimated summary odds ratios (ORs), which ranged between 2.13 for the most-efficacious and 1.37 for the least efficacious antidepressant, all of which are considered medium to low effect sizes. The effect of psychotherapy with concomitant antidepressants on major depressive disorder was reported to have an OR of 2.93, corresponding to a medium effect size. Psychotherapy alone, at six months, was found to have an OR of 1.42, considered a low effect size (Karyotaki et al., 2016). The meta-analysis by Bandelow et al. (2015) investigated the effect of psychotherapy and pharmacotherapy separately, as well as combined, and found that medications were associated with a significantly higher effect size (d=2.02) than psychotherapies (d=1.22) in treating anxiety disorders. When psychotherapy and pharmacotherapy were combined the effect size was 2.12. All of these are considered very large to huge effect sizes of treatment. These effect sizes are roughly comparable to those calculated by the meta-analysis investigating psilocybin-assisted therapy for the treatment of anxiety disorders. In this study, the effect size of psilocybin treatment was 1.38, indicating a very large effect of treatment. These effects on anxiety symptoms remained large through follow-up data points as well (g=1.16) (Goldberg et al., 2020).

Treatment-resistant depression is operationally defined as failure of at least two courses of treatment (Goodwin et al., 2022). This type of depression is often treated with brain stimulation, including electroconvulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS). Recently, a new form of treatment has been approved by the FDA, intranasal esketamine (FDA, 2019). Finally, antipsychotic or anticonvulsant medications may be taken in conjunction with standard antidepressants. Bipolar type 2 disorder can be treated with antidepressant medications, psychotherapy, or certain other mood stabilizers, like lithium or valproate (NIMH, 2024x). However, while individuals with bipolar type 2 disorder were included in one study (Rosenblat et al., 2024), there have been no RCTs designed to specifically investigate the use of psilocybin as a treatment for this condition. Anxiety disorders are typically treated with psychotherapy (CBT, others), medication (antidepressants, anti-anxiety medications, beta-blockers), or a combination of the two (NIMH, 2024a).

Specific treatments for treatment-resistant depression were also evaluated. Electroconvulsive therapy was found to have an OR of 4.77, which can be considered a large effect size of treatment (Pagnin et al., 2004). In an analysis of rTMS, those receiving the treatment were nearly three times as likely to reach remission than those who were not (Vida et al., 2023). Finally, intranasal esketamine has been shown to have a small effect on treatment-resistant depression (Jawad et al., 2022). While the large effect sizes demonstrated by psilocybin-assisted therapy in the treatment of treatment-resistant depression may appear comparable to at least ECT and rTMS, again this is a comparison between a small number of trials (for psilocybin) and a much larger pool of data for ECT and rTMS. While promising, more clinical trials exploring the efficacy of psilocybin are necessary.

Alcohol use disorder

This phase II, double-blind, placebo-controlled randomized a total of 95 participants with a diagnosis of alcohol use disorder to one of two groups, psilocybin (n=49) or placebo (diphenhydramine; n=46). All participants received four therapy sessions before treatment, two eight-hour sessions with the drug (separated by four weeks), and four non-drug follow-up psychotherapy sessions after each treatment session. Psilocybin doses were calculated by participant body weight. During the first drug session participants received 25 mg/70 kilogram (kg) of body weight, with the option to increase to 50 mg/70 kg of body weight at the second session. Similarly, dosing for diphenhydramine was 50mg for session one and an optional increase to 100 mg for session two. The primary endpoint was 38 weeks. After the final non-drug integrative session, participants in the control condition were offered to be part of an open-label trial, in which they repeated the above experiment with psilocybin (Bogenschutz et al., 2022).

During the first drug session participants received 25 mg/70 kg of body weight, with the option to increase to 50 mg/70 kg of body weight at the second session. Similarly, dosing for diphenhydramine was 50 mg for session one and an optional increase to 100 mg for session two. The primary endpoint was 38 weeks. After the final non-drug integrative session, participants in the control condition were offered to be part of an open-label trial, in which they repeated the above experiment with psilocybin. At the end of the study, participants who received psilocybin had a lower mean percentage of heavy drinking days (9.7 percent) than those who received diphenhydramine (23.6 percent). Participants who received psilocybin also had a mean lower percentage of total drinking days (29.4 percent) than those in the diphenhydramine group (42.8 percent), and lower mean drinks per day (1.2 drinks/day versus 2.3 drinks/per day, respectively). All measures were statistically different between the groups, favoring psilocybin. There was also a trend toward abstinence in those that received psilocybin (22.9 percent of participants) as compared with the control condition (8.9 percent) at the end of the trial (Bogenschutz et al., 2022).

Cluster headache

The RCT investigating cluster headache was an exploratory, double-blind, placebo-controlled trial (Schindler et al., 2022). A total of 16 participants were randomly assigned to either the psilocybin group (n=8) or the placebo group (n=8). Starting 14 days before the first experimental session, and lasting until the end of the experiment, participants kept a headache diary in which they logged the date, time, duration, and intensity (on a 0 through 10 scale) of every cluster headache. Psilocybin was dosed by body weight (0.143 mg/kg of body weight), and treatment occurred over three 6-hour experimental sessions, each separated by approximately 5 days. The main outcome investigated was the number of cluster headache attacks (frequency) three weeks after the first drug session. The study also assessed the duration of these attacks and the intensity of the pain. While there was a reduction in attack frequency of cluster headache in the psilocybin group, there was no statistical difference in cluster headache frequency between the two groups. Furthermore, there were no differences in the duration of the attacks, or the intensity of the pain. When separating data between participants that experience chronic versus episodic cluster headaches, the effect of psilocybin treatment was higher in those with chronic than episodic type, but neither group saw a statistically significant reduction.

Adverse effects of psilocybin in clinical trials

In the RCT that directly compared psilocybin to escitalopram, the percentage of patients who experienced anxiety, dry mouth, sexual dysfunction, or reduced emotional responsiveness were all higher in the escitalopram group than the psilocybin group (Carhart-Harris et al., 2021). One particular adverse effect associated with these trials is suicidal ideation. Because these trials included individuals with treatment-resistant depression (TRD), there were a handful of reports of suicidal ideation, behavior, or self-injury, both in psilocybin and control groups. Individuals with TRD are often at an increased risk of suicidal ideation. Increased suicide risk with serotonergic antidepressant drugs has been a noted concern in the literature. Individuals with TRD have been through several rounds of ineffective treatment, and therefore may consider psychedelics as a last resort. Given the recent media hype around psychedelics as "cure-all" drugs, it is conceivable that if psilocybin-assisted treatment is perceived as being ineffectual as well, demoralization and hopelessness (and potentially further suicidal behavior) may ensue in this population (Gukaysan, 2023).

Abuse potential and toxicity

While rare, two cases of Tako-Tsubo cardiomyopathy following the consumption of psychoactive fungi have been reported (Kotts et al., 2022; Nef et al., 2008). Two cases of rhabdomyolysis following ingestion of large amounts of psilocybin-containing mushrooms have also been reported; one occurred in an individual that experienced concurrent psilocybin-induced psychosis (Suleiman et al., 2022), and one occurred in an individual with hepatitis C, resulting in acute renal failure, posterior encephalopathy with cortical blindness, all of which were treated successfully (Bickel et al., 2005). However, a clinical trial investigating the pharmacokinetics indicated that, at clinical doses, renal clearance of intact psilocin accounted for less than 2 percent of the total clearance, suggesting that no dose reduction is needed for subjects with even mild-to-moderate renal impairment (Brown et al., 2017). In terms of emergency room visits, the only predictor associated with higher risk of emergency medical presentations is young age (Kopra et al., 2022). There was one report in the literature of an 18-year-old experiencing hallucinogen persisting perception disorder after consumption of psilocybin-containing mushrooms and cannabis together, which persisted for more than eight months before resolving spontaneously (Espiard et al., 2005).

LSD

LSD is an ergoline, a special class of tryptamine, with the (R)-amphetamine structure embedded within it (Kwan et al., 2022), and has a high affinity for nearly all of the 14 serotonin receptors in humans, as well as certain dopamine receptors and adrenergic receptors (Kroeze et al., 2015). The rigid structure of LSD, along with its binding at certain dopamine receptors, may be part of the mechanism that prolongs the drug effects (Marona-Lewicka et al., 2005). LSD acts in many of the same brain regions as both MDMA and psilocybin, producing overall similar effects of heterogeneous excitation and inhibition (Kwan et al., 2022), and increasing functional connectedness between regions (Müller et al., 2017; Preller et al., 2018).

A single trial for LSD therapy for opioid use disorder was conducted in the 1960s in a prison population, which raises concerns around scientific ethics and consent. No current trials for the disorder have been run, and so this condition was not included in the review.

Anxiety disorders

Both studies were double-blind, placebo-controlled, phase II clinical trials, with similar methods. In each study, participants were randomized to one of two groups, receiving either a 200 microgram (µg) dose of LSD or a 20 µg dose, which acted as an active control. Regardless of trial or condition, all participants received a single non-drug preparatory session, two 8-hour treatment sessions with a team of therapists, and one to three non-drug integrative sessions after each treatment.

In the first study, LSD-assisted therapy was shown to significantly reduce both the State (p=0.02) and Trait (p=0.03) components of the anxiety scale as compared with the control condition two months after the last treatment. The effect sizes of treatment on these components were also found to be very large (d=1.2 and d=1.1, respectively) (Gasser et al., 2014). Data from the second trial corroborated that of the first, in which LSD-assisted therapy resulted in a significant decrease in both the State (p=0.017) and Trait (p=0.007) components of the STAI 16 weeks after the second treatment session, as compared with the control condition (Holze et al., 2023). The effect sizes of treatment were considered moderate to large (d=-0.75, d=-0.87 respectively). A key secondary outcome was the effect on comorbid depression, measured by the Hamilton Depression Rating Scale (HAMD) and the Beck Depression Inventory (BDI). Symptoms of depression decreased significantly on both scales following LSD-assisted therapy as compared with the control condition (HAMD; p=0.0004; BDI: p=0.02) (Holze et al., 2023).

Comparison of efficacy, anxiety disorders

The effect size of psychotherapy versus control groups was moderate on self-reported measures (Hedge's g=0.84) and large on clinician-rated instruments (g=1.09) (Cuijpers et al., 2014). Holze et al (2023) found that the effect size of LSD-assisted therapy on the STAI as a whole was large (d=-0.87). Looking at each component of the STAI, this meta-analysis found moderate effects of treatment on both the State aspect (g=0.73) and the Trait aspect (g=0.64) (Cuijpers et al., 2014). In comparison, the effect sizes of LSD-assisted therapy on the State component of the STAI was found to be very large to moderate (d=1.2 (Gasser et al., 2014), d=-0.75 (Holze et al., 2023)), and were found to range from very large to large for the Trait component (d=1.1 (Gasser et al., 2014), d=-0.87 (Holze et al., 2023)). As calculated by the meta-analysis, the effects of standard psychotherapy on comorbid depression were moderate (g=0.71) (Cuijpers et al., 2014). Analyses were further broken down by measurement instrument. When using the HAMD, the effect of treatment on depression was large (g=0.91) and moderate when using the BDI (g=0.80) (Cuijpers et al., 2014). In comparison, the effect sizes of LSD-assisted therapy on depressive symptoms were found to be very large (HAMD: d=1.1) to moderate (BDI: d=-0.72) on the same scales.

Alcohol use disorder

The methodology varied widely between the studies conducted in the 1960s and 1970s. In total, these studies included a total of 550 participants, 327 of whom were exposed to an experimental dose of LSD. The doses of LSD employed in these studies ranged anywhere from 300 micrograms (µg) to 800 µg, with one study dosing instead 3 µg/kg of body weight. Most studies included a therapeutic component in at least one group that received LSD, but a corresponding therapeutic component was not always employed equally in the control

condition. Furthermore, not all studies included a control group. Each study followed-up with patients after treatment, ranging from one to twelve months post-treatment. Apart from the methodological concerns, another particular caveat of these studies is that the overwhelming majority of participants in these studies were male. Ultimately, the conclusions drawn by each of these studies indicated that treatment with LSD provided no meaningful benefit over other therapeutic modalities in the treatment of alcohol use disorder.

The meta-analysis by Krebs and Johansen (2012) reported a statistically significant beneficial effect on improving symptoms of alcohol misuse at the first-reported follow-up session (p=0.0003) (Krebs and Johansen, 2012). When evaluating dichotomized data (improved vs. not improved) at the first follow-up, 59 percent of LSD patients, as compared with 38 percent of control patients, were considered "improved", which was also statistically significant (p=0.0003). The analysis further indicated that treatment with LSD provided significant beneficial effects on alcohol misuse in both the short-term (2-3 months post-treatment; p=0.01) and medium-term (6 months post-treatment; p=0.01). There was no statistical difference between the groups in the long-term (considered 12 months post-treatment). Investigating the effect of treatment on total abstinence, it was found that LSD showed significantly greater beneficial effects over control groups at the first reported follow-up (1-3 months post-treatment; p=0.004) and the short-term follow-up (2-3 months post-treatment; p=0.03). There were no statistical differences between the groups at the medium-term follow-up (Krebs & Johansen, 2012).

Comparison of efficacy, alcohol use disorder

The meta-analysis by Krebs and Johansen (2012) provided a direct statistical comparison of LSD against current treatments by calculating the pooled benefit difference (Krebs and Johansen, 2012). In terms of improvement on alcohol misuse, the pooled benefit difference between daily naltrexone use and control groups was calculated to be 11 percent, and the pooled benefit difference between daily acamprosate and control groups was 1 percent. The analysis was unable to calculate the pooled benefit difference for the study on disulfiram. In comparison, the pooled benefit difference between LSD groups and control groups was 16 percent. In the analysis of abstinence from alcohol, the pooled benefit difference of daily naltrexone use versus control conditions was 3 percent, this measure was 11 percent between acamprosate and control conditions, and 11 percent between disulfiram and control conditions. The pooled benefit difference in the maintenance of abstinence following LSD treatment versus control groups was 15 percent (Krebs and Johansen, 2012).

Adverse effects of LSD in clinical trials

Special consideration regarding the action of these types of psychedelic drugs on the heart is included in the guidance document for clinical investigation of psychedelics developed by the FDA (FDA, 2023). While “flashbacks” were experienced by participants in the trials, none of these instances were reported to be distressing. Furthermore, no participants met the criteria for a diagnosis of hallucinogen-persisting perception disorder (HPPD), which requires that lingering perceptual disturbances cause significant distress or impairment (APA, 2022).

Drug-drug interactions

LSD is metabolized by a number of cytochrome P450 (CYP) enzymes (Wagman et al., 2019); therefore, any medications that interact with these enzymes will likely result in an interaction.

Community research and population statistics

Unpublished data

The trial by MindMed, Inc. was a randomized, double-blind, placebo-controlled 12-week trial using their proprietary formulation of LSD called MM120. A total of 198 participants with generalized anxiety disorder were enrolled into one of five groups: placebo, 200 micrograms (µg), 100 µg, 50 µg, or 25 µg dose of MM120. Each participant received a single administration of MM120 or placebo, with no psychotherapy intervention. This single dose (based on 100 µg results) resulted in statistically and clinically significant reductions in anxiety measurements out to week 12. This was true for comorbid depression scores as well. At the end of the study, 65 percent of participants showed a reduction in anxiety, and nearly 50 percent of the participants showed remission from the condition. Adverse effects were mild-to-moderate, and transient (most not lasting after treatment day). Most common were illusions or hallucinations, nausea, headache, anxiety, and increased blood pressure. There were no drug-related serious adverse effects (Hopkins, 2023).

A search of ClinicalTrials.gov on June 5, 2024, indicated that a number of clinical trials have been registered for each of the three drugs. There have been 104 clinical trials registered investigating MDMDA. Of these, 56 have been completed, 8 are active, 17 are currently recruiting, and 14 have not yet begun recruiting. For psilocybin, 175 clinical trials have been registered. Of these, 41 have been completed, 20 are active, 60 are currently recruiting, and 33 have not yet begun recruiting. Finally, 24 clinical trials have been registered to investigate LSD. Of these, 17 have been completed, none are currently active, 6 are currently recruiting, and 1 has not yet begun recruiting. Overall, the number of registered clinical trials indicates that research surrounding these drugs as treatments for various health conditions is of interest, ongoing, and will continue for the foreseeable future.

National general use statistics

In young adults (19 through 30 years old), the all-time high of reported use was 8.9 percent in 2023. Reported MDMA use temporarily spiked in 2014 (6.1 percent) and 2020 (4.7 percent). Use of LSD saw an all-time high in 2020 (4.7 percent). General statistics on substance use reported by the Centers for Disease Control (CDC) do not include psychedelics or hallucinogens as a category (NCHS, 2021).

Adult health data in Minnesota

Data from the Health Trends Across Communities from the Minnesota Electronic Health Records Consortium (MNEHR) uses summary reports from electronic health records on a range of chronic, behavioral, and mental health conditions, as well as conditions related to drug use. The information comes from eleven health systems that make up the MNEHR, and represents around 90 percent of health care for Minnesotans. The reported

prevalence estimates include Minnesota residents who were seen at any participating health system within the last three years and received a diagnosis related to use of drugs of interest in the last five years.

The prevalence of health conditions related to hallucinogen rose from 1,950 reports in 2020 to 2,300 reports in 2023 statewide, each representing less than 1 percent of the total population. The prevalence of health conditions associated with psychostimulant use rose from 27,670 in 2020 to 32,840 in 2023, though this also represent less than 1 percent of the population (MNEHR, 2024).

Poison control data

Regarding data from poison control centers, it is important to note that reporting is voluntary, which may result in an underrepresentation of the true occurrence of exposures. Exposures are defined as actual or suspected contact with any substance, regardless of toxicity or clinical manifestation. There may be cases where an exposure involves multiple substances, as well as cases involving a single substance.

Appendix I: Scientific literature review methods

The scientific duties outlined in the legislation were addressed by three questions. Corresponding to the first duty, the question was "What are the health conditions that each drug shows efficacy or effectiveness in treating?" (“Question 1”). The scientific question (“Question 2”) corresponding to the second duty was “What is the efficacy or effectiveness of each drug in treating the above-named conditions as compared with current gold-standard treatments?” Finally, the task force voted to include a third scientific question (“Question 3”), asking “What are the risks associated with each drug as a therapeutic treatment?”

All methods were determined a priori, and all components of the search strategy were approved by the Psychedelic Medicine Task Force. All searches were conducted using PubMed. Searches addressed each of the three scientific questions for each drug. From these search results, follow-up searches based on works cited and related citations were run to ensure thorough data collection. Following each search, resulting citations were uploaded to Mendeley citation manager for deduplication. Next, citations were added to manual spreadsheets for further analysis. The inclusion or exclusion of search results was applied individually to each remaining result through reading the title, abstract, and methods, as available. Following this, results from Question 2 were further subject to critical appraisal before final analysis.

Following each search, conditional formatting was used to determine if each study met the inclusion criteria approved by the task force. For Question 1, the criteria were as follows: The search was limited to all peer-reviewed observational studies, primary studies, systematic reviews, meta-analyses, and clinical practice guidelines in which either the efficacy or effectiveness of MDMA, psilocybin, or LSD was investigated in the adult population (18 years old or above). There were no restrictions on the date of publication, location, language, exposure to the drug or setting in which exposure occurred.

For Question 2, the criteria were as follows: The search was limited to all peer-reviewed randomized controlled trials (RCTs), meta-analyses, systematic reviews, and clinical practice guidelines in which the efficacy of MDMA, psilocybin, or LSD was investigated in the adult population (18 years old or above). There were no restrictions on the date of publication, location, language, exposure to the drug or setting in which exposure occurred. To be able to compare the efficacy of psychedelic drugs against current standard treatments, an additional search was run. Current standard treatments for each health condition were identified through searches of the appropriate and corresponding institute within the National Institutes of Health. The search in PubMed was subsequently restricted to meta-analyses investigating the efficacy of the current standard treatments for the health condition in question, in the adult population (18 years old or above). There were no restrictions on the date of publication, location, or language of publication. Due to the large volume of research, the results were limited to the first 50 results returned and sorted by "Best Match."

While case reports were excluded from analysis for Questions 1 and 2, they were included in the search for Question 3 (the potential risks of each drug as a therapeutic treatment). The search was still restricted to peer-reviewed publications, but there was no restriction on age, date of publication, location, language, exposure to the drug or setting in which exposure occurred. Supplemental searches for risk information from related citations were run to ensure thorough data collection.

For all questions, deduplication was run following the search to remove duplicate results before the application of inclusion criteria. The title, abstract and methods of each result were analyzed using conditional formatting. For Question 1, for each drug, results were broadly categorized into related, over-arching health conditions. For Question 2, all studies that met inclusion criteria were next assessed using critical appraisal tools (CATs). Standard academic CATs were obtained from the Joanna Briggs Institute (JBI; Aromataris et al., 2024). The appropriate type of CAT for each type of study was used. Following critical appraisal, articles were read in full and further determined if they continued to meet criteria for inclusion. From those that remained, relevant data were extracted. Systematic reviews that only reported on RCTs that were already analyzed for inclusion in the report were discarded, as they provided no new information, while those that included clinical trials not found in the search were included. Meta-analyses were included if they provided results from more than one primary RCT for the drug being studied. To compare the efficacy of psychedelic drugs versus current standard treatments, a separate search was run. Meta-analyses were prioritized, especially those that provided direct statistical comparisons. Like the search for primary RCTs, results that met inclusion criteria were further assessed with CATs before analysis. For Question 3, following the application of inclusion criteria remaining results were assigned to over-arching categories (e.g., studies in healthy volunteers, case studies, etc.) and analyzed further.

Between the three drugs, the initial search for Question 1 yielded a total of 620 results. Of these, 58 were duplicates. For Question 2, there were a total of 269 results returned between the three drugs, 98 of which were duplicate results. After removing duplicates for each drug, applying exclusion criteria, and critical assessment, 62 results were included in the final analysis. To compare the efficacy of each drug against current standard treatments, a secondary search was run to identify these treatments. Between all three drugs, the search returned 574 results, with 147 being duplicate references between the three drugs. Following deduplication, exclusion criteria, and critical assessment, a total of 52 results were analyzed. For Question 3, there were a total of 2,156 results between all three drugs, with 41 duplicates. Following deduplication and the application of exclusion criteria, a total of 382 results were analyzed. Between all drugs and all questions, there were a total of 3,625 results returned, and a total of 555 of these were duplicate results.

