

The uncontrolled experiment – Psychedelic use in the wild



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Holmøy, B. & Andersen, K. A. A. (2025). Persistent Altered States: Psychological Treatment of Psychedelic Adverse Effects. *Tidsskrift for Norsk psykologforening*. <https://doi.org/10.52734/HGSN7664>

Psychedelics are widely used outside clinical settings. We need psychedelic epidemiology to learn more about the risks and benefits of recreational use.

In their article titled ‘Persistent Altered States: Psychological Treatment of Psychedelic Adverse Effects’, Holmøy and Andersen (2025) present a clinically focused overview of the phenomenology and symptoms of mental health problems after psychedelic use, as well as challenges in and recommendations for psychotherapeutic work on such problems. As a researcher in psychedelic epidemiology, I wish to comment on their important article by taking a wider view, from the clinical difficulties they describe to the millions of people who use psychedelics every year in the wild; an uncontrolled experiment on a vast scale, outside the clinic and without the guardrails of clinical trials.

Clinical evidence

Research on psychedelics has grown in volume and improved in quality over the past two decades, especially research on psilocybin, the main psychoactive compound in so-called magic mushrooms. For example, one of the largest psilocybin trials to date randomly assigned 233 patients with treatment-resistant depression to receive a synthetic formulation of psilocybin at one of three doses (25 mg, 10 mg or 1 mg as a control) alongside psychological support. The group receiving 25 mg showed a significantly greater reduction in depression scores at three weeks compared with the group receiving 1 mg (Goodwin et al., 2022). Similar results have emerged from other rigorously designed trials, including in patients with major depressive disorder (e.g., Raison et al., 2023), underscoring the potential of psilocybin and other 5-HT_{2A} receptor agonist psychedelics in the treatment of depression and other psychiatric disorders.

The safety record of these substances is also encouraging under controlled conditions (Hinkle et al., 2024; Yao et al., 2024), but those conditions are worth spelling out, because trials of this kind often use restrictive eligibility criteria and exclude people with potential risk factors, including a history of psychotic disorders; they verify the compound and control the dose; and they typically have trained professionals in the room for the duration of the session (Johnson et al., 2008). In other words, the promising findings so far apply to carefully selected patients treated under carefully controlled

conditions, which is important to remember when considering psychedelic use from a public health perspective.



Shifting policy

Alongside the growing body of clinical data, the legal status of psychedelics such as psilocybin has begun to shift, particularly in the United States (US), where much of the scientific work has been conducted. For instance, in 2019, Denver and Oakland became the first US cities to effectively decriminalise psilocybin – a watershed in psychedelic legal history which, in many ways, opened the way to regulated access in Oregon, Colorado and New Mexico (Siegel et al., 2023). And these state-level changes have been accompanied by movement at the federal level, including an executive order signed in April 2026 that, among other things, directs the US Food and Drug Administration (FDA) to issue national priority vouchers to qualifying breakthrough-designated psychedelics and, together with the Drug Enforcement Administration, establish a pathway for eligible patients to access psychedelics under the Right to Try Act (Executive Order 14401, 2026). Notably, within a week of the order, the FDA had issued three national priority vouchers to companies developing psychedelics for psychiatric indications (US Food and Drug Administration, 2026). While these measures can accelerate review, they do not in themselves establish that a treatment is safe or effective. And yet, it is now widely expected that the first psilocybin treatment will receive FDA approval in the coming months. If and when it does, thousands of people in the US will gain access to psilocybin as a medicine. Millions of people, however, are already taking it.

Mushrooms in the wild

These policy changes have not occurred in a vacuum. The public has been changing both its attitudes towards psychedelics and its pattern of use in recent years (Barnett et al., 2024; Walsh et al., 2024). For example, between 2019 and 2023, past-year psilocybin use increased by 44% among US adults aged 18 to 29 and by 188% among adults aged 30 and over (Rockhill et al., 2025). It is now estimated that approximately three per cent of the adult population – roughly eight million adults – used psilocybin last year in the US alone (Simonsson et al., 2026a).

The trials to date have enrolled a comparatively small number of participants, each of them screened, dosed and supervised. But millions of people every year are now taking the same substance with few, if any, of those safeguards. It is, in effect, a large and uncontrolled experiment, and understanding this experiment is, in many ways, the task of psychedelic epidemiology.

Psychedelic epidemiology

Research on psychedelic use in naturalistic settings has frequently reported positive results on outcomes such as wellbeing and mental health (Carvalho et al., 2026). These findings should, however, be interpreted in light of methodological problems common in the field (Simonsson et al., 2026b). For instance, much of the research has relied on convenience samples, often recruited using materials that explicitly mention psychedelics, which may disproportionately attract participants with favourable attitudes towards these substances or positive experiences of their use. These substances are also often grouped into broad categories, such as *hallucinogens* or *psychedelics*, even when the compounds in question have distinct pharmacological and risk–benefit profiles. This aggregation can mask

substance-specific harms and benefits alike. And it makes observed outcomes difficult to attribute to any particular compound.



Not all psychedelics are equal

In light of these limitations, my colleagues and I conducted a study using data from a US online panel survey weighted to produce nationally representative estimates, the National Survey Investigating Hallucinogenic Trends, which asked about each substance separately. Alongside psilocybin, we focused on LSD and MDMA, which are also commonly used and researched, as well as ibogaine and 5-MeO-DMT, which are far less studied but are quickly gaining cultural and scientific prominence (Simonsson et al., 2026a).

While reported benefits were common across substances among people who had used them in the past year, the balance between benefit and harm appeared to differ across substances, with psilocybin and ibogaine at opposite ends. For example, among people who had used psilocybin in the past year, improved mental health attributed to the substance was reported about eleven times as often as worsened mental health (51.2% versus 4.7%), whereas among those who had used ibogaine the two were nearly even (37.2% versus 34.5%). The results for LSD and MDMA generally lay between those for psilocybin and ibogaine, while those for 5-MeO-DMT were similar to those for ibogaine (Simonsson et al., 2026a).

In order to gain deeper insight into what people actually experienced, those who had used a substance in the past three months were asked about specific adverse effects. Notably, commonly reported adverse effects attributed to the substance included anxiety, fear or panic (20.2% for psilocybin versus 53.1% for ibogaine) and changes in vision (32.4% versus 49.8%). These findings should be interpreted with caution, however, especially given that the study was cross-sectional and the outcomes were self-attributed (Simonsson et al., 2026a).

The treatment gap

Despite the study limitations, the findings suggest that psychedelic use in naturalistic settings is not without risks, the risks appear to differ by substance, and they include the kind of difficulties (e.g., anxiety, changes in vision) that clinicians may encounter in practice. Other work, including from Norway, shows that such difficulties can persist well beyond the acute effects (Kvam et al., 2023), yet what remains almost entirely unknown is how best to treat them once they have arisen.

Holmøy and Andersen (2025) take a first step toward filling this gap. Their article does not show that any treatment is effective, but it gives clinicians a starting point for supporting people who struggle after psychedelic use. As the field develops, research on therapeutic promise must be matched by research on recovery from adverse outcomes.

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