Stimulant Use Disorder Practice Update

July 12, 2021

In this document:

Overview

Stimulants—including cocaine, methamphetamine, and other amphetamine-type substances—are one of the most common illicit psychoactive substances used around the world. Although recent Canadian prevalence data for stimulant use is sparse, a survey of individuals accessing harm reduction services in BC found that methamphetamine was the most commonly used drug in 2018, with 69% of participants reporting its use in the past 7 days;[1] this was an increase from 47% in 2015.[2] While cocaine use has reportedly been decreasing in BC,[1] it is increasing across Canada, with 2.5% of Canadians of 15 reported cocaine use in the past year in 2017 compared to 0.9% in 2013.[3]

Stimulants are increasingly being detected in illicit drug toxicity deaths. A review of completed cases by the BC Coroner's Service found that between 2018 and 2020, post-mortem toxicology detected cocaine in 49% of illicit drug toxicity deaths and amphetamine or methamphetamine in 39% of illicit drug toxicity deaths.[4] Notably, the detection of methamphetamine in illicit drug toxicity deaths has increased from 14% in 2012 to 43% in 2020.[5,6] In addition, drug checking data from BC over the past several years indicates that, although infrequent in comparison with opioid adulteration, stimulants such as cocaine and methamphetamine are also at risk of being adulterated with fentanyl (approximately 2.1% of all expected stimulant samples, with 4.1% of expected crack cocaine and 6.5% of expected methamphetamine samples were adulterated with fentanyl from September 2020 to January 2021).[7]

Following the March 17, 2020, BC declaration of a public health emergency due to the COVID-19 pandemic, the BCCSU, Ministry of Mental Health and Addictions, and Ministry of Health mobilized a group of expert clinicians, people with lived experience, and other health system stakeholders to rapidly develop interim clinical guidance, *Risk Mitigation in the Context of Dual Pandemics,* which built on "*Prescriber Guidelines for Risk Mitigation in the Context of Dual Public Health Emergencies"* from Vancouver Coastal Health Authority. It was recognized that the COVID-19 pandemic would compound the harms and challenges of the toxic drug supply and overdose emergency declared in April 2016, and would increase risks for people who use drugs, including the ongoing risk of drug toxicity deaths and other harms related to the illicit toxic drug supply, the risk of infection and spread of COVID-19 among those with underlying health conditions and who face social marginalization, and risks due to withdrawal for those who must self-isolate or quarantine to prevent the spread of COVID-19. The interim clinical guidance provides guidance on prescribing stimulants in order to support individuals at risk of withdrawal to social distance, self-isolate, or quarantine in order to reduce transmission of COVID-19 and reliance on a limited and toxic drug supply.

This practice update describes current treatment options for individuals who use stimulants, including acute intoxication or overdose, withdrawal, and stimulant use disorder. This update also describes clinical experience and preliminary data from a year of Risk Mitigation prescribing and implications for care in order to reduce individuals' risk of drug toxicity deaths due to stimulants.

Current Treatment Options

Stimulant Intoxication

Acute stimulant intoxication or overdose can present with symptoms such as:

- Mania
- Paranoia
- Severe delirium
- Elevated blood pressure
- Agitation
- Sweating
- Skin-picking
- Abnormal movement (e.g., ataxia, choreoathetosis)

As there are no medications currently approved for treating stimulant intoxication or overdose, these symptoms are primarily managed with supportive therapy, which may include providing hydration and food or a safe place to rest.[8]

Stimulant Withdrawal

Symptoms of stimulant withdrawal generally present a few hours to several days after last using the substance. Some individuals may also experience symptoms that last weeks or months, such as sleep or mood disturbances.[9,10] Symptoms of stimulant withdrawal may include:

- Craving
- Depressed mood
- Vivid, unpleasant dreams
- Fatigue
- Insomnia or hypersomnia
- Increased appetite
- Psychomotor agitation or impairment
- Agitation and irritability
- Cognitive impairment