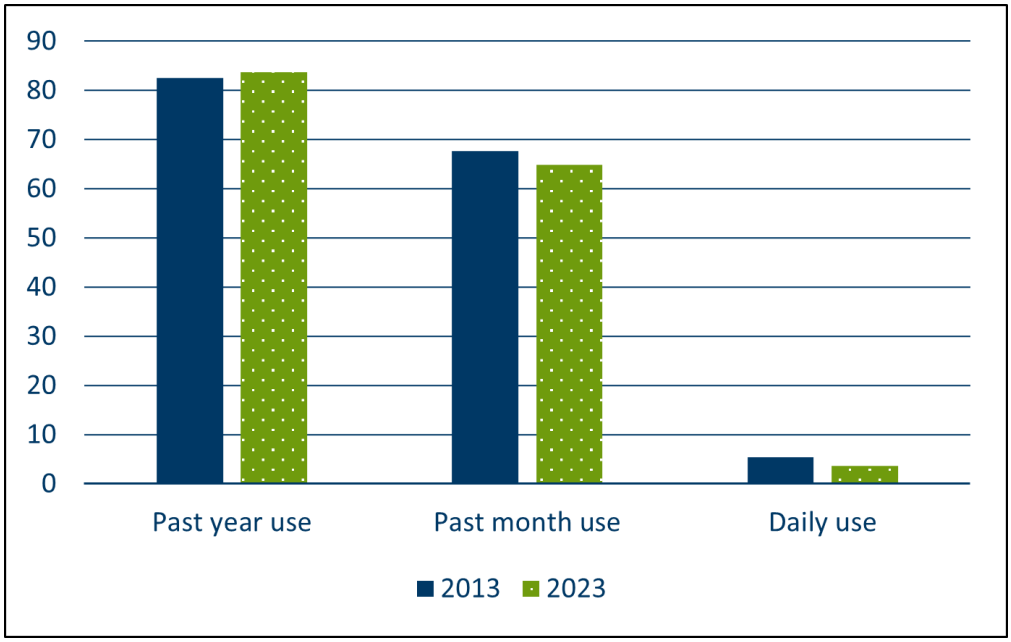
Appendix J: Alcohol and cannabis population statistics

As a comparison with the population statistics reported for psychedelic drugs, the task force presents population statistics for both alcohol and cannabis use. Cannabis is sometimes referred to a marijuana, per the source of the information provided. According to these data, these substances are (and have historically been) used substantially more than any psychedelic drug.

National general use

The Monitoring the Future survey series (Patrick et al., 2024) indicates that reported past year alcohol use by young adults (aged 19 through 30) increased slightly (1.5 percent) in the 10-year period between 2013 and 2023. However, alcohol use in the past 30 days decreased approximately 4 percent in the same 10-year period, while daily use in the past 30 days has decreased approximately 35 percent from 2013 to 2023 (Figure 1).

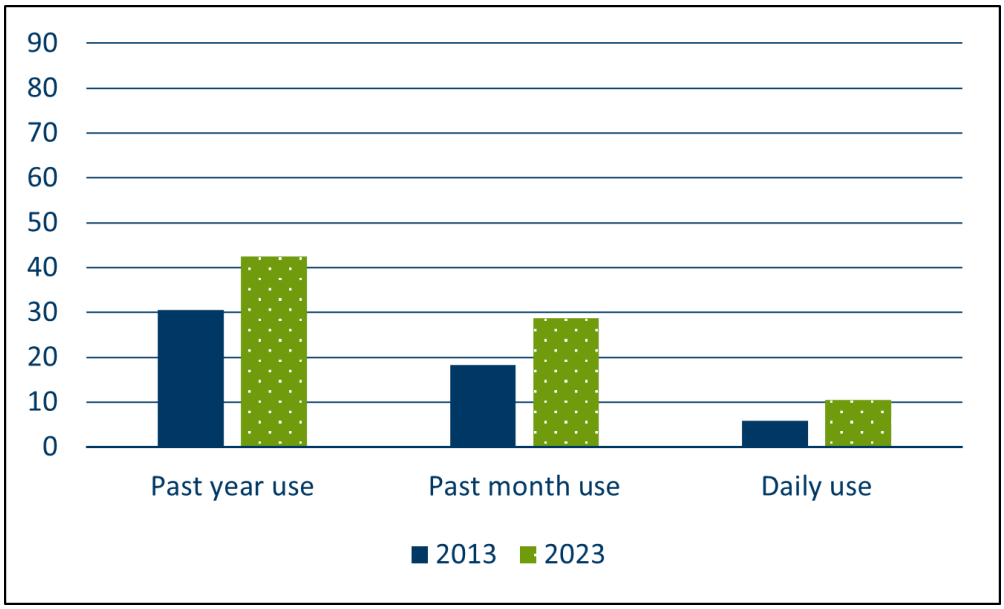
Appendix Figure 1. Percentage of reported alcohol use in 2013 and 2023, ages 19-30



Source: Adapted from Patrick et al., 2024

The same study reports cannabis use (Patrick et al., 2024). In young adults (19 through 30 years old), past year cannabis use has increased approximately 38 percent between 2013 and 2023, reaching an all-time high in 2022 (43.6 percent). Reported past month use has increased nearly 57 percent between 2013 and 2023, also reaching an all-time high of 29 percent in 2021. Finally, self-reported daily use in the past 30 days has increased 76 percent between 2013 and 2023, though is down slightly from the 2022 all-time high (11.3 percent) (Figure 2). While reported use of any hallucinogen in the past year increased from 2013 to 2023 (from 3.8 percent to 8.9 percent), it is still substantially less than both reported alcohol and cannabis use (Patrick et al., 2024).

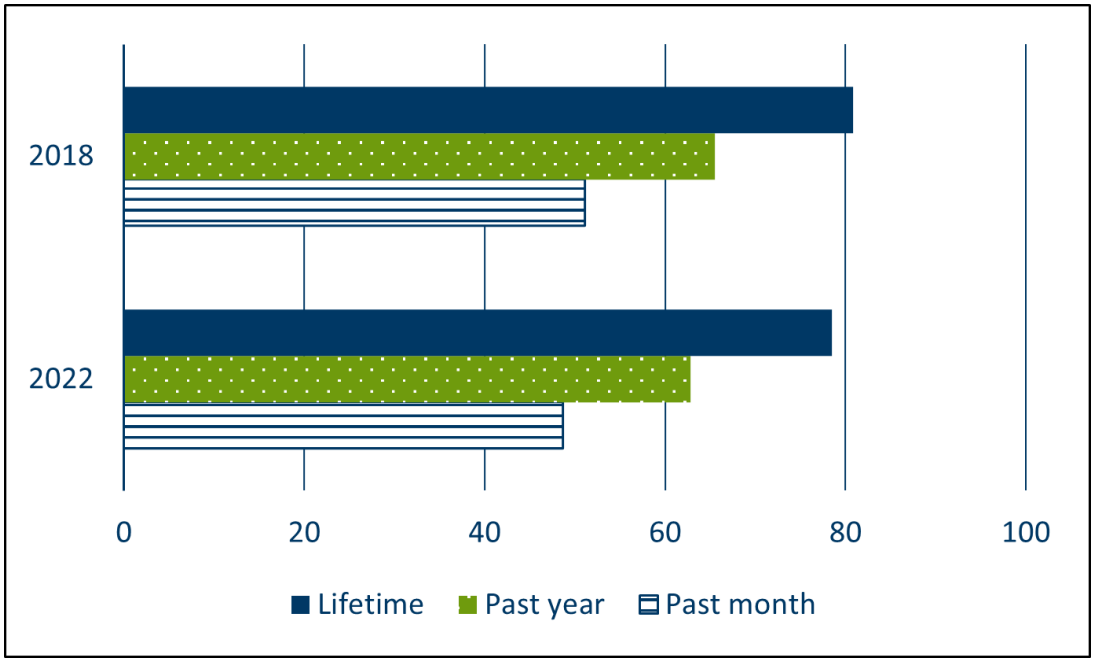
Appendix Figure 2. Percentage of reported cannabis use in 2013 and 2023, ages 19-30



Source: Adapted from Patrick et al., 2024

The annual National Survey on Drug Use and Health sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA) reports national estimates of substance use in the United States in individuals aged 12 and above (SAMHSA, 2019, 2023a). In this population, estimated lifetime use, past year use, and past month use of alcohol all decreased slightly in the years between 2018 and 2022 (Figure 3).

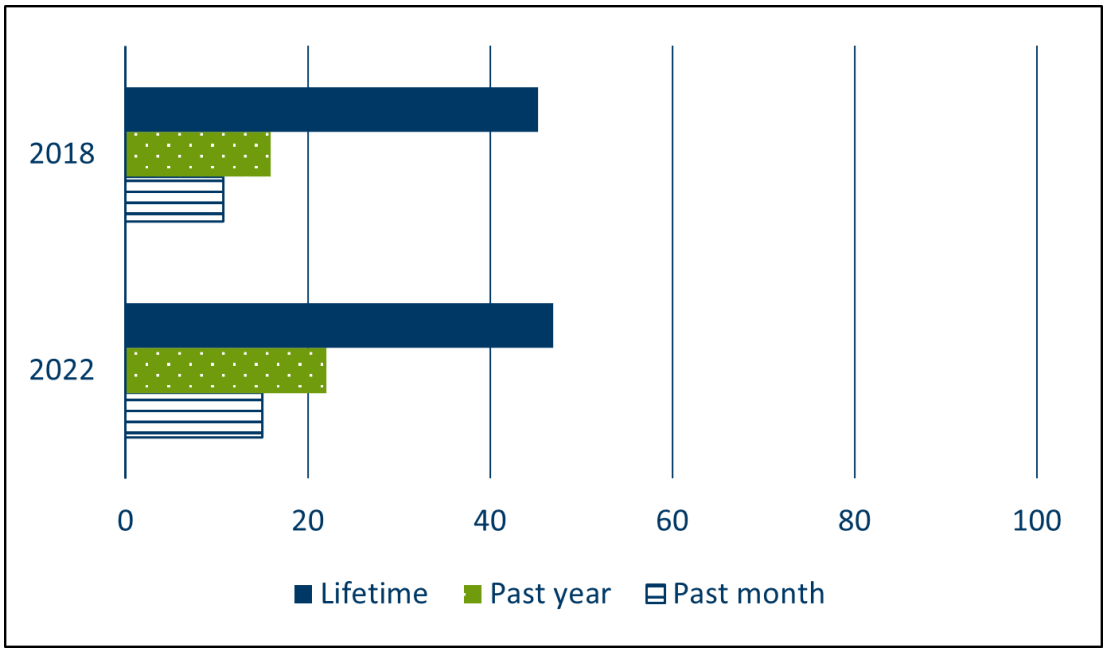
Appendix Figure 3. Estimated percentage of alcohol use in 2018 and 2022, ages 12 and above



Source: Adapted from SAMHSA, 2019, 2023a

Similarly, estimated lifetime use of marijuana (cannabis) increased slightly between 2018 and 2022 in individuals aged 12 and above, while estimated past year and past month use in 2022 each increased by approximately 38 percent and 30 percent, respectively, as compared with 2018 (Figure 4) (SAMHSA 2019; 2023a). As of 2022, the estimated percent of both estimated past year alcohol and cannabis use are substantially higher than estimated past year us of MDMA (7.8 percent), psilocybin (7.8 percent), and LSD (11 percent) (SAMHSA, 2023a).

Appendix Figure 4. Estimated percentage of marijuana use in 2018 and 2022, ages 12 and above



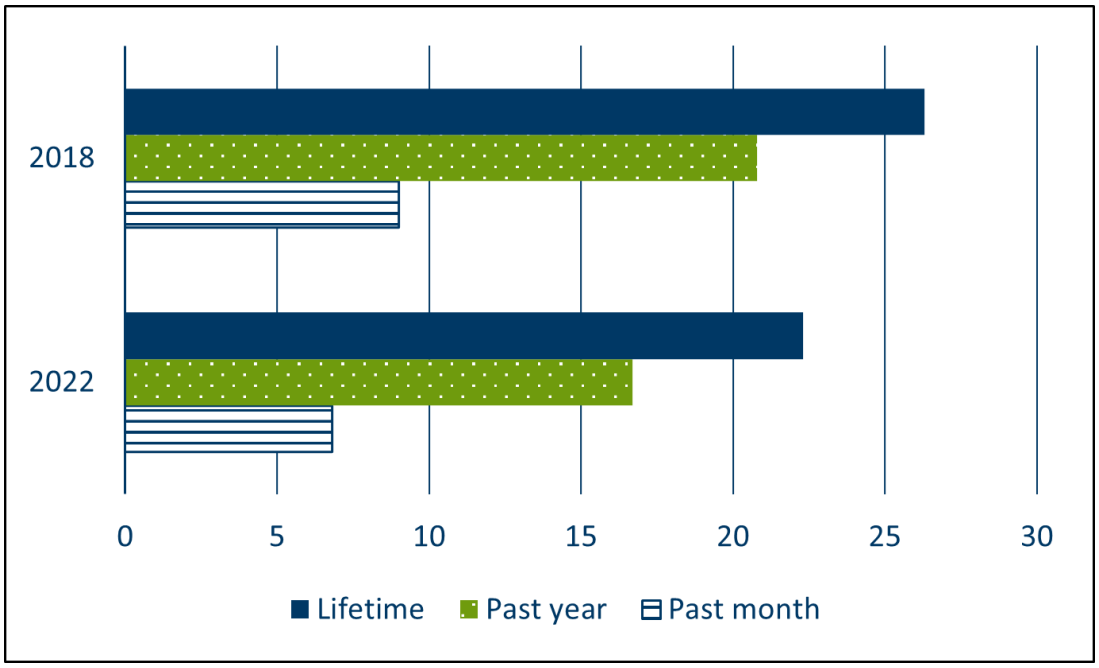
Source: Adapted from SAMHSA, 2019, 2023a

Youth Access

As of 2021, the Centers for Disease Control and Prevention (CDC) Youth Risk Behavior Surveillance System (CDC, 2021) reported that 22.7 percent of high school students reported drinking in the past 30 days. This survey also reports that 27.8 percent have reported ever trying marijuana, with 13.8 percent reporting use in the past 30 days. These numbers are much higher than those students who have reported ever trying any hallucinogen (6.5 percent) (CDC, 2021).

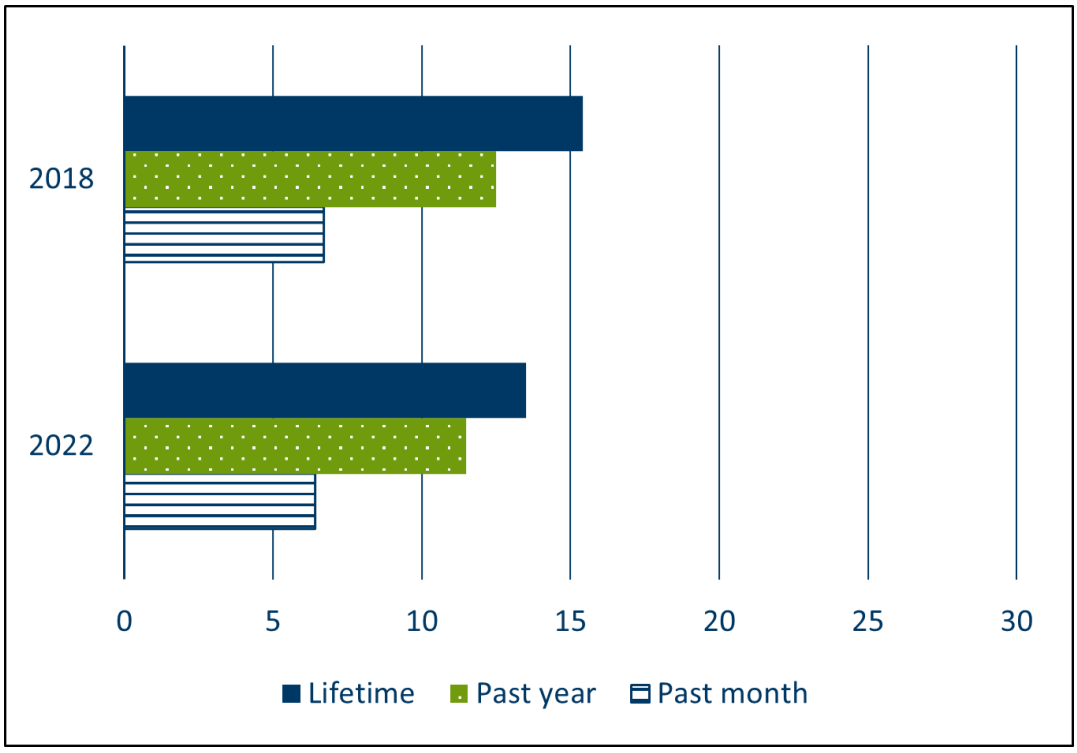
The National Survey on Drug Use and Health also estimated lifetime use of alcohol and marijuana (cannabis) in adolescents aged 12-17 (SAMHSA, 2019, 2023a). In this age group, the estimated percentage of those having ever used alcohol has decreased from 2018 to 2022. This is true for both past year and past month use as well (Figure 5). Estimated lifetime, past year, and past month use of marijuana also decreased between 2018 and 2022 (Figure 6). A decrease in estimated lifetime use of both MDMA (0.8 percent to 0.5 percent) and LSD (1.3 percent to 1.1 percent) between 2018 and 2022 was also reported but estimates of any lifetime use of psilocybin have increased from 0.8 percent to 1.3 percent, representing a 38 percent increase (SAMHSA 2019, 2023a). However, these numbers are still substantially lower than lifetime use of alcohol or marijuana.

Appendix Figure 5. Estimated percentage of alcohol use in 2018 and 2022, ages 12 through 17



Source: Adapted from SAMHSA, 2019, 2023a

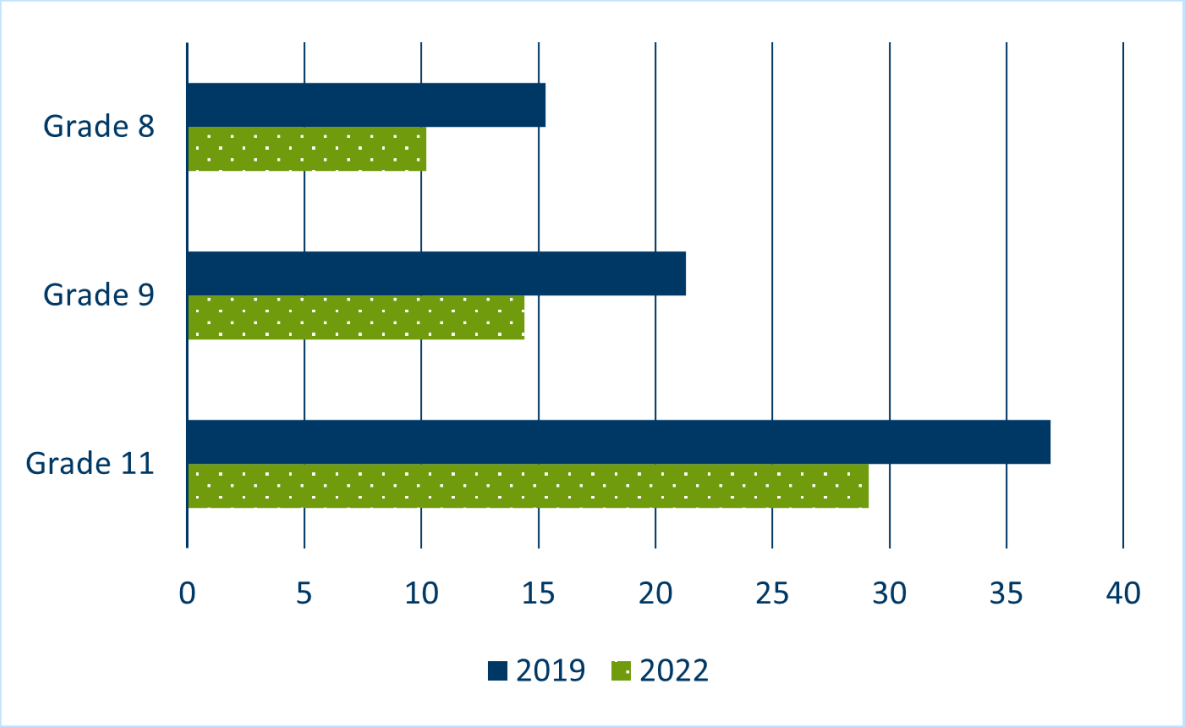
Appendix Figure 6. Estimated percentage of marijuana use in 2018 and 2022, ages 12 through 17



Source: Adapted from SAMHSA, 2019, 2023a

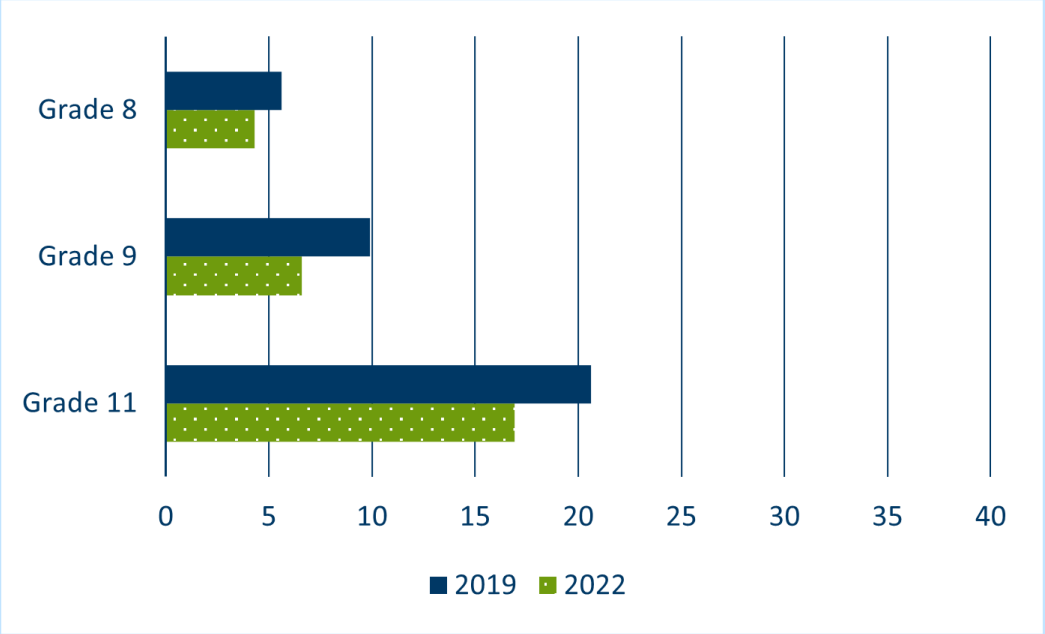
The Minnesota Student Survey includes a section on self-reported substance use, including alcohol, marijuana, and hallucinogen use in the past 12 months (Minnesota Department of Education [MDE], 2022). The percentage of students who reported any past-year use of alcohol has decreased noticeably in grades 8, 9, and 11 between 2019 and 2022 (Figure 7). This trend is true for self-reported use of marijuana as well (Figure 8). On the other hand, self-reported use of LSD, psilocybin, or PCP has increased slightly between 2019 and 2022 in grades 9 (from 1.4 percent to 1.7 percent) and 11 (2.9 percent to 3.0 percent). There was no change in grade 8 self-reports. In this same time period, the use of MDMA, GHB or ketamine decreased in grades 8 (1 percent to 0.7 percent) and 9 (1.1 percent to 0.8 percent), but increased slightly in grade 11 (1.3 percent to 1.4 percent) (MDE, 2022). However, self-reported alcohol and marijuana use were greater in all grades in both 2019 and 2022.

