July 2025, Vol 3, Issue 3

APSI NEWS BUZZ

ISSN No. 2584-2730 (Online)

The Official Newsletter of Addiction Psychiatry Society of India (APSI)

Theme: Psychedelics in Psychiatry: Promise, Peril, and Policy

THEMATIC ARTICLES

- PSYCHEDELICS AS TREATMENT FOR PSYCHIATRIC DISORDERS
- PSYCHEDELIC USE DISORDER?
- LEGALITY OF PSYCHEDELICS AS MEDICINE

SCAN ME

SPECIAL COVERAGE

WORLD DRUG REPORT 2025

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Editorial

Neither Panacea nor Poison: The Psychedelics and Psychiatry Tango

Vinit Patel, Ravindra Rao

From soma in the Vedic texts to peyote in Native American rituals, from Mayan mushroom ceremonies to the bhang of Indian festivals, psychoactive substances have long been woven into human culture. What unites these practices across time and geography is not casual indulgence but context: sacred rituals, bounded occasions, and community-sanctioned use. Substances were embedded in spiritual frameworks that gave them meaning and boundaries, making their use both sacred and, in many ways, safer (1).

Mushroom rituals were widespread and deeply ritualised in Mesoamerica. The Mayans consumed "k'aizalaj Okox" (Psilocybe cubensis), known to the Aztecs as "teonanacatl" or "flesh of the gods," often in ceremonies mediated by priests or shamans who acted as bridges between the physical and spiritual worlds. Mushroom stones carved more than 3,500 years ago, unearthed across Mexico and Central America, testify to the antiquity of these practices (2). These substances were understood as entheogens—tools for communion with divine powers, prophecy, and healing—rather than recreational agents (3). Even today, some indigenous societies preserve these ceremonies, carefully embedding safeguards to prevent misuse. Indigenous use was not limited to sacred ceremonies alone. Spirit medicines also played broader roles in community life — in palliative care, fostering creativity, strengthening social bonds, and, at times, even for hedonistic purposes. In the Greco-Roman world, the Eleusinian Mysteries centred on the ingestion of kykeon, a psychoactive drink thought to contain LSD-like compounds, showing that entheogenic practices extended well beyond Mesoamerica and India, spanning continents and millennia (4). By contrast, the hedonistic use of hallucinogens for pleasure exclusively is a much more recent phenomenon, emerging largely in Euro-American countercultures.

The very word psychedelic is another case in point. A Greek neologism coined in the mid-20th century by psychiatrist Humphry Osmond and popularised by Aldous Huxley and later Michael Pollan, it bundled together a loose grouping of hallucinogens—from LSD to mushrooms to ayahuasca—once tied to counterculture and now reframed as both spiritual and medical panaceas (5). As Yuria Celidwen notes, many indigenous communities of the Global South instead refer to these substances as spirit medicines, embedding them in relational, ecological, and cultural systems (3). The contrast underscores that "psychedelic" is not timeless, but a Western construct layered onto traditions with very different meanings.

It is against the erosion of these traditions, and the vacuum left by prohibitive laws, that a modern revival has taken shape. The past two decades have seen what many call a psychedelic renaissance. Substances once relegated to counterculture are re-entering the medical mainstream, driven largely by unmet needs in mental health care. For conditions such as

treatment-resistant depression, PTSD, end-of-life distress, and substance use disorders, existing pharmacological options are often limited in efficacy and slow to act. Psychedelics, paired with psychotherapy, have emerged as promising, if controversial, alternatives (4,5). Advocates argue that these compounds may even help address the so-called "diseases of despair"—suicide, overdose, and alcohol-related harm—when combined with structured psychotherapeutic care, raising hopes of a new class of treatments in psychiatry (5).

This resurgence has not been merely confined to research labs. Spiritual tourism such as ayahuasca retreats in South America, psilocybin journeys in Europe, peyote ceremonies in North America has flourished alongside the quest for healing. Closer home, the parallel rise of non-pharmacological approaches such as yoga and mindfulness-based sādhanās reflects a shared search for meaning and recovery beyond conventional medicine. Yet, like any powerful tool, psychedelics attract both seekers of healing and seekers of escape. The hope of rapid transformation can slip into the desire for a quick fix, mirroring patterns of problematic use familiar from other substances. For some, the pursuit takes on ascetic undertones, echoing the ideal of transcendence; for others, it risks replaying the excesses of the hippie counterculture of the 1970s.

This revival, however, is not occurring in isolation. It unfolds alongside wider global debates on drug regulation, where cannabis offers both inspiration and warning. The World Drug Report 2025 highlights that while cannabis remains the most widely used controlled substance worldwide, its trajectory is instructive for today's psychedelic debates. What began as a movement for medical access of cannabis in a handful of jurisdictions has, within two decades, led to widespread legalization across many countries. The result has been not only increased availability of cannabis but also greater daily use among youth, the proliferation of high-THC products, and rising psychiatric morbidity, a cautionary reminder of how policy can (and often does) outpace science (6).

Psychedelics now stand at a similar crossroads. In 2024, the U.S. Food and Drug Administration rejected MDMA-assisted therapy for PTSD, citing methodological limitations and safety concerns (7,8). By contrast, Australia's Therapeutic Goods Administration reclassified psilocybin and MDMA in 2023, allowing psychiatrists to prescribe them under strict controls (9), and Canada continues to provide access through its Special Access Program for patients with serious, treatment-resistant conditions (10). The global picture is therefore uneven: enthusiasm and reform in some countries, hesitation and caution in others. The WDR warns that expanding non-medical use, from microdosing communities to psychedelic retreats, is already creating blurred boundaries between therapy, wellness, and recreation (6).

Within this shifting landscape, our three thematic contributions examine psychedelics from scientific, clinical, and policy angles. The first, "Psychedelics in Psychiatric Treatment: From Research to Practice," reviews the expanding scientific literature on psilocybin, MDMA, LSD,

and related substances in conditions such as depression, PTSD, and substance use disorders. While the findings are encouraging, the article also highlights the limitations of current evidence. The article reminds us that the therapeutic promise of psychedelics must be tempered by methodological caution (4). The second article, "Psychedelic Use Disorder: A Clinical Myth or Emerging Reality?" adds an important corrective to the prevailing optimism. Although psychedelics are often regarded as non-addictive, the authors underscore clinical scenarios of persistent use and consequent problems thereof. They also examine how nosology frameworks in DSM-5 and ICD-11 accommodate (or fail to accommodate) these presentations. Finally, "Treatment on Trial: Can India's Drug Laws Accommodate Psychedelic Medicine?" situates these discussions within our own legal and policy framework. The article outlines how the NDPS Act creates barriers for scientific research, clinical trials, and eventual therapeutic use of psychedelics. By contrasting India's position with regulatory reforms in other jurisdictions, it highlights a pressing policy dilemma: how to enable scientific inquiry without opening the floodgates to misuse.

Together, these pieces show how optimism, caution, and regulation must be held in balance. But they also raise a broader question—are psychedelics destined to follow the same arc as cannabis? The answer is not yet clear—but the parallels are striking. Public enthusiasm, anecdotal reports, and market forces are moving faster than clinical trials, ethical guidelines, or policy reforms. For India, this moment offers both a warning and an opportunity. The warning is that policy inertia can be as harmful as premature liberalisation. If research pathways are blocked under rigid prohibition, we risk scientific stagnation. If, on the other hand, enthusiasm is allowed to outrun safeguards, we may replicate the unintended consequences seen with cannabis.

While these debates dominate headlines, the realities of everyday addiction care remain equally pressing. In Basic sciences section, we feature a novel fMRI study that used the film Trainspotting to examine heroin addiction and recovery, demonstrating how naturalistic cues can illuminate brain mechanisms of craving and their change with treatment. Our Alcohol and Tobacco section reviews two recent meta-analyses on smokeless tobacco cessation. The findings underscore the efficacy of varenicline and nicotine replacement therapy, while also exposing persistent gaps in South Asian research, an omission particularly relevant for India, where smokeless tobacco use remains widespread. In Recent Advances, an innovative analysis of Reddit posts on methadone and buprenorphine is highlighted. Using advanced natural language processing, the study maps patient experiences of treatment, withdrawal, and provider interactions. Such digital ethnography offers valuable, real-time insights into patient perspectives that are often absent in clinical trials. Our Special Populations section examines integrated models of opioid substitution therapy and hepatitis C care for homeless people who inject drugs. While these examples draw from Western contexts, the lessons for India lie in adapting low - threshold, outreach - based approaches to reach marginalised and unstably

housed person who inject drug (PWID). The newsletter also gives a summary of the recently released World Drug Report in June 2025, providing important insights on impact of drug use globally.

Beyond trials and policies, lived experience reminds us what recovery looks like in practice. This issue also carries a moving patient perspective, "The Far Side of Addiction: Day 100+." In it, the writer reflects on the fragile but determined journey of early recovery — crossing the symbolic milestone of 100 days of abstinence. The narrative captures the ambivalence of progress: pride in small victories, the weight of cravings, the ever-present risk of relapse, and the importance of support systems, including treatment, that sustain hope. For clinicians and policymakers, such testimonies are reminders that abstinence is not just a statistic but a lived experience, often hard-earned and deeply personal. We invite our readers to engage with these narratives, and to contribute similar reflections from their own practice or patient networks, so that Newsbuzz can remain not just a forum for evidence, but also for empathy.

As usual, we look forward to your feedback and suggestions to improve the newsletter.

Happy reading!!