There are currently no medications approved for treating stimulant withdrawal. Treatment primarily consists of supportive therapy, which may include providing adequate nutrition, supporting sleep hygiene, and mental health assessments and supports. Some individuals may benefit from support with cognitive behavioural therapy (CBT) to manage their withdrawal symptoms.[8]

Stimulant Use Disorder

Stimulant use, as defined by DSM-5 criteria (see Appendix 1), is associated with an increased risk of a number of health complications, including[8]:

- Cardiovascular disease (such as myocardial infarction, renal insult, and stroke)
- Psychiatric conditions (including psychosis, depression, and suicidal ideation)
- Blood-borne virus transmission (such as HIV or Hepatitis C)

To date, the evidence on pharmacotherapy for the treatment of stimulant use disorders is limited and inconclusive, although some evidence of benefit (e.g., prolonging abstinence) and the absence of harms have prompted calls for further investigation into the use of prescribed psychostimulants as replacement for illicit stimulants (see Evidence Supporting Prescription of Stimulants to Reduce Harms, below). Recent trials of other, non-psychostimulant pharmacotherapy options have shown some promise in reducing methamphetamine use compared to treatment with placebo, including extended-release injectable naltrexone plus oral extended-release bupropion[11] and mirtazapine.[12]

Due to the limited and inconclusive evidence supporting the use of pharmacotherapy, psychosocial treatment is currently the standard of care for stimulant use disorder. In particular, contingency management, community reinforcement[a], CBT, the Matrix Model, and self-help groups based on the 12-step program have been recommended, although there is a lack of guidance on which of these interventions should be considered first.[13]

The efficacy of contingency management in the treatment of stimulant use disorders is supported by a large body of evidence.[14-18] A 2018 network meta-analysis comparing psychosocial interventions for cocaine and amphetamine use found that contingency management alone or in combination with either community reinforcement approach or CBT had the highest efficacy at achieving abstinence from stimulants compared to treatment as usual[b] and other psychosocial interventions (alone or in combination).[13] In particular, contingency management in combination with community reinforcement approach was found to be superior for abstinence during treatment (numbered needed to treat [NNT]=2.1), at the end of treatment (NNT=4.1), and at the longest follow-up after treatment completion (NNT=3.7). This combination of interventions was also superior in retaining participants (NNT=3.3).[13]

Contingency management has had relatively poor uptake, due to a variety of barriers including cost, practical concerns, and philosophical objections,[19-21] making it inaccessible for many individuals with stimulant use disorder. These barriers have been compounded by the additional challenges of running group-based programming in the current context of the COVID-19 pandemic, with contingency management programs having to adapt to support physical distancing and infection control.[22] In light of this, other psychosocial interventions may provide benefit to individuals when contingency management and/or community reinforcement approach are not available, or for those who prefer a different treatment approach. Specialist-led, manualized CBT has shown effectiveness at reducing cocaine use post-treatment[23] as well as methamphetamine use.[18] Individuals may experience positive outcomes from CBT even from short periods of treatment (as few as 2–4 sessions).[18] However, while CBT was found to have superior retention to treatment as usual, it was not superior for abstinence.[13] Additionally, accessing this intervention may be challenging, as it requires a specialist with training in manualized CBT techniques that are specific to substance use disorders. The Matrix Model has shown promising results for treatment retention, program completion, and in-treatment performance. Participants in this program receive a combination of CBT, family education, individual counselling, 12-step fellowship participation, and drug testing over a 16-week intensive treatment protocol.[24]

---

[a] Community reinforcement includes a combination of interventions such as coping skills training and social, familial, recreational, and vocational reinforcements.

[b] Treatment as usual was defined in this study as non-specific therapy including case management and any unstructured, non-manualized psychosocial intervention.

