Incorporating prescription psychostimulants into the continuum of care for people with stimulant use disorder in Canada

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Canada is facing an ongoing crisis of poisonings from unregulated drugs. Synthetic opioids like fentanyl are a known driver, but stimulant use is also rising. For example, in nearly half of all opioid deaths in Canada in 2022, a stimulant was also detected. Accessing the unregulated supply of stimulants can pose several risks, including increased rates of infectious disease, mental health concerns (e.g., sleep impairments, psychosis), overdose and all-cause mortality. These risks are particularly acute among people with underlying health conditions, and people facing structural vulnerabilities relating to housing and financial security, legal status and racial discrimination. Similarly to opioid agonist treatment, prescribed psychostimulants can support the management of cravings and withdrawal symptoms in patients with stimulant use disorder and can be prescribed with the overall goal of supporting reductions in illegal stimulant use.

No pharmacologic treatment for stimulant use disorder has been approved in Canada. Nevertheless, psychostimulants are increasingly prescribed as harm reduction for stimulant use disorder in Canada, following evidence from clinical trials in Europe, Australia and the United States.² Prescribed psychostimulants like methylphenidate and dextroamphetamine are central nervous system stimulants, which increase extracellular concentrations of dopamine and norepinephrine by blocking the neuronal reuptake of the neurotransmitters or promoting their release or both.

Psychostimulant prescribing has expanded in Canada since 2020, when the federal minister of health issued a letter to provincial and territorial ministers of health and regulatory colleges to encourage action on increasing access to safer pharmaceutical-grade alternatives to the contaminated drug supply. To date, British Columbia is the only province to issue a Safer Supply Policy Directive, including guidance for prescribing psychostimulants to people at risk of overdose.³

Since the 2020 federal directive, psychostimulants have been prescribed for stimulant use disorder in Canada for a small proportion of patients, primarily by general practitioners, addiction medicine specialists and nurse practitioners.^{4,5} In the first year of implementation in BC, prescribed psychostimulant medications reportedly reached 1220 people, reflecting less than 3% of people estimated to have stimulant use disorder.⁶

Key points

- Illegal stimulant use (methamphetamine use in particular) is rising in Canada and is associated with substantial morbidity and mortality
- Accumulating evidence supports treatment of stimulant use disorder with prescribed psychostimulants, but no pharmacologic treatments for stimulant use disorder are currently approved in Canada.
- Off-label prescribing of psychostimulants for stimulant use disorder has been implemented on a small scale in certain jurisdictions in Canada.
- In the context of an unregulated supply of stimulants, implementation of psychostimulant prescribing can be considered by clinicians who provide care to patients with stimulant use disorder to reduce the use of and harms from illegal stimulant use.

The lack of widespread implementation of prescribed psychostimulants may be explained, in part, by the fact that the evidence base for pharmacologic treatment of stimulant use disorder is newer than for pharmacologic treatments of other substance use disorders. Evidence of the effectiveness of prescribed psychostimulants has been limited by restrictive outcome measures (i.e., abstinence), small sample sizes and inappropriate interventions (e.g., low doses) in early clinical trials.^{7,8} A recent systematic review of the effectiveness of prescribed psychostimulants included 38 clinical trials with 2889 patients. It concluded that prescribed psychostimulants constitute a safe, effective intervention for stimulant use disorder, particularly in the treatment of cocaine dependence and when prescribed at 60 mg or more (of prescription amphetamines or methylphenidate) per day.² Outcomes observed in these studies include reduced use of illegal stimulants, improvement in physical and mental health, and improved focus and attention for patients with concurrent attention-deficit/hyperactivity disorder. This emerging evidence can support prescribers' level of confidence in off-label prescribing of psychostimulants to patients with stimulant use disorder (and particularly for patients with attention-deficit/hyperactivity

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disorder and stimulant use disorder). Prescribed psychostimulants could be offered alongside nonpharmacologic interventions (e.g., contingency management) to provide patients with a comprehensive range of treatment options across the continuum of care.

Implementation of prescribed psychostimulants has been called for in settings where patients are in regular contact with care, such as at opioid agonist treatment clinics.² In BC, psychostimulants are most commonly prescribed by physicians already serving clients with substance use disorders and are dispensed daily at community pharmacies. Daily dispensation is intended to promote safety, but daily pharmacy visits have been identified as a logistical barrier to engagement in opioid agonist treatment and prescribed psychostimulants.9 As such, take-home dosing for prescribed psychostimulants (as is offered for opioid agonist treatment) has been proposed. Concerns over diversion of prescribed psychostimulants have been raised and can be reduced by establishing standardized protocols, including waiting to initiate take-home dosing until the patient has titrated to an optimal dose, regular monitoring for adverse events to confirm the suitability of the medication to the client's goals and needs, and urine drug screens to monitor for the presence of the medication. Reinstating witnessed dosing may be indicated where safety is a concern; for example, if the patient is not taking the medication as directed, or where new adverse events arise.

Although safety concerns have been reported as a barrier to implementation, systematic reviews have concluded that prescribed psychostimulants for stimulant use disorder are well tolerated and not associated with serious adverse events. 7.8 Psychosis induced by prescribed psychostimulants is more rare than psychosis with illegal stimulant use, which a 2014 review suggested occurs in as many as 40% of people using methamphetamine. 10 In the context of the crisis of poisonings from unregulated drugs, the potential risks and benefits of prescribed psychostimulants must be weighed against the risks of harm from ongoing illegal stimulant use. Introducing prescribed psychostimulants for people already using illegal stimulants, alongside monitoring for adverse events, is a reasonable approach to reduce the harms associated with continued contact with an unregulated stimulant supply.

Several actions can be taken to advance the implementation of prescribed psychostimulants in Canada. Researchers must consolidate efforts to conduct implementation studies to fill existing knowledge gaps and inform timely updates of clinical and program protocols. Centres with mandates to issue clinical guidance for harm reduction and substance use treatment services can publish and regularly update clinical guidance as new evidence emerges. Substance use treatment programs and clinics that serve patients with stimulant use disorder can establish protocols to systematically incorporate prescribed psychostimulants into the range of interventions offered. This process can be conducted collaboratively, incorporating patients and multidisciplinary care teams, drawing from the resources available from the growing settings across Canada where psychostimulant prescribing has been implemented. This process will require adaptation of existing protocols for dosing and dispensing prescribed psychostimulants, according to the clinical setting (e.g., prescriber experience,

frequency of patient contact) and patient population (e.g., goals, patterns of illegal stimulant use).

Broader implementation of prescribed psychostimulants as an effective option in the continuum of care for stimulant use disorder is needed in Canada; this practice would help the growing number of patients seeking to reduce their reliance on the illegal stimulant supply during the ongoing unregulated drug poisoning crisis.

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