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THEMATIC ARTICLES

Psychedelics in Psychiatric Treatment: From Research to Practice

Omar Afroz, Rohit Verma

Psychedelics are substances that carry the capacity to alter emotions, perception, and thought processes (1). Based on the chemical class, typical psychedelics can be divided into tryptamines (such as psilocybin), phenylethylamines (such as mescaline), and ergolines [such as lysergic acid diethylamide (LSD)]. Apart from these, psychedelics also include substances with related psychoactive properties, such as dissociatives such as ketamine. Some of these substances have been used in spiritual rituals in various indigenous areas for centuries, such as mushrooms containing psilocybin, among others. In recent times, there has been increasing interest in the use of psychedelics in psychiatric treatment (2).

Evidence for Efficacy in Mental Illness

Most of the current evidence for psychedelics in mental health is for depression, anxiety disorders, substance use disorders, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), eating disorders, and mental health issues associated with terminal illnesses (3). The first double blind controlled study in modern times was published in 2011, in which psilocybin (0.2 mg/kg) was used for the treatment of anxiety and depressive symptoms in 12 patients with advanced cancer. Psilocybin was found to improve anxiety (significant at 1 and 3 months) and depressive symptoms (significant at 6 months) (4). Subsequently, many RCTs involving various psychedelics have been published.

A recent systematic review and meta-analysis of 126 studies involving psychedelics found that Psilocybin and Ayahuasca have the largest number of articles on treating mood disorders, at 28 and 7, respectively. While there were several double blind RCTs involving psilocybin, most Ayahuasca studies were open-label trials, with few RCTs. There were 18 studies on MDMA which was tried for the treatment of PTSD, while LSD had six articles each on the treatment of mood disorders and alcohol use disorder. Psilocybin was found to have the greatest effect on anxiety and depression (Hedges' g = -1.49), followed by Ayahuasca, MDMA, and LSD. Moreover, two studies also found reduced suicidality (as a preliminary finding) after administration of Psilocybin and Ayahuasca (5). Notably, Ketamine was not included in this review.

A systematic review that included 49 RCTs found that Ketamine (racemic > Esketamine) was effective in treating depression, with higher doses (≥ 0.5 mg/kg) associated with greater effects. The largest effect size (-0.73) was seen for high-dose racemic ketamine. The effect was rapid after a single dose, peaking at 24 hours and subsequently returning to baseline. Repeated doses were found to have sustained antidepressant effects compared to controls (6). Another meta-analysis on treatment-resistant depression included 28 studies and reported rapid and strong

reduction in symptoms after a single 0.5 mg/kg intravenous infusion (standardised mean difference, SMD=0.68) (7). The effect was noticed as early as 4 hours after administration and peaked at 24 hours, subsequently decreasing at 7 days. Repeated administration (3 times a week for 2 weeks) was found to have higher efficacy and a more sustained response. A meta-analysis including seven articles reported that Esketamine used in the perioperative period was found to reduce the incidence of postpartum depression (8). The effect was sustained at 42 days after delivery and was not associated with increased risk of adverse effects.

A recent scoping review on the therapeutic use of psychedelics for substance use disorders found that among psychedelics, LSD and Ketamine had the most robust evidence. The greatest number of studies were for alcohol use disorder (AUD), followed by opioid use disorder (OUD), and Cocaine use disorder (CoUD). The included studies involved several double RCTs on psychedelics, in addition to two meta-analyses for LSD. Ketamine was found to have the strongest evidence (in multiple RCTs) for cocaine use disorder, followed by AUD and OUD. Similarly, LSD was found to have robust evidence for AUD. In addition, Psilocybin was found to have evidence for AUD (RCT) and tobacco use disorder (open study), Ayahuasca for CoUD (observational study), and Ibogaine for opioid use disorder (observational study). The review reported limited evidence for cannabis use disorder, sedative use disorder, and addictive behaviours (9). One of the meta-analyses included in this review involved six RCTs on LSD, with over 500 participants in total, and found that compared to placebo, LSD had a higher reduction in alcohol misuse and a greater likelihood of complete abstinence (odds ratios 1.96 and 1.8, respectively) (10).

A meta-analysis on psychedelic use for psychological symptoms in cancer patients reported that Ketamine (four RCTs) had a significant and rapid effect (Hedges' g = -1.37) on symptoms (11). Psilocybin (three RCTs) was also found to have a large effect (Hedges' g = -3.13). Studies on MDMA and LSD were found to lack rigorous methodologies (11). A Cochrane review, which included six studies on psychedelic use (Psilocybin, LSD, and MDMA) in patients with life-threatening diseases, reported that these agents may decrease anxiety and depressive symptoms (12). The evidence for the effect of these agents on existential distress was inconclusive.

A meta-analysis including 9 studies on MDMA assisted psychotherapy for PTSD reported a significant reduction of symptoms (SMD = -1.10) compared to control (13). Both response and remission rates were improved, without any significant increase in adverse effects. Similar findings were reported by another meta-analysis, which included 5 trials (14). A meta-analysis of 10 studies on Ketamine for PTSD (including five RCTs) reported improvement in symptoms 24 hours after Ketamine administration and at the end of treatment (which varied in duration for different studies) (15). The effect size, which was significant at the treatment endpoint, was found to be 0.25.

A systematic review on the use of psychedelics in OCD and related disorders found most articles to be in the form of preclinical data and case reports (psilocybin and LSD), with two trials involving psilocybin (16). Overall, Psilocybin was reported to have a significant reduction of symptoms of OCD and body dysmorphic disorder for some patients. A systematic review of nine studies on Ketamine for OCD (including 2 RCTs) reported that a single administration of 0.5 mg/kg intravenous Ketamine was associated with rapid and significant reduction of symptoms (17).

Limitations of Studies on Efficacy in Mental Illness

There are various methodological issues of psychedelic studies for the treatment of mental illnesses such as inadequate blinding, expectancy effects, heterogeneity and variability in procedures and dosing, and low generalizability (18). Other issues include a lack of data on long-term safety and efficacy, the role of drug versus psychotherapy in therapeutic effects, problems with informed consent considering the unpredictability of psychedelic experiences, vulnerability of participants to coercion, and inequity in availing treatments (19). Moreover, there are concerns about selection bias, lack of control groups, placebo effects, and conflicts of interest (20).

Mechanism of Action in the Treatment of Mental Illnesses

Various possible mechanisms have been proposed. Classical psychedelics are partial agonists at 5HT2A receptors causing excitatory postsynaptic currents and an increase in firing rates. These receptors are expressed in cortical (prefrontal cortex - PFC) and subcortical (basal ganglia, hypothalamus, and brainstem) areas which are involved in mood, learning, memory, and sleep-wake cycles. In addition, these receptors are expressed in brain areas involved in visual perception, attention, and higher-order association. In addition, activity on trace amino-associated receptor (TAAR) leading to subsequent inhibition of dopaminergic activity may be involved in the efficacy of psychedelics for addiction and depression (1, 21).

The psycho-plastogen model proposes that psychedelics rapidly promote both structural and functional neuroplasticity. This is mediated by postsynaptic glutamate release and AMPA receptor activation, leading to the release of brain-derived neurotrophic factor (BDNF) and enhanced signalling of mammalian target of rapamycin (mTOR), causing upregulation of genes involved in neuroplasticity. Moreover, Ketamine, by blocking NMDA receptors, allows glutamate to bind to AMPA receptors, leading to its antidepressant effects (1).

Some psychedelics, such as LSD and MDMA, increase levels of oxytocin, which is involved in sociability and empathy. This may lead to prosocial tendencies, allowing social manipulations to occur during the session, ultimately leading to the beneficial therapeutic effects. Moreover, the anti-inflammatory effects of psychedelics, mediated through 5HT2A activity on “trigger

-neurons," are implicated in their therapeutic effects. Psychedelics may also release the inhibition of the PFC on the thalamus, leading to sensory overload and altered perceptions, and decrease default mode network (DMN) activity, causing loosening of maladaptive beliefs. Disruption of coordination between cortical areas and the Claustrum, leading to reduced cognitive control, has also been proposed (1).

Psychological mechanisms include experiences of altered states leading to mystical experiences and insights, enhancing meaning and purpose. Psychedelics may also increase cognitive flexibility and mindfulness. Moreover, increased suggestibility caused by psychedelics may lead to a change in beliefs and worldview. Increase of social connectedness and unity may also lead to enhanced meaning and relief from depression and anxiety related to death. Finally, psychedelics may provide a window for the development of health behaviours and habits (1).

Protocols for Therapeutic Use

Among psychedelics, Ketamine was first approved for treatment-resistant depression (TRD) in combination with antidepressants. Recently, it has been approved as a monotherapy (Esketamine nasal spray) for TRD. However, the FDA declined the approval of MDMA for PTSD, and most other psychedelics are currently not approved for therapeutic use. As Ketamine is the only approved psychedelic, this chapter will discuss its administration in detail. An NHS protocol for Ketamine administration mentions the following (22):

The indication for ketamine administration is TRD (defined as ≥ 3 Antidepressants for 6 weeks) with active symptoms.

- **Before administration:** informed consent should be taken from the patient. The patient should be accompanied by an attendant. An anaesthetist should be available and prescribe Ketamine. The patient should be examined in detail and relevant investigations should be conducted before treatment. The patient is advised to avoid solid food for 4 hours and clear liquids for 2 hours before the procedure.
- **Ketamine administration:** ketamine (diluted in NS) is given at a dose of 0.5 mg/kg through the intravenous route over 40 minutes using a syringe driver. BP, PR, and SPO2 should be monitored during administration of ketamine. Rating scales such as Montgomery-Asberg Depression Rating Scale (MADRS) can be applied pre- and post-treatment for response and adverse effects. Patient should be observed for one hour after ketamine administration.
- **Post-administration:** the patient should be discharged with the attendant. The frequency of sessions is Weekly. 6 sessions is recommended for the acute phase, followed by maintenance sessions if needed.

In addition, it is recommended that the setting should have resuscitation facilities, with at least one treatment provider certified in advanced cardiac life support (ACLS) or be able to access experts immediately. The ECT suite is reported to be an ideal setting for administering Ketamine. The dose of Ketamine should be optimized based on efficacy and adverse effects (23).

The dose of Ketamine should be optimized based on efficacy and adverse effects. Management for common side effects includes Ondansetron for nausea, Acetaminophen for headache, slowing the infusion for tachycardia/hypertension, and Beta-blockers for hypertension. Other adverse effects such as increased salivation, nightmares, hallucinations, and agitation, may also require intervention. It is recommended that the vital signs be monitored every 15 minutes during the 1 hour after the treatment, and the patient should be advised not to drive or operate machinery for the next 24 hours (23).

Future Direction

There is a need for studies with more robust methodologies, including larger sample sizes, long-term follow-ups, and adequate blinding. Optimization of protocols and dosing, and delineating the role of psychotherapy, is also required. Other areas such as microdosing of psychedelics and the use of Norketamine (a metabolite of Ketamine), also warrant further research (24).

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Psychedelic Use Disorder: A Clinical Myth or Emerging Reality?

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The term "psychedelics" has commonly been used by both the general public and researchers to refer to hallucinogens. Historical records document the use of cannabis, ayahuasca, and hallucinogenic mushrooms in sacred religious and spiritual ceremonies. A major milestone in the synthetic production of psychedelics occurred in 1943, when Dr. Albert Hofmann, a Swiss chemist, first stumbled upon LSD. Living to the age of 102, he would likely take satisfaction in its resurgence today, as rigorous scientific research begins to uncover its therapeutic potential. Psychedelics are typically classified by their chemical structures such as indoleamines, ergolines, or phenylethylamines, or by their mechanism of action, with classical psychedelics acting on serotonin receptors and non-classical ones affecting other pathways (1).

Over the past two decades, there has been a resurgence of interest in the therapeutic potential of psychedelics, particularly in the treatment of psychiatric disorders such as major depressive disorder, posttraumatic stress disorder (PTSD), and obsessive-compulsive disorder (OCD). Much of the evidence comes from early-phase clinical trials, which suggest promising outcomes (2). However, concerns regarding potential misuse, psychological risks, addiction, and diversion continue to inform a cautious regulatory stance. These concerns underscore the importance of rigorous methodology and careful oversight as the field moves toward establishing psychedelics within the framework of evidence-based psychiatric care.

The fall and rise of Psychedelics

Following a surge of interest in the 1950s and 60s, research into the therapeutic potential of psychedelics was largely suspended for nearly five decades due to regulatory restrictions and sociopolitical concerns. Over the past 20 years, there has been a renewed focus on these compounds, resulting in a growing body of preliminary research. In recognition of this emerging evidence, the U.S. Food and Drug Administration (FDA) has granted “breakthrough therapy” designation to two psilocybin-based formulations currently under investigation for treatment-resistant depression. MDMA has also received a breakthrough designation for its potential use in treating posttraumatic stress disorder in 2019 (though it subsequently declined to approve the new drug application in 2024 mainly due to limitations in study design of phase 3 trials) (3, 4).

Although current regulations classify psychedelics as Schedule I substances, placing them in the same category as heroin, recent research has prompted calls to reconsider this classification. If approved for medical use, psychedelics may be more appropriately placed in Schedule IV, alongside medications such as benzodiazepines (5). In contrast to many commonly misused substances, psychedelics have been found to pose relatively lower risk. A harm assessment

study conducted by Nutt and colleagues rated LSD and psilocybin among the least harmful substances, with scores of 7 and 6 out of 100, respectively, while substances such as alcohol and heroin scored significantly higher (6). These findings suggest that psychedelics carry a substantially lower risk of harm to individuals and society.

Epidemiological data further indicate that lifetime use of psychedelics is associated with lower rates of psychological distress, suicidal ideation, and suicide attempts. The task force report by the Canadian Network for Mood and Anxiety Treatments (CANMAT) 2023 states that the evidence for the safety of psychedelics is of low quality. But, based on the expert opinion, the long-term likelihood of developing hallucinogen use disorder or hallucinogen-persisting perception disorder appears to be low (particularly in individuals without a history of psychosis) (7).

Continuing risk of Psychedelics

Although there is growing evidence for the potential therapeutic benefits of psychedelics, their use is not entirely without risk. Adverse effects have been reported, particularly in vulnerable individuals and in cases involving high doses or unregulated sources. A systematic review and meta-analysis by Sabe et al. examined the incidence of psychedelic-induced psychosis in both the general population and individuals with preexisting mental illness. The review found that most psychotic reactions occurred among individuals who obtained psychedelics from illicit markets or consumed novel psychoactive substances not used in controlled clinical trials (8).

Reported adverse reactions range from acute, transient panic responses and brief psychotic episodes to persistent psychosis characterized by flashbacks and other non-specific psychotic symptoms. While classical psychedelics such as psilocybin and LSD are generally associated with lower risk in supervised settings, non-classical compounds and derivatives, including phenethylamines, lysergamides, and synthetic tryptamines, have been associated with more severe complications. These include serotonin syndrome, seizures, coma, cerebral edema, prolonged respiratory failure, renal failure, multi-organ failure, metabolic acidosis, rhabdomyolysis, and long-term neurological impairment (9, 10, 11). Social consequences may arise from impaired judgment, leading to high-risk behaviors and harm to others.

Are We Being Overcautious? Evidence from clinical research

Psychedelics have consistently ranked low in terms of dependence risk, although some evidence suggests that the possibility of misuse cannot be entirely ruled out. This lower risk is likely attributable to the fact that serotonergic hallucinogens do not exert direct effects on the brain's dopaminergic reward pathways, which are central to the reinforcing properties of most addictive substances (8).

In a comprehensive review, Johnson et al. (2018) assessed the abuse potential of medical

psilocybin using the eight-factor framework outlined in the Controlled Substances Act. Their findings indicated that psilocybin demonstrates limited reinforcing effects. Utilizing the Addiction Research Centre Inventory (ARCI), they found that psychedelics such as LSD and psilocybin were associated with substantially lower abuse potential compared with substances known for compulsive and repetitive use patterns (6, 12).

Classic psychedelics are generally well tolerated in clinical and research settings. While serious adverse events have been documented, these have primarily occurred in non-clinical contexts (13). The severe consequences sometimes reported in recreational settings have not been observed in recent trials conducted under medical supervision. A systematic review has identified specific personality traits and psychological states that may influence the subjective experience of psychedelic use. Individuals with high levels of absorption, openness, and acceptance, as well as those in a psychological state characterized by surrender, tend to report more favorable outcomes. In contrast, those with low levels of these traits or in a state of apprehension or psychological preoccupation are more likely to encounter acute adverse effects (12, 14).

Because psychedelics intensify emotional experiences, the context of use, often referred to as "set and setting," is crucial. In unprepared individuals or unsafe environments, the effects may escalate into distressing psychological states or, in rare instances, risky behavior. While such events are less common than those associated with other psychoactive substances, particularly alcohol, they tend to be highly publicized, shaping public perception of the risks (12, 13). Despite public concern, scientific literature consistently classifies psychedelics as significantly less harmful than alcohol and many other controlled substances, both at the individual and societal levels. Nevertheless, ongoing research is needed to better quantify the incidence of rare, but serious, adverse effects and to develop safeguards for clinical use.

It is also important to interpret psychedelic research with a clear understanding of its inherent methodological limitations. These include the presence of multiple confounders, difficulties in maintaining blinding, limited data on acute and chronic dose-response relationships, and patient expectancy effects. Questions have also been raised about the validity and sensitivity of outcome measures commonly used in psychedelic studies, such as the Hallucinogen Rating Scale (5).

Nosology

It is also important to examine the evolving nosological classification of psychedelics. Use of psychedelics is not very different from other substances – “Any consumption of psychedelic substances, whether for therapeutic, spiritual, recreational, or exploratory purposes” is considered use. However, use of psychedelics in a manner inconsistent with intended or recommended use, increasing risk of harm, which includes taking unsupervised high doses

without preparation, combining psychedelics with other substances, and using despite medical and psychiatric contraindications, is different from “use” and is widely regarded as “misuse”(15). "Hallucinogen abuse" is defined in the DSM-IV-TR as a pattern of drug use resulting in recurrent significant adverse consequences from the repeated ingestion of hallucinogens.

The DSM-5 criteria for Hallucinogen Use Disorder (≥2 of 11 criteria over 12 months) include craving, failed attempts to cut down, neglecting major obligations, continued use despite harm, tolerance, but no withdrawal. Hallucinogen Persisting Perceptual Disorder, as defined by DSM-5, is the re-experiencing of perceptual symptoms like those experienced while intoxicated that are clinically impairing and not better explained by another cause.

As per ICD-11, Hallucinogen Dependence is rare, and hallucinogen withdrawal is not very well described. The typical signs and symptoms of withdrawal are not very well studied, and hence, this criterion is not included in the diagnosis of dependence. In contrast to ICD-10, ICD-11 does not have a specifically defined category for hallucinogen persisting perception disorder but talks about acute intoxication with hallucinogens, described as a clinically significant, transient condition following consumption of hallucinogens that may include changes in cognition, affect, perception, behavior, and autonomic system. Among the psychiatric disorders related to hallucinogen use, Hallucinogen-Induced Psychotic Disorder, described in both DSM-5 and ICD-11, is the most frequently seen, although worldwide it is still uncommon.