While 12-step programs were found to be less effective at achieving abstinence and had lower retention than contingency management plus community reinforcement approach, they are frequently recommended for the treatment of stimulant use disorder.[13] A 2013 multi-site randomized controlled trial (n=471) evaluating 12-step facilitation compared to treatment as usual[25] for individuals with stimulant use disorders found that those with greater attendance and involvement in program activities were more likely to experience lower rates of stimulant use during the program and abstinence from stimulant use at the end of the program.[26,27] Additionally, individuals who obtained sponsors[c] through their 12-step program were more likely to have maintained abstinence at follow-up.[29] While further research on the efficacy of recovery-based programming for stimulants is needed, they may provide some benefit to individuals who have experienced success from such programs previously.

There is limited evidence on the efficacy of bed-based (also called residential) treatment models for stimulant use disorder. However, bed-based programs have resulted in improved treatment outcomes for individuals with other substance use disorders, and some individuals with stimulant use disorder may benefit, particularly those who previously attended bed-based programs and experienced beneficial outcomes, unstably housed patients, or those in dangerous living situations.[8]

Psychosocial Treatment Programs for Stimulant Use Disorder

Cognitive Behavioural Therapy

- Specialist-led approach
- May be available in many communities

Contingency Management

- Pender Community Health Centre (Vancouver)
- St. Paul's Hospital (Vancouver)
- Rewarding Recovery
    - Fraser North Day Evening Weekend Program (New Westminster)
    - Fraser South Day Evening Weekend Program (Surrey)

Matrix Model

- Three Bridges Community Health Centre (Vancouver)

Evidence Regarding Stimulant Replacement

Although the evidence supporting the use of medications—including psychostimulants—for treating stimulant use disorder is limited and inconclusive, available studies suggest that prescribed stimulants appear promising and merit further investigation.[15,30-37] It should be noted, however, that most of the studies included in the above systematic reviews and meta-analyses excluded individuals with severe psychiatric comorbidities (e.g., psychotic or bipolar disorders) and/or did not assess for other common comorbidities such as attention deficit hyperactivity disorder (ADHD)[33-37]; thus, the relative safety of stimulant prescribing for individuals with a history of or active psychiatric disease is unknown. There have been additional methodological limitations in the existing literature that have made it difficult to

[c] Sponsorship involves a participant receiving mentorship from another member of the program who has achieved long-term recovery, and has previously been associated with greater abstinence and treatment outcomes in the context of alcohol use disorder.[28]

synthesize the existing data with any certainty—for example, a wide range of outcomes have been measured, with abstinence the most commonly reported outcome.[37] However, abstinence may not be a possible or preferrable goal for all people who use illicit stimulants; reductions in use, safer use, and reduced withdrawal symptoms may be more clinically meaningful outcomes that reflect the complex nature of addiction and better align with patient goals.[37] Regarding outcomes other than abstinence, some individual studies have found statistically significant reductions in cravings, positive urine drug tests, and depressive symptoms.[37]

A 2020 systematic review and meta-analysis restricted analysis to trials of medications with similar behavioural effects and deemed most analogous to cocaine or amphetamine-type substances.[33] This meta-analysis found that prescription psychostimulants likely promote sustained abstinence and may reduce use throughout the trial and extend duration of abstinence. The overall effect was primarily influenced by studies that used prescription amphetamines (mostly dextroamphetamine) for treatment of cocaine use disorder specifically. **The meta-analysis provides preliminary evidence that supports the use of medications with a more "potent" agonist effect (e.g., dextroamphetamine) vs. medications with a less "potent" effect (e.g., modafinil), and that higher doses are more effective than lower doses.[33]** The meta-analysis authors conclude that there is an urgent need to further explore prescribed psychostimulants in implementation studies to better define the methods and outcomes that would indicate treatment success.[33] In addition, a 2016 placebo-controlled, randomized controlled trial found that sustained-release dextroamphetamine resulted in significantly fewer days of cocaine use than placebo, in individuals receiving injectable diacetylmorphine for opioid use disorder who had co-morbid cocaine use disorder.[38,39] A 2021 case study from Crosstown Clinic in Vancouver reported on the use of sustained-release dextroamphetamine for an individual with co-occurring opioid and cocaine use disorder, who was receiving iOAT and using 10–15 rocks of crack daily. After 4 weeks of dextroamphetamine treatment, the patient's use was reduced to an average of 1–2 rocks twice a week; other benefits included abscesses and chronic wounds healing, increased cognitive alertness, and meeting patient-identified goals.[40]

It should also be noted that, while methamphetamine is currently the most widely-used illicit stimulant in BC, the evidence base supporting the use of medications for the treatment of stimulant use disorder is largely focused on cocaine use. A 2020 systematic review that examined all pharmacotherapy for meth/amphetamine use disorders, including non-stimulant medications, concluded that no pharmacotherapy yielded convincing results, and noted that most studies were both underpowered and had low completion rates. However, several agents showed promise, including stimulant agonist treatment (dexamphetamine and methylphenidate), naltrexone, and topiramate.[37] The authors also note that future research should include additional outcome measures (such as reduction in days used) and address the heterogeneous nature of meth/amphetamine use disorder. In addition, a 2021 phase-2, open-label, single-group study (n=16) of oral lisdexamfetamine (brand name Vyvanse, among others) for treatment of methamphetamine use disorder found that doses up to 250mg/day were safe and well tolerated.[41] Although methamphetamine use decreased from a median of 21 days to 13 days over the 4-week dose escalation period, the study was not powered to establish efficacy. It should be noted, also, that these findings are limited by small sample size and short duration of treatment. Despite these limitations, this study provides preliminary evidence of safety, tolerability, and acceptability of higher doses of lisdexamfetamine in individuals with methamphetamine use disorder and may encourage further larger-scale trials of this medication.

In light of promising but equivocal research on the provision of stimulants to treat stimulant use disorder, the standard of care continues to be psychosocial treatment (see Current Treatment Options, above).

However, the increasing toxicity of the illicit drug supply requires additional practice options in order to reduce overdose and other harms; clinical experience with *Risk Mitigation* prescribing suggests that prescribing stimulants as a harm reduction measure may be an appropriate practice option in some situations.

Clinical Experience from Risk Mitigation Prescribing

Using PharmaNet[42] and other Ministry of Health[43-45] data available through the BCCDC COVID-19 Cohort (BCC19C), an estimated 6,498 people were dispensed Risk Mitigation Guidance (RMG) prescriptions from March 27 2020 to February 28, 2021.[d] While the majority (58%) were prescribed opioid medications, a significant number (n=1220, 18.8%) were prescribed stimulant medications (other medications prescribed include benzodiazepines and alcohol withdrawal medications). Overall, there were 179,349 unique medication dispensations, more than 70% of which were for opioids, and approximately 20% of which were for stimulants.

Preliminary data from the BC COVID-19 Cohort indicates that, of 6,498 persons who were dispensed RMG medications from March 27, 2020 to February 28, 2021, 82 persons died during that period. Of the persons who died, 33 (40%) were prescribed opioids only, 9 (11%) were prescribed stimulants or stimulants and opioids, 6 (7%) were prescribed alcohol withdrawal medications and another RM medication (unspecified), and the rest (34; 42%) were prescribed only alcohol withdrawal medications or only benzodiazepines. Of the 82 persons who died, 7 had an active dispensation on the day they died (n=4 opioids; n=3 alcohol withdrawal management medications). The cause of death for a high proportion of deaths (n=37; 45%) is not specified due to the lag in Vital Statistics data. Of those deaths where cause is specified (n=45; 55%), none were due to illicit drug toxicity death. Among persons who received *Risk Mitigation* prescriptions that were not active on the day they died, the average length between prescription end date and death was 41 days for stimulant medications, 56 days for opioid medications, 86 days for benzodiazepine medications and 72 days for alcohol withdrawal management medications.

Prescribing Stimulants to Reduce Reliance on the Illicit Drug Supply

Since the *Risk Mitigation* interim clinical guidance was published, clinical experience of prescribing stimulants to reduce the risk of COVID-19 transmission and reliance on the illicit drug supply has emerged. Clinical experience suggests that the stimulant medications currently available have, overall, had limited benefit for people who use illicit stimulants; however, some individuals report significant benefit in terms of reduced reliance on the illicit drug supply (for example, using prescribed stimulants for some but not all doses in a day) as well as improved functional and social outcomes such as executive function, focus, and improvements in interpersonal relationships.

For this reason, a trial of prescribed stimulants to reduce the risks associated with the illicit drug supply has emerged as a potential practice option to help individuals with stimulant use disorder to reduce their reliance on the illicit drug supply and support engagement in care. The intervention described below should be understood as a potential harm reduction measure based on limited clinical experience,

[d] The BCC19C was established at the Provincial Health Service Authority (PHSA) as a surveillance platform to integrate various datasets including data on BC-wide laboratory tests, COVID-19 surveillance case data, HealthLink 811 calls, prescription drug dispensations, medical visits, ambulance dispatches, Intensive Care Unit (ICU) admissions, and mortality—all integrated with existing administrative data sources such as the Chronic Disease Registry, hospital admissions, and the Provincial Client Roster.

intended to reduce the harms associated with an increasingly toxic illicit drug supply. All individuals with stimulant use disorder should be engaged in a discussion around their substance use and general health goals and be offered evidence-based psychosocial treatment for stimulant use disorder, if applicable. Until a policy and related provincial protocols to guide the provision of pharmaceutical alternatives to reduce risk of overdose and drug-related harms are available from the provincial government of BC, clinical judgment paired with thorough assessment, consideration of patient preference and goals, discussion of potential risks and benefits, and informed consent may indicate that trialing prescription dextroamphetamine or methylphenidate in combination with psychosocial supports is a reasonable approach to reduce risk of overdose and other harms, as well as reliance on the illicit drug supply for individuals who use stimulants who decline treatment or continue to experience cravings and withdrawal necessitating accessing the illicit stimulant supply despite accessing psychosocial and other treatment interventions. If dextroamphetamine or methylphenidate is trialed for this purpose, an evaluation of the benefit of this intervention to the patient should be performed (see Assessment and Continuing Care).

Assessment

The following considerations for eligibility should be assessed and documented in the patient's health record:

- Ongoing active stimulant use
  AND
- At high risk of overdose or other harms related to illicit stimulant use

Assessment for eligibility should include the following:

- Active substance use assessment (i.e., type of substance, quantity used, frequency of use, route of administration)
  - Note: Not all patients who qualify for these medications will use stimulants daily. For example, people who use stimulants often have a binge pattern of use rather than daily use and would still benefit from support in order to reduce their reliance on the illicit drug supply and risk of overdose and other harms
- Substance use and treatment history
- History of overdose and other drug related harms (e.g., infections, criminalization)
- Comorbid mental and physical conditions
- Prescribed medication(s)
- Current access to a prescriber (i.e., GP, addiction medicine physician, nurse practitioner)

For patients using illicit stimulants:

- Assess current level of use and presence of withdrawal symptoms and cravings
  - Example questions include:
    - What drugs do you currently use? How do you use them?
    - What kind, how much, and how often?
    - How much money are you spending on drugs?
- If not patient has not previously received a stimulant use disorder diagnosis, assess using DSM-5 criteria
- Assess mental health (Note: If any of the below are present, consider consultation with an addiction psychiatrist or psychiatrist, if available)

    - Use extreme caution if there is a known diagnosis or indications of psychosis or bipolar disorder. Prescribing stimulants may worsen mental health symptoms for individuals with these conditions
    - Patients with psychosis or bipolar disorder should be receiving treatment or offered or referred to treatment for these conditions when prescription psychostimulants are offered
    - Patients with a history of severe psychosis that directly resulted in suicide attempts or aggression may experience worsening of mental health on psychostimulant prescribing, especially if use of street amphetamines does not decrease.
    - If clinical judgment indicates that the risk of overdose outweighs all other risks of harm for these patients, and psychostimulants are prescribed as a trial, close follow up is indicated
    - Methylphenidate may be preferred over dextroamphetamine for individuals with co-occurring mental health conditions[46]
- Assess overall physical health
- Cardiac assessment, including hypertension and history of any cardiac conditions (see contraindications below)

Dosing

If clinical judgment and patient preference indicate that a trial of psychostimulants is appropriate, the following protocol may be used:

For patients with active stimulant use disorder:

- Prescribe dextroamphetamine[e]:
    - Dextroamphetamine SR 10-20mg PO BID provided daily with a maximum total daily dose of 40mg BID per day[f]

AND/OR

    - Dextroamphetamine IR 10-20mg PO BID-TID with a maximum total daily dose of 80mg Dexedrine per day

OR

- Prescribe methylphenidate[g]:
    - Methylphenidate SR 20-40mg PO OD with maximum total daily dose of 100mg/24hrs **AND/OR**
    - Methylphenidate IR 10-20mg PO BID daily to maximum total daily dose of 100mg methylphenidate per day

[e] Dexedrine is FDA Pregnancy Category 3.
[f] In some clinical practices, doses of 60mg BID are being used; however, there is limited data to support this practice.
[g] Methylphenidate is FDA Pregnancy Category C.

Medication Selection and Dosing

- Medication selection should take into account patient preference and current use, and may include only slow-release, only immediate-release, or a combination of the two
- Total daily doses of >60mg of both dextroamphetamine and methylphenidate may be more effective than lower doses[33]
- The selected medication and dose should be documented in the patient's health record

Contraindications

- Do not prescribe stimulants for a person with unstable angina or moderate to severe hypertension. Prescribe with caution in those with a cardiac history.
- Dextroamphetamine:
    - CAD, structural heart disease, cardiomyopathy, cardiac arrhythmias, or other serious cardiac conditions should generally not be treated with prescription stimulants, allergy or intolerance to the medication or any ingredients. If prescribing to a to a patient with a cardiac condition, ensure ongoing documentation that the benefits continue to outweigh any risks.
- Methylphenidate:
    - Marked anxiety, agitation, glaucoma, motor tics, a personal or family history of Tourette's, and concurrent use of MOAIs or within 14 days of MOAI administration since hypertensive crisis may result, serious cardiac conditions (as above for dexamphetamine), allergy or intolerance to the medication or any ingredients.

Patient Education

- Patients with concurrent psychotic or bipolar disorder should be warned of the potential worsening of symptoms with prescribed stimulant medications and advised to stop or reduce dose and/or present for medical help early should this occur
- Patients should be educated on potential side effects (e.g., heart palpitations, sleeplessness, anxiety, psychotic or manic symptoms) and advised that medication effects may be different than usually experienced with illicit stimulants
- Discuss safe storage and develop a plan (e.g., if living in an SRO or supportive housing, medication could be stored and dispensed by staff)

Monitoring and Follow up

- Provide close monitoring during initiation
- Prescription length should be based on individual patients' follow-up requirements

The assessment and informed consent process should include a discussion and documentation of the potential risks and benefits of pandemic prescribing, as well as a discussion of continuing care. This should include a discussion of patient goals, as well as which clinical and psychosocial parameters would indicate that the patient is benefitting from the intervention, and which clinical and psychosocial parameters would indicate that the patient is not benefitting from the intervention, and how the treatment plan would change if the patient is not benefitting. See Appendix: Informed Consent for an example of how to discuss the intervention and seek informed consent.

Assessment and Continuing Care

Following an initial trial period (i.e., 2–4 weeks), a thorough assessment of clinical and psychosocial indicators, as well as patient goals, should be performed, to determine whether the patient is benefitting from the intervention. The results of this assessment along with expert consultation (e.g., addiction psychiatrist, 24/7 Line), where appropriate, and patient preference should inform the decision to continue or discontinue this intervention and be appropriately documented in the patient's medical record. Clear indication of patient benefit, supported by clinical judgment and aligned with patient goals, supports the continuation of this intervention.

Indications that the patient is benefitting

Clinical

- Reduction or cessation of illicit stimulant use
- Reduced risk of overdose
- Lack of cravings
- Management of withdrawal symptoms
- Improved overall wellbeing
- Functional outcomes such as increased focus and executive function
- Consistent urine drug tests positive for prescribed medication(s)[h]
    - Amphetamines may be detected in urine drug tests for 2–5 days after use. Urine drug testing for amphetamines has low specificity and is prone to false positives[47] due to a high degree of cross-reactivity with other substances.[48] For this reason, it may be challenging to isolate the use of prescribed medications from the use of illicit amphetamines through point-of-care urine drug testing. Confirmatory testing should be ordered if the results would alter clinical management.
    - Cocaine can be detected for up to day in a urine drug test, while benzoylecgonine (a cocaine metabolite) can be detected up to 4 days after use. Urine drug tests for cocaine metabolites are highly reliable.

Psychosocial[i]

- Reduced need to engage in high-risk and criminalized activities (e.g., sex work) to support substance use
- Seeking or gaining employment or volunteer activities
- Integrating new activities
- Reconnecting with family and friends (e.g., improved social functioning)

---

[h] Note that consistent urine drug tests positive for prescribed medications **and** negative for illicit substances are *not* required in order to continue this intervention. Many individuals may continue to use a combination of prescribed and illicit stimulants. It is recognized that each dose of prescribed, regulated stimulants reduces risk of overdose and other harms from the illicit drug supply.

[i] Structural barriers such as lack of affordable and accessible housing or suitable employment may make these difficult to achieve for individuals who are otherwise benefitting from the intervention. Improvements in these domains are not required, but—where possible—may be additional indications that the patient is benefitting and should continue to receive this intervention.

- Attaining safe housing and accessing other social services

Indications that the patient is not benefitting

Clinical

- No change or increased intensity of illicit substance use
- No change or increased overdose risk
- Ongoing cravings and withdrawal symptoms
- Urine drug tests consistently negative for prescribed medication(s) or other indications of diversion
- No change in wellbeing or social functioning
- Consistently missed doses
- Development or worsening of psychosis or bipolar disorders

If thorough assessment of patient-identified goals and indicators of clinical and psychosocial stability indicate that the patient is not benefitting from the intervention despite attempts at optimizing dosing and concurrent psychosocial treatments and supports, it may be appropriate to discontinue the intervention and explore alternative harm reduction, treatment, and recovery options. Alternative options may include referral to additional or alternative psychosocial treatment options (such as contingency management, CBT, or bed-based treatment options), providing patient education and referral to harm reduction services and supplies, referral to psychosocial and community supports, or a combination. The assessment, treatment plan, and rationale should be documented in the patient's medical record. It may be helpful to consult the 24/7 Line for assistance in determining whether the intervention is or is not beneficial, and next steps.

Peer Navigators and Advocacy

Clinical experience from the past year indicates that the inclusion of peer navigators and patient advocates on the care team can help support engagement in care, including both continued engagement with prescribing to reduce reliance on the illicit drug supply and with substance use disorder treatment. Peer navigators and advocates can support engagement in care in the following ways:

- Outreach
- Explaining interventions and treatment options and what to expect
- Completing intake forms in a setting that is comfortable for the patient
- Supporting patients to attend appointments (including reminders, providing rides)
- Accompanying patients to appointments, if requested
- Facilitating access to treatment, harm reduction, and primary care services (e.g., vaccination)
- Providing advocacy when individuals encounter challenges accessing treatