Psychedelics to Relieve Psychological Suffering Associated with a Life-Threatening Diagnosis: Time for a Canadian Policy Discussion

Thérapie psychédélique pour soulager la souffrance psychologique associée à un diagnostic menaçant la vie : discussion en cours sur les politiques canadiennes

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Abstract

In Canada, the conversation to enable access to therapeutic psychedelics is under way. With recent federal initiatives, Canadians can request access to psychedelic-assisted therapies (PATs) to alleviate enduring and intolerable psychological suffering (EIPS) associated with

life-threatening conditions on a case-by-case basis. The resurgence of past research concerning the therapeutic potential of PATs, promising preliminary results from contemporary clinical trials, public and media interest and the recognition of traditional Indigenous use of psychedelics have facilitated a change in the popular narrative around these stigmatized substances. A lack of access to PATs for treating EIPS, especially at end of life, is a public policy problem worth addressing.

Résumé

Il y a actuellement, au Canada, un débat entourant l'accès aux thérapies psychédéliques. Grâce aux récentes initiatives du gouvernement fédéral, les Canadiens peuvent demander, au cas par cas, l'accès à des thérapies assistées par des psychédéliques (TAP) pour soulager les souffrances psychologiques persistantes et intolérables (SPPI) associées à des conditions potentiellement mortelles. La résurgence des recherches passées concernant le potentiel thérapeutique des TAP, les résultats préliminaires prometteurs des essais cliniques contemporains, l'intérêt du public et des médias ainsi que la reconnaissance de l'usage autochtone traditionnel des substances psychédéliques ont favorisé un changement dans le discours populaire sur ces substances stigmatisées. Le manque d'accès aux TAP pour atténuer les SPPI, en particulier en fin de vie, est une question de politique publique qui mérite d'être abordée.

Introduction

In recent years, Canadian perceptions of controlled substances have shifted along with changes in drug policy, including provisions for access to medical cannabis (Fischer et al. 2016). More changes are anticipated. Global drug policy is also shifting. The United Nations has removed cannabis from its strictest control (UN 2020), enabling federal shifts in policy. Research and conversation about the therapeutic use of psychedelic substances abound internationally and nationally. Canada's leading medical journal reported that the medicinal use of psychedelics was "just around the corner" (Dyck 2015: 1080), "opening clinical and therapeutic doors long closed" (Tupper et al. 2015: 1059). Over 50 terminally ill Canadians have received legal access to psilocybin-containing mushrooms to alleviate psychological distress at end of life (EOL). Canadian healthcare professionals have acquired access to psilocybin for training in psychedelic-assisted therapies (PATs) (Dubinski 2020). Canadians, including policy makers and medical practitioners, are interested in exploring psychedelic options to improve quality of life (QOL) at EOL and to reduce psychological disturbances more generally.

We use the term *psychedelics* to refer to lysergic acid diethylamide (LSD), ketamine, psilocybin, 3,4-methylenedioxymethamphetamine (MDMA), N,N-dimethyltryptamine (DMT) and N,N-dipropyltryptamine (DPT). Each of these have been – to varying degrees – the most researched for safety and efficacy within an EOL care context. PAT refers to the use of psychedelic substances as an adjunct to a psychotherapeutic modality.

Enduring and Intolerable Psychological Suffering

The Medical Assistance in Dying (MAID) legislation (Bill C-14) in 2016 marked the creation of a clinical condition called enduring and intolerable psychological suffering (EIPS) as an indication for MAID (Government of Canada 2016). The original provision conceptualized EIPS as a form of suffering arising when coping with an incurable and terminally advanced physical disease. The text of the Bill states that patients may have cause for MAID if "that illness, disease or disability or that state of decline causes them enduring physical or psychological suffering that is intolerable to them and that cannot be relieved under conditions that they consider acceptable" (Government of Canada 2023: 286).

As a construct defined within a legal and political framework, EIPS does not correspond with recognized psychiatric disorders, contributing to a lack of information about the condition's determinants and diagnosis. Nonetheless, the construct of EIPS points to a condition long recognized by clinicians in palliative care, hence the historical use of palliative sedation as a last-resort intervention for terminally ill patients. Some have referred to EIPS as existential distress, death anxiety or demoralization in an EOL context, which has been treated with conventional treatments such as pharmacotherapies and psychotherapies (Bauereiß et al. 2018; Vehling and Kissane 2018). Existentially oriented distress is a condition both immemorial and new that has come under the radar of psychiatric nosology.

Research on MAID has found that most requests are motivated by existential suffering associated with a life-threatening diagnosis (Cha 2017; Downar et al. 2020; Li and Kain 2018), which is neither inadequate pain or physical symptom control nor, strictly speaking, a desire for death. Rather, MAID may allow individuals to have control over the timing and manner of their death, alleviating some death and dying-related concerns.

Though EIPS may not have a high prevalence, it is difficult to manage when it does occur. The first line of treatment may involve conventional pharmacotherapy or psychotherapy or their combination, but for those who do not respond to them, MAID is the next legally accessible option – the second line of treatment. We propose that PATs may be well suited to alleviate existentially oriented psychological suffering and can be an effective option (Schimmel et al. 2022; Yaden et al. 2021).

Palliative Sedation and MAID

MAID signalled a change in public perception that it is acceptable to have the right to die and to determine the medical options that would promote dignity in death at EOL. Before MAID, EIPS at EOL may have been controversially addressed for some with palliative sedation – an intervention to sedate a person that may hasten death as a secondary effect but is not the primary intent. The use of palliative sedation has been extended to include the alleviation of non-physical symptoms such as fear, anxiety and psycho-existential distress (Heijltjes et al. 2020), and in some jurisdictions, it can be the sole reason for the request for palliative sedation. The legal status of palliative sedation, particularly for the indication of psychological suffering, is unsettled in Canada. There is no legislation addressing it, and no court cases have tested it.

Despite calls for caution (Laupacis 2020), access to MAID continues to broaden rapidly. As of 2024, eligibility will include those whose sole diagnosis is a mental illness (Karel 2021; van Veen et al. 2022). Given the finality of MAID or palliative sedation and the pace of cultural change, stakeholders may welcome the inclusion of PATs as an alternate or additional treatment option.

Are PATs Safe and Effective Enough?

Contemporary clinical trials examining psilocybin and MDMA in patients with life-threatening illnesses have demonstrated physiological and psychological safety in a medical setting (Griffiths et al. 2016; Grob et al. 2011; Ross et al. 2016; Wolfson et al. 2020). Psilocybin-assisted therapy led to a decrease in depression, anxiety and existential distress and an increase in QOL and life meaning sustained at six months (Griffiths et al. 2016). In one study, participants requested additional sessions to reinforce clinical benefits (Grob et al. 2011). These results are promising and remarkable, though the evidence is preliminary. The clinical trials were relatively small, the populations were heterogenous and the initial research did not have the statistical power or methodological rigour to definitively demonstrate efficacy within EOL populations. More studies are needed to clarify both indications and contraindications and to continue to explore the safety of PATs.

However, the large effect sizes, amount of clinician and researcher commentary and increasing public engagement should not be ignored. A decision logic that supports good enough evidence that improves QOL at EOL may be helpful, especially given that the regulatory and medical boundary includes MAID. EOL care decisions that are clinically relevant may be the ones that (1) consider patient-relevant benefits that outweigh any harms, (2) apply to the patients being treated and (3) are the best available options (Howick 2011).

A tempered approach may be appropriate. The findings so far probably do not support the immediate widespread rollout and unmitigated access to PATs. However, providing funds to facilitate the study of psychedelic interventions can be recommended as can easing administrative restrictions to provide streamlined case-by-case access for those experiencing EIPS within a MAID context. We also recommend that policy discussions begin now about how to meet the demand for PATs (see Table 1).

Approval Processes

There may be several approval processes for the therapeutic use of psychedelics. A recent example is by way of requesting subsection 56(1) class exemption of the *Controlled Drugs and Substances Act* (*CDSA*) (1996). Approval and access to illicit substances and last-resort interventions for therapeutic purposes, typically for conditions that have not responded to conventional therapies, have a long-standing history in Canada's medical and legal landscape. The scope of use for palliative sedation was expanded under the umbrella of compassionate care using the principles of informed consent and potentially life-shortening symptom relief (Downie and Liu 2018) to include EIPS as an indication. The approval process for MAID

TABLE 1. Three overarching questions to guide the policy discussion

Question 1	Who can be allowed to facilitate a therapeutic experience with a patient undergoing a psychedelic intervention?
	This question may raise follow-up questions about training and certification processes, healthcare professional affiliations, Indigenous and other traditional ethnocultural healers and types of clinical or healing approaches that would fulfill the psychotherapeutic or facilitation portion.
Question 2	Where can a patient undergo a psychedelic intervention?
	Issues raised may include the location of psychedelic administration (e.g., hospital, home, community clinic, Indigenous and other traditional ethnocultural contexts), the necessary physical and aesthetic elements within the setting (e.g., furniture, décor, temperature, sound) and questions about accessibility.
Question 3	Which psychedelic substances can be administered?
	Issues raised may concern the decision about which psychedelics will be part of a medicinal treatment model, including substances that have been more researched (e.g., psilocybin, DPT, LSD) or those with a history of use in traditional healing practices (e.g., ayahuasca). There may also be questions about production and methods of procurement.

DPT = N,N-dipropyltryptamine; LSD = lysergic acid diethylamide.

was the subject of judicial consideration, the law was changed and policies were created to make MAID accessible.

Cannabis has undergone a complex approval process and may offer insight into how psychedelics could pass this process. Similar to psychedelics, cannabis had a '60s stigma that produced an enduring negative counterculture image. There was mixed scientific evidence for its therapeutic properties and discouragement of medical research based on it. Some cannabis products were made accessible for medical use before the *Marihuana Medical Access Regulations* (2001) and the *Marihuana for Medical Purposes Regulations* (2013). Examples of these products included nabilone, which was approved in 1982 for chemotherapy-induced nausea and vomiting not responding to conventional therapy, and in 2005, Canada became the first country to approve Sativex – a cannabis-derived prescription medicine used for multiple sclerosis neuropathic pain and cancer pain.

Precedents for the Therapeutic Use of Psychedelics

There are a few legal means to access psychedelic substances at EOL. Each avenue provides a different potential for medical support and involves various methods of procurement of the substance. Clinical trial enrolment is the most common and the long-standing method of access. More recently, the Public Prosecution Service of Canada issued a revision to simple possession offences under the *CDSA* (1996), whereby law enforcement is advised to avoid prosecuting simple drug possession cases unless there are significant public health and safety concerns and only when prosecution serves the public interest (Public Prosecution Service of Canada 2020). This directive allows individuals at EOL to procure and consume psychedelics without criminal prosecution. Outside a clinical trial context, the only legal provision for

"medical" access is the case-by-case basis subsection 56(1) class exemption of the *CDSA* (1996). It has been used to give patients access to psilocybin-containing mushrooms since August 2020.

On January 5, 2022, Health Canada announced its amendment to the Special Access Program (SAP), allowing practitioners with prescription privileges to request access to restricted drugs (including psychedelics such as psilocybin, LSD and MDMA) within a model of PAT for Canadians experiencing mental disorders unrelieved by existing treatments. Through subsection 56(1) class exemption of the *CDSA*, healthcare workers were provided case-by-case access to PAT training. In February 2022, Health Canada began denying subsection 56(1) exemptions to terminally ill Canadians and healthcare workers seeking access to psilocybin for medicinal and training purposes. This decision has not been publicly explained, and lobbying to grant exemptions continues (Office of the Commissioner of Lobbying of Canada 2022). The Centre for Addiction and Mental Health (CAMH) has recently received Canada's first federal grant from the Canadian Institutes of Health Research (CIHR) to study psilocybin's effects on treatment-resistant depression (CAMH 2022). The federal funding agency has also issued a request for proposals to support early phase clinical trials exploring the use of psilocybin-assisted psychotherapy to treat mental health disorders and substance use, including at EOL (CIHR 2022). Perhaps support can be expanded to consider innovative trial designs.

In the US, outside of approved clinical trials, there is an expanded access program that provides a pathway for seriously ill patients to access investigational drugs (Darrow et al. 2020). However, increased access to legal psilocybin therapy began as an Oregon state-led initiative to provide medically available psilocybin services for a two-year period, activated by special interest and lobby groups (Investing News Network 2022). During this period, information will be gathered on this experimental policy to inform how and whether to create a comprehensive regulatory framework for providing this service. Taking a different approach, Australian medical regulators have rejected an application to have psychedelics legalized for clinical use due to a lack of clinical scientific evidence (Landis-Hanley 2021). To back this evidence base, the Australian government has provided millions of dollars to fund psychedelic research by the country's universities. Meanwhile, the European Medicines Agency is conducting large-scale trials of psilocybin to alleviate treatment-resistant depression.

Pan-Canadian Rollout: Issues to Consider

The federal aspect is well developed at this point, with recent changes to the SAP enabling access to psychedelics. However, there are no approaches to access that are province- or territory-specific. The first steps to establishing such pan-Canadian approaches would entail regulatory changes, legislative changes and consultation with key stakeholders, including the government, scientific and clinical communities, drug development companies and special interest and patient groups. To expand the current policy discussion that is under way, there are three questions that will need to be discussed (see Table 1).

Many issues will be similar to those related to the medicalization of cannabis. However, there are important exceptions – namely, that a licensed health professional will likely be required to administer the psychedelic within a supervised psychotherapeutic setting. Issues with product licensure, production and manufacturing may follow a similar pathway as the one for cannabis. As such, four points will need to be considered: (1) the licensing and certification of the providers, (2) the creation of appropriate settings for administration and follow-up, (3) funding models and payment schemes within an EOL context and (4) the evaluation of outcomes.

There may be provincial and territorial variations in creating access to medicinal psychedelics. British Columbia has several initiatives that model potential ways of delivering psychedelic therapies, including training programs for those interested in providing PAT. Historically, Saskatchewan and Ontario were at the forefront of research on mescaline and LSD in Canada. Current Canadian research is largely under way in Ontario, Quebec and British Columbia, exploring psilocybin's effects on mood disorders and EOL distress, ketamine's antidepressant effects and MDMA's potential to alleviate post-traumatic stress disorder. These provinces may be the first to tackle issues of creating access to medicinal psychedelics for EOL care and to establish working models that other provinces and territories can adapt. It is worthwhile to consider the diversity both ethnoculturally and clinical-professionally, especially as it relates to Indigenous Peoples' right to traditional healing modalities and their use of traditional Indigenous medicines (Muscat et al. 2021). Thus, it is important to recognize that diversity in the licensing and certification process for providers of PAT may need to exist, which is consistent with existing variations in the licensure for health professionals across Canada. Provinces and territories may also consider establishing training programs open to certifying various professionals beyond those with a regulated clinical designation.

EOL Psychedelic Use: There Is Little to Lose and a Lot to Gain

With municipal discussions to decriminalize controlled substances for personal consumption, access to MAID for those who are not close to their natural death and upcoming changes to MAID's eligibility criteria that will enable access for persons whose only medical condition is a mental illness – the potential clinical benefits of making PATs accessible as part of palliative care may outweigh the risks. The most recent changes to Bill C-7 may not adequately address Canada's commitment to providing access to acceptable and alternative options (Government of Ontario n.d.). Since palliative care aims to improve QOL at EOL, alternative interventions addressing a person's psychological suffering and loss of life's meaning in the face of death should be made accessible. Psychedelics may constitute such an alternative. Canadians have the right to access all treatment options available and should not have to choose between a legal but, for some, inadequate solution and an illegal but potentially more effective one.

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