Conclusion

To conclude, psychedelics may be seen as a difficult child, once misunderstood, mishandled, and cast aside by regulatory barriers, but they are now re-emerging as powerful tools with potential therapeutic substance despite the threats of harm and risk of addiction. With careful research, responsible use, and robust safeguards, psychedelics may yet fulfill the promise that early pioneers envisioned: not as recreational curiosities, but as transformative agents for treatment of psychiatric conditions.

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Treatment on Trial: Can India's Drug Laws Accommodate Psychedelic Medicine?

Ashwin Mohan

Psychedelics have a long and complex history of thousands of years of usage in ancient cultures and rituals, modern rediscovery in the middle of the last century, their unbridled use in popular culture leading to eventual stigmatization and prohibition, and their incorporation into international drug laws. However, there has been a huge resurgence of interest in psychedelics in the 21st century leading to research, clinical trials and treatments for many mental health conditions and addictions (1, 2). These research initiatives have also led to policy and ethical concerns and also challenged traditional drug laws that have failed to keep up with the science leading to a regulatory landscape that still looks up to this class of substances with the narrow perspective of enforcement rather than embracing them as therapeutic tools.

This article aims to give a birds-eye view of the current global regulatory landscape followed by the Indian scenario. It also attempts to suggest ways of incorporating these therapies in the Indian context.

Historical context

The modern era of psychedelics began in 1938 when Swiss chemist Albert Hofmann accidentally synthesized LSD while working at Sandoz Laboratories. In 1943, he inadvertently ingested a small amount, leading to the discovery of its powerful psychoactive effects. This accidental creation dramatically changed the use of psychedelics among the wider public (2). During the 1950s, psychedelics were studied for their psychiatric benefits, with research suggesting their potential to treat depression, addiction, and other mental disorders. However, as their recreational use became widespread in the 1960s, especially during the hippie movement and the Anti-war sentiment, a political and social pushback led to increasing restrictions.

Even though there was extensive growing body of clinical research on hallucinogens, especially with LSD, which at the time was being distributed in the US for investigational purposes, there was still no federal legal requirement in the Federal Food, Drug and Cosmetic Act of 1938 (in the US) requiring pharmaceutical manufacturers to demonstrate proof of clinical efficacy through adequate and well controlled clinical trials. It was on October 10th, 1962, in response to the thalidomide tragedy, the Kefauver-Harris Drug Amendments to the Federal FD&C Act, known officially as the "Drug Amendments of 1962" was signed into public law. This crucial legislation significantly increased the FDA's regulatory controls on the new chemical entities for humans. For any new drug substance, pharmaceutical companies were now required to submit as part of their New Drug Application (NDA), adequate and well-controlled studies,

demonstrating their drug to be both safe and effective for the clinical indication(s). The Controlled Substances Act emerged along with other international drug control treaties that included, the international "Single Drug Convention" of 1961, the "Psychotropic Convention" of 1971, and other efforts from nations to harmonize their drug regulatory frameworks (1). By the 1970s and 1980s, governments around the world classified psychedelics as illegal substances, effectively halting scientific exploration for decades. Since then, psychedelics have remained illegal in most places globally, with only limited exceptions for indigenous or religious use.

Today, there appears to be rapidly growing awareness, and immense interest generated for the potential of several psychedelic drugs to become medically approved for various psychiatric disorders. This comes at a time when the research into neuroscience treatments have reduced significantly. The FDA has recently granted breakthrough therapy designation to psilocybin and MDMA for depression and PTSD, respectively. Similarly, Australia has recently authorized the use of psilocybin and MDMA for specific psychiatric conditions under regulated settings.

Although a comprehensive discussion regarding legal status of different psychedelics in different countries is not possible due to space constraints, but the current status of some of these substances in different countries is presented. As of 2025, the following countries have legalized the use of psychedelics: Bahamas (Psilocybin), Bolivia (Ayahuasca), Bolivia (Ayahuasca), Jamaica (Psilocybin), Peru (Ayahuasca). The following countries have decriminalized the use of psychedelics: Argentina, Armenia, Austria, Belgium, Chile, Colombia, Costa Rica, Croatia, Czechia, Ecuador, Estonia, Italy, Latvia, Lithuania, Netherlands, Portugal, Slovenia, Spain and Ukraine. The following countries have permitted medical use: United States, Switzerland, Israel, Australia and Denmark. In other countries, the use of psychedelics, either for recreational or medical use, remains illegal (2).

The varieties of Psychedelic Law

As can be seen above, the varieties of psychedelic law include: Decriminalization, supported adult use (no prescription needed for personal use), Medical use, legal use for religious purposes, and complete legalization (3).

The Indian context

In India, the Drugs for therapeutic uses are approved by the Central Drugs Standard Control Organisation (CDSCO) and are governed by the provisions of the Drugs and Cosmetics Act (D&C Act, 1940) and Rules (D&C Rules, 1945) (4). The standard approval process includes the application for a new drug, evaluation including regulatory evaluation, followed by possible permissions to conduct a bioequivalence study or a clinical trial and then a review by the Subject Expert committee. If these hurdles are cleared, then the data and reports are evaluated

after which a final approval is given (5). This is a time-consuming process, usually taking years. In addition, conducting a clinical trial has its own challenges.

If the particular drug is covered under the Narcotic drugs and Psychotropic Substances Act and Rules (NDPS Act and Rules) (6), then it adds much more stringent layers of regulation involving different regulatory authorities and compliances. A detailed review is beyond the scope of this article. Although the NDPS Act carves out an exception for the use of these substances for 'medical and scientific purposes', in reality, the act is draconian and stringent and skewed towards enforcement. Thus, it makes for a difficult regulatory environment to work with.

At present, no psychedelics are approved for use in India.

Barriers to clinical and research use

The public health need for new medicinal treatments to support patients who find available medicines ineffective or unacceptable due to side-effects, compliance, and cost demands are enormous. Apart from the humongous regulatory barriers as detailed above, other barriers include: Researching psychedelics and marijuana for potential development into prescription medicines, training therapists and working to establish a network of clinical treatment centres, supporting scientific research into neuroscience, creativity, and spirituality, Educating the public at large about the potential risks and benefits from psychedelic and marijuana use. Other challenges include commercialization, and patents, insurance coverage, methods and types of legalization and issues of access, equity and availability. There are also clinical barriers including those related to treatment guidelines, lack of standard algorithms, dosing, and other clinical challenges (1, 2, 7, 8).

As seen above, a set of complicated ethical and policy issues need to be resolved if these medications are to contribute meaningfully to advancing mental health.

Lessons from global frameworks

In the beginning of this article, I had detailed about the current global scenario as far as the regulation of psychedelics are concerned. This offers some lessons for us in the Indian scene. However, in India, we do not have a stratification of risk for the use of psychotropic substances and the regulatory framework is the same for all kinds of illicit substances without exception. Thus, in the absence of a change in regulatory framework, most of the global initiatives are bound to fail in our country. The NDPS Act and the D&C Act being central acts require the parliament to pass amendments. This is extremely difficult, if not impossible. The states have little control over approvals except for framing rules under the act.

Even if psychedelics are approved for medical use (and not recreational use), it brings about many challenges including, but not limited to the degree of reforms (broad or narrow; all psychedelics or some; for which conditions); for medical use or recreational use or both (contexts, amounts, possession issues, penalties); logistical issues (supply, context of supply, manufacture and transport, storage); and compliance (record keeping, submission of returns).

What needs to change

A brief overview of the regulatory, ethical and policy challenges were listed above regarding the use of psychedelics in India. There are challenges at multiple levels and multiple areas that are not easy to fulfil or circumvent. There are multiple layers involved ranging from the regulatory to institutional to societal and cultural issues. Navigating such a maze of entities requires sustained efforts at different levels. Needless to add, it requires enormous funding.

As evident from the provisions of the international and Indian statutes, science is just one of the considerations in health policy. These regulations were developed during a time of fear, politics, and misinformation and even lack of knowledge about mental disorders and their treatments, as well as about psychedelic substances that led to derailing research and complete stoppage into their clinical use. But new emerging clinical scientific information have led to the resurgence of interest in research and potential therapeutic application of certain psychedelic substances.

I will end with quotes of Captain Beloiun, A US core Commissioned Officer for an enduring science-centred, research-guided mental health policy (1):

"*We must seek the truth, through science, by pursuing research.*"

"*We must have the acknowledgment, willingness, and resolve, to engage in clinically validating potential paradigm shifting treatment endeavours, even when at times they may run counter to cultural norms, cherished ideologies, and time-honoured belief systems.*"

"*As a nation, if we can overcome fear and lead the world by putting humanity on the moon, we must overcome 50 years of legacy fear and lead in this research.*"

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SPECIAL SECTION

Summary of World Drug Report 2025

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The World Drug Report provides an annual overview of the major developments in drug markets for various drug categories. It is a flagship publication of UNODC (United Nations Office on Drugs and Crime) and offers a comprehensive analysis of trends in drug production, trafficking, consumption, and their health, social, and environmental consequences. The World Drug Report 2025 was released on 26th June 2025 and comprises of four main sections: Key Findings; Drug Market Patterns and Trends; Contemporary Issues on Drugs; and Special Points of Interest.

The key findings have been reported in four main areas namely latest trends in drug markets, latest trends in drug demand and harm, drug policy updates and in focus: sex and age differences and topical deep dives. The first and most urgent finding is the surge in global drug use, reaching alarming new heights. Drug consumption has soared, placing immense strain on already overburdened health and social systems. The report estimates that 316 million people aged 15–64 (about 6% of the global population) have used an illicit substance in 2023, more than 5.2% from 2013, showing an alarming rise. This rise has outpaced population growth, reflecting deeper economic and geopolitical distress. Global production of cocaine reached a record-breaking 3,700+ tonnes in 2023, while consumption has jumped from 17 million in 2013 to 25 million in 2023, spreading beyond its traditional strongholds into Asia, Africa, and parts of Europe. Synthetic drugs, including amphetamines, methamphetamines (notably Captagon), and fentanyl, are also surging. Fentanyl and new synthetic opioids such as nitazenes are rising in prominence. These highly potent substances are cheap to produce, easily concealed, and increasingly responsible for clusters of fatal overdoses. Their proliferation has complicated overdose prevention and burdened health systems. The pre-existing and emerging use of drug mixtures and concoctions, such as “nyaope” (containing heroin, cannabis and other adulterants such as phenacetin and caffeine), and more recently “karkoubi” (mixture of cannabis and clonazepam) and “kush” (containing cannabis, fentanyl, tramadol, etc.), is an increasing threat to public health in some African countries.

The second key finding is the alarming evolution of organised crime. Advanced technologies, leveraging encrypted communication platforms, digital marketplaces, cryptocurrency, and blockchain-based financial layering have made detection of criminal network difficult. They also benefit from clandestine chemical innovation, allowing them to continually adapt their products and methods. Major busts by law enforcements no longer now dismantle the networks rather they trigger shifts to a new route, smarter concealment or use of sharper tactics. These criminal networks are growing more sophisticated, adaptive, and resilient with passage of time.

Thirdly, the human health and social toll of this drug upsurge remains vast. Drug use disorders has affected around 64 million people worldwide which is a 13% increase since 2013. Despite being a large population suffering from drug use disorders, access to treatment is woefully limited with only 8–9% of those with drug use disorders receiving any form of treatment. Treatment of opioid overdose by naloxone and opioid agonist therapies remain uncommon in many countries. However, stigma, criminalisation, and exclusion compound the barriers to help.

The World Drug Report has also highlighted environmental damage from drug activity. Illicit coca and poppy cultivation, especially in the Andes, as well as clandestine meth labs in Europe, are causing deforestation, land degradation, severe water and air pollution, and biodiversity loss. Each pound of methamphetamine produced generates roughly five pounds of toxic waste, still cleanup efforts are underfunded and environmental restoration remains a secondary priority in national drug policies.

In the section on drug market patterns and trends, the report notes a dramatic shift in the opium supply following Afghanistan's 2022 opium ban. This collapse of cultivation has led to compensation by substituting synthetic opioids like fentanyl into markets which was previously dominated by heroin. The Golden Triangle—spanning Myanmar, Laos, Thailand, and southern China—remains one of the world's most potent synthetic-drug hotspots. Methamphetamine seizures in this region saw a 24% year-on-year surge. In South-East Asia, methamphetamine remains the primary drug of concern, while the non-medical use of ketamine is also notably high in the region. Use of cocaine as primary drug of use has also increased in the south-east Asian region from almost 0 in 2017 to 1500 persons in 2022. Asia has also showed the largest gender gap in cannabis use globally, with 90 out of every 100 past-year cannabis users being men. The region also accounts for the highest number of people who inject drugs worldwide—an estimated 5.2 million in 2022. Among this population, 615,000 are living with HIV and 2.8 million with hepatitis C. The highest prevalence of HIV among people who inject drugs is found in South-West Asia (29.5%), while East and South-East Asia report the highest prevalence of hepatitis C (65%), raising serious public health concerns.

There has been a change and evolution in demographics and user behaviour globally. Women increasingly access synthetic substances through social circles and digital channels, while young people explore unsupervised psychedelic experiences. Cannabis use continues to increase globally, more so among adolescents. Drug use, including injecting drug use, remains one of the drivers of new HIV and hepatitis C infections. Drug treatment availability, coverage and accessibility remain limited globally, particularly in Africa and Asia. The criminal justice response remains focused on offences related to drug use and possession. Criminalization of drug-related offences and severity of punishment varies across countries. Inequalities in the availability of pharmaceutical opioids for medical use continue to be significant.

In the section on contemporary issues on drugs, the report emphasises the right to health at its core. The report states that drug policy must align with fundamental rights, ensuring access to care, equity, and inclusion, even for people who use drugs or are incarcerated. However, presence of stigma, criminalisation, and marginalisation block harm reduction and treatment access worldwide. In regions affected by conflict, displacement, and economic crisis, drug use is becoming a coping mechanism, particularly among youth who lack stable family support. Mental health strain and limited access to safe and legal economies drive many toward substances as self-medication or survival tools. The report also finds that gender inequality remains astutely stark. Women are significantly less likely to access treatment than men, and stigma around female drug use remains persistent. In some contexts, such as Sierra Leone, women exposed to powerful synthetic drugs face elevated risks of sexual violence. Harm-reduction and treatment services continue to lack gender-sensitive design, reinforcing barriers to support and recovery.

In the section on special points of interest, the report draws attention to three thematic areas. The first is complex Impacts of Drug Use which shows that drug use reverberates far beyond individual health and management demands integrated strategies that combine health, social care, prevention, psychosocial support, and harm reduction—not simply clinical or punitive solutions. The section on special point of interest also focuses upon evolving organised crime dynamics and environmental harm of illicit drug activities, taking Europe as an example.

The report also provides policy recommendations to address these layered challenges and outlines five strategic directions. The first is cross-sectoral integration of health systems, justice systems, environmental management, and community development to deliver a more unified and effective response to drug-related issues. The second recommendation is promoting the integration of digital forensics with on-the-ground operations for sustained and targeted enforcement efforts. The report's third recommendation is expansion of prevention, treatment & harm reduction such as use of opioid substitution therapy and supervised consumption spaces, naloxone distribution and screening. These services should be community-based and gender-sensitive, recognizing the varied needs of people who use drugs and those in marginalized settings. The report repeatedly emphasises upon embedding environmental remediation and restoration into drug policy planning and budgeting, acknowledging the environmental impact of drug production and trafficking. In its fifth recommendation the report envisages leveraging technology and international cooperation to improve drug response to global drug challenge. The report also notes certain emerging gaps & new threats such as use of nitazenes, pharmaceutical diversion of medications intended for pain relief or mental health, increase use of new psychoactive substances, including synthetic cannabinoids, benzodiazepines, cathinones and shifting substance trends in displaced youths.

In conclusion, the 2025 World Drug Report issues a stark warning that the global drug crisis is escalating in scope, complexity, and consequence. The record levels of production and consumption of various substances such as cocaine, ATS, fentanyl, and nitazenes have increased and are spreading through sophisticated criminal networks and reaching vulnerable populations worldwide. The fallout is high and encompasses of overdose deaths, disease, social fracture, and environmental destruction. However, the report also shows a path forward and offers a clear blueprint for transformation. It urges a new paradigm that is integrated, evidence-based, rights-centred, and aware towards environment. It calls for a shift from fragmented, punitive responses toward smart with involving cross-sector cooperation. The report highlights that only this holistic, multi-level strategy can address the intertwined challenges of drug supply, demand, ecological impact, social justice, and resilience.

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SECTION UPDATES

A Movie, the Brain, and the Journey of Recovery: What 'Trainspotting' Revealed About Heroin Addiction

Poulami Basu, Ankita Chattopadhyay

Drug addiction, especially heroin use disorder (HUD), has long been understood through the lens of neurobiology, with the orbitofrontal cortex (OFC) playing a central role in how individuals assign "value" to rewards like drugs vs. other life stimuli like food or relationships. According to the various models of addiction including the impaired response inhibition and salience attribution (iRISA) model, recurrent substance use hijacks the brain's reward system, leading to compulsive drug-seeking and weakened control over behavior (1, 2). Yet much of what we know comes from artificial lab setups using static images of drug cues—which fail to capture the complexity of real-life situations where competing stimuli (drug vs. non-drug) fight for attention.

A recent study from the Icahn School of Medicine at Mount Sinai has used a surprising tool to explore heroin addiction and recovery: a movie (3).

The researchers wanted to understand how the brain responds to drug-related cues and how this response changes with treatment. So, they asked two groups—30 people recovering from heroin addiction and 25 healthy individuals—to watch the first 17 minutes of the film Trainspotting, which includes scenes of heroin use, social situations, and daily life.

The study employed a longitudinal fMRI design to examine shared brain responses to a drug-themed movie in individuals with heroin use disorder (iHUD) compared with healthy controls (HC). Thirty inpatient iHUD and twenty-five age- and sex-matched HC watched the first 17 minutes of Trainspotting during scanning, with repeated sessions approximately 15 weeks apart. Functional data were preprocessed using fMRIPrep, followed by custom preprocessing (motion correction, smoothing, high-pass filtering, and confound regression). Inter-subject correlation and reverse correlation approaches were applied to identify synchronized brain activity within regions of interest, particularly the orbitofrontal cortex (OFC), during drug versus non-drug scenes. Movie segments were independently labeled for drug content, and scene-specific craving ratings were collected post-scan to correlate neural responses with subjective craving. Statistical analyses employed bootstrapping and permutation testing to determine drug-biased synchronization and its longitudinal changes with treatment.

Key Findings

The study showed that at baseline, people with heroin addiction had significantly stronger drug-related brain synchronization than healthy controls (HC) in 28 cortical regions, including the orbitofrontal cortex (OFC), insula, and prefrontal cortex [false discovery rate (FDR) corrected at $p < 0.05$]. After about 15 weeks of inpatient treatment, HUD participants showed a significant reduction in drug-biased brain responses across 12 regions, including the

OFC, compared to HC. Importantly, reductions in OFC synchronization were significantly correlated with reductions in scene-induced craving ($r = 0.54$, $P = 0.0023$, $q = 0.016$ FDR corrected).

Why This Matters

Traditional brain studies often use static images to study addiction, but real life is dynamic and full of competing cues—both drug-related and non-drug-related. Movies provide a more natural way to study how people respond to complex, emotional situations.

This is one of the first studies to show that the brain's response to drug cues in a natural setting like a film can be used as a marker for craving and recovery. It also suggests that the brain can "retrain" itself with treatment, adjusting how it reacts to familiar drug cues.

What Makes This Unique

While brain responses to drug cues and their links to craving have been studied before, this research stands out because it combines several novel elements. Instead of static images, it used a naturalistic movie to mimic real-life experiences, and it applied a group-level synchronization approach to show how people with heroin addiction shared brain reactions during drug scenes. Most importantly, it followed participants over 15 weeks of treatment, revealing that these synchronized brain signals not only decreased with recovery but also closely tracked reductions in craving. This integration of naturalistic fMRI, group synchronization, and longitudinal design makes the study distinctive.

What's Next?

This kind of research could help develop better tools to track progress in addiction treatment. It could even lead to therapies that involve naturalistic media, such as films or virtual environments, to help retrain the brain.

The findings also open the door for similar studies in other conditions like depression or anxiety, using real-life content instead of artificial lab tasks.

Final Thought

Movies often reflect our emotions and struggles. In this case, Trainspotting became more than a story—it became a mirror into the addicted brain. And as treatment helped reduce craving, the brain quietly rewrote its script, one scene at a time.

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Evidence for smokeless tobacco cessation intervention: Updates from two recent systematic reviews and meta-analyses

Darshan Shadakshari

Smokeless tobacco (SLT) use includes products like chewing tobacco, gutka, snuff, and snus, which are a persistent global health challenge. Most of it is concentrated in South and Southeast Asia, with varied adverse consequences including oral cancers, cardiovascular diseases, and poor reproductive outcomes. Despite this, substantial research attention is given to smoking cessation, with less exploration of smokeless tobacco cessation interventions. Two recent systematic reviews and meta-analyses have attempted to summarise the existing evidence and gaps, providing comprehensive insight into practical strategies for SLT cessation.

Overview of the reviews

Livingstone-Banks et al. (2025) have published an assessment of both behavioural and pharmacological interventions for SLT cessation as part of the Cochrane Database of Systematic Reviews, which was conducted using 43 randomised controlled trials (RCTs) involving approximately 20,346 participants worldwide, with the majority from North America and some representation from South Asia (1).

Pradhan et al. (2025) in contrast, have focused solely on evaluating the efficacy of pharmacological interventions and comparing them with behavioral modification for adult SLT users. The review primarily included 19 RCTs with 4575 participants, featuring balanced geographical representation, including studies from the USA, Norway, Sweden, India, Bangladesh, and Pakistan, which is critical given SLT's burden in the region (2).

Pharmacotherapy

Pradhan and others primarily evaluated different pharmacological options and noted that pooled results showed a statistically significant benefit of pharmacotherapy over behavioural interventions at 6 months (OR 1.21; 95% CI: 1.03 to 1.43), with low heterogeneity (I^2 = 19%). Varenicline (OR 1.99; 95% CI: 1.48 to 2.68; I^2 = 0%) demonstrated the highest efficacy, with an estimated 99% improvement in abstinence, based on data from three studies. Nicotine patch showed 46% higher quit rate than behavioural modification (OR 1.46; 95% CI: 1.07-1.98; I^2 = 0%), suggesting a consistent benefit. Similarly, nicotine lozenges in 6 studies outperformed behavioural modification with a 41% increase in odds of cessation (OR 1.41; 95% CI: 1.08 to 1.83; I^2 = 30%).

In contrast to this, bupropion and nicotine gum did not yield statistically significant results (three studies each). While both bupropion (OR 1.18, 95% CI 0.51 to 2.73, I^2 = 67%) and nicotine gum (OR 1.64, 95% CI 0.82 to 3.37, I^2 = 59%) did not demonstrate statistically significant benefit for SLT cessation, nicotine gum showed a more substantial effect estimate and directionality

more consistent with benefit abstinence. In contrast, confidence for bupropion's effectiveness indicated greater variability in effectiveness, with directionality ranging from potential benefit to potential harm.

The Cochrane review corroborated the findings with its meta-analysis, suggesting moderate certainty evidence supporting varenicline (RR 1.35; 95% CI: 1.08 to 1.68) and low certainty evidence for NRT, with no benefit from bupropion. NRT (RR 1.18; 95% CI: 1.05-1.33) was analysed as a combined category in this review, which limited insights into product-specific effectiveness.

It is essential to note that both reviews included only NRT, Varenicline, and bupropion, as these were the most commonly studied agents. There were no eligible trials that included other agents such as cytisine or nortriptyline. Additionally, combination NRT was not evaluated separately from individual NRT, as only a limited number of trials were available.

Behavioural interventions

The Cochrane review provided a detailed breakdown of behavioral interventions. The interventions were categorized into counselling, brief advice, and other approaches, including self-help materials, telephone support, and digital tools.

Studies related to counselling included individual or group delivery by trained healthcare professionals with sessions aimed at enhancing motivation, discussing coping strategies, and supporting quit attempts. Overall, the certainty of the evidence of effectiveness was moderate and suggested that counselling increases quit rates significantly compared to minimal or no support (RR 1.76; 95% CI: 1.44 to 2.16; $I^2 = 69\%$). Studies related to brief advice included short, structured messages delivered in under 15 minutes by clinicians and community workers to motivate SLT cessation. Brief advice was also practical with moderate certainty of evidence in increasing cessation compared to no support (RR 1.24; 95% CI: 1.03 to 1.48; $I^2 = 49\%$). However, it was less impactful than counselling. Others, including self-help materials, telephone support, and digital tools, were also evaluated, but had limited evidence and higher heterogeneity.

Methodological considerations

Although both the reviews were methodologically rigorous with PRISMA and Cochrane standards, several considerations were noteworthy:

- Underrepresentation of South and Southeast Asia in the Cochrane trial despite being the region with the highest SLT burden.
- Lack of trials on other pharmacotherapies like cytisine, nortriptyline or combination NRT as in the case of smoking tobacco

- Inconsistent use of biochemical validation of abstinence outcomes, limiting the objectivity of quit rate reporting
- High heterogeneity in study designs, intervention, intensity, and population characteristics.

The review by Livingstone-Banks et al. suggested that future trials should prioritize more representative products and populations, particularly in South Asia.

Conclusions

These two high-quality SRMAs represent the current evidence in SLT cessation research. While behavioral interventions offer support, particularly in low-resource settings, Varenicline and NRT (particularly nicotine patch) demonstrate superior efficacy in improving abstinence rates. Future research must address the geographical and cultural gaps in evidence, ensuring that interventions are not only practical but also equitable and accessible across diverse populations.

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Digital Dialogues: Understanding Patients' Perspectives on Opioid Use Disorder Treatment Through Online Social Media Discourse

Shinjini Choudhury

A growing body of research has attempted to analyse social media for public health purposes. One of such popular social media forums is Reddit. Reddit users interact through a platform resembling an online forum. Discussions on Reddit take place through posts—submissions that initiate conversations—and comments, which are responses to either posts or other comments. These interactions occur within topic-specific communities known as subreddits. Users who attain a certain level of community standing can create new subreddits. Features such as throwaway and anonymous accounts and thematic forums create the opportunity for in-depth discussion less susceptible to social desirability bias. In the past, discussions on Reddit have contributed to health care research, including experiences related to substance use (1, 2, 3).

A group of researchers explored two subreddits on medications for opioid use disorder (MOUD) which had the largest number of members – "r/Methadone" and "r/suboxone" in a mixed methods study to identify the challenges faced by individuals on MOUD (4). Natural Language Processing (NLP) methods were applied to 37, 278 original unique posts collected from the above two subreddits, excluding polls and comments, covering all content posted from their creation in 2011 up to 31 December 2022, capturing over a decade of user-generated discussions. In order to understand the key topics being discussed in these posts, the researchers used a technique called Correlated Topic Modelling – a statistical method which identifies and groups related themes or topics based on the words used in the text. Topic modelling is a type of machine learning which is used to detect hidden thematic structures in a large text body. Instead of assigning labels manually, topic models automatically group words which frequently occur together and infer the topics present in each document. Correlated topic modelling allows for correlation between topics which is more realistic and useful similar to some real world discussions where topics might naturally co-occur. A total of 27 challenge related topics were identified in r/Methadone and 34 in r/suboxone. These topics were grouped in three macro-classes: healthcare related issues, medication related issues, and treatment discontinuation. Some of the key differences between the two subreddit groups arose from dispensing differences.

Among healthcare related issues, both logistical and interpersonal barriers encountered by the patients in accessing MOUD emerged as a significant area of discussion. Posts concerning healthcare service-related challenges accounted for 20.1% in r/Methadone, compared to 14.7% in r/Suboxone. Logistical difficulties commonly involved issues such as transporting medication and stringent clinic requirements, particularly for methadone. Interpersonal challenges included reports of negative interactions with healthcare providers and clinic staff.

In medication-related issues, patients frequently voiced concerns related to the effects and management of their medications. Medication-related discussions comprised 41.6% of posts in r/Methadone and 53.9% in r/Suboxone. Key issues included withdrawal symptoms, cravings, dosing difficulties, and adverse effects. Many patients also demonstrated knowledge about dosing adjustments and tapering strategies. Patients' discussions on treatment discontinuation revealed the complexity surrounding the topic. Discontinuation discussions were more prominent in r/Methadone (6.39%) compared to r/suboxone (0.55%). Patients shared personal experiences and strategies for tapering MOUD, often without adequate guidance from healthcare providers. Patients frequently expressed a strong motivation to discontinue methadone treatment, citing issues such as increasing tolerance and financial strain.

Although the study presents important advantages, there are some limitations as well. One of the primary limitations is the anonymity of the participants due to which there is no detailed information on their OUD diagnosis or sociodemographic parameters. The second limitation arises from the representativeness of the study sample, which raises concerns of self-selection bias. Some concerns were also based on the unsupervised NLP method which the researchers attempted to address by comprehensive evaluation of a set of potential topic model solutions through quantitative and qualitative methods.

In conclusion, the study delves into the challenges of persons taking MOUD through the use of a popular social media platform, Reddit. The study findings suggest a need for changes in policy and practice of MOUD, particularly focusing on the delivery of patient centred care, enhancing patient autonomy and flexibility while aiming to improve patient engagement and treatment outcomes.

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Taking Cure to the Curbside: How integrating infectious disease and OST Care for the Homeless can drive HCV Elimination in India

Tamonud Modak

The World Health Organization has set an ambitious goal: eliminate hepatitis C (HCV) as a public health threat by 2030. Achieving that target will depend on closing persistent gaps for people least served by traditional systems, especially people who inject drugs (PWID) and those experiencing homelessness. India bears a considerable share of the global hepatitis C burden. According to the WHO's 2024 Global Hepatitis Report, India accounted for approximately 5.5 million people with HCV (1). Despite the scale of the problem, diagnosis rates remain low—only about 28% of HCV cases in India are detected (2). The infection disproportionately affects PWID with prevalence surveys showing HCV positivity rates higher than 50% in most studies (3). Reinfection following successful direct-acting antiviral (DAA) therapy is also high. A study in Imphal documented 13.2 reinfections per 100 person-years among PWID, with the highest risk seen in younger individuals aged 18–24 years (4). These findings underscore the urgent need for expanded screening, harm reduction, and follow-up strategies to curb HCV transmission in high-risk and underserved communities. The burden of HCV is very high, and the overlap between PWID and homelessness is pivotal in driving the burden. Modeling data suggest homelessness will account for more than one in ten new HCV infections among PWID this decade (5). Most of the evidence on the intersection of homelessness, PWID, and HCV comes from western countries. There is limited information in India HCV among the PWID homeless. This article explores some recent advances in integrated low-threshold treatment HCV, HIV, and opioid use which can provide us with insights on strengthening low-threshold, outreach-oriented OST–HCV services that can engage PWID where they are. In India, significant gaps remain in local OST–HCV integration, underscoring the need for innovations that bring cure and prevention to the curbside, where they are most urgently needed.

A study from Baltimore reviewed the challenges and opportunities in treating HCV among PWIDs through an integrated mobile clinic in Baltimore City (6). The clinic provides low-threshold services, combining OST with infectious disease management. The study revealed significant drop-outs: only 22% of those with confirmed HCV started medication, and a mere 10% achieved a documented cure. Key barriers identified include homelessness, insurance restrictions, and venous access issues. The study underscores the necessity for rapid point-of-care HCV RNA testing, simplified treatment guidelines, and the facilitation of same-day testing and treatment. The authors emphasized that implementing patient-centered, integrated care models can significantly improve HCV treatment uptake among marginalized populations. A key conclusion that can be drawn from the study was that mere provision in integrated care may not be enough. Progress toward HCV elimination requires ease of access in testing, treatment accessibility, and addressing social determinants like homelessness.

There is evidence that a test and treat approach i.e. provision of HCV care at point-of-care testing site may be effective in dealing with people suffering from homelessness. A study evaluated this model in in San Francisco (7). The researchers found that treatment success in this approach was high, with 67% sustained virologic response at 12 weeks (SVR12) in the intention-to-treat analysis and 84% among those who completed therapy. These rates were comparable to clinical trials. Importantly, all treatments were well-tolerated, with no severe adverse events or deaths reported. They describe that offering treatment in familiar, accessible community locations, providing wrap-around services such as food support and harm reduction supplies, and ensuring rapid linkage to care (most participants started treatment within a week of diagnosis) were some of the factors that facilitated success. These findings underscore that point-of-diagnosis treatment in nonclinical settings is feasible, acceptable, and effective at achieving cure in populations that typically face significant barriers to care. This approach has the potential to bridge gaps in the HCV care continuum, reduce viral transmission, and advance efforts toward hepatitis C elimination, especially among those who are often hard to reach through traditional healthcare settings.

Although there is emerging evidence that integrated low threshold delivery of OST and HCV treatment is effective, especially among the homeless, there are challenges to its implementation. A qualitative study evaluated the operational difficulties of operating such mobile units and offered insights into both their effectiveness and the practical challenges of implementation especially with the homeless (8).

The study found that trust, patient-centered care, and harm reduction are essential to engagement with the population. Although mobile teams were able to initiate OST, provide naloxone, deliver basic medical care (e.g., wound care, vaccinations, STI testing), and link patients to community resources, this was driven by key facilitators, strong referral networks and established community partnerships. Several barriers were noted: difficulties finding safe and acceptable parking locations, variable relationships with law enforcement, funding difficulties, and uncertainty about long-term sustainability of the model. Staff also reported emotional toll of working in high-stress street environments. The authors recommended that expansion of such services can be done provided that there are adequate funding mechanisms, integrating harm reduction, embedding safety and support structures for staff, and building trust through community linkages.

Hepatitis C elimination by 2030 will remain out of reach unless health systems innovate to reach people most excluded from care—particularly PWIDs experiencing homelessness. Evidence from integrated mobile clinics in the U.S. and other high-burden settings demonstrates that low-threshold, community-based models combining OST, HCV care, and HIV services are both feasible and effective. These interventions overcome stigma, logistical barriers, and fragmented systems by taking services directly to encampments, shelters, and

community spaces. However, their success depends not only on clinical delivery but also on supportive infrastructure: trust-building, patient-centered care, harm reduction integration, and sustainable financing. For India, which bears a substantial HCV burden and faces high reinfection rates among PWID, the lessons are clear—traditional clinic-based care is insufficient. Mobile and outreach-based integrated care models offer a powerful strategy to close diagnostic gaps, prevent reinfection, and advance toward elimination targets.

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CREATIVE SECTION

So, I just reached 100 days of sobriety for the first time in my life.

That's 25 years (almost 26, still hanging on) of breathing — and over 12 of them spent smoking. It's just a hundred days in what will, hopefully, be a long life. But I wouldn't be telling the truth if I didn't say this: these 2,400 hours have changed everything for me.

I've even been told to pen a letter to myself, to celebrate this sobriety. Most assume this would be easy for a writer — pour a drink, play music, and let the words flow. That's a lie. Writing about addiction is like dragging a bell through mud: difficult, messy, and humbling. Every attempt risks failure — but also offers a chance to learn.

Addiction does this — it weaponizes the thing you hold most dear, your mind, and pits it against logic. And logic, in an addict's hands, is treacherous.

When I look back at Day 1, I honestly don't have the words to describe how I was feeling. The hundred-day mark had always been an internal milestone, a mental checkpoint I'd never reached.

The last time I tried to quit weed and cigarettes, I failed on Day 80. That was two years ago. And in a cruel twist, I kept counting the days long after I'd relapsed — more than double my actual sober stretch. A pitiful habit soaked in regret and huge personal disappointment.

This time, things were different.

I was under the guidance of Dr. YYY (*name of doctor withheld*) and the excellent tobacco cessation program at ZZZ (*name of the facility*). I was prescribed bupropion, which helped regulate the dopamine crash that inevitably follows nicotine withdrawal. I used nicotine patches — starting at 14mg, tapering to 7mg, and now, used only as an emergency fallback. That shift alone — needing less — was something I never thought I'd be proud of. But I am.

My own trick was redefining relapse as a "slip." I thought if the word had less power, it might loosen the grip. It wasn't foolproof — I did once fiend for ten minutes on a friend's vape outside a pub in Shoreditch. But I forgave myself, wrote about it, and kept the clock running. That forgiveness was as important as the discipline. Because the real turning point was not perfection — it was deciding, in room 115 at ZZZ *(name of facility withheld)*, across from Dr.YYY *(name of doctor withheld)*, what I wanted my life to be.

The earliest battles were mental. The hardest part wasn't the craving — it was the inner monologue that tried to rationalize it. In those moments, I didn't trust myself. Every thought

felt like a trick. “Just one.” “You’ve had a hard day.” “This won’t count.” Addiction is cunning — it borrows your voice and weaponizes your logic. And when that happens, it becomes hard to tell if you’re actually choosing, or just surrendering in slow motion.

Addiction has many faces. If it belongs to a genre, it’s tragedy— Shakespearean in scope. But the scripts are unfinished, always. Anyone in this fight has a chance to write their own ending.

Close to Day 100, I was in that same room at ZZZ when a resident doctor came in with news about another patient. The man’s daughter had come to cancel his appointment: he had relapsed. The patient had begged his daughter not to say anything, even turned angry. But she came anyway, carrying the weight of his failure into that room, alone. Two years ago, hearing that might have triggered me to want to smoke. But now, it just made me sad. I empathized with her, and I wished I could help. It was a reminder that abstinence is always tough — but it is possible, doable, and necessary.

That’s what I want people to know: recovery isn’t about willpower. It’s about building a system you can lean on when your own thinking turns against you. For me, that system included medication, structure, and professional help. And it worked.

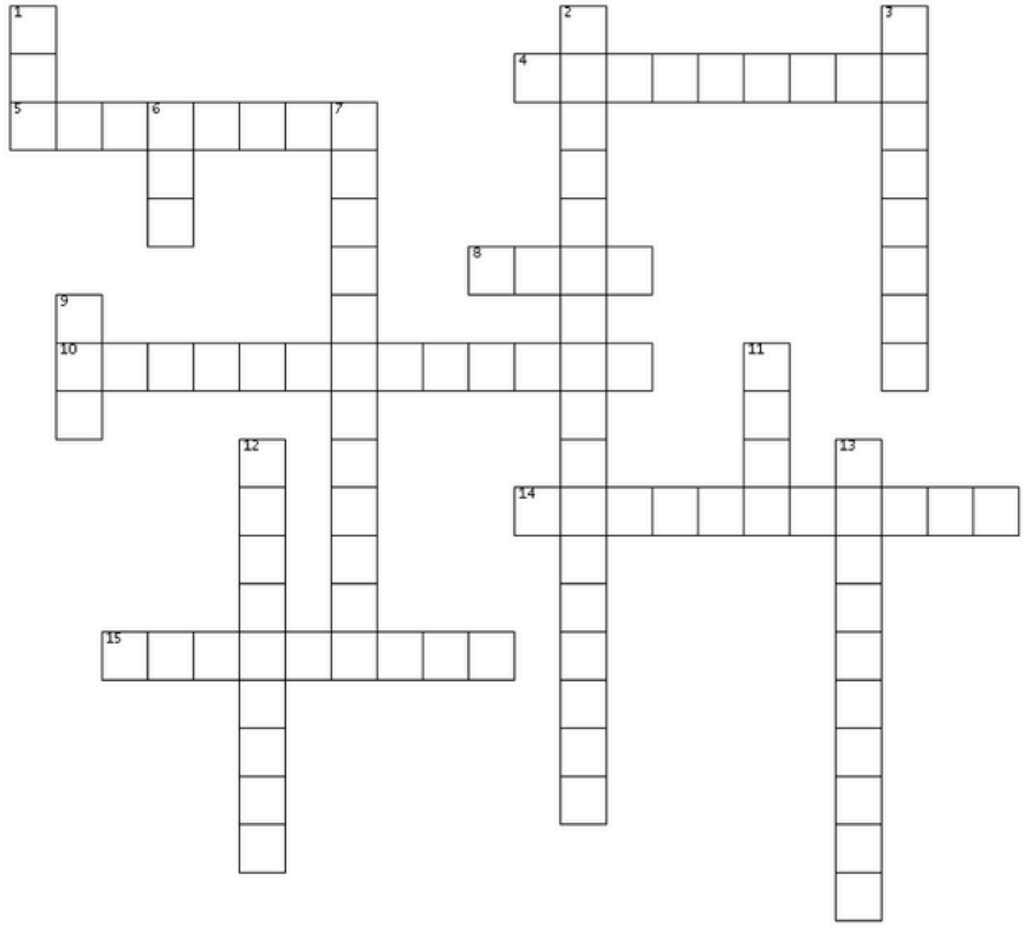
But this is where the fight changes. Past a hundred days, the cravings lose their teeth, and a new danger creeps in: complacency. Addiction no longer shouts, it waits — in boredom, in celebrations, in those quiet moments when discipline feels like overkill. Day 100 isn’t immunity; it’s a checkpoint. The work now is to build structure so strong that even when I stop counting the days, the system holds.

In 100 days, I got back more than I expected: my time, my lungs, my peace of mind. I started moving, eating better, sleeping deeper. I began writing more — less than I’d like, but enough to remind myself I still can.

I’m not here for applause or to give answers. But if you’re struggling, if you’ve failed before, I’m just saying: try systems, not just strength. Treatment has helped me in ways I’ll always be grateful for. I paid one rupee to sit across from a doctor who didn’t tell me what I wanted to hear — but what I needed to.

This isn’t a victory lap. It’s just a signal from the road — a hundred days out, with many more ahead. I don’t know what Day 1,000 looks like yet. But I’d like to find out.

And this time, I will.



Down

1. Psychedelic sometimes called the "spirit molecule" (3)
2. Legal model focusing on reducing criminal penalties without full legalization (15)
3. Dissociative anesthetic studied for depression (8)
6. US agency regulating drug approvals (abbr.) (3)
7. Blending of senses, such as "hearing colors" (12)
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4. Psychoactive cactus alkaloid (9)
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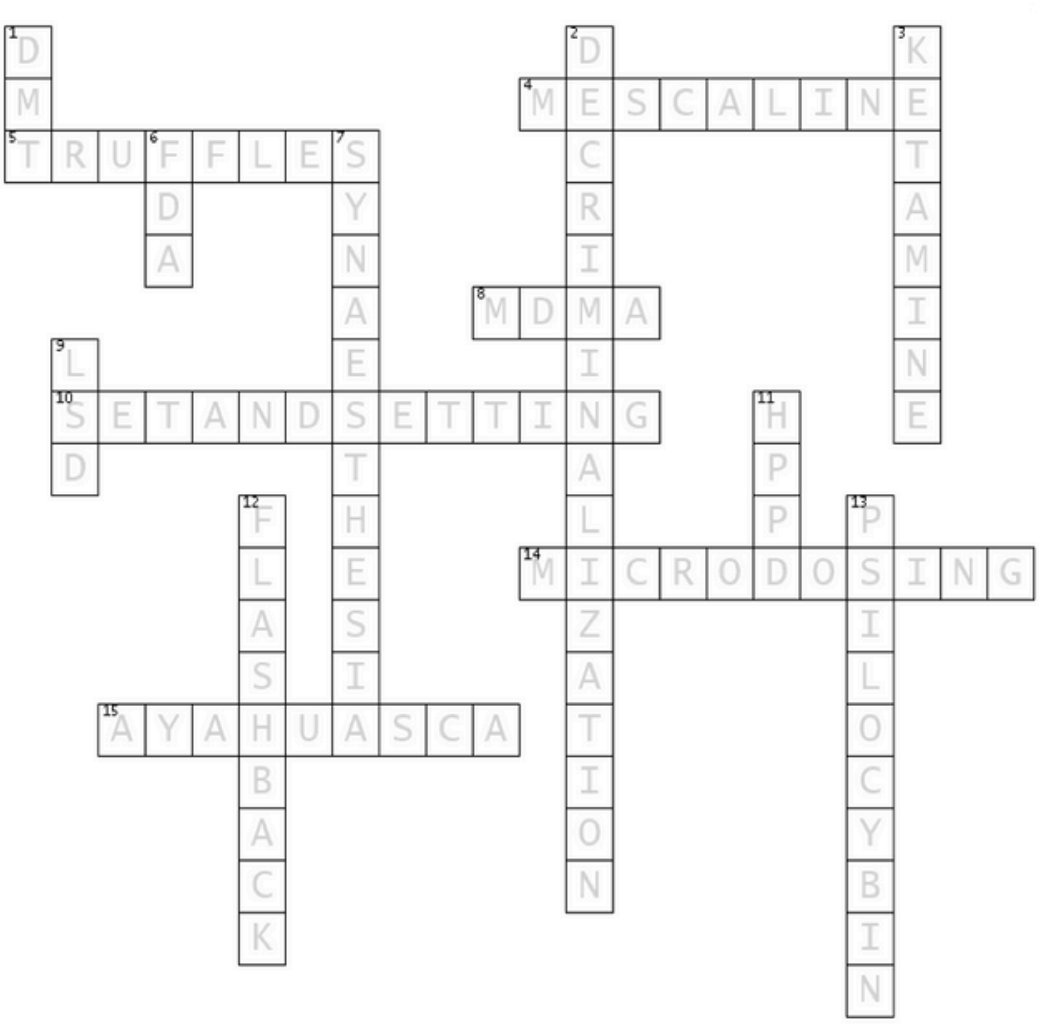
8. The "club drug" being tested for PTSD therapy (4)
10. Term describing mindset and environment shaping psychedelic experience (3,3,7)
14. Psychedelic practice of taking sub-perceptual doses (11)
15. Indigenous brew containing DMT, used in Amazonian rituals (8)

Solutions Mindbender



ADDICON, 2025

When: November 5-7, 2025

Where: Indore, Madhya Pradesh, India

Link: https://addicon2025.com/

36th Annual Meeting and Scientific Symposium

Organised by: American Academy of Addiction Psychiatry

When: November 6-9, 2025

Where: San Francisco, CA

Link: https://aaap.societyconference.com/v2/?card=registration

ISAM, 2026

Organised by: International Society of Addiction Medicine (ISAM) & Vereniging voor Vreemdelingenverkeer, Netherlands

When: Oct 1-3, 2026

Where: Rotterdam, Netherlands

Link: https://hr25.hri.global/hr25-virtual/

57th ASAM Annual Conference

Organised by: American Society of Addiction Medicine

When: April 23 - 26, 2026

Where: Manchester Grand Hyatt, San Diego, CA

Link: https://www.asam.org/education/signature-courses/live-conference-events

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Contact Details

National Drug Dependence Treatment Centre (NDDTC)

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Links to the Addiction Psychiatry Society of India below