Appendix Figure 7. Percentage of self-reported past year alcohol use by grade in Minnesota, 2019 and 2022



Source: Adapted from MDE, 2022

Appendix Figure 8. Percentage of self-reported past year marijuana use by grade in Minnesota, 2019 and 2022



Source: Adapted from MDE, 2022

Adult Health Data in Minnesota

For adults in Minnesota, statistics on the prevalence of diagnosed health conditions related to drug use have been compiled for the state by the Minnesota Electronic Health Records Consortium (MNEHR) (MNEHR, 2024). Please see the Community Research section for a description of data sources. The reported prevalence estimates that follow include Minnesota residents who were seen at any participating health system within the last three years and received a diagnosis related to use of alcohol or cannabis in the last five years.

The reported prevalence of health conditions related to the use of alcohol rose only marginally between 2020 (133, 150) and 2023 (157,890), representing 2.7 percent and 2.8 percent of the state's population, respectively. Similarly, the prevalence of health conditions related to cannabis use followed the same trend, increasing slightly from 2020 (53,080) to 2023 (66,600), representing 1.1 percent and 1.2 percent of the population, respectively. In comparison, while the reported prevalence of health conditions related to use of hallucinogens (psilocybin, LSD, peyote, and PCP) rose over the period between 2020 and 2023, from 1,860 reports to 2,180 reports statewide, each represents less than 1 percent of the total population. In this dataset MDMA is grouped with other psychostimulants including methamphetamine, and so determining conditions related specifically to MDMA is difficult. However, in both 2020 and 2023 the prevalence of reports related to this category each represented less than 1 percent of the population. Overall, a larger number of adults in the state of Minnesota present with health conditions related to the use of alcohol and cannabis than to psychedelic drugs.

Toxicity and Overdose Statistics

The National Center for Health Statistics reports that the rates of alcohol-induced deaths have increased approximately 7 percent per year from 2000 to 2018. This figure jumped drastically with a 26 percent increase between 2019 and 2020 (Spencer et al., 2022). For the years between 2017 and 2020, there were on average 0.7 deaths from alcohol poisoning per 100,000 people (age-adjusted rate). For that same period, in Minnesota the rate was on average 1.0 per 100,000 people (age-adjusted rate) (MDH, 2021). On the other hand, deaths or overdoses attributed solely to marijuana use have not been reported (NIDA, 2019). Rather, accidents (e.g., motor vehicle crashes) may occur when under the influence, which may in some instances result in mortality (National Academies, 2017). Currently, the National Center for Health Statistics does not include data regarding psychedelic drugs, suggesting that overdoses do not occur frequently enough to be reported in their own category (Spencer et al., 2024).

Poison Control Data

The American Association of Poison Control Centers reports calls to poison control centers across the nation and publishes an annual report. Regarding data from poison control centers, it should be noted that reporting is voluntary, which may result in an underrepresentation of the true occurrence of exposures. Exposures are defined as actual or suspected contact with any substance, regardless of toxicity or clinical manifestation. There may be cases where an exposure involves multiple substances, as well as cases involving a single substance. Data on calls regarding alcohol and cannabis in Minnesota were unavailable.

Data from the National Poison Data System indicate that since 2018 calls regarding a single exposure to alcohol in the form of ethanol-containing beverages has increased overall; however, there was a noticeable spike in calls in 2020 (Table 1). This increase has also occurred steadily regarding those under 20 years old (Gummin et al., 2019, 2020, 2021, 2022, 2023). Numbers reported in all categories presented here are substantially larger than corresponding categories for any of the psychedelic drugs investigated in this report (See Community Research section).

Table 1. Calls to poison control regarding alcoholic beverages, nationwide, 2018 through 2022

Year	Total calls	Total calls, ages 20 and below
2018	7.312	3,067
2019	7,937	3,544
2020	8,340	3,874
2021	7,758	3,419
2022	7,964	3,954

Source: Gummin et al., 2019, 2020, 2021, 2022, 2023

Similarly, the National Poison Data System reports calls on a number of different preparations of marijuana (cannabis) (Gummin et al., 2019, 2020, 2021, 2022, 2023). Data presented here is the aggregate of a number of

common forms: Concentrated extracts, dried plant, edible preparation, oral capsule or pill (non-pharmaceutical), and other or unknown preparation. Calls regarding a single exposure of one of the above-listed forms of cannabis have risen sharply, approximately tripling between 2018 and 2022 (Table 2). The total number of calls have nearly quadrupled for those less than 20 years old in this same five-year period. Furthermore, in 2018, 32.8 percent of calls were specifically in regard to edible preparations; in 2022 this number was 66.8 percent. Similar to alcohol, the number of reported calls regarding these types of cannabis preparations are substantially larger than the number of calls received for psychedelic substances (see Community Research section).

Table 2. Calls to poison control regarding certain cannabis products, nationwide, 2018 through 2022

Year	Total calls	Total calls, ages 20 and below
2018	5,231	3,067
2019	6,792	3,989
2020	9,332	6,455
2021	11,573	8,334
2022	15,738	11,498

Source: Gummin et al., 2019, 2020, 2021, 2022, 2023

Appendix K: Other state efforts

Minnesota is neither the first nor the only state exploring legislation around psychedelic medicine. As both Oregon (Oregon Health Authority, accessed November 11, 2024) and Colorado (Colorado Department of Regulatory Agencies, accessed November 11, 2024) have been leading the nation in this area, much of their work informed the task force's work. This includes aspects that worked well and those that have not. Notably, the high costs involved in the program in Oregon, including to get a license and to engage as a patient with the medicine, have been prohibitive to the majority of the state's citizens.

The following description of state initiatives is what is currently findable, however many states are exploring a variety of access or research options, and ongoing evaluation of what is happening in other states is recommended. A new resource has been created, called Psychedelic Alpha, which has been trying to catalogue what is happening in this space, with one page dedicated to US drug policy reforms with psychedelics (Psychedelic Alpha, accessed December 6, 2024). The Psychedelic Alpha website is actively maintained by volunteers and a collaboration between Calix Law and the UC Berkeley Center for the Science of Psychedelics, though it has some notable errors and thus should not be viewed as the only source on other states efforts. Another resource is available to find out the status of legislation moving through in different states, and at the federal level, through the LegiScan bill tracker website (LegiScan, accessed November 11, 2024). This resource was used to go through state-by-state to see what legislation has passed in each state, with verification on each state's respective legislative website to look at the status of the bills. Most of what is described below relates to the most recent legislative efforts from 2024, with some historical bills addressed, however more information on the history of legislation in each state can be found summarized on the Psychedelic Alpha "Psychedelic Legalization & Decriminalization Tracker" website (Psychedelic Alpha, accessed December 6, 2024).

So far two states (Oregon and Colorado) have approved state-regulated psychedelic medicine programs through voter-initiated ballot measures. Nearly all other states are instead aiming to pass new laws through their state legislature. While almost all of these efforts have been either rejected by their legislatures, or approved and then vetoed by the Governor (California and Arizona), one state (Utah) did successfully pass a bill, however it's unclear how they will source psychedelic medicines, as the law is currently written. The most common approach that is approved by a state legislature is to create working groups or task forces, similar to what the task force did here in Minnesota, or have allocated funding for more research under "pilot programs" that are essentially funding programs for local institutions to conduct more clinical trials through currently federal legal channels with investigational drug products (e.g., those that are allowed by FDA and DEA to be used for research).

The following is a list of state legislative efforts (in alphabetical order):

- Alabama: No legislation on record at the time of report writing.
- Alaska Legislature (2024). Senate Bill HB228. (Alaska State Legislature, September 2024). Creates a task force to determine how best to regulate psychedelic medicines in the state, once approved by the FDA. Signed into law.
- Arizona Legislature (2024). Senate Bill SB1570. (AZ Leg, accessed November 11, 2024). Would have created psilocybin services and licensing structure. It was passed by the legislature but vetoed by the Governor.

- Arkansas: No legislation on record at the time of report writing.
- California Legislature (2024).
    - Senate Bill SB1012 (California Legislative Information, accessed November 11, 2024): Would create a psychedelic medicine program with licensed facilitators, however it is currently stalled in committee and placed on suspense file due to the projected high cost of the program.
    - Senate Bill SB-58 (California Legislative Information, accessed November 11, 2024): Would have decriminalized certain psychedelic substances, which passed through the legislature, but was vetoed by the Governor.
    - Two additional bills were introduced and then cancelled by the bill authors before their hearings:
        - Senate Bill SB-803 (California Legislative Information, accessed November 11, 2024)
        - Assembly Bill AB-941 (California Legislative Information, accessed November 11, 2024).
- Colorado legislature and ballot initiatives. In 2022, voters in Colorado approved proposition 122 to create the Natural Medicine Health Act (NMHA), allowing for facilitated services for a variety of natural psychedelic medicines, both for clinical and peer-supported facilitation, allowing for personal cultivation and decriminalization of various plant medicines.
- SB23-290 was passed by the legislature in 2023 to amend the NMHA, where among other things, created a federally recognized American tribes and Indigenous community working group to discuss the implications of legalizing plant medicines and the impacts that will have on Tribes and other Indigenous communities that use these plant medicines. This working group will issue their report with recommendations in early 2025 (Colorado General Assembly, accessed November 11, 2024).
- Connecticut Legislature (2024). House Bill HB 5297 (Connecticut General Assembly, 2024): Would have decriminalized possession of small amounts of psilocybin mushrooms, which passed through several committees before dying in the Transportation Committee (CT News Junkie, April 2024).
- Delaware, Florida, Georgia: No legislation on record at the time of report writing.
- Hawaii: There have been multiple bills over the years that have introduced that subsequently died in committee, however a Breakthrough Therapies Task Force was created in August of 2023 (Office of the Governor of Hawaii, August 2023).
    - HB 1340/SB 1531 (Hawai'i State Legislature, accessed November 11, 2024): Would have created an advisory council related to breakthrough therapies, but was discharged (i.e., died in committee).
    - HB 1337/SB 1454 (Hawai'i State Legislature, accessed November 11, 2024): Would create a working group related to therapeutic psilocybin. Was carried over into the 2024 sessions, but no updates on its status have been posted since December 2023, suggesting it may have died in committee.
    - HB 2630/SB 3019 (Hawai'i State Legislature, accessed November 11, 2024): Would have established a regulatory framework for administration of therapeutic psilocybin, but died in committee.
- Idaho: No legislation on record at the time of report writing.
- Illinois Legislature (2024). Senate Bill SB2612, Senate Bill SB3695, and House Bill BH0001 (Illinois General Assembly, accessed November 11, 2024): Would create the Compassionate Use and Research of Entheogens (CURE) Act, allowing for facilitated psychedelic medicine services and

licensing, funding, and descheduling of psilocybin and psilocin from the state Controlled Substances Act. This is currently still moving through committee and thus still pending.

- Indiana Legislature (2024). House Bill HB1259 (Indiana General Assembly, accessed November 11, 2024) and Senate Bill SB139 both were introduced to create a similar program to allocate funding for more research into the therapeutic uses of psilocybin. HB1259 was signed into law in March 2024.
- Iowa Legislature (2023). House File HF240 (The Iowa Legislature, accessed November 11, 2024) removes psilocybin and psilocin from the state Controlled Substances Act. It's unclear whether this was approved, as the initial source says it was voted to pass, but a more recent source indicates it died in committee (Bill Track 50, accessed November 11, 2024).
- Kansas, Kentucky, Louisiana: No legislation on record at the time of report writing.
- Maine Legislature (2024). Senate Bill SB194 (Maine Legislature, accessed November 11, 2024) will create the Commission to Study Pathways for Creating a Psilocybin Services Program in Maine. It passed through several committees and is being carried over until the next session.
- Maryland Legislature (2024). Senate Bill SB1009 (Maryland General Assembly, accessed November 11, 2024) and House Bill HB0548 (Maryland General Assembly, accessed November 11, 2024) were introduced "establishing the Task Force on Responsible Use of Natural Psychedelic Substances to study and make recommendations related to the use of natural psychedelic substances; and requiring the Task Force to submit a report of its findings and recommendations to the Governor and the General Assembly on or before July 31, 2025." This was passed and signed by the Governor in May 2024.
- Massachusetts: Question 4 (An Initiative Petition For a Law Relative to the Regulation and Taxation of Natural Psychedelic Substances, accessed November 11, 2024) was rejected by voters in the November 2024 general election. This program would have created a state-regulated program for therapeutic use and licensing for facilitation of natural psychedelic medicines, allow for home cultivation, and decriminalize these behaviors in the state. Several bills have been introduced related to this, however none have progressed through, according to a search on LegiScan (LegiScan, accessed November 11, 2024), which notably does not return ballot initiatives (like Question 4).
- Michigan Legislature (2024). Senate Bill SB0499 (Michigan Legislature, accessed November 11, 2024) and House Bill HB5980 (Michigan Legislature, accessed November 11, 2024) have been introduced in the Fall of 2024 to legalize the cultivation, possession, and use of personal amounts of mushrooms containing psilocin and psilocybin for people 18 years or older with a confirmed diagnosis of post-traumatic stress disorder (PTSD).
- Mississippi: No legislation on record at the time of report writing.
- Missouri Legislature (2024). House Bill HB1830 (Missouri House of Representatives, accessed November 11, 2024) and Senate Bill SB0768 (Missouri Senate, accessed November 11, 2024) were introduced in 2024. The House dropped the bill from the calendar in May 2024, however the Senate bill was put on the perfection calendar, meaning it was reviewed favorably and is in the queue to be discussed on the floor, as of May 2024.
- Montana Legislature (2023). House Bill HB955 (Montana Legislature, accessed November 11, 2024) was introduced in 2023 to legalize psilocybin for post-traumatic stress disorder (PTSD), however it died in committee.
- Nevada Legislature (2023). Senate Bill SB242 (Nevada Legislature, accessed November 11, 2024) created a Psychedelic Medicine Working Group (NV.gov, accessed November 11, 2024) to research and create a report about therapeutic uses of psilocybin/psilocin to the legislature.

- New Hampshire Legislature (2024). House Bill HB1693 (The General Court of New Hampshire, accessed November 11, 2024) was introduced to legalize therapeutic access for psychedelic medicines including MDMA, LSD, and mescaline, for people with qualifying conditions. The bill was deemed unworkable and died in committee (Marijuana Moment, October 2024). They agreed there should be more research, but current state law prohibits clinical trials with Schedule I drugs within the state.
- New Jersey Legislature (2024). Bills A3852 (New Jersey Legislature, accessed November 11, 2024) and S2283 (New Jersey Legislature, accessed November 11, 2024) have been introduced to create the Psilocybin Behavioral Health Access Services Act.
- In 2021, S3256 reclassified possession of psilocybin as disorderly persons offense (New Jersey Legislature, accessed December 4, 2024).
- New Mexico Legislature (2024). SM 12 (New Mexico Legislature, accessed November 11, 2024) was passed by the legislature to create a working group to "study the efficacy of using psilocybin mushrooms for therapeutic treatments."
- New York Legislature (2024). There are several bills that have been introduced in New York, none of which have progressed through the system beyond their initial committee assignments.
    - Assembly Bill A8349A (The New York State Senate, accessed November 11, 2024) and Senate Bill S7832A (The New York State Senate, accessed November 11, 2024) "Establishes the psilocybin assisted therapy pilot program for veterans and first responders."
    - Assembly Bill A3582 (The New York State Senate, accessed November 11, 2024) and Senate Bill S3520 (The New York State Senate, accessed November 11, 2024) "Relates to medical use of psilocybin; establishes a psilocybin assisted therapy grant program; makes an appropriation therefore."
    - Assembly Bill A10375 (The New York State Senate, accessed November 11, 2024) also "Allows the growth, cultivation, and adult use of psilocybin for the treatment of certain health conditions."
- North Caroline Legislature (2024). House Bill HB727 (North Carolina General Assembly, accessed November 11, 2024) was introduced to create the "Breakthrough Therapies Research/Advisory Act" to create a grant program and advisory board to fund clinical research with psychedelic medicines. It appears it's still in committee and has not been approved.
- North Dakota, Ohio: No legislation on record at the time of report writing.
- Oklahoma Legislature (2023). House Bill HB2107 (Oklahoma State Legislature, accessed November 11, 2024) was introduced to allow research trials with psilocybin to be conducted in the state, however it died in committee.
- Oregon legislature and ballot initiatives. In 2020, Oregon voters approved two ballot measures to create psilocybin services (measure 109) and state-wide decriminalization of all drugs for possession of personal use quantities (measure 110).
- The Oregon legislature repealed measure 110 in 2024 through SB4002, overriding the will of the voters to recriminalize possession of all drugs (Oregon State Legislature, accessed November 11, 2024).
- In 2024, the Oregon legislature passed SB303, where data collection from psilocybin services centers becomes mandatory in 2025 (Oregon Health Authority, accessed November 11, 2024).
- Voters in several Oregon cities voted in the 2024 general election to ban psilocybin service centers (Oregon Capital Chronicle, November 2024).
- Pennsylvania: No legislation on record at the time of report writing.

- Rhode Island Legislature (2024). House Bill H7047 (State of Rhode Island in General Assembly, accessed November 11, 2024) was introduced to amend the current law on controlled substances to permit a person to be in possession of less than one ounce of psilocybin and permits psilocybin to be securely cultivated within a person's residence for personal use. The bill died in committee (LegiScan, accessed November 11, 2024).
- South Carolina, South Dakota, Tennessee: No legislation on record at the time of report writing.
- Texas Legislature (2021). House Bill 1802 (Texas Legislature Online, accessed November 11, 2024), Relating to a study on the use of alternative therapies for treating post-traumatic stress disorder.
    - Additional, more recent bills have been introduced relating to the establishment of a Psilocybin Research Advisory Council (Texas Legislature Online, accessed November 11, 2024), and the other relating to a study on the use of alternative therapies for treating post-traumatic stress disorder (Texas Legislature Online, accessed November 11, 2024), both of which died in committee in 2023.
- Utah Legislature (2024). Senate Bill 0266 (Utah State Legislature, accessed November 11, 2024) was passed and allows any psychedelic medicine granted "Breakthrough Therapy" designation by the FDA to be used in two of their state-wide hospital systems. However, the bill itself does not provide a pathway for legal access to these medicines, as pharmaceutical companies that have been granted this status by the FDA are not willing to provide their product to state-programs that are still federally illegal. It is unclear how Utah will source psychedelic medicines.
- Vermont Legislature (2024). Senate Bill SB114 (Vermont General Assembly, accessed November 11, 2024) created a Psychedelic Therapy Advisory Working Group to research and submit a report to the legislature on the medical uses and ways to create a therapeutic program with psychedelic medicines.
    - House Bills H439 (Vermont General Assembly, accessed November 11, 2024) and H371 (Vermont General Assembly, accessed November 11, 2024) were also introduced in 2023 to decriminalize psychedelic medicines, however those died in committee.
- Virginia: No legislation on record at the time of report writing.
- Washington Legislature (2023). SB5263 (Washington State Legislature, accessed November 11, 2024) was introduced originally to cover the creation of a task force working group, a pilot program to fund more clinical trials with psilocybin, and other sections related a state-regulated program and removal of criminal penalties. This was passed by the legislature, and the Governor partially vetoed the bill, approving only the sections for the task force and the pilot program.
- West Virginia Legislature (2024). HB4473 (West Virginia Legislature, accessed November 11, 2024) was introduced to remove psilocybin and certain cannabinoids from the state Controlled Substances Act. It died in committee.
- Wisconsin Legislature (2024). SB727 (Wisconsin State Legislature, accessed November 11, 2024) and AB753 (Wisconsin State Legislature, accessed November 11, 2024) were introduced for creating a medicinal psilocybin treatment fund and a pilot program for psilocybin treatment for PTSD. Failed to pass through a joint senate resolution.
- Wyoming, Washington, DC: No legislation on record at the time of report writing.

Appendix L: Data collection considerations

Discussions with lawyers who have been closely following the rescheduling recommendation for cannabis revealed that this was made possible because of well-collected data from state medical programs. According to the report submitted by HHS, made available through a Freedom of Information Act request (US Department of Health and Human Services, August 2023) from HHS and DEA, there were only two states that had sufficient quality data to inform this recommendation: Maryland and Minnesota. Data collection on activity surrounding Schedule I drugs poses risks, however the track record in the state for the medical cannabis programs data collection efforts did not result in a federal subpoena for access to such data for prosecution of federal laws, beyond this request from HHS for their rescheduling evaluation. However, there are concerns about data confidentiality and privacy protections, which are typically protected under HIPAA, however this does not extend to programs that are in violation of federal laws. Thus, a detailed database of state-regulated activity that are technically federal crimes may put a variety of stakeholders at risk of federal consequences, including but not limited to, prescribers and pharmacies having DEA licenses revoked, federal employees losing benefits, parental rights being questioned or revoked, employment or government assisted housing being at risk, and prosecution for drug diversion/trafficking. While this did not occur under state programs with medical cannabis, it's unclear if the same discretion to "look the other way" will be applied here for psychedelic medicine programs. Best practices will need to be implemented to protect identifiable information for all parties involved that will come into contact with any psychedelic medicine program or services, including not collecting any identifiable data from individuals, and creating state laws about what data is allowed to be shared. Given the existing relationship with data collection, management, and sharing under the medical cannabis program, similar practices could be implemented for a psychedelic medicine program to keep Minnesotans insulated from federal involvement, while also collaborating with the federal government to help inform national drug policy reforms around psychedelic medicines.

One simple to way to mitigate conflicts with federal laws around data privacy and protections is to brand a program as research, which allows a Certificate of Confidentiality (National Institute of Health, accessed November 11, 2024) to be obtained by the federal government, granted by either FDA or NIH, where HIPAA would then apply. This is the approach being used in Oregon through a research study at OHSU to collect data from the psilocybin service centers and to help centers comply with the new state law (SB303, Oregon Health Authority, accessed November 11, 2024) that mandates data collection at psilocybin service centers. The platform for this database is live (OPEN, accessed November 11, 2024), and a paper was published describing the data collection plan (Korthuis, et al., 2024). However, this potentially conflates research with healthcare delivery, as state programs in Oregon, and soon in Colorado, are currently aiming to operate, which may pose some challenges. Should a similar approach be used here in Minnesota, it is advised that any data collection efforts that are required allow people to opt into the program, rather than opting out so people are able decide if they want to participate and what information will be collected about them, and what kind of risks they are putting themselves in by using these services. Any such efforts should be clearly outlined in any informed consent document for clients wanting to use such services and being able to determine whether it is worth the risk to their data privacy and confidentiality.

Minnesota should continue to watch how this is being implemented in Oregon, and eventually Colorado, and consider factors already in place here in the state related to the Minnesota Data Practices Act (Laws of Minnesota 2024, Chapter 13), and leveraging the success of data collection from the Division of Medical Cannabis that helped inform the federal rescheduling recommendation for cannabis (Minnesota Office of Cannabis Management, accessed November 11, 2024).

Appendix M: Resources

The following are resources for more information on various aspects of psychedelic medicine, particularly as they pertain to the recommendations.

Recommendation 1

American Medical Association (AMA) decriminalization policies (https://www.ama-assn.org/system/files/a24-handbook-refcomm-b.pdf)

American Psychological Association (APA) perspective on psychedelic medicine (https://www.apa.org/monitor/2024/06/psychedelics-as-medicine)

Drug decriminalization policy in Portugal (https://drugpolicy.org/wp-content/uploads/2023/08/dpa-drug-decriminalization-portugal-health-human-centered-approach_0.pdf) since 2001

Drug Policy Alliance report on drug decriminalization and recriminalization (https://drugpolicy.org/news/oregon-set-to-recriminalize-drugs-return-to-failed-approach-of-arresting-jailing-people-for-possession/) in Oregon

"Grow, gather, gift" model of decriminalization developed by Decriminalize Nature (https://www.decriminalizenature.org/about/dn-s-ethos)

MAPS training (https://maps.org/2024/03/11/psychedelic-crisis-assessment-and-intervention/) for psychedelic-assisted therapy for first-responders

Minneapolis, MN Executive Order (https://www.minneapolismn.gov/government/mayor/executive-orders/executive-order-2023-01/) deprioritizing entheogenic plants

Minnesota Medical Association (MMA) endorses decriminalization of drug possession (https://www.mnmed.org/application/files/3916/8676/6277/MMA_Decriminalization_HR_Policies.pdf)

Minnesota Medical Association's Frequently Asked Questions (https://www.mnmed.org/application/files/3716/8686/1476/MMA.FAQ.DrugDecrim.Final.pdf)

Minnesota Statutes 2023, Chapter 152 (https://www.revisor.mn.gov/statutes/cite/152)

Minnesota Statues 2023, section 340A.902 (https://www.revisor.mn.gov/statutes/cite/340A.902)

McHenry, A. E. & Siegler, A. "Drug Policy: State of the Evidence," February 2024, https://www.house.mn.gov/comm/docs/WhVCIbMAokmkyoIOz32oUg.pdf.

Open Society Foundations, "A Quiet Revolution: Drug Decriminalisation Policies in Practice Across the Globe," July 2012, https://www.opensocietyfoundations.org/publications/quiet-revolution-drug-decriminalisation-policies-practice-across-globe.

Policy report (https://chacruna.net/wp-content/uploads/2021/11/2021-Comprehensive-Report.pdf) on two years of psilocybin decriminalization in Denver, CO

Psilocybin-containing truffles (https://dutchreview.com/culture/truffles-in-the-netherlands-psychedelic-trip/) for sale in the Netherlands

Students for Sensible Drug Policy, "Just Say Know Drug Education," accessed November 11, 2024, https://ssdp.org/our-work/just-say-know/.

US Department of Justice, Introduction to DARE: Drug Abuse Resistance Education Program; Program Brief," 1991, https://www.ojp.gov/ncjrs/virtual-library/abstracts/introduction-dare-drug-abuse-resistance-education-program-program.

Wikipedia, "Drug Abuse Resistance Education," accessed November 11, 2024, https://en.wikipedia.org/wiki/Drug_Abuse_Resistance_Education.

Recommendation 2

21 C.F.R. § 312.81 (2024). (https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312/subpart-E/section-312.81) Code of Federal Regulations, Title 21

American Psychiatric Association position on psychedelic medicine (https://www.psychiatry.org/news-room/news-releases/apa-releases-official-positions-on-issues-affectin)

Colonial extraction (https://chacruna.net/maria-sabina-mushrooms-and-colonial-extractivism/) of psychedelic medicines

Convention on biological diversity [CBD], "The Nagoya Protocol on Access and Benefit Sharing": https://www.cbd.int/abs/about/default.shtmlAmerican Psychological Association (APA) perspective on psychedelic medicine (https://www.apa.org/monitor/2024/06/psychedelics-as-medicine)

Funding for research on the impact of drug policy changes (https://grants.nih.gov/grants/guide/notice-files/NOT-DA-24-010.html) on public health outcomes

Minnesota Mycological Society (https://minnesotamycologicalsociety.org/about-the-mms/)

Minnesota Office of Cannabis Management (https://mn.gov/ocm/)

Minnesota Statutes 2023, section 151.375. (https://www.revisor.mn.gov/statutes/cite/151.375) Minnesota Right to Try Act

National Archives, Code of Federal Regulations Title 21, Chapter I, Subchapter D, Page 312, Subpart E, § 312.81, March 24, 2004, https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312/subpart-E/section-312.81.

National Institute of Health, "Notice of Special Interest (NOSI): Impacts of Psychedelic and Dissociative Drug Policy Changes on Public Health Outcomes," July 13, 2023, https://grants.nih.gov/grants/guide/notice-files/NOT-DA-24-010.html.

National Institutes of Health (NIH) certificates of confidentiality (https://www.hhs.gov/ohrp/regulations-and-policy/guidance/certificates-of-confidentiality/index.html) for protection of research subjects

Open Psychedelic Evaluation Nexus, accessed November 11, 2024, https://www.openpsychedelicscience.org/.

Psilocybin facilitators sue Oregon Health Authority over access (https://www.axios.com/local/portland/2024/07/02/magic-mushrooms-hospice-psilocybin-oregon-lawsuit)

Right to Try Act. (2018). Public Law 115-176. (https://www.congress.gov/115/bills/s204/BILLS-115s204enr.pdf) Federal Right to Try Act

The Fireside Project (https://firesideproject.org/)

The Office of the Minnesota Attorney General. (2024). Drug Free Zones. State.mn.us. https://www.ag.state.mn.us/consumer/Publications/DrugFreeZones.asp. Accessed November 15, 2024.

US Department of Health and Human Services, "Basis for the recommendation to reschedule marijuana into Schedule III of the Controlled Substances Act," August 29, 2023, page 81, https://www.dropbox.com/scl/fi/pw3rfs9gm6lg80ij9tja6/2023-01171-Supplemental-Release-1.pdf?rlkey=v5atj0tcnhxhnszyyzcwdcvvt&e=4&st=jygniear&dl=0.

Recommendation 3

21 C.F.R. § 312.81 (2024). (https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312/subpart-E/section-312.81)

Conducting clinical trials with decentralized elements (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/conducting-clinical-trials-decentralized-elements)

Education and research programs of Attorney General, 21 U.S.C. § 872e (https://www.govinfo.gov/app/details/USCODE-2023-title21/USCODE-2023-title21-chap13-subchapI-partE-sec872)

Funding for research on the impact of drug policy changes (https://grants.nih.gov/grants/guide/notice-files/NOT-DA-24-010.html) on public health outcomes

Funding opportunities (https://www.justice.gov/grants) from the Department of Justice

Minnesota Office of Cannabis Management (https://mn.gov/ocm/)

Lykos Therapeutics, "A Multi-site Expanded Access Program for MDMA-assisted Psychotherapy for Patients With Treatment-resistant PTSD (EAMP1)," November 5, 2024, https://clinicaltrials.gov/study/NCT04438512.

National Institute of Health, "Notice of Special Interest (NOSI): Impacts of Psychedelic and Dissociative Drug Policy Changes on Public Health Outcomes," July 13, 2023, https://grants.nih.gov/grants/guide/notice-files/NOT-DA-24-010.html.

National Institute of Mental Health, "Notice of Information on NIMH's Considerations for Research Involving Psychedelics and Related Compounds," November 16, 2022, https://grants.nih.gov/grants/guide/notice-files/NOT-MH-23-125.html.

Online tracker for psychedelic medicine legislation (https://psychedelicalpha.com/data/psychedelic-laws)

US Food and Drug Administration, "Conducting Clinical Trials With Decentralized Elements," September 2024, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/conducting-clinical-trials-decentralized-elements.

US Department of Veterans Affairs [VA], "To improve care for Veterans, VA to fund studies on new therapies for treating mental health conditions," January 5, 2024, https://news.va.gov/press-room/to-improve-care-for-veterans-va-to-fund-studies-on-new-therapies-for-treating-mental-health-conditions/.

Recommendation 4

American Medical Association (AMA) decriminalization policies (https://www.ama-assn.org/system/files/a24-handbook-refcomm-b.pdf)

Cannabis social clubs in Spain (https://internationalcbc.com/what-is-the-status-of-cannabis-clubs-in-spain/) and Malta (https://internationalcbc.com/an-estimated-750-people-have-joined-maltas-legal-cannabis-clubs/)

Colorado Natural Medicine Program (https://dpo.colorado.gov/NaturalMedicine)

Convention on biological diversity (CBD), "The Nagoya Protocol on Access and Benefit Sharing": https://www.cbd.int/abs/about/default.shtml

Creating Health Equity in Minnesota (https://www.health.state.mn.us/communities/equity/about/creatinghealthequity.html)

FDA recall of Diamond Schruumz (https://www.fda.gov/food/outbreaks-foodborne-illness/investigation-illnesses-diamond-shruumz-brand-chocolate-bars-cones-gummies-june-2024) products and subsequent warning from the Minnesota Department of Agriculture (https://www.mda.state.mn.us/minnesota-officials-urge-residents-not-consume-mushroom-based-microdose-chocolates-candies)

Laws of Minnesota 2023, Chapter 27 (https://www.revisor.mn.gov/statutes/cite/27/full)

Laws of Minnesota 2023, Chapter 342 (https://www.revisor.mn.gov/statutes/cite/342/full)

Minneapolis, MN Executive Order (https://www.minneapolismn.gov/government/mayor/executive-orders/executive-order-2023-01/) deprioritizing entheogenic plants

Minnesota Department of Agriculture Certified Wild Mushroom Harvester Database (https://www.mda.state.mn.us/certified-wild-mushroom-harvester-database)

Minnesota Office of Cannabis Management, "First Draft of Proposed Cannabis Rules," July 31, 2024, https://mn.gov/ocm/assets/first-draft-of-cannabis-rules_tcm1202-639141.pdf.

Minnesota Office of Cannabis Management, "Tribal Nations," accessed November 11, 2024, https://mn.gov/ocm/tribal-nations/.

Minnesota Mycological Society (https://minnesotamycologicalsociety.org/about-the-mms/)

Oregon Psilocybin Services (https://www.oregon.gov/oha/ph/preventionwellness/pages/oregon-psilocybin-services.aspx)

Policy report (https://chacruna.net/wp-content/uploads/2021/11/2021-Comprehensive-Report.pdf) on two years of psilocybin decriminalization in Denver, CO

Psilocybin-containing mushrooms are the most-used psychedelic drug (https://www.rand.org/news/press/2024/06/27.html)

Report on Health Disparities in Minnesota (https://mncmsecure.org/website/Reports/Community%20Reports/Disparities%20by%20RELC/2022MY%20Disparities%20by%20RELC_FINAL.pdf), October 2023

Tryptomics, "Testing Result Report," May 21, 2024, https://www.tryptomics.com/_files/ugd/05d377_4f502cdb2f864aea9a225df15a4f52ac.pdf?index=true.

U.S. Const. amend. X, § 4.2 (https://constitution.congress.gov/browse/essay/amdt10-4-2/ALDE_00013627/)

University of California, Berkeley poll on public support of psychedelics (https://psychedelics.berkeley.edu/berkeley-psychedelics-survey-2023/)

Veterans affairs

Cronk, T.M. (2017). President Signs Bill to Extend Veteran's Choice Health Care Law (https://www.defense.gov/News/News-Stories/Article/Article/1158092/president-signs-bill-to-extend-veterans-choice-health-care-law/)

Funding mechanism from the VA for psychedelic medicine research (https://news.va.gov/press-room/to-improve-care-for-veterans-va-to-fund-studies-on-new-therapies-for-treating-mental-health-conditions/)

Heroic Hearts Project (https://heroicheartsproject.org/)

Heroic Hearts Project research with King's College London (https://heroicheartsproject.org/about/hhp-research/)

Minnesota Veteran Suicide Statistics, 2021 (https://www.mentalhealth.va.gov/docs/data-sheets/2021/2021-State-Data-Sheet-Minnesota-508.pdf)

Operation Deep Dive (https://docs.house.gov/meetings/VR/VR00/20220929/115166/HHRG-117-VR00-Wstate-LorraineJ-20220929-SD001.pdf)

Reason for Hope (https://www.reason-for-hope.org/)

Ryan, S. (Host). (2019—present). Pete Hegseth - Secretary of Defense Nominee | SRS. Vigilance Elite. https://www.youtube.com/watch?v=DoN5ovwB8s4

The Douglas Mike Day Psychedelic Therapy to Save Lives Act of 2023 spending bill by the Department of Defense (https://www.congress.gov/bill/118th-congress/house-bill/3684/text) was passed to fund more psychedelic medicine research for military personnel

The Wounded Warrior Project's government affairs (https://www.woundedwarriorproject.org/programs/government-affairs)

Veterans Choice Program (VCP) https://www.publichealth.va.gov/exposures/publications/oef-oif-ond/post-9-11-vet-fall-2015/veterans-choice-program.asp

Veterans Exploring Treatment Solutions (VETS) https://vetsolutions.org/.

Veterans Mental Health Coalition (VMHC) https://vmhlc.org/

Willink, J., & Charles, E. (Hosts). (2015—present). Under reported [Audio podcast]. DEFCOR Network. https://www.youtube.com/watch?v=lDffjkSecaU

Other resources, news articles, and government reports

21 U.S.C. § 872d (https://www.govinfo.gov/content/pkg/USCODE-2023-title21/pdf/USCODE-2023-title21-chap13-subchapI-partE-sec872.pdf)

21 U.S.C. § 872e (https://www.govinfo.gov/content/pkg/USCODE-2023-title21/pdf/USCODE-2023-title21-chap13-subchapI-partE-sec872.pdf)

Alaska State Legislature, "HB 228: An Act establishing the Alaska task force for the regulation of psychedelic medicines approved by the United States Food and Drug Administration; and providing for an effective date," September 19, 2024, https://www.akleg.gov/basis/Bill/Detail/33?Root=HB228.

Adlin, B. (2024a, August 20). Federal Court Hears Doctor's Dispute With DEA Over Giving Psilocybin To Terminally Ill Cancer Patients. Marijuana Moment. https://www.marijuanamoment.net/federal-court-hears-doctors-dispute-with-dea-over-giving-psilocybin-to-terminally-ill-cancer-patients/

Adlin, B. (2024b, September 19). Georgia Pharmacy Begins Selling Medical Marijuana To Patients In Defiance Of DEA Warnings About Federal Law. Marijuana Moment. https://www.marijuanamoment.net/georgia-pharmacy-begins-selling-medical-marijuana-to-patients-in-defiance-of-dea-warnings-about-federal-law/

Adlin, B. (2024c, October 9). New Hampshire Lawmakers Recommend State Consider Psychedelic Therapy Access Options. Marijuana Moment. https://www.marijuanamoment.net/new-hampshire-lawmakers-recommend-state-consider-psychedelic-therapy-access-options/.

American Indian Religious Freedom Act Amendments of 1994 [AIRFA]. H.R. 4230, 103rd Congress. (1994). https://www.congress.gov/bill/103rd-congress/house-bill/4230/text

American Psychological Association [APA]. (2020). Treatments for PTSD. https://www.apa.org. https://www.apa.org/ptsd-guideline/treatments.

An Initiative Petition for a Law Relative to the Regulation and Taxation of Natural Psychedelic Substances, "The Natural Psychedelic Substances Act," accessed November 11, 2024, https://s3.documentcloud.org/documents/25040955/23-13_petition_text.pdf.

Arizona Legislature, "Bill History for SB1570," accessed November 11, 2024, https://apps.azleg.gov/BillStatus/BillOverview/81143.

Busby, M. (2024, October 10). Psychedelic Mushrooms Are Getting Much, Much Stronger. WIRED. https://www.wired.com/story/breeding-stronger-magic-mushrooms/

California Institute of Integral Studies, "Exploring the Evolving Role of Chaplains in Psychedelic-Assisted Therapy on NPR," October 3, 2023, https://www.ciis.edu/news/exploring-evolving-role-chaplains-psychedelic-assisted-therapy-npr.

California Legislative Information, "SB-1012 The Regulated Psychedelic Facilitators Act and the Regulated Psychedelic-Assisted Therapy Act," accessed November 11, 2024, https://leginfo.legislature.ca.gov/faces/billStatusClient.xhtml?bill_id=202320240SB1012.

California Legislative Information, "SB-58 Controlled substances: decriminalization of certain hallucinogenic substances," accessed November 11, 2024, https://leginfo.legislature.ca.gov/faces/billStatusClient.xhtml?bill_id=202320240SB58.

California Legislative Information, "SB-803 Heal Our Heroes Act," accessed November 11, 2024, https://leginfo.legislature.ca.gov/faces/billStatusClient.xhtml?bill_id=202320240SB803.

California Legislative Information, "AB-941 Controlled substances: psychedelic-assisted therapy," accessed November 11, 2024, https://leginfo.legislature.ca.gov/faces/billStatusClient.xhtml?bill_id=202320240AB941.

Centers for Disease Control [CDC]. (2021). Youth Online: High School YRBS - United States 2021 Results | DASH | CDC. NCCD.CDC.gov. Retrieved from: https://tinyurl.com/bdhjy3sf

Chacruna. (2021, June 21) "DEA Denies Soul Quest's Religious Exemption: Impacts on the Ayahuasca Community." https://chacruna.net/dea_denies_soul_quest_religious_exemption_ayahuasca/.

Chacruna Institute for Psychedelic Plant Medicines & Hoots, A. (2021). Guide to RFRA and Best Practices for Psychedelic Plant Medicine Churches. San Francisco, CA: Chacruna Institute for Psychedelic Plant Medicines. https://chacruna.net/guide_rfra_best_practices_psychedelic_churches/. ISBN 979-8-9852933-3-3

Chen, A. (2017, April 20). Some of the Parts: Is Marijuana's "Entourage Effect" Scientifically Valid? Scientific American. https://www.scientificamerican.com/article/some-of-the-parts-is-marijuana-rsquo-s-ldquo-entourage-effect-rdquo-scientifically-valid/

Colorado General Assembly, "SB23-290: Natural Medicine Regulation And Legalization," accessed November 11, 2024, https://leg.colorado.gov/bills/sb23-290.

COMPASS Pathways. (2018, October 23). COMPASS Pathways Receives FDA Breakthrough Therapy Designation for Psilocybin Therapy for Treatment-resistant Depression. Retrieved from: https://www.prnewswire.com/news-releases/compass-pathways-receives-fda-breakthrough-therapy-designation-for-psilocybin-therapy-for-treatment-resistant-depression-834088100.html

Connecticut General Assembly, "Substitute for Raised H.B. No. 5297: an act concerning the decriminalization of possession of small amounts of psilocybin," 2024, https://www.cga.ct.gov/asp/cgabillstatus/cgabillstatus.asp?selBillType=Bill&bill_num=HB05297&which_year=2024.

Constitution Annotated, "ArtI.S8.C1.2.1 Overview of Spending Clause," accessed November 11, 2024, https://constitution.congress.gov/browse/essay/artI-S8-C1-2-1/ALDE_00013356/.

CT News Junkie. (2024, April 18) "Psilocybin Decriminalization Bill Dies In Transportation Committee After Referral." https://ctnewsjunkie.com/2024/04/18/psilocybin-decriminalization-bill-dies-in-transportation-committee-after-referral/.

Cybin. (2024, March 13). Cybin Receives FDA Breakthrough Therapy Designation for its Novel Psychedelic Molecule CYB003 and Announces Positive Four-Month Durability Data in Major Depressive Disorder. Cybin Corp. https://ir.cybin.com/investors/news/news-details/2024/Cybin-Receives-FDA-Breakthrough-Therapy-Designation-for-its-Novel-Psychedelic-Molecule-CYB003-and-Announces-Positive-Four-Month-Durability-Data-in-Major-Depressive-Disorder/default.aspx.

Drug Enforcement Agency [DEA]. (2020). What Are Hallucinogens? Drug Enforcement Administration. https://www.dea.gov/sites/default/files/2020-06/Hallucinogens-2020.pdf

Drug Enforcement Agency [DEA]. (2024). National Drug Threat Assessment 2024. Drug Enforcement Administration. https://www.dea.gov/sites/default/files/2024-05/5.23.2024%20NDTA-updated.pdf

Drug Enforcement Administration [DEA], April 10, 2024, https://iowamedicalmarijuana.org/cases/olsen-dea-2021.html

Estrada, Á. (1989). Vida de María Sabina: La sabia de los hongos. Siglo XXI Editores México.

Executive Order 13132: Federalism, August 4, 1999. Federal Register, Vol. 64, No. 153 (https://www.govinfo.gov/content/pkg/FR-1999-08-10/pdf/99-20729.pdf)

Fierce Healthcare. (2024, September 9) "Texas sues HHS over rule that limits access to reproductive health information by law enforcement." https://www.fiercehealthcare.com/regulatory/texas-sues-hhs-over-rule-limits-access-reproductive-health-information-law-enforcement.

Food and Drug Administration [FDA]. (2019, March 5). FDA approves new nasal spray medication for treatment-resistant depression; available only at a certified doctor's office or clinic. U.S. Food and Drug Administration. https://www.fda.gov/news-events/press-announcements/fda-approves-new-nasal-spray-medication-treatment-resistant-depression-available-only-certified

Food and Drug Administration [FDA]. (2023). Psychedelic drugs: Considerations for clinical investigations guidance for industry (Draft guidance). Docket: FDA-2023. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/psychedelic-drugs-considerations-clinical-investigations.

Government of British Columbia. (2023, March 7). Decriminalizing Personal Possession of Illicit Substances - Province of British Columbia. Www2.Gov.bc.ca. https://www2.gov.bc.ca/gov/content/overdose/decriminalization

Guzmán, G. (2019). The hallucinogenic mushrooms: Diversity, traditions, use and abuse with special reference to the genus Psilocybe. In Fungi from Different Environments (pp. 256-277). CRC Press.

Hawai'i State Legislature, "HB1340 HD2 SD2," accessed November 11, 2024, https://www.capitol.hawaii.gov/session/measure_indiv.aspx?billtype=HB&billnumber=1340&year=2024.

Hawai'i State Legislature, "HB1337," accessed November 11, 2024, https://www.capitol.hawaii.gov/session/measure_indiv.aspx?billtype=HB&billnumber=1337&year=2024.

Hawai'i State Legislature, "HB2630 HD2," accessed November 11, 2024, https://www.capitol.hawaii.gov/session/measure_indiv.aspx?billtype=HB&billnumber=2630&year=2024.

Hopkins, J. (2023, April 14). MindMed Collaborators Announce Positive Topline Data from Phase 2 Trial of Lysergide (LSD) in Major Depressive Disorder (MDD). MindMed. https://mindmed.co/news/press-release/mindmed-collaborators-announce-positive-topline-data-from-phase-2-trial-of-lysergide-lsd-in-major-depressive-disorder-mdd/

Illinois State Legislature, "Bill Status of HB0001: Illinois CURE Act," accessed November 11, 2024, https://www.ilga.gov/legislation/BillStatus.asp?DocNum=1&GAID=17&DocTypeID=HB&SessionID=112&GA=103.

Indiana General Assembly, "House Bill 1259: Health care matters," accessed November 11, 2024, https://iga.in.gov/legislative/2024/bills/house/1259/details.

International Narcotics Control Board [INCB]. (2003). List of psychotropic substances under international control. Retrieved from https://web.archive.org/web/20051205125434/http://www.incb.org/pdf/e/list/green.pdf

Iowa Legislature, "House File 240," accessed November 11, 2024, https://www.legis.iowa.gov/legislation/BillBook?ga=90&ba=HF240.

Iowa Legislature. Bill Track 50, "IA HF240," accessed November 11, 2024, https://www.billtrack50.com/billdetail/1563708.

Jaeger, K. (2021, June 21). Texas Will Study Benefits Of Psychedelics For Military Veterans Under Bill Enacted Without Governor's Signature. Marijuana Moment. https://www.marijuanamoment.net/texas-will-study-benefits-of-psychedelics-for-military-veterans-under-bill-enacted-without-governors-signature/

Law Enforcement Action Partnership, accessed November 11, 2024, https://lawenforcementactionpartnership.org/.

LegiScan, accessed November 11, 2024, https://legiscan.com/.

LegiScan, "Results for MA legislative search about psilocybin," accessed November 11, 2024, https://legiscan.com/gaits/search?state=MA&keyword=psilocybin.

LegiScan, "Rhode Island House Bill 7047," accessed November 11, 2024, https://legiscan.com/RI/bill/H7047/2024.

Lykos Therapeutics, "A Multi-site Expanded Access Program for MDMA-assisted Psychotherapy for Patients With Treatment-resistant PTSD (EAMP1)," May 11, 2024, https://clinicaltrials.gov/study/NCT04438512.

Maine Legislature, "Resolve, to Establish the Commission to Study Pathways for Creating a Psilocybin Services Program in Maine," accessed November 11, 2024, https://legislature.maine.gov/legis/bills/display_ps.asp?LD=1914&snum=131.

Marlan, D. (2021, March 24). The Myth of Psychedelic Exceptionalism - Bill of Health. Blog.petrieflom.law.harvard.edu. https://blog.petrieflom.law.harvard.edu/2021/03/24/psychedelic-exceptionalism-drug-policy/. Accessed November 9, 2024.

Maryland General Assembly, "SB 1009: Task Force on Responsible Use of Natural Psychedelic Substances," accessed November 11, 2024, https://mgaleg.maryland.gov/mgawebsite/Legislation/Details/SB1009?ys=2024RS.

Maryland General Assembly, "HB 0548: Task Force on Responsible Use of Natural Psychedelic Substances," accessed November 11, 2024, https://mgaleg.maryland.gov/mgawebsite/Legislation/Details/HB0548?ys=2024RS.

Michigan Legislature, "Senate Bill 499 of 2023," accessed November 11, 2024, https://legislature.mi.gov/Bills/Bill?ObjectName=2023-SB-0499.

Michigan Legislature, "House Bill 5980 of 2024," accessed November 11, 2024, https://legislature.mi.gov/Bills/Bill?ObjectName=2024-HB-5980.

Mind Medicine, Inc. "MindMed Announces First Patient Dosed in Phase 3 Voyage Study of MM120 in Generalized Anxiety Disorder (GAD)," accessed December 16, 2024, https://ir.mindmed.co/news-events/press-releases/detail/169/mindmed-announces-first-patient-dosed-in-phase-3-voyage-study-of-mm120-in-generalized-anxiety-disorder-gad.

Minnesota Department of Education [MDE]. Data Reports and Analytics. (2022). Public.education.mn.gov. https://public.education.mn.gov/MDEAnalytics/DataTopic.jsp?TOPICID=242

Minnesota Department of Health [MDH]. (2023). Estimates of Alcohol Poisoning Deaths. Minnesota Department of Health. https://www.health.state.mn.us/communities/alcohol/documents/alcoholpoison2021.pdf

Minnesota Department of Health [MDH]. (2024). Data Projects - MNDOSA. Retrieved from: https://www.health.state.mn.us/communities/injury/data/mndosa.html

Minnesota Electronic Health Records Consortium [MNEHR]. (2024). Health Trends Across Communities in Minnesota Dashboard | Minnesota EHR Consortium. Retrieved from https://mnehrconsortium.org/health-trends-across-communities-minnesota-dashboard

Minnesota Office of Cannabis Management, "Data Collection Background and Surveys," accessed November 11, 2024, https://mn.gov/ocm/dmc/data-reports/data-collection/.

Minnesota Regional Poison Center [MNRPC]. (2024). Annual Reports. Minnesota Regional Poison Center. https://mnpoison.org/about-the-poison-center/annual-reports/

Minnesota Senate Media Services, "Senate Floor Session - Part 1 - 05/03/24," May 6, 2024, https://www.youtube.com/watch?v=95jiOSzaAZY&t=24233s.

Missouri House of Representatives, "HB 1830," accessed November 11, 2024, https://house.mo.gov/Bill.aspx?bill=HB1830&year=2024&code=R.

Missouri Senate," SB 768," accessed November 11, 2024, https://www.senate.mo.gov/24info/BTS_Web/Bill.aspx?SessionType=R&BillID=349.

Montana Legislature, "HB 955: Legalize psilocybin use for PTSD/mental illness treatment," accessed November 11, 2024, https://bills.legmt.gov/#/bill/20231/LC1208.

Multidisciplinary Association for Psychedelic Studies [MAPS]. "Psychedelic Science 2023," accessed November 11, 2024, https://2023.psychedelicscience.org/sessions/mechanisms-and-time-course-of-psilocybin-induced-neuroplasticity-in-healthy-human-volunteers/.

National Academies of Science, Engineering, and Medicine, "Cannabis Policy Impacts Public Health and Health Equity," 2024, https://nap.nationalacademies.org/catalog/27766/cannabis-policy-impacts-public-health-and-health-equity.

National Archives, Code of Federal Regulations Title 21, Chapter I, Subchapter D, Page 312, Subpart E, § 312.81, March 24, 2004, https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-312/subpart-E/section-312.81.

National Center for Health Statistics [NCHS]. (2021) Health, United States: Table SubsUse. Hyattsville, MD. Available from: https://www.cdc.gov/nchs/hus/data-finder.htm

National Institute on Drug Abuse [NIDA]. (2019). Cannabis (Marijuana) DrugFacts. National Institute on Drug Abuse; National Institute on Drug Abuse. https://nida.nih.gov/publications/drugfacts/cannabis-marijuana

National Institute of Mental Health [NIMH]. (2023). Post-traumatic stress disorder. National Institute of Mental Health. https://www.nimh.nih.gov/health/topics/post-traumatic-stress-disorder-ptsd.

National Institute of Mental Health [NIMH]. (2024a). Anxiety Disorders. Retrieved from: https://www.nimh.nih.gov/health/topics/anxiety-disorders#:~:text=Cognitive%20behavioral%20therapy&text=It%20teaches%20people%20different%20ways.

National Institute of Mental Health [NIMH]. (2024b). Social Anxiety Disorder: More Than Just Shyness. Retrieved from: https://www.nimh.nih.gov/health/publications/social-anxiety-disorder-more-than-just-shyness#part_6258.

National Institute of Mental Health [NIMH]. (2024c). Depression. Retrieved from https://www.nimh.nih.gov/health/topics/depression#:~:text=Depression%20is%20usually%20treated%20with,a%20combination%20of%20the%20two.

National Institute of Mental Health [NIMH]. (2024d). Bipolar Disorder. National Institute of Mental Health. Retrieved from: https://www.nimh.nih.gov/health/topics/bipolar-disorder

National Institute of Neurological Disorders and Stroke [NINDS]. (2023). Cluster headache. Retrieved from: https://www.ninds.nih.gov/health-information/disorders/headache#:~:text=only%20brief%20remissions.-,Cluster%20headache,migraine%2Dlike%20aura%20and%20nausea.

National Institute on Alcohol Abuse and Alcoholism [NIAAA]. (2024). Understanding alcohol use disorder. Retrieved from: https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/understanding-alcohol-use-disorder--.

National Library of Medicine, "Visual Surround Suppression and Perceptual Expectation Under Psilocybin," June 3, 2024, https://clinicaltrials.gov/study/NCT04424225.

Nevada Legislature, "SB 242," accessed November 11, 2024, https://www.leg.state.nv.us/App/NELIS/REL/82nd2023/Bill/10067/Overview.

NV.gov, "Psychedelic Medicines Working Group," accessed November 11, 2024, https://dhhs.nv.gov/Resources/Psychedelic_Medicines_Working_Group/.

The General Court of New Hampshire, "HB1693-FN," accessed November 11, 2024, https://www.gencourt.state.nh.us/bill_Status/billinfo.aspx?id=1610.

Nielson, J. L. & Megler, J. D. "Ayahuasca as a Candidate Therapy for PTSD," *The Therapeutic Use of Ayahuasca*, pp 41-58, https://link.springer.com/chapter/10.1007/978-3-642-40426-9_3.

Nielson, J. L., Megler, J. D., & Canvar, C. "A Qualitative Assessment of Risks and Benefits of Ayahuasca for Trauma Survivors," *Ayahuasca Healing and Science,* pp 81-98, https://link.springer.com/chapter/10.1007/978-3-030-55688-4_5.

New Jersey Legislature, “Bill A3852 Acs (ACS): Psilocybin Behavioral Health Access and Services Act,” accessed November 11, 2024, https://www.njleg.state.nj.us/bill-search/2024/A3852.

New Jersey Legislature, “Bill S2283 ScsSca (SCS/1R): Psilocybin Behavioral Health Access and Services Act,” accessed November 11, 2024, https://www.njleg.state.nj.us/bill-search/2024/S2283.

New Jersey Legislature, “Bill S3256: Reclassifies possession of psilocybin as disorderly persons offense,” accessed December 4, 2024, https://www.njleg.state.nj.us/bill-search/2020/S3256.

New Mexico Legislature, “2024 Regular Session - SM 12: Study Psilocybin for Therapeutic Treatments,” accessed November 11, 2024, https://www.nmlegis.gov/Legislation/Legislation?chamber=S&legtype=M&legno=12&year=24.

The New York State Senate, “Assembly Bill A8349A,” accessed November 11, 2024, https://www.nysenate.gov/legislation/bills/2023/A8349/amendment/A.

The New York State Senate, “Senate Bill S7832A,” accessed November 11, 2024, https://www.nysenate.gov/legislation/bills/2023/S7832/amendment/A.

The New York State Senate, “Assembly Bill A3581A,” accessed November 11, 2024, https://www.nysenate.gov/legislation/bills/2023/A3581/amendment/A.

The New York State Senate, “Senate Bill S3520A,” accessed November 11, 2024, https://www.nysenate.gov/legislation/bills/2023/S3520/amendment/A.

The New York State Senate, “Assembly Bill A10375,” accessed November 11, 2024, https://www.nysenate.gov/legislation/bills/2023/A10375.

North Carolina General Assembly, “House Bill 727,” accessed November 11, 2024, https://www.ncleg.gov/BillLookUp/2023/H727.

Office of the Governor of Hawaii, “Office of the Governor – News Release – Breakthrough Therapies Task Force Signals New Era of Wellness and Resilience,” August 29, 2023, https://governor.hawaii.gov/newsroom/office-of-the-governor-news-release-breakthrough-therapies-task-force-signals-new-era-of-wellness-and-resilience/.

Oklahoma State Legislature, “HB 2107 by Pae and Brooks,” accessed November 11, 2024, http://www.oklegislature.gov/BillInfo.aspx?Bill=hb2107&Session=2400.

Oregon State Legislature, “HB 4002 Enrolled,” accessed November 11, 2024, https://olis.oregonlegislature.gov/liz/2024R1/Measures/Overview/HB4002.

Oregon Health Authority, “Oregon Psilocybin Services - Senate Bill 303 and Data Collection Information,” accessed November 11, 2024, https://www.oregon.gov/oha/ph/preventionwellness/pages/psilocybin-sb303-and-data-collection.aspx.

Oregon Capital Collection, "More than a dozen Oregon communities vote to ban psilocybin businesses," November 6, 2024, https://oregoncapitalchronicle.com/2024/11/06/more-than-a-dozen-oregon-communities-vote-to-ban-psilocybin-businesses/.

Oregon Health Authority, "Oregon Psilocybin Services," accessed November 11, 2024, https://www.oregon.gov/oha/ph/preventionwellness/pages/oregon-psilocybin-services.aspx.

Oregon Health Authority, "Healthier Together Oregon: 2020-2024 State Health Improvement Plan," accessed November 11, 2024, https://www.oregon.gov/oha/ph/about/pages/healthimprovement.aspx.

Patrick, M. E., Miech, R. A., Johnston, L. D., & O'Malley, P. M. (2024). Monitoring the Future Panel Study annual report: National data on substance use among adults ages 19 to 65, 1976–2023 (PDF). Monitoring the Future Monograph Series. Ann Arbor, MI: Institute for Social Research, University of Michigan.

Pennington, S., Stark, N., & Esselman, D.M. (2024, May 28). State–Federal Synergy Advancing Psychedelic Policy Reform: Toward Safe, Equitable, and Efficient Access to Treatment. Radicle Institute. https://radicleinstitute.org/s/Radicle-Institute_StateFederal-Synergy-Advancing-Psychedelic-Policy-Reform.pdf.

Psychedelic Alpha, "Psychedelic Legalization & Decriminalization Tracker," accessed December 6, 2024, https://psychedelicalpha.com/data/psychedelic-laws.

Psychedelic Medicine Task Force, January 2024 Meeting, https://www.youtube.com/watch?v=duRNlJcjdbU .

Psychedelic Medicine Task Force, February 2024 meeting, https://www.youtube.com/watch?v=xInti7y4c6s.

Psychedelic Medicine Task Force, March 2024 meeting, https://www.youtube.com/watch?v=UysnyQBdxTA.

Psychedelic Medicine Task Force, April 2024 meeting, https://www.youtube.com/watch?v=q2xZ30TtiYs.

Psychedelic Medicine Task Force, May 2024 meeting, https://www.youtube.com/watch?v=qy__vuQCBP4.

Psychedelic Medicine Task Force, June 2024 meeting, https://www.youtube.com/watch?v=4QqsidflKNU.

Psychedelic Society of Minnesota, "Legislative Initiatives and Consulting with Indigenous Peoples," March 5, 2024, https://www.youtube.com/watch?v=T4d2iUdW8Mk&t=1s.

Psychedelic Society of Minnesota, "Updates from the Psychedelic Space - Fall 2024," October 6, 2024, https://www.youtube.com/watch?v=_3qd8KCc0Y4.

RAND, "Considering Alternatives to Psychedelic Drug Prohibition," June 27, 2024, https://www.rand.org/pubs/research_reports/RRA2825-1.html.

Religious Freedom and Restoration Act of 1993 [RFRA]. H.R. 1308, 103rd Congress (1993-1994). https://www.congress.gov/bill/103rd-congress/house-bill/1308/text

Shulgin, Alexander T. and David E. Nichols. "Characterization of Three New Psychotomimetics." In The Psychopharmacology of Hallucinogens, edited by Richard C. Stillman and Robert E. Willette. New York: Pergamon Press, 1978.

Substance Abuse and Mental Health Services Administration, "Welcome to SAMHSA data," accessed November 11, 2024, https://www.samhsa.gov/data/.

Spencer, M. R., Curtin, S. C., & Garnett, M. F. (2022). Alcohol-induced death rates in the United States, 2019–2020. NCHS Data Brief No. 448. Hyattsville, MD: National Center for Health Statistics. 2022. DOI: https://dx.doi.org/10.15620/cdc:121795.

Spencer M.R., Garnett M.F., & Miniño, A.M. (2024). Drug Overdose Deaths in the United States, 2002–2022. NCHS Data Brief, no 491. Hyattsville, MD: National Center for Health Statistics. DOI: https://dx.doi.org/10.15620/cdc:135849.

State of Rhode Island in General Assembly, "2024 -- H 7047: Relating to Food And Drugs -- Uniform Controlled Substances Act" accessed November 11, 2024, https://webserver.rilegislature.gov/BillText/BillText24/HouseText24/H7047.pdf.

Swanson, L., Jungers, S., Varghese, R., Cullen, K.R., Evans, M.D., Nielson, J.L., & Schallmo, M-P. "Enhanced visual contrast suppression during peak psilocybin effects: A psychophysical study," accessed November 11, 2024, https://osf.io/preprints/psyarxiv/5rm62.

Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality [SAMHSA]. (2019). National Survey on Drug Use and Health 2018. Retrieved from: https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables

Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality [SAMHSA]. (2023a). National Survey on Drug Use and Health 2022. Retrieved from: https://www.samhsa.gov/data/report/2022-nsduh-detailed-tables

Substance Abuse and Mental Health Services Administration [SAMHSA] (2023b). Drug Abuse Warning Network: Findings from Drug-Related Emergency Department Visits, 2022; Publication PEP23-07-03-001. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data.

Texas Legislature Online, "HB 1802: Relating to a study on the use of alternative therapies for treating post-traumatic stress disorder," accessed November 11, 2024, https://capitol.texas.gov/BillLookup/History.aspx?LegSess=87R&Bill=HB1802.

Texas Legislature Online, "HB 4423: Relating to the establishment of the Psilocybin Research Advisory Council," accessed November 11, 2024, https://capitol.texas.gov/BillLookup/History.aspx?LegSess=88R&Bill=HB4423.

Texas Legislature Online, "HB 4288: Relating to a study on the use of alternative therapies for treating post-traumatic stress disorder," accessed November 11, 2024, https://capitol.texas.gov/BillLookup/History.aspx?LegSess=88R&Bill=HB4288.

The Church of the Eagle and the Condor [CEC]. (2023). Settlement. The Church of the Eagle and the Condor. Retrieved from https://www.churchofeagleandcondor.org/settlement.html

The New York Times [NYT]. (2023, November 10). 'Is This Hell?' The Pilot Accused of Trying to Crash a Plane Tells His Story. The New York Times. https://www.nytimes.com/2023/11/10/us/alaska-airlines-pilot-joseph-emerson-mushrooms.html

Thomson Reuters, "Ayahuasca Church's Tax-Exempt Status Denial Appeal Should Not Be Reheard, IRS Tells Court," October 30, 2024, https://tax.thomsonreuters.com/news/ayahuasca-churchs-tax-exempt-status-denial-appeal-should-not-be-reheard-irs-tells-court/.

United States Court Of Appeals For The Ninth Circuit, "Amicus Curiae Brief of the States of Washington, Arizona, Delaware, Illinois, Michigan, Minnesota, Ohio, and Oregon, and the District of Columbia in Support of Petitioners and Granting the Petition," accessed November 11, 2024, https://emergelawgroup.com/wp-content/uploads/2021/05/State-Amici.pdf.

US Department of Justice, "Administrative Procedures Act," accessed November 11, 2024, https://www.justice.gov/sites/default/files/jmd/legacy/2014/05/01/act-pl79-404.pdf.

US Food and Drug Administration, "Expanded Access," February 28, 2024, https://www.fda.gov/news-events/public-health-focus/expanded-access.

US Food and Drug Administration, "Right to Try," accessed November 11, 2024, https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/right-try.

Usona Institute. (2019, November 22). FDA grants Breakthrough Therapy Designation to Usona Institute's psilocybin program for major depressive disorder. Retrieved from: https://www.usonainstitute.org/updates/fda-grants-breakthrough-therapy-designation-to-usona-institutes-psilocybin-program-for-major-depressive-disorder

Utah State Legislature, "S.B. 266 Medical Amendments," accessed November 11, 2024, https://le.utah.gov/~2024/bills/static/SB0266.html.

Vermont General Assembly, "S.114 (Act 126): An act relating to the establishment of the Psychedelic Therapy Advisory Working Group," accessed November 11, 2024, https://legislature.vermont.gov/bill/status/2024/S.114.

Vermont General Assembly, "H.439: An act relating to decriminalizing certain chemical compounds found in plants and fungi that are commonly used for medicinal, spiritual, religious, or entheogenic purposes," accessed November 11, 2024, https://legislature.vermont.gov/bill/status/2024/H.439.

Vermont General Assembly, "H.371: An act relating to removal of criminal penalties for possessing, dispensing, or selling psilocybin and establishment of the Psychedelic Therapy Advisory Working Group," accessed November 11, 2024, https://legislature.vermont.gov/bill/status/2024/H.371.

Washington State Legislature, "SB 5263 - 2023-24: Concerning access to psilocybin services by individuals 21 years of age and older," accessed November 11, 2024, https://app.leg.wa.gov/billsummary?BillNumber=5263&Year=2023&Initiative=false.

Wasson, R. G. 1957. Seeking the magic mushroom. Life 49, no. 19 (May 13): 100–102, 109–120.

West Virginia Legislature, “House Bill 4473,” accessed November 11, 2024, https://www.wvlegislature.gov/Bill_Status/Bills_history.cfm?input=4473&year=2024&sessiontype=RS&btype=bill.

Wisconsin State Legislature, “Senate Bill 727: An Act to create 20.285 (1) (qh), 20.285 (1) (qi), 25.14 (1) (a) 14m., 25.17 (1) (jw), 25.51 and 36.25 (16) of the statutes; Relating to: creating a medicinal psilocybin treatment fund and a pilot program to study the effects of medicinal psilocybin treatment on patients with post-traumatic stress syndrome at the University of Wisconsin-Madison and making an appropriation. (FE)” accessed November 11, 2024, https://docs.legis.wisconsin.gov/2023/proposals/reg/sen/bill/sb727.

Wisconsin State Legislature, “Assembly Bill 753: An Act to create 20.285 (1) (qh), 20.285 (1) (qi), 25.14 (1) (a) 14m., 25.17 (1) (jw), 25.51 and 36.25 (16) of the statutes; Relating to: creating a medicinal psilocybin treatment fund and a pilot program to study the effects of medicinal psilocybin treatment on patients with post-traumatic stress syndrome at the University of Wisconsin-Madison and making an appropriation. (FE),” accessed November 11, 2024, https://docs.legis.wisconsin.gov/2023/proposals/reg/asm/bill/ab753.

World Science Festival, “Psychedelics for the Frontlines: A Police Officer on the Healing Potential of MDMA for PTSD,” September 26, 2022, https://www.youtube.com/watch?v=ugZemizXHB0.

Yeomans, K. (2022, November 2). Cultural and Anthropological Review of Resources. Oregon Psilocybin Services; State of Oregon. https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/Documents/Cultural-Anthropological-Review-2022.pdf

Appendix N: Peer-reviewed academic references

Abraham, H. D. (1982). A chronic impairment of colour vision in users of LSD. The British Journal of Psychiatry, 140(5), 518-520.

Alchakee, A., Ahmed, M., Eldohaji, L., Alhaj, H., & Saber-Ayad, M. (2022). Pharmacogenomics in psychiatry practice: the value and the challenges. International Journal of Molecular Sciences, 23(21), 13485.

American Psychiatric Association [APA]. (2022). Diagnostic and statistical manual of mental disorders (5th ed., text rev.). https://doi.org/10.1176/appi.books.9780890425787

Antolino-Lobo, I., Meulenbelt, J., van den Berg, M., & van Duursen, M. B. (2011). A mechanistic insight into 3, 4-methylenedioxymethamphetamine ("ecstasy")-mediated hepatotoxicity. Veterinary Quarterly, 31(4), 193-205.

Aromataris E, Lockwood C, Porritt K, Pilla B, Jordan Z, eds. (2024) JBI Manual for Evidence Synthesis. JBI. Available from: https://synthesismanual.jbi.global. https://doi.org/10.46658/JBIMES-24-01

Baldauf, S. L., & Palmer, J. D. (1993). Animals and fungi are each other's closest relatives: congruent evidence from multiple proteins. Proceedings of the National Academy of Sciences, 90(24), 11558-11562.

Bandelow, B., Reitt, M., Röver, C., Michaelis, S., Görlich, Y., & Wedekind, D. (2015). Efficacy of treatments for anxiety disorders: A meta-analysis. International Clinical Psychopharmacology, 30(4), 183-192.

Barbee, G. A., Berry-Cabán, C. S., Barry, J. D., Borys, D. J., Ward, J. A., & Salyer, S. W. (2009). Analysis of mushroom exposures in Texas requiring hospitalization, 2005–2006. Journal of Medical Toxicology, 5, 59-62.

Bayne, T., & Carter, O. (2018). Dimensions of consciousness and the psychedelic state. Neuroscience of Consciousness, 2018(1), niy008.

Becker, A. M., Holze, F., Grandinetti, T., Klaiber, A., Toedtli, V. E., Kolaczynska, K. E., Duthaler, U., Varghese, N., Eckert, A., Grünblatt, E., & Liechti, M. E. (2022). Acute effects of psilocybin after escitalopram or placebo pretreatment in a randomized, double-blind, placebo-controlled, crossover study in healthy subjects. Clinical Pharmacology & Therapeutics, 111(4), 886-895.

Belouin, S. J., Averill, L. A., Henningfield, J. E., Xenakis, S. N., Donato, I., Grob, C. S., Berger, A., Magar, V., Danforth, A.L., & Anderson, B. T. (2022). Policy considerations that support equitable access to responsible, accountable, safe, and ethical use of psychedelic medicines. Neuropharmacology, 1-6. https://doi.org/10.1016/j.neuropharm.2022.109214

Ben-Shabat, S., Fride, E., Sheskin, T., Tamiri, T., Rhee, M. H., Vogel, Z., Bisogno, T., De Petrocellis L., Vincenzo Di Marzo, V., & Mechoulam, R. (1998). An entourage effect: inactive endogenous fatty acid glycerol esters enhance 2-arachidonoyl-glycerol cannabinoid activity. European Journal of Pharmacology, 353(1), 23-31.

Benzenhöfer, U., & Passie, T. (2010). Rediscovering MDMA (ecstasy): The role of the American chemist Alexander T. Shulgin. Addiction, 105(8), 1355-1361.

Bernhard, M. K., & Ulrich, K. (2009). Recurrent cortical blindness after LSD-intake. Fortschritte der Neurologie-Psychiatrie, 77(2), 102-104.

Benzenhöfer U, Passie T. Rediscovering MDMA (ecstasy): the role of the American chemist Alexander T. Shulgin. Addiction. 2010 Aug;105(8):1355-61. doi: 10.1111/j.1360-0443.2010.02948.x.

Bickel, M., Ditting, T., Watz, H., Roesler, A., Weidauer, S., Jacobi, V., Gueller, S., Betz, C., Fichtlscherer, S., & Stein, J. (2005). Severe rhabdomyolysis, acute renal failure and posterior encephalopathy after 'magic mushroom' abuse. European Journal of Emergency Medicine, 12(6), 306-308.

Bogenschutz, M. P., Ross, S., Bhatt, S., Baron, T., Forcehimes, A. A., Laska, E., Mennenga, S.E., O'Donnell, K., Owens, L.T., Podrebarac, S., Rotrosen, J., Tonigan, J.S., & Worth, L. (2022). Percentage of heavy drinking days following psilocybin-assisted psychotherapy vs placebo in the treatment of adult patients with alcohol use disorder: A randomized clinical trial. JAMA Psychiatry, 79(10), 953-962.

Bonson, K. R., & Murphy, D. L. (1995). Alterations in responses to LSD in humans associated with chronic administration of tricyclic antidepressants, monoamine oxidase inhibitors or lithium. Behavioural Brain Research, 73(1-2), 229-233.

Bonson, K. R., Buckholtz, J. W., & Murphy, D. L. (1996). Chronic administration of serotonergic antidepressants attenuates the subjective effects of LSD in humans. Neuropsychopharmacology, 14(6), 425-436.

Bowen, W. T., Soskin, R. A., & Chotlos, J. W. (1970). Lysergic acid diethylamide as a variable in the hospital treatment of alcoholism: A follow-up study. The Journal of Nervous And Mental Disease, 150(2), 111-118.

Brauer, R. B., Heidecke, C. D., Nathrath, W., Beckurts, K. T. E., Vorwald, P., Zilker, T. R., Schweigart, U., Hölscher, A.H., & Siewert, J. R. (1997). Liver transplantation for the treatment of fulminant hepatic failure induced by the ingestion of ecstasy. Transplant International, 10, 229-233.

Brown, R. T., Nicholas, C. R., Cozzi, N. V., Gassman, M. C., Cooper, K. M., Muller, D., Thomas, C.D., Hetzel, S.J., Henriquez, K.M., Ribaudo, A.S., & Hutson, P. R. (2017). Pharmacokinetics of escalating doses of oral psilocybin in healthy adults. Clinical Pharmacokinetics, 56, 1543-1554.

Burgess, A., Hays, H. L., Badeti, J., Spiller, H. A., Rine, N. I., Gaw, C. E., Ding, K., & Smith, G. A. (2024). Delta-8 tetrahydrocannabinol, delta-10 tetrahydrocannabinol, and tetrahydrocannabinol-O acetate exposures reported to America's Poison Centers. Clinical Toxicology, 62(4), 256-266.

Campbell, G. A., & Rosner, M. H. (2008). The agony of ecstasy: MDMA (3, 4-methylenedioxymethamphetamine) and the kidney. Clinical Journal of the American Society of Nephrology, 3(6), 1852-1860.

Carhart-Harris, R. L., Kaelen, M., Whalley, M. G., Bolstridge, M., Feilding, A., & Nutt, D. J. (2015). LSD enhances suggestibility in healthy volunteers. Psychopharmacology, 232, 785-794.

Carhart-Harris, R., Giribaldi, B., Watts, R., Baker-Jones, M., Murphy-Beiner, A., Murphy, R., Martell, J., Allan Blemings, A., Erritzoe, D., & Nutt, D. J. (2021). Trial of psilocybin versus escitalopram for depression. New England Journal of Medicine, 384(15), 1402-1411.

Carhart-Harris, R. L., Roseman, L., Haijen, E., Erritzoe, D., Watts R, R., Branchi, I., & Kaelen, M. (2018). Psychedelics and the essential importance of context. Journal of Psychopharmacology, 1-7. DOI: 10.1177/0269881118754710

Carod-Artal, F. J. (2015). Hallucinogenic drugs in pre-Columbian Mesoamerican cultures. Neurología (English Edition), 30(1), 42-49.

Carvalho, M., Pontes, H., Remiao, F., L Bastos, M., & Carvalho, F. (2010). Mechanisms underlying the hepatotoxic effects of ecstasy. Current Pharmaceutical Biotechnology, 11(5), 476-495.

Castellanos, D. & Gralnik, L. M. (2016). Synthetic cannabinoids 2015: an update for pediatricians in clinical practice. World journal of clinical pediatrics, 5(1), 16.

Cavarra, M., Falzone, A., Ramaekers, J. G., Kuypers, K. P., & Mento, C. (2022). Psychedelic-assisted psychotherapy—A systematic review of associated psychological interventions. Frontiers in psychology, 13, 887255.

Chan, C. C., Fishman, M., & Egbert, P. R. (1978). Multiple ocular anomalies associated with maternal LSD ingestion. Archives of Ophthalmology, 96(2), 282-284.

Celidwen, Y., Redvers, N., Githaiga, C., Calambás, J., Añaños, K., Chindoy, M. E., Vitale, R., Rojas, J. N., Mondragón, D., Rosalío, Y. V., & Sacbajá, A. (2022). Ethical principles of traditional Indigenous medicine to guide western psychedelic research and practice. Lancet regional health. Americas, 18, 100410. https://doi.org/10.1016/j.lana.2022.100410.

Cipriani, A., Furukawa, T. A., Salanti, G., Chaimani, A., Atkinson, L. Z., Ogawa, Y., Leucht, S., Ruhe, H.G., Turner, E.H., Higgins, J.P.T., Egger, M., Takeshima, N., Hayasaka, Y., Imai, H., Shinohara, K., Tajika, A., Ioannidis, J.P.A., & Geddes, J. R. (2018). Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: A systematic review and network meta-analysis. The Lancet, 391(10128), 1357-1366.

Colasanti, A., Guo, Q., Giannetti, P., Wall, M. B., Newbould, R. D., Bishop, C., Onega, M., Nicholas, R., Ciccarelli, O., Muraro, P.A., Malik, O., Owen, D.R., Young, A.H., Gunn, R.G., Piccini, P., Matthews, P.M., & Rabiner, E. A. (2016). Hippocampal neuroinflammation, functional connectivity, and depressive symptoms in multiple sclerosis. Biological Psychiatry, 80(1), 62-72.

Crossin, R., Cleland, L., Wilkins, C., Rychert, M., Adamson, S., Potiki, T., Pomerleau, A.C., MacDonald, B., Faletanoai, D., Hutton, F., Noller, G., Lambie, I., Sheridan, J.L., George, J., Mercier, K., Maynard, K., Leonard, L., Walsh, P., Ponton, R., ... Boden, J. (2023). The New Zealand drug harms ranking study: A multi-criteria decision analysis. Journal of Psychopharmacology, 37(9), 891-903.

Cuijpers, P., Sijbrandij, M., Koole, S., Huibers, M., Berking, M., & Andersson, G. (2014). Psychological treatment of generalized anxiety disorder: A meta-analysis. Clinical Psychology Review, 34(2), 130-140.

Danforth, A. L., Grob, C. S., Struble, C., Feduccia, A. A., Walker, N., Jerome, L., Yazar-Klosinski, B., & Emerson, A. (2018). Reduction in social anxiety after MDMA-assisted psychotherapy with autistic adults: A randomized, double-blind, placebo-controlled pilot study. Psychopharmacology, 235(11), 3137-3148.

Davis, A. K., Barrett, F. S., May, D. G., Cosimano, M. P., Sepeda, N. D., Johnson, M. W., Finan, P.H., & Griffiths, R. R. (2021). Effects of psilocybin-assisted therapy on major depressive disorder: A randomized clinical trial. JAMA Psychiatry, 78(5), 481-489.

Dean, J. G., Liu, T., Huff, S., Sheler, B., Barker, S. A., Strassman, R. J., Wang, M. W., & Borjigin, J. (2019). Biosynthesis and extracellular concentrations of N, N-dimethyltryptamine (DMT) in mammalian brain. Scientific Reports, 9(1), 9333.

Degenhardt, L., Bruno, R., & Topp, L. (2010). Is ecstasy a drug of dependence?. Drug and Alcohol Dependence, 107(1), 1-10.

Dishotsky, N. I., Loughman, W. D., Mogar, R. E., & Lipscomb, W. R. (1971). LSD and genetic damage: Is LSD chromosome damaging, carcinogenic, mutagenic, or teratogenic?. Science, 172(3982), 431-440.

Dolder, P. C., Müller, F., Schmid, Y., Borgwardt, S. J., & Liechti, M. E. (2018). Direct comparison of the acute subjective, emotional, autonomic, and endocrine effects of MDMA, methylphenidate, and modafinil in healthy subjects. Psychopharmacology, 235, 467-479.

Erritzoe, D., Barba, T., Greenway, K.T., Murphy, R., Martell, J., Giribaldi, B., Timmermann, C., Murphy-Beiner, A., Baker Jones, M., Nutt, D., Weiss, B., & Carhart-Harris, R. (2024). Effect of psilocybin versus escitalopram on depression symptom severity in patients with moderate-to-severe major depressive disorder: Observational 6-month follow-up of a phase 2, double-blind, randomised, controlled trial. eClinicalMedicine.

Espiard, M. L., Lecardeur, L., Abadie, P., Halbecq, I., & Dollfus, S. (2005). Hallucinogen persisting perception disorder after psilocybin consumption: a case study. European Psychiatry, 20(5-6), 458-460.

Farah, R., Kerns, A. F., Murray, A. C., & Holstege, C. P. (2024). Psilocybin exposures reported to US poison centers: National trends over a decade. Journal of Adolescent Health, 74(5), 1053-1056.

Feduccia, A. A., Jerome, L., Yazar-Klosinski, B., Emerson, A., Mithoefer, M. C., & Doblin, R. (2019). Breakthrough for trauma treatment: Safety and efficacy of MDMA-assisted psychotherapy compared to paroxetine and sertraline. Frontiers in Psychiatry, 10, 650.

Freedman, D. X. (1963). Psychotomimetic drugs and brain biogenic amines. American Journal of Psychiatry, 119(9), 843-850.

Gable, R. S. (2004). Comparison of acute lethal toxicity of commonly abused psychoactive substances. Addiction, 99(6), 686-696.

Gasser, P., Holstein, D., Michel, Y., Doblin, R., Yazar-Klosinski, B., Passie, T., & Brenneisen, R. (2014). Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. The Journal of Nervous and Mental Disease, 202(7), 513-520.

George, J. R., Michaels, T. I., Sevelius, J., & Williams, M. T. (2020). The psychedelic renaissance and the limitations of a White-dominant medical framework: A call for indigenous and ethnic minority inclusion. Journal of Psychedelic Studies, 4(1), 4-15.

Goldberg, S. B., Pace, B. T., Nicholas, C. R., Raison, C. L., & Hutson, P. R. (2020). The experimental effects of psilocybin on symptoms of anxiety and depression: A meta-analysis. Psychiatry Research, 284, 112749.

Goodwin, G. M., Aaronson, S. T., Alvarez, O., Arden, P. C., Baker, A., Bennett, J. C., Bird, C., Blom, R.E., Brennan, C., Brusch, D., Burke, L., Campbell-Coker, K., Carhart-Harris, R., Cattell, J., Daniel, A., DeBattista, C., Dunlop, B.W., Eisen, K., Feife, D., … Malievskaia, E. (2022). Single-dose psilocybin for a treatment-resistant episode of major depression. New England Journal of Medicine, 387(18), 1637-1648.

Goodwin, G. M., Croal, M., Feifel, D., Kelly, J. R., Marwood, L., Mistry, S., O'Keane, V., Peck, S.K., Simmons, H., Sisa, C., Stansfield, S.C., Tsai, J., Williams, S., & Malievskaia, E. (2023). Psilocybin for treatment resistant depression in patients taking a concomitant SSRI medication. Neuropsychopharmacology, 48(10), 1492-1499.

Green, A. R., Mechan, A. O., Elliott, J. M., O'Shea, E., & Colado, M. I. (2003). The pharmacology and clinical pharmacology of 3, 4-methylenedioxymethamphetamine (MDMA, "ecstasy"). Pharmacological Reviews, 55(3), 463-508.

Greer, G. & Strassman, R.J. (1985) Information on "Ecstasy." American Journal of Psychiatry, 142:1391.

Greer, G. & Tolbert, R. (1986). Subjective reports of the effects of MDMA in a clinical setting. Journal of Psychoactive Drugs, 18:319–27. doi: 10.1080/02791072.1986.10472364

Greer, G. R. & Tolbert, R. (1998). A method of conducting therapeutic sessions with MDMA. Journal of Psychoactive Drugs, 30(4), 371-379. doi: 10.1080/02791072.1998.10399713

Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., Cosimano, M.P., & Klinedinst, M. A. (2016). Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. Journal of Psychopharmacology, 30(12), 1181-1197.

Grob, C. S., Danforth, A. L., Chopra, G. S., Hagerty, M., McKay, C. R., Halberstadt, A. L., & Greer, G. R. (2011). Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. Archives of General Psychiatry, 68(1), 71-78.

Grof, S., & Dytrych, Z. (1965). Blocking of LSD reaction by premedication with Niamid. Activitas Nervosa Superior, 7(3), 306.

Gukasyan, N. (2023). On blinding and suicide risk in a recent trial of psilocybin-assisted therapy for treatment-resistant depression. Med, 4(1), 8-9.

Gukasyan, N., Griffiths, R. R., Yaden, D. B., Antoine, D. G., & Nayak, S. M. (2023). Attenuation of psilocybin mushroom effects during and after SSRI/SNRI antidepressant use. Journal of Psychopharmacology, 37(7), 707-716.

Gummin, D. D., Mowry, J. B., Beuhler, M. C., Spyker, D. A., Bronstein, A. C., Rivers, L. J., Pham, N.P.T., & Weber, J. (2021). 2020 annual report of the American association of poison control centers' national poison data system (NPDS): 38th annual report. Clinical Toxicology, 59(12), 1282-1501.

Gummin, D. D., Mowry, J. B., Beuhler, M. C., Spyker, D. A., Frooks, D. E., Dibert, K. W., Pham, N.P.T., & Ryan, M. L. (2020). 2019 annual report of the American association of poison control centers' national poison data system (NPDS): 37th annual report. Clinical Toxicology, 58(12), 1360-1541.

Gummin, D. D., Mowry, J. B., Beuhler, M. C., Spyker, D. A., Rivers, L. J., Feldman, R., Brown, K., Pham, N.P.T., Bronstein, A.C., & Weber, J. A. (2022). 2021 annual report of the National Poison Data System©(NPDS) from America's poison centers: 39th annual report. Clinical Toxicology, 60(12), 1381-1643.

Gummin, D. D., Mowry, J. B., Beuhler, M. C., Spyker, D. A., Rivers, L. J., Feldman, R., Brown, K., Pham, N.P.T., Bronstein, A.C., & DesLauriers, C. (2023). 2022 Annual report of the national poison data system®(NPDS) from America's Poison Centers®: 40th annual report. Clinical Toxicology, 61(10), 717-939.

Gummin, D. D., Mowry, J. B., Spyker, D. A., Brooks, D. E., Beuhler, M. C., Rivers, L. J., Hashem, H.A., & Ryan, M. L. (2019). 2018 Annual report of the American Association of Poison control centers' National Poison Data System (NPDS): 36th annual report. Clinical Toxicology, 57(12), 1220-1413.

Haden, M., & Woods, B. (2020). LSD overdoses: three case reports. Journal of studies on alcohol and drugs, 81(1), 115-118.

Haikazian, S., Chen-Li, D. C., Johnson, D. E., Fancy, F., Levinta, A., Husain, M. I., Mansur, R.B., McIntyre, R.S., & Rosenblat, J. D. (2023). Psilocybin-assisted therapy for depression: A systematic review and meta-analysis. Psychiatry Research, 115531.

Halberstadt, A. L., & Geyer, M. A. (2011). Multiple receptors contribute to the behavioral effects of indoleamine hallucinogens. Neuropharmacology, 61(3), 364-381.

Han, D. D., & Gu, H. H. (2006). Comparison of the monoamine transporters from human and mouse in their sensitivities to psychostimulant drugs. BMC Pharmacology, 6, 1-7.

Harrington, R. D., Woodward, J. A., Hooton, T. M., & Horn, J. R. (1999). Life-threatening interactions between HIV-1 protease inhibitors and the illicit drugs MDMA and γ-hydroxybutyrate. Archives of Internal Medicine, 159(18), 2221-2224.

Hasler, F., Studerus, E., Lindner, K., Ludewig, S., & Vollenweider, F. X. (2009). Investigation of serotonin-1A receptor function in the human psychopharmacology of MDMA. Journal of Psychopharmacology, 23(8), 923-935.

Henry, J. A., & Hill, I. R. (1998). Fatal interaction between ritonavir and MDMA. The Lancet, 352(9142), 1751-1752.

Hernández Santiago, F., Martínez-Reyes, M., Pérez-Moreno, J., & Mata, G. (2017). Pictographic representation of the first dawn and its association with entheogenic mushrooms in a 16th century Mixtec Mesoamerican Codex. Revista Mexicana de Micología, 46, 19-28.

Hinkle, J. T., Graziosi, M., Nayak, S. M., & Yaden, D. B. (2024). Adverse events in studies of classic psychedelics: A systematic review and meta-analysis. JAMA Psychiatry.

Hofmann, A. (1979). How LSD originated. Journal of Psychedelic Drugs, 11(1-2), 53-60.

Hollister, L. E., Shelton, J., & Krieger, G. (1969). A controlled comparison of lysergic acid diethylamide (LSD) and dextroamphetamine in alcoholics. American Journal of Psychiatry, 125(10), 1352-1357.

Holze, F., Caluori, T. V., Vizeli, P., & Liechti, M. E. (2021a). Safety pharmacology of acute LSD administration in healthy subjects. Psychopharmacology, 1-13.

Holze, F., Gasser, P., Müller, F., Dolder, P. C., & Liechti, M. E. (2023). Lysergic acid diethylamide–assisted therapy in patients with anxiety with and without a life-threatening illness: A randomized, double-blind, placebo-controlled phase II study. Biological Psychiatry, 93(3), 215-223.

Holze, F., Ley, L., Müller, F., Becker, A. M., Straumann, I., Vizeli, P., Kuehne, S.S., Roder, M.A., Duthaler, U., Kolaczynska, K.E., Varghese, N., Eckert, A., & Liechti, M. E. (2022). Direct comparison of the acute effects of lysergic acid diethylamide and psilocybin in a double-blind placebo-controlled study in healthy subjects. Neuropsychopharmacology, 47(6), 1180-1187.

Holze, F., Vizeli, P., Ley, L., Müller, F., Dolder, P., Stocker, M., Varghese, N., Eckert, A., Borgwardt, S., & Liechti, M. E. (2021b). Acute dose-dependent effects of lysergic acid diethylamide in a double-blind placebo-controlled study in healthy subjects. Neuropsychopharmacology, 46(3), 537-544.

Honyiglo, E., Franchi, A., Cartiser, N., Bottinelli, C., Advenier, A. S., Bévalot, F., & Fanton, L. (2019). Unpredictable behavior under the influence of “magic mushrooms”: A case report and review of the literature. Journal of Forensic Sciences, 64(4), 1266-1270.

Hoorn, E.J. (2001). A fatal case of Ecstasy poisoning. Paediatrics & Child Health, 6(7):491.

Horita, A., & Weber, L. J. (1961). The enzymic dephosphorylation and oxidation of psilocybin and pscilocin by mammalian tissue homogenates. Biochemical Pharmacology, 7(1), 47-54.

Hoskins, M., Pearce, J., Bethell, A., Dankova, L., Barbui, C., Tol, W. A., van Ommeren, M., de Jong, J., Seedat, S., Chen, H., & Bisson, J.I. (2015). Pharmacotherapy for post-traumatic stress disorder: Systematic review and meta-analysis. The British Journal of Psychiatry, 206(2), 93-100.

Isbell, H., & Logan, C. R. (1957). Studies on the diethylamide of lysergic acid (LSD-25): II. Effects of chlorpromazine, azacyclonol, and reserpine on the intensity of the LSD-reaction. AMA Archives of Neurology & Psychiatry, 77(4), 350-358.

Jansen, K. L. (1999). Ecstasy (MDMA) dependence. Drug and Alcohol Dependence, 53(2), 121-124.

Jawad, M. Y., Di Vincenzo, J. D., Ceban, F., Jaberi, S., Lui, L. M., Gillissie, E. S., Alnafeesi, Y., Rosenblat, J.D., & McIntyre, R. S. (2022). The efficacy and safety of adjunctive intranasal esketamine treatment in major depressive disorder: A systematic review and meta-analysis. Expert Opinion on Drug Safety, 21(6), 841-852.

Johnson, F. G. (1970). A comparison of short-term treatment effects of intravenous sodium amytal-methedrine and LSD in the alcoholic. Canadian Psychiatric Association Journal, 15(5), 493-497.

Johnson, M. W., Garcia-Romeu, A., & Griffiths, R. R. (2017). Long-term follow-up of psilocybin-facilitated smoking cessation. The American Journal of Drug and Alcohol Abuse, 43(1), 55-60.

Johnson, M. W., Garcia-Romeu, A., Cosimano, M. P., & Griffiths, R. R. (2014). Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction. Journal of Psychopharmacology, 28(11), 983-992.

Johnson, M. W., Griffiths, R. R., Hendricks, P. S., & Henningfield, J. E. (2018). The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substances Act. Neuropharmacology, 142, 143-166.

Johnson, M. W., Richards, W. A., & Griffiths, R. R. (2008). Human hallucinogen research: Guidelines for safety. Journal of Psychopharmacology, 22(6), 603-620.

Johnson, M. W., Sewell, R. A., & Griffiths, R. R. (2012). Psilocybin dose-dependently causes delayed, transient headaches in healthy volunteers. Drug and Alcohol Dependence, 123(1-3), 132-140.

Jones, K. A., Srivastava, D. P., Allen, J. A., Strachan, R. T., Roth, B. L., & Penzes, P. (2009). Rapid modulation of spine morphology by the 5-HT2A serotonin receptor through kalirin-7 signaling. Proceedings of the National Academy of Sciences, 106(46), 19575-19580.

Joshi, S., Rivera, B. D., Cerdá, M., Guy, G. P., Strahan, A., Wheelock, H., & Davis, C. S. (2023). One-year association of drug possession law change with fatal drug overdose in Oregon and Washington. JAMA psychiatry, 80(12), 1277-1283.

Kalant, H. (2001). The pharmacology and toxicology of “ecstasy” (MDMA) and related drugs. Canadian Medical Association Journal, 165(7), 917-928.

Kaplan, K., Kurtz, F., & Serafini, K. (2018). Substance-induced anxiety disorder after one dose of 3, 4-methylenedioxymethamphetamine: A case report. Journal of Medical Case Reports, 12, 1-5.

Karyotaki, E., Smit, Y., Henningsen, K. H., Huibers, M. J. H., Robays, J., De Beurs, D., & Cuijpers, P. (2016). Combining pharmacotherapy and psychotherapy or monotherapy for major depression? A meta-analysis on the long-term effects. Journal of Affective Disorders, 194, 144-152.

Keeler, M. H. (1967). Chlorpromazine antagonism of psilocybin effect. International Journal of Neuropsychiatry, 3(1), 66.

Kim, K., Che, T., Panova, O., DiBerto, J. F., Lyu, J., Krumm, B. E., Wacker, D., Robertson, M.J., Seven, A.B., Nichols, D.E., Shoichet, B.K., Skiniotis, G., & Roth, B. L. (2020). Structure of a hallucinogen-activated Gq-coupled 5-HT2A serotonin receptor. Cell, 182(6), 1574-1588.

Kindred, R., Bates, G. W., & McBride, N. L. (2022). Long-term outcomes of cognitive behavioural therapy for social anxiety disorder: A meta-analysis of randomised controlled trials. Journal of Anxiety Disorders, 92, 102640.

Klein, A. K., Chatha, M., Laskowski, L. J., Anderson, E. I., Brandt, S. D., Chapman, S. J., McCorvy, J.D., & Halberstadt, A. L. (2020). Investigation of the structure–activity relationships of psilocybin analogues. ACS Pharmacology & Translational Science, 4(2), 533-542.

Kloft, L., Otgaar, H., Blokland, A., Toennes, S. W., & Ramaekers, J. G. (2022). Remembering Molly: Immediate and delayed false memory formation after acute MDMA exposure. European Neuropsychopharmacology, 57, 59-68.

Ko, K., Knight, G., Rucker, J. J., & Cleare, A. J. (2022). Psychedelics, mystical experience, and therapeutic efficacy: A systematic review. Frontiers in Psychiatry, 13, 917199.

Kopra, E. I., Ferris, J. A., Winstock, A. R., Young, A. H., & Rucker, J. J. (2022). Adverse experiences resulting in emergency medical treatment seeking following the use of magic mushrooms. Journal of Psychopharmacology, 36(8), 965-973.

Kotts, W. J., Gamble, D. T., Dawson, D. K., & Connor, D. (2022). Psilocybin-induced takotsubo cardiomyopathy. BMJ Case Reports CP, 15(5), e245863.

Krebs, T. S., & Johansen, P. Ø. (2012). Lysergic acid diethylamide (LSD) for alcoholism: Meta-analysis of randomized controlled trials. Journal of Psychopharmacology, 26(7), 994-1002.

Kroeze, W. K., Sassano, M. F., Huang, X. P., Lansu, K., McCorvy, J. D., Giguère, P. M., Sciaky, N., & Roth, B. L. (2015). PRESTO-Tango as an open-source resource for interrogation of the druggable human GPCRome. Nature Structural & Molecular Biology, 22(5), 362-369.

Kuiper H, Alley C, Harris Z, Kuiper Rauch C, Robbins M, Rodriguez P, Tomczak P, Urrutia J, Magar V. Psychedelic public health: State of the field and implications for equity. Soc Sci Med. 2024 Sep;357:117134. doi: 10.1016/j.socscimed.2024.117134. Epub 2024 Jul 14. PMID: 39173415.

Kuniyoshi, S. M., & Jankovic, J. (2003). MDMA and Parkinsonism. New England Journal of Medicine, 349(1), 96-97.

Kuwahara, T., Nakakura, T., Oda, S., Mori, M., Uehira, T., Okamoto, G., Yoshino, M., Sasakawa, A., Yajima, K., Umemoto, A., Takada, K., Makie, T., & Yamamoto, Y. (2008). Problems in three Japanese drug users with Human Immunodeficiency Virus infection. The Journal of Medical Investigation, 55(1, 2), 156-160.

Kwan, A. C., Olson, D. E., Preller, K. H., & Roth, B. L. (2022). The neural basis of psychedelic action. Nature Neuroscience, 25(11), 1407-1419.

Lee, D. J., Schnitzlein, C. W., Wolf, J. P., Vythilingam, M., Rasmusson, A. M., & Hoge, C. W. (2016). Psychotherapy versus pharmacotherapy for posttraumatic stress disorder: Systemic review and meta-analyses to determine first-line treatments. Depression and anxiety, 33(9), 792-806.

Liechti, M. E., & Vollenweider, F. X. (2001). Which neuroreceptors mediate the subjective effects of MDMA in humans? A summary of mechanistic studies. Human Psychopharmacology: Clinical and Experimental, 16(8), 589-598.

Lim, T. H., Wasywich, C. A., & Ruygrok, P. N. (2012). A fatal case of 'magic mushroom' ingestion in a heart transplant recipient. Internal Medicine Journal, 42(11).

Ludwig, A., Levine, J., Stark, L., & Lazar, R. (1969). A clinical study of LSD treatment in alcoholism. American Journal of Psychiatry, 126(1), 59-69.

Ly, C., Greb, A. C., Cameron, L. P., Wong, J. M., Barragan, E. V., Wilson, P. C., Burback, K.F., Zarandi, S.S., Sood, A., Paddy, M.R., Duim, W.C., Dennis, M.Y., McAllister, A.K., Ori-McKenney, K.M., Gray, J.A., & Olson, D. E. (2018). Psychedelics promote structural and functional neural plasticity. Cell Reports, 23(11), 3170-3182.

Mackey, T. K., & Liang, B. A. (2012). Integrating biodiversity management and indigenous biopiracy protection to promote environmental justice and global health. American Journal of Public Health, 102(6), 1091-1095.

Majić, T., Brandt, L., & Montag, C. (2022). Anxiety-related symptoms following the sporadic use of ecstasy – A case study. Journal of Psychoactive Drugs, 54(4), 378-385.

Marks, M. (2023). State-regulated psychedelics on a collision course with FDA. JAMA.

Malcolm, B., & Thomas, K. (2022). Serotonin toxicity of serotonergic psychedelics. Psychopharmacology, 239(6), 1881-1891.

Marona-Lewicka, D., Thisted, R. A., & Nichols, D. E. (2005). Distinct temporal phases in the behavioral pharmacology of LSD: dopamine D 2 receptor-mediated effects in the rat and implications for psychosis. Psychopharmacology, 180, 427-435.

Marseille, E., Stauffer, C. S., & Agrawal, M. (2023). Group psychedelic therapy: Empirical estimates of cost-savings and improved access. Frontiers in Psychiatry, 14, 1293243.

Mason, N. L., Kuypers, K. P. C., Müller, F., Reckweg, J., Tse, D. H. Y., Toennes, S. W., Hutten, N.R.P.W., Jansen, J.F.A., Stiers, P., Feilding, A., & Ramaekers, J. G. (2020). Me, myself, bye: Regional alterations in glutamate and the experience of ego dissolution with psilocybin. Neuropsychopharmacology, 45(12), 2003-2011.

McPheeters, M., O'Connor, E. A., Riley, S., Kennedy, S. M., Voisin, C., Kuznacic, K., Coffey, C.P., Edlund, M.D., Bobashev, G., & Jonas, D. E. (2023). Pharmacotherapy for alcohol use disorder: A systematic review and meta-analysis. JAMA, 330(17), 1653-1665.

Meikle, S., Carter, O., & Bedi, G. (2024). Psychedelic-assisted psychotherapy, patient vulnerability and abuses of power. Australian & New Zealand Journal of Psychiatry, 58(2), 104-106.

Meyer, J. S. (2013). 3, 4-methylenedioxymethamphetamine (MDMA): Current perspectives. Substance Abuse and Rehabilitation, 83-99.

Migliaccio, G. P., Shieh, T. L. N., Byrn, S. R., Hathaway, B. A., & Nichols, D. E. (1981). Comparison of solution conformational preferences for the hallucinogens bufotenin and psilocin using 360-MHz proton NMR spectroscopy. Journal of Medicinal Chemistry, 24(2), 206-209.

Mitchell, J. M., Bogenschutz, M., Lilienstein, A., Harrison, C., Kleiman, S., Parker-Guilbert, K., Ot'alora G, M., Garas, W., Paleos, C., Gorman, I., Nicholas, C., Mithoefer, M., Carlin, S., Poulter, B., Mithoefer, A., Quevedo, S., Wells, G., Klaire, S.S., van der Kolk, B., … Doblin, R. (2021). MDMA-assisted therapy for severe PTSD: A randomized, double-blind, placebo-controlled phase 3 study. Nature Medicine, 27(6), 1025.

Mitchell, J. M., Ot'alora G, M., van der Kolk, B., Shannon, S., Bogenschutz, M., Gelfand, Y., Paleos, C., Nicholas, C.R., Quevedo, S., Balliett, B., Hamilton, S., Mithoefer, M., Kleiman, S., Parker-Guilbert, K., Tzarfaty, K., Harrison, C., de Boer, A., Doblin, R., Yazar-Klosinski, B., & MAPP2 Study Collaborator Group. (2023). MDMA-assisted therapy for moderate to severe PTSD: A randomized, placebo-controlled phase 3 trial. Nature Medicine, 29(10), 2473-2480.

Mithoefer, M. C., Mithoefer, A. T., Feduccia, A. A., Jerome, L., Wagner, M., Wymer, J., Holland, J., Hamilton, S., Yazar-Klosinski, B., Emerson, A., & Doblin, R. (2018). 3, 4-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy for post-traumatic stress disorder in military veterans, firefighters, and police officers: A randomised, double-blind, dose-response, phase 2 clinical trial. The Lancet Psychiatry, 5(6), 486-497.

Mithoefer, M. C., Wagner, M. T., Mithoefer, A. T., Jerome, L., & Doblin, R. (2011). The safety and efficacy of±3, 4-methylenedioxymethamphetamine-assisted psychotherapy in subjects with chronic, treatment-resistant posttraumatic stress disorder: The first randomized controlled pilot study. Journal of Psychopharmacology, 25(4), 439-452.

Monte, A. A., Schow, N. S., Black, J. C., Bemis, E. A., Rockhill, K. M., & Dart, R. C. (2024). The rise of psychedelic drug use associated with legalization/decriminalization: An assessment with the nonmedical use of prescription drugs survey. Annals of Emergency Medicine, 83(3), 283-285.

Montoya, A. G., Sorrentino, R., Lukas, S. E., & Price, B. H. (2002). Long-term neuropsychiatric consequences of "ecstasy" (MDMA): A review. Harvard Review of Psychiatry, 10(4), 212-220.

Moreno, F. A., Wiegand, C. B., Taitano, E. K., & Delgado, P. L. (2006). Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder. Journal of Clinical Psychiatry, 67(11), 1735-1740.

Müller, F., Dolder, P. C., Schmidt, A., Liechti, M. E., & Borgwardt, S. (2018). Altered network hub connectivity after acute LSD administration. NeuroImage: Clinical, 18, 694-701.

Musha, M., Ishii, A., Tanaka, F., & Kusano, G. (1986). Poisoning by hallucinogenic mushroom hikageshibiretake (Psilocybe argentipes K. Yokoyama) indigenous to Japan. The Tohoku Journal of Experimental Medicine, 148(1), 73-78. Gable, 2004

National Academies of Sciences, Engineering, and Medicine [NASEM]. (2017) The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research. Washington, DC: National Academies Press. doi: 10.17226/24625.

National Academies of Sciences, Engineering, and Medicine [NASME]. 2024. Cannabis Policy Impacts Public Health and Health Equity. Washington, DC: The National Academies Press. https://doi.org/10.17226/27766.

Nayak, S. M., Gukasyan, N., Barrett, F. S., Erowid, E., Erowid, F., & Griffiths, R. R. (2021). Classic psychedelic coadministration with lithium, but not lamotrigine, is associated with seizures: An analysis of online psychedelic experience reports. Pharmacopsychiatry, 54(05), 240-245.

Nef, H. M., Möllmann, H., Hilpert, P., Krause, N., Troidl, C., Weber, M., Rolf, A., Dill, T., Hamm, C., & Elsässer, A. (2009). Apical regional wall motion abnormalities reminiscent to Tako-Tsubo cardiomyopathy following consumption of psychoactive fungi. International Journal of Cardiology, 134(1), e39-e41.

Nichols, D. (2003). Hypothesis on Albert Hofmann's Famous 1943 'Bicycle Day'. Foredrag holdt på kon.

Nichols, D. E. (1986). Differences between the mechanism of action of MDMA, MBDB, and the classic hallucinogens. Identification of a new therapeutic class: Entactogens. Journal of Psychoactive Drugs, 18(4), 305-313.

Nichols, D. E. (2016). Psychedelics. Pharmacological Reviews, 68(2), 264-355.

Nichols, D. E., & Grob, C. S. (2018). Is LSD toxic?. Forensic Science International, 284, 141-145.

Nutt, D. J., King, L. A., & Phillips, L. D. (2010). Drug harms in the UK: A multicriteria decision analysis. The Lancet, 376(9752), 1558-1565.

Oehen, P., Traber, R., Widmer, V., & Schnyder, U. (2013). A randomized, controlled pilot study of MDMA (±3, 4-Methylenedioxymethamphetamine)-assisted psychotherapy for treatment of resistant, chronic Post-Traumatic Stress Disorder (PTSD). Journal of Psychopharmacology, 27(1), 40-52.

Ona, G. (2018). Inside bad trips: Exploring extra-pharmacological factors. Journal of Psychedelic Studies, 2(1), 53-60.

Ot'alora G, M., Grigsby, J., Poulter, B., Van Derveer III, J.W., Giron, S.G., Jerome, L., Feduccia, A.A., Hamilton, S., Yazar-Klosinski, B., Emerson, A., Mithoefer, M.C., & Doblin, R. (2018). 3, 4-Methylenedioxymethamphetamine-assisted psychotherapy for treatment of chronic posttraumatic stress disorder: A randomized phase 2 controlled trial. Journal of Psychopharmacology, 32(12), 1295-1307.

Pagnin, D., de Queiroz, V., Pini, S., & Cassano, G. B. (2008). Efficacy of ECT in depression: A meta-analytic review. Focus, 6(1), 155-162.

Papaseit, E., Vázquez, A., Pérez-Maná, C., Pujadas, M., de la Torre, R., Farré, M., & Nolla, J. (2012). Surviving life-threatening MDMA (3, 4-methylenedioxymethamphetamine, ecstasy) toxicity caused by ritonavir (RTV). Intensive Care Medicine, 38, 1239-1240.

Parrott, A. C. (2001). Human psychopharmacology of Ecstasy (MDMA): A review of 15 years of empirical research. Human Psychopharmacology: Clinical and Experimental, 16(8), 557-577.

Passie, T., Halpern, J. H., Stichtenoth, D. O., Emrich, H. M., & Hintzen, A. (2008). The pharmacology of lysergic acid diethylamide: a review. CNS Neuroscience & Therapeutics, 14(4), 295-314.

Peck, S. K., Shao, S., Gruen, T., Yang, K., Babakanian, A., Trim, J., Finn, D.M., & Kaye, W. H. (2023). Psilocybin therapy for females with anorexia nervosa: a phase 1, open-label feasibility study. Nature Medicine, 29(8), 1947-1953.

Pleet, M. M., White, J., Zamaria, J. A., & Yehuda, R. (2023). Reducing the harms of nonclinical psychedelics use through a peer-support telephone helpline. Psychedelic Medicine, 1(2), 69-73.

Pentney, A. R. (2001). An exploration of the history and controversies surrounding MDMA and MDA. Journal of Psychoactive Drugs, 33(3), 213-221.

Perez, N., Langlest, F., Mallet, L., De Pieri, M., Sentissi, O., Thorens, G., Seragnoli, F., Zullino, D., Kirschner, M., Kaiser, S., Solmi, M., & Sabé, M. (2023). Psilocybin-assisted therapy for depression: A systematic review and dose-response meta-analysis of human studies. European Neuropsychopharmacology, 76, 61-76.

Pilgrim, J. L., Gerostamoulos, D., & Drummer, O. H. (2011). Pharmacogenetic aspects of the effect of cytochrome P450 polymorphisms on serotonergic drug metabolism, response, interactions, and adverse effects. Forensic Science, Medicine, and Pathology, 7, 162-184.

Preller, K. H., & Vollenweider, F. X. (2018). Phenomenology, structure, and dynamic of psychedelic states. Behavioral Neurobiology of Psychedelic Drugs, 221-256.

Preller, K. H., Burt, J. B., Ji, J. L., Schleifer, C. H., Adkinson, B. D., Stämpfli, P., Seifritz, E., Repovs, G., Krystal, J.H., Murray, J.D., Vollenweider, F.X., & Anticevic, A. (2018). Changes in global and thalamic brain connectivity in LSD-induced altered states of consciousness are attributable to the 5-HT2A receptor. eLife, 7, e35082.

Raison, C. L., Sanacora, G., Woolley, J., Heinzerling, K., Dunlop, B. W., Brown, R. T., Kakar, R., Hassman, M., Trivedi, R.P., Robison, R., Gukasyan, N., Nayak, S.M. Hu, X., O'Donnell, K.C., Kelmendi, B., Sloshower, J., Penn, A.D., Bradley, E., Kelly, D.F., ... Griffiths, R. R. (2023). Single-dose psilocybin treatment for major depressive disorder: A randomized clinical trial. JAMA, 330(9), 843-853.

Resnick, O., Krus, D. M., & Raskin, M. (1964). LSD-25 action in normal subjects treated with a monoamine oxidase inhibitor. Life Sciences.

Roseman, L., Nutt, D. J., & Carhart-Harris, R. L. (2018). Quality of acute psychedelic experience predicts therapeutic efficacy of psilocybin for treatment-resistant depression. Frontiers in Pharmacology, 8, 974.

Rosenblat, J. D., Meshkat, S., Doyle, Z., Kaczmarek, E., Brudner, R. M., Kratiuk, K., Mansur, R.B., Schulz-Quach, C., Sethi, R., Abate, A., Ali, S., Bawks, J., Blainey, M.G., Brietzke, E., Cronin, V., Danilewitz, J., Dhawan, S., Di Fonzo, A., Di Fonzo, M., ... McIntyre, R. S. (2024). Psilocybin-assisted psychotherapy for treatment resistant depression: A randomized clinical trial evaluating repeated doses of psilocybin. Med. 5(3), 190-200.

Ross, S., Bossis, A., Guss, J., Agin-Liebes, G., Malone, T., Cohen, B., Mennenga, S.E., Belser, A., Kalliontzi, K., Babb, J., Su, Z., Corby, P., & Schmidt, B. L. (2016). Rapid and sustained symptom reduction following psilocybin

treatment for anxiety and depression in patients with life-threatening cancer: A randomized controlled trial. Journal of Psychopharmacology, 30(12), 1165-1180.

Sard, H., Kumaran, G., Morency, C., Roth, B. L., Toth, B. A., He, P., & Shuster, L. (2005). SAR of psilocybin analogs: Discovery of a selective 5-HT2C agonist. Bioorganic & Medicinal Chemistry Letters, 15(20), 4555-4559.

Sarparast, A., Thomas, K., Malcolm, B., & Stauffer, C. S. (2022). Drug-drug interactions between psychiatric medications and MDMA or psilocybin: A systematic review. Psychopharmacology, 239(6), 1945-1976.

Schindler, E. A., Sewell, R. A., Gottschalk, C. H., Flynn, L. T., Zhu, Y., Pittman, B. P., Cozzi, N.V., & D'Souza, D. C. (2024). Psilocybin pulse regimen reduces cluster headache attack frequency in the blinded extension phase of a randomized controlled trial. Journal of the Neurological Sciences, 460, 122993.

Schindler, E. A., Sewell, R. A., Gottschalk, C. H., Luddy, C., Flynn, L. T., Zhu, Y., Lindsey H., Pittman B.P., Cozzi, N.V., & D'Souza, D. C. (2022). Exploratory investigation of a patient-informed low-dose psilocybin pulse regimen in the suppression of cluster headache: Results from a randomized, double-blind, placebo-controlled trial. Headache: The Journal of Head and Face Pain, 62(10), 1383-1394.

Schmid, Y., Enzler, F., Gasser, P., Grouzmann, E., Preller, K. H., Vollenweider, F. X., Rudolf Brenneisen, R., Müller, F., Borgwardt, S., & Liechti, M. E. (2015). Acute effects of lysergic acid diethylamide in healthy subjects. Biological Psychiatry, 78(8), 544-553.

Searchfield, G. D., Poppe, T. N. E. R., Durai, M., Jensen, M., Kennedy, M. A., Maggo, S., Shekhawat, G.S., Spiegel, D., Sundram, F., & Wise, K. (2020). A proof-of-principle study of the short-term effects of 3, 4-methylenedioxymethamphetamine (MDMA) on tinnitus and neural connectivity. International Journal of Neuroscience, 130(7), 671-682.

Shahar, O., Botvinnik, A., Shwartz, A., Lerer, E., Golding, P., Buko, A., Hamid, E., Kahn, D., Guralnick, M., Blakolmer, K., Wolf, G., Lotan, A., Lerer, L., Lerer, B., & Lifschytz, T. (2024). Effect of chemically synthesized psilocybin and psychedelic mushroom extract on molecular and metabolic profiles in mouse brain. Molecular Psychiatry, 1-15.

Shao, L. X., Liao, C., Gregg, I., Davoudian, P. A., Savalia, N. K., Delagarza, K., & Kwan, A. C. (2021). Psilocybin induces rapid and persistent growth of dendritic spines in frontal cortex in vivo. Neuron, 109(16), 2535-2544.

Shulgin, A. T., & Nichols, D. E. (1978). Characterization of three new psychotomimetics. In *The Psychopharmacology of Hallucinogens* (pp. 74-83). Pergamon.

Siegel, J. S., Palanca, B. J., Ances, B. M., Kharasch, E. D., Schweiger, J. A., Yingling, M. D., Snyder, A.Z., Nicol, G.E., Lenze, E.J., & Farber, N. B. (2021). Prolonged ketamine infusion modulates limbic connectivity and induces sustained remission of treatment-resistant depression. Psychopharmacology, 238, 1157-1169.

Siegel, J. S., Subramanian, S., Perry, D., Kay, B. P., Gordon, E. M., Laumann, T. O., Reneau, T.R., Metcalf, N.V., Chacko, R.V., Gratton, C., Horan, C., Krimmel, S.R., Shimony, J.S., Schweiger, J.A., Wong, D.F., Bender, D.A., Scheidter, K.M., Whiting, F.I., Padawer-Curry, J.A., ... Dosenbach, N. U. (2024). Psilocybin desynchronizes the human brain. Nature, 1-8.

Simmler, L. D., Hysek, C. M., & Liechti, M. E. (2011). Sex differences in the effects of MDMA (ecstasy) on plasma copeptin in healthy subjects. The Journal of Clinical Endocrinology & Metabolism, 96(9), 2844-2850.

Simonsson, O., Mosing, M. A., Osika, W., Ullén, F., Larsson, H., Lu, Y., & Wesseldijk, L. W. (2024). Adolescent psychedelic use and psychotic or manic symptoms. JAMA psychiatry, 81(6), 579-585.

Singer, L. T., Moore, D. G., Fulton, S., Goodwin, J., Turner, J. J., Min, M. O., & Parrott, A. C. (2012a). Neurobehavioral outcomes of infants exposed to MDMA (Ecstasy) and other recreational drugs during pregnancy. Neurotoxicology and Teratology, 34(3), 303-310.

Singer, L. T., Moore, D. G., Min, M. O., Goodwin, J., Turner, J. J., Fulton, S., & Parrott, A. C. (2021b). One-year outcomes of prenatal exposure to MDMA and other recreational drugs. Pediatrics, 130(3), 407-413.

Smart, R. G., Storm, T., Baker, E. F., & Solursh, L. (1966). A controlled study of lysergide in the treatment of alcoholism. I. The effects on drinking behavior. Quarterly Journal of Studies on Alcohol, 27(3), 469-482.

Smithies, V., Broadbear, J., Verdejo-Garcia, A., & Conduit, R. (2014). Dysfunctional overnight memory consolidation in ecstasy users. Journal of Psychopharmacology, 28(8), 751-762.

Strassman, R. J. (1995). Hallucinogenic drugs in psychiatric research and treatment perspectives and prospects. The Journal of Nervous and Mental Disease, 183(3), 127-138.

Straumann, I., Ley, L., Holze, F., Becker, A. M., Klaiber, A., Wey, K., Duthaler, U., Varghese, N., Eckert, A., & Liechti, M. E. (2023). Acute effects of MDMA and LSD co-administration in a double-blind placebo-controlled study in healthy participants. Neuropsychopharmacology, 48(13), 1840-1848.

Strauss, D., Ghosh, S., Murray, Z., & Gryzenhout, M. (2022). An overview on the taxonomy, phylogenetics and ecology of the psychedelic genera Psilocybe, Panaeolus, Pluteus and Gymnopilus. Frontiers in Forests and Global Change, 5, 813998.

Studerus, E., Vizeli, P., Harder, S., Ley, L., & Liechti, M. E. (2021). Prediction of MDMA response in healthy humans: A pooled analysis of placebo-controlled studies. Journal of Psychopharmacology, 35(5), 556-565.

Suleiman, M., Basu, A., Belal, S., & Jacob, T. (2022). From mushrooms to myolysis: A case of rhabdo in psilocybin-induced mood and psychotic disorder. The Journal of Nervous and Mental Disease, 210(8), 638-639.

Swanson, L. R. (2018). Unifying theories of psychedelic drug effects. Frontiers in pharmacology, 9, 172.

Swanson, L., Jungers, S., Varghese, R., Cullen, K.R., Evans, M.D., Nielson, J.L., & Schallmo, M-P. (2024). Enhanced visual contrast suppression during peak psilocybin effects: Psychophysical results from a pilot randomized controlled trial. Journal of Vision, 24(12): 5, 1-19.

Takahashi, T., Takahashi, K., Ido, T., Yanai, K., Iwata, R., Ishiwata, K., & Nozoe, S. (1985). 11C-labelling of indolealkylamine alkaloids and the comparative study of their tissue distributions. The International Journal of Applied Radiation and Isotopes, 36(12), 965-969.

Tancer, M., & Johanson, C. E. (2007). The effects of fluoxetine on the subjective and physiological effects of 3, 4-methylenedioxymethamphetamine (MDMA) in humans. Psychopharmacology, 189, 565-573.

Thompson, M. R., Callaghan, P. D., Hunt, G. E., Cornish, J. L., & McGregor, I. S. (2007). A role for oxytocin and 5-HT1A receptors in the prosocial effects of 3, 4 methylenedioxymethamphetamine ("ecstasy"). Neuroscience, 146(2), 509-514.

Timmermann, C., Roseman, L., Williams, L., Erritzoe, D., Martial, C., Cassol, H., Laureys, S., Nutt, D., & Carhart-Harris, R. (2018). DMT models the near-death experience. Frontiers in Psychology, 9, 395026.

Tsosie, R. L., Grant, A. D., Harrington, J., Wu, K., Thomas, A., Chase, S., Barnett, D., Hill, S.B., Belcourt, A., Brown, B., & Plenty Sweetgrass-She Kills, R. (2022). The six Rs of Indigenous research. Tribal College Journal of American Indian Higher Education, 33(4).

Vaidya, V. A., Marek, G. J., Aghajanian, G. K., & Duman, R. S. (1997). 5-HT2A receptor-mediated regulation of brain-derived neurotrophic factor mRNA in the hippocampus and the neocortex. Journal of Neuroscience, 17(8), 2785-2795.

van Amsterdam, J., Opperhuizen, A., & van den Brink, W. (2011). Harm potential of magic mushroom use: A review. Regulatory toxicology and pharmacology, 59(3), 423-429.

van Wel, J. H., Kuypers, K. P., Theunissen, E. L., Bosker, W. M., Bakker, K., & Ramaekers, J. G. (2012). Effects of acute MDMA intoxication on mood and impulsivity: role of the 5-HT2 and 5-HT1 receptors. PloS One, 7(7), e40187.

Vanattou-Saïfoudine, N., McNamara, R., & Harkin, A. (2012). Caffeine provokes adverse interactions with 3, 4-methylenedioxymethamphetamine (MDMA, 'ecstasy') and related psychostimulants: Mechanisms and mediators. British Journal of Pharmacology, 167(5), 946-959.

Vardy, M. M., & Kay, S. R. (1983). LSD psychosis or LSD-induced schizophrenia?: A multimethod inquiry. Archives of General Psychiatry, 40(8), 877-883.

Verrico, C. D., Miller, G. M., & Madras, B. K. (2007). MDMA (Ecstasy) and human dopamine, norepinephrine, and serotonin transporters: implications for MDMA-induced neurotoxicity and treatment. Psychopharmacology, 189, 489-503.

Vida, R. G., Sághy, E., Bella, R., Kovács, S., Erdősi, D., Józwiak-Hagymásy, J., Zemplényi, A., Tényi, T., Osváth, P., & Voros, V. (2023). Efficacy of repetitive transcranial magnetic stimulation (rTMS) adjunctive therapy for major depressive disorder (MDD) after two antidepressant treatment failures: Meta-analysis of randomized sham-controlled trials. BMC Psychiatry, 23(1), 545.

Vizeli, P., & Liechti, M. E. (2017). Safety pharmacology of acute MDMA administration in healthy subjects. Journal of Psychopharmacology, 31(5), 576-588.

Vizeli, P., Straumann, I., Holze, F., Schmid, Y., Dolder, P. C., & Liechti, M. E. (2021). Genetic influence of CYP2D6 on pharmacokinetics and acute subjective effects of LSD in a pooled analysis. Scientific Reports, 11(1), 10851.

Vollenweider, F. X., Gamma, A., Liechti, M., & Huber, T. (1998). Psychological and cardiovascular effects and short-term sequelae of MDMA (“ecstasy”) in MDMA-naïve healthy volunteers. Neuropsychopharmacology, 19(4), 241-251.

von Rotz, R., Schindowski, E. M., Jungwirth, J., Schuldt, A., Rieser, N. M., Zahoranszky, K., Seifritzb, E., Nowakb, A., Nowakb, P., Jänckec, L., Preller, K.H., & Vollenweider, F. X. (2023). Single-dose psilocybin-assisted therapy in major depressive disorder: A placebo-controlled, double-blind, randomised clinical trial. EClinicalMedicine, 56.

Wacker, D., Wang, C., Katritch, V., Han, G. W., Huang, X. P., Vardy, E., McCorvy, J.D., Jiang, Y., Chu, M., Siu, F.Y., Liu, W., Xu, H.E., Cherezov, V., Roth, B.L., & Stevens, R. C. (2013). Structural features for functional selectivity at serotonin receptors. Science, 340(6132), 615-619.

Wacker, D., Wang, S., McCorvy, J. D., Betz, R. M., Venkatakrishnan, A. J., Levit, A., Lansu, K., Schools, Z.L., Che, T., Nichols, D.E., Shoichet, B.K., Dror, R.O., & Roth, B. L. (2017). Crystal structure of an LSD-bound human serotonin receptor. Cell, 168(3), 377-389.

Wagmann, L., Richter, L. H., Kehl, T., Wack, F., Bergstrand, M. P., Brandt, S. D., Stratford, A., Maurer, H.H., & Meyer, M. R. (2019). In vitro metabolic fate of nine LSD-based new psychoactive substances and their analytical detectability in different urinary screening procedures. Analytical and Bioanalytical Chemistry, 411, 4751-4763.

Watts, B. V., Schnurr, P. P., Mayo, L., Young-Xu, Y., Weeks, W. B., & Friedman, M. J. (2013). Meta-analysis of the efficacy of treatments for posttraumatic stress disorder. The Journal of Clinical Psychiatry, 74(6), 11710.

Williams, K., Romero, O. S. G., Braunstein, M., & Brant, S. (2022). Indigenous Philosophies and the "Psychedelic Renaissance". Anthropology of Consciousness, 33(2), 506-527.

Wolfson, P. E., Andries, J., Feduccia, A. A., Jerome, L., Wang, J. B., Williams, E., Carlin, S.C., Sola, E., Hamilton, S., Yazar-Klosinski, B., Emerson, A., Mithoefer, M.C., & Doblin, R. (2020). MDMA-assisted psychotherapy for treatment of anxiety and other psychological distress related to life-threatening illnesses: A randomized pilot study. Scientific Reports, 10(1), 20442.

Wsół, A. (2023). Cardiovascular safety of psychedelic medicine: current status and future directions. Pharmacological Reports, 75(6), 1362-1380.

Yan, C. G., Chen, X., Li, L., Castellanos, F. X., Bai, T. J., Bo, Q. J., Cao, J., Chen, G.M., Chen, N.X., Chen, W., Cheng, C., Cheng, Y.Q., Cui, X.L., Duan, J., Fang, Y.R., Gong, Q.Y., Guo, W.B., Hou, Z.H., Hu, L., ... Zang, Y. F. (2019). Reduced default mode network functional connectivity in patients with recurrent major depressive disorder. Proceedings of the National Academy of Sciences, 116(18), 9078-9083.

Yarmolinsky, A., & Rettig, R. A. (Eds.). (1995). Federal regulation of methadone treatment. Washington (DC): National Academies Press (US).

Yerubandi, A., Thomas, J. E., Bhuiya, N. M. A., Harrington, C., Zapata, L. V., & Caballero, J. (2024). Acute Adverse Effects of Therapeutic Doses of Psilocybin: A Systematic Review and Meta-Analysis. JAMA Network Open, 7(4), e245960-e245960.

Appendix O: Mushroom cultivation suggestions

This section outlines priorities submitted from legacy cultivators and should be used when factoring in sourcing psilocybin-mushrooms and other plant medicines in any state-regulated program. Other state initiatives have not had representation of cultivators and thus suggestions from that community are provided here.

Manufacture/cultivation

- Protections/priority for local/legacy manufacturers/cultivators in the market.
    - Limitations to out-of-state producers.
        - Current market sees influx of out of state products which is undermining and pushing local people out of the market, a legal market needs to support local people and stimulate local economy.
- Non-prohibitive licensing (e.g., in terms of cost, taxes, restrictions, etc.)
    - Legal market cannot be restricted to who has the most money, an emphasis on small scale local producers disallows monopolization of the space.
- Licensing priority for legacy market/in-state producers
    - Folks currently criminalized by state and federal laws deserve priority and respect over new-to-the-space venture capitalists. Licensing priority for folks with relevant drug offenses should be considered.
- Licensing models that create space for small businesses to flourish (e.g., different licensing, regulation, taxes based on business size, etc.).
    - Mitigate monopolization and allow space for small business to thrive, the community has subsisted on many small-scale growers throughout prohibition, there is room for everyone to create a professional life and impact.
- Licensing limitations predicated on state residency (e.g., out-of-state cannot get in-state licensing without residency for two years).
    - Local, local, local. See first bullet point.
- Distribution businesses require quota of product sourced from local manufacturers/cultivators.
    - See first bullet point.
- Bundled licensing allowing cultivators/manufacturers to hold distribution/retail licensing (e.g., retail space allowable on same property as small scale or otherwise cultivation space, permitted zoning for joined retail/farming, etc.).
    - Small scale producers should not be pigeonholed into wholesale producers effectively drowning their business from large scale competition, direct to retail needs to be allowed for small scale producers and business to thrive. Perhaps wholesale manufacture license and retail manufacture license holding different restrictions?
- Caregiver programs allowing remuneration under minimal regulation/licensing.
- Options allocated to micro- or side businesses/hobbyist, this is not retail (e.g., not licensed for store front or otherwise but license allowing remuneration of products under certain circumstances). This is in allowance of legacy community to continue operation with local cultivators who for whatever reason are not pursuing legal retail or licensing.
- Exemptions to mandated testing regulations/labeling requirements.
    - Current testing can be cost prohibitive for producers, further considering relative potency or otherwise changes from crop to crop, further products used in spiritual practice should not

be put under invasive scrutiny potentially disrupting sacred rites. If testing is mandated, funds should be allocated from tax revenue and be allocated to cover state sponsored testing services at no cost to the producer.

Ecological/sustainability

- Outdoor cultivation of psychoactive mushrooms or plants to be allowed unless it is determined substantial local ecological impact could be proved.
- This is to create nonrestrictive entry to certain species which cannot be easily grown indoors without substantial knowhow and financial investment. likely this should be looked as well for mass production as that is where local ecological impact would likely stem from, however current understanding dictates minimal ecological impact overall.
- Cultivation/distribution is allowing of all psychoactive species, not just specific ones.
- Psychoactive mushrooms consist of several hundred different species, all species are to be allowed, same is said for plant varietals.
- Restrictions set on import of wild harvested plants/fungi as well as domestic wild harvest plants/fungi.
- Licensing for any import/domestic wild harvested plant or fungi should be heavily vetted and restricted to ensure safe and sustainable harvesting practices, as well restricted to folks with a bona fide need (e.g., communities with direct relationship to locality of import for spiritual practices, such as how ayahuasca is permitted under cultivated varietals of plant admixtures, harvested plant admixtures from South America are restricted to communities showing direct relation to said locality or spirituality and showing sustainable harvesting practices).
- Emphasis on local cultivation needs to be done to ensure minimal impact on foreign ecologies and protect said communities.
- Considerations made to classification of psychoactive mushrooms species under their own specific category (e.g., mushroom species/cultivars considered independent substances not under a blanket term of psilocybin mushrooms).
    - This would matter in case of quantity limits; independent species can be classified as differing substances acting towards differing use cases. Taking the Colorado idea of limits based on annual need. A blanket covering all species limits the quantity substantially for those who use several/many species for differing use cases.