Psychedelic Medicine:

A Rapid Review of Therapeutic Applications and Implications for Future Research:

Executive Summary

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Objectives

We conducted a rapid but comprehensive review to synthesize the current state of knowledge in the expanding body of work concerning the therapeutic applications of psychedelic substances[1]. Specifically, we aimed to:

- Summarize the extant body of research on psychedelic substances for the treatment and support of people experiencing mental health and substance use disorders;
- Provide an overview of issues and considerations relevant to research and development in this area;
- Highlight gaps in knowledge and opportunities for research investment in the Canadian context.

Key Findings

- The use of certain psychedelics, namely psilocybin, LSD, ketamine, and possibly ayahuasca and iboga/ibogaine, for substance use disorders show promise as emergent therapeutic modalities for addressing a range of substance use health conditions that continue to respond inadequately to existing treatments and health interventions.
- Psilocybin-assisted therapies have demonstrated safety, tolerability, and moderate efficacy in early-stage clinical trials in reducing symptoms of depressive disorders, substance use dependence, and existential distress due to advanced or terminal disease.
- MDMA-assisted therapy for PTSD is in advanced stages in the process of regulatory drug approval and Phase 3 clinical trials, while ketamine-assisted therapy for PTSD and treatment-resistant depression is demonstrated to be rapid acting and moderately effective for short durations.
- There is promise for psychedelic treatments for a variety of other health conditions, such as chronic pain/headache, eating disorders, traumatic brain injury, and neurocognitive disorders, that remain under-studied due to logistical roadblocks (e.g., funding, access to illicit research substances).

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[1] **Search Process and Terms:** We undertook a rapid review using a highly structured search string of key words and phrases in several iterations to focus on the references of most relevance to the project objectives. The analysis focused on human clinical studies inclusive of clinical trials, observational studies, and case reports, as well as research methods, risk assessments, and regulatory considerations. Work focused on animal models, neuroscience, and psychopharmacological mechanisms were excluded, although some individual studies and reviews clearly touch on both foundational mechanisms and clinical therapeutics.

- There is a need for larger, rigorously designed and multi-site Phase 3 clinical trials that include a placebo control and long-term follow-up to demonstrate more evidence for the efficacy of all psychedelic substances reviewed in this report, as well as consistency in language and definition (microdose vs. low dose, treatment resistance, for example)
- Psychotherapeutic or other supportive processes that occur before, during, and after the dosing session(s) must be considered integral to the efficacy of the therapeutic use of psychedelics. Practice standards remain to be confirmed.

Table 1: Authors' assessment of the evidence as insufficient, preliminary, modest, or compelling

	Substance Use Disorders	Depressive Disorders	Post-Traumatic Stress Disorder	Palliative care/ end of life distress	Eating Disorders (AN, BN, BDD)
LSD	Preliminary	Insufficient	Insufficient	Preliminary	Insufficient
MDMA	Insufficient	Modest	Compelling	Insufficient	Preliminary
Psilocybin	Compelling	Compelling	Insufficient	Compelling	Preliminary
Ayahuasca	Preliminary	Modest	Insufficient	Insufficient	Preliminary
Ketamine	Compelling	Compelling	Modest	Insufficient	Preliminary
Iboga/Ibogaine	Compelling	Insufficient	Preliminary	Insufficient	Insufficient

Recommendations and Considerations:

- **Safety:** Of all psychedelics, psilocybin presents the greatest safety profile. Client selection, preparation, and safe setting are paramount; therapist abuse in psychedelic therapies must be addressed. Suggestibility and vulnerability are significant.
- **Research Design:** We advocate for diversity in research design that includes observational, naturalistic, ethnographic, randomized controlled trials, and clinical modes of investigation as supportive evidence.
- **Diversity/Equity:** Psychedelic medicine is entrenched in a system that engenders racialized and gendered biases, and invisibilizes disability and LGTBQ2S+ communities, among others. This must be addressed at various levels (policy, education, research design, etc.).
- **Indigenous Autonomy:** Native/Indigenous/First Nations peoples have the right to autonomous practice in healing and spiritual modalities. Policy, education, and access concerning these emergent psychedelic treatments must involve their participation, and recognize and respect this right.