

High time? Psychedelics on cannabis-like fast track to legalization

■ Cite as: *CMAJ* 2022 December 19;194:E1695-6. doi: 10.1503/cmaj.1096029

Posted on cmajnews.com on December 02, 2022

Alberta will soon become the first province to regulate psychedelic-assisted therapy. But, as with cannabis, momentum for medical access to psychedelics is outpacing research to guide their use.

Earlier this year, Health Canada amended its Special Access Program to allow physicians to request otherwise illegal psychedelics like psilocybin (also known as magic mushrooms) and MDMA (ecstasy) for research and to treat patients who haven't responded to other therapies.

In October, Alberta announced it would amend provincial mental health regulations to lay the groundwork for the expanding use of psychedelics in the treatment of mental disorders.

"The evidence is emerging that psychedelic-assisted therapy holds a lot of promise in treating mental health issues like posttraumatic stress disorder and treatment-resistant depression," said Mike Ellis, Alberta's associate minister of mental health and addictions at the time.

The exact mechanisms at work are still unclear, but it's thought that psychedelics promote neural plasticity in key circuits relevant to brain health, including those involved in mood, cognition, perception, and regulating stress responses.

Starting in January, clinics in Alberta wishing to provide psychedelic-assisted therapy must obtain a provincial license, appoint a psychiatrist to oversee the treatment, and ensure staff meet qualification and training standards, among other requirements.

Cribbing from the cannabis playbook

Access to psychedelics will still require Health Canada's case-by-case approval, but advocates say provincial regulations are the next step in a steady push for legalization that's closely following the cannabis playbook.

Civil disobedience, legal challenges, and medical access were instrumental in securing public and political support for the broader legalization of cannabis, said Dana Larsen, a long-time drug reform advocate.

Larsen operated an unlicensed cannabis dispensary in Vancouver in the years leading up to that drug's legalization, and now runs one of the many psilocybin dispensaries proliferating across Canada in anticipation of a similar regulatory shift.

When dispensaries first began selling drug paraphernalia like bongos and pipes in the 1990s, and then seeds and dried cannabis for medical use, "they would get raided and have problems with the police," Larsen said.

Over time, however, enforcement dropped off. "The courts were not willing to give people significant penalties for selling these kinds of items," Larsen explained. "It was a lot of work for the police and we just kind of outnumbered them."

The civil disobedience of the 90s culminated in a landmark ruling in *R. v. Parker*, which held that it was unconstitutional to block medical access to cannabis. The decision facilitated the implementation of medical cannabis regulations in 2001 and paved the way for the legalization of recreational cannabis in 2018.

"That was kind of a necessary precursor to legalization, having this massive civil disobedience movement happening," Larsen says. "And I think it's going to be very similar with mushrooms."

Health Canada is already facing legal challenges over access to psilocybin.

In July, a group of more than 100 health professionals linked with TheraPsil, a medical psilocybin advocacy group, sought a judicial review of Health Canada's refusal to grant access to the drug for training purposes.

According to Health Canada, training could be obtained by participating in clinical trials, but the health professionals argued that's not an appropriate venue.

TheraPsil is also crowdfunding for an upcoming constitutional challenge to restrictions on medical access to psilocybin, building on precedents set by medical cannabis rulings.

Previously, TheraPsil helped patients access psilocybin directly via section 56 exemptions under Canada's *Controlled Drugs and Substances Act*. But the group says Health Canada stopped approving those exemptions when it started providing psychedelics to clinicians under the Special Access Program.

As of last year, Health Canada had approved a total of 64 exemptions but acknowledged it hadn't responded to 150 other requests.

According to TheraPsil's John Gilchrist, limiting "reasonable access" to psilocybin violates Canadians' constitutional right to life, liberty, and security of the person. Similar charter challenges have successfully overturned restrictions on medical assistance in dying and safe injection sites.

TheraPsil is one of several advocacy groups, including the Multidisciplinary Association of Psychedelic Studies and the Canadian Psychedelic Association, proposing alternative frameworks for the legalization of psilocybin modelled on medical cannabis regulations.

Under TheraPsil's framework, Gilchrist said, "a patient would be allowed to grow psilocybin mushrooms themselves, a third party could grow psilocybin mushrooms for that patient, or they could access natural mushrooms or synthetic psilocybin through a licensed dealer."

Alberta's regulations are much narrower in scope, Gilchrist noted.

For example, by focusing exclusively on psychiatric treatment, the regulations limit the use of psychedelics for other conditions like chronic pain and shut out doctors who are already providing the service legally under Health Canada's Special Access Program without the involvement of a psychiatrist.

Evidence lagging legalization

More research is needed for psychedelics to meet the same bar for approval as other medicines. But legalization for medical use may come first, as seen with cannabis, which still hasn't met drug approval standards two decades later.

Psilocybin and MDMA are furthest along the research pipeline.

The Canadian Institutes for Health Research are funding phase 1 and 2 trials of psilocybin-assisted psychotherapy for substance use and mental disorders, and phase 3 research was slated to begin in the United States by the end of 2022.

Earlier this year, a small randomized controlled study led by Natalie Gukasyan of the Johns Hopkins University School of Medicine showed that 58% of patients with severe depression who received two doses of psilocybin together with therapy had a substantial and sustained remission in symptoms a year later compared to other patients on a waiting list for the treatment.

"The early signals that we're getting from this, and a couple of the other studies are interesting, and they are exciting," Gukasyan said. "At our centre, we've administered psilocybin to hundreds of participants at this point and we have a pretty good safety track record of low rates of severe adverse events."

However, she noted, "This is still an experimental treatment that doesn't have the typical level of evidence that there is for an approved treatment for depression."

Oregon recently became the first U.S. state to legalize the personal use of psilocybin for people over age 21, as well as medical use at licensed service centres under the direction of a trained facilitator, although it's unclear what that training will involve.

"There's not even a requirement that they are formally clinically trained, which is concerning to me," Gukasyan said.

Private sector investment in psychedelic therapy has exploded recently, but the time and resources involved remain a barrier to

many health professionals participating in research and treatment.

"It's an eight-hour drug administration visit when you're doing the psilocybin therapy, not even counting eight hours of prep before and over a number of follow-up sessions afterward [to integrate the experience]," Gukasyan said. "There's a lot of speculation about what this is actually going to look like [outside of a clinical trial]."

Mark Haden of the University of British Columbia's School of Population and Public Health says it is possible psilocybin will be legalized for medical use before it's approved as a therapeutic product.

Meanwhile, MDMA-assisted therapy for posttraumatic stress disorder is in phase 3 trials and on track for medical legalization in 2023, according to Haden. He previously coauthored a public-health model for regulating psychedelics.

Alberta's regulations will "provide structure when those laws change," Haden said. However, efforts to restrict psychedelic therapy to medical facilities "misunderstand how to work with this medicine effectively, efficiently and appropriately."

"How you set people up for the experience, what they bring to the experience, the environment that they take it in," all matter as much as the specific medicine and dosage given, he explained.

One of the reasons for the relative safety of psychedelic use in many cultural and sacred traditions is that a person's "set," or expectations and psychological profile, and "setting" are carefully structured in those contexts.

Being in a hospital won't necessarily help with these factors, and "makes the whole thing more expensive," Haden said.

Dosing poses a challenge, too. So far, most research on psilocybin uses synthetics; real-world treatment may use naturally occurring mushrooms, which vary in potency and chemical makeup.

"Health Canada does not like unknown substances with unknown dosages; you can't do a clinical trial on that," Haden said.

The medical risks of psychedelics are often minimal, and much of the persistent negative perceptions of psychological risks are unsupported by the available evidence, according to a narrative review in the *Journal of Psychopharmacology*. However, the potential for rare adverse effects, such as psychotic episodes or overdose, increases

at higher doses or when psychedelics are mixed with other substances.

Generally, people with a predisposition toward psychotic illness are excluded from clinical treatment with psychedelics, the authors noted. "With such screening, no psychotic episodes have been documented in modern clinical trials to the best of our knowledge."

Critical gaps remain in understanding how psychedelics will interact with other psychiatric medications.

"There are zero clinical studies to date on how psilocybin will affect people who are on psychiatric medications. Those that do exist are on healthy volunteers who are given a psychiatric medication for a couple weeks at most," said Aryan Sarparast of the Oregon Health & Science University School of Medicine. He highlighted the issue in a systematic review in March.

Without data on drug-to-drug interactions, seriously ill patients must taper off existing medications completely before starting psychedelic therapy.

"Physicians in Canada likely will be deciding on if the risk of coming off one treatment is worth the benefit of an alternative treatment. This is a tough decision that requires expert knowledge on psychiatric medications, psychedelics, and how those two things play together," Sarparast said.

Colorado recently became the second U.S. state to legalize psilocybin via a midterm election ballot initiative. The measure legalizes personal use, growing and sharing of psilocybin, as well as several other naturally occurring psychedelic compounds including DMT and mescaline. By 2024, these drug will also be available in state-regulated centres.

Oregon and Colorado's permissive legalization schemes will allow governments to assess the drug's large-scale health impact and may contribute to Canadian legalization efforts as well.

Kevin Zannese, Ottawa, Ont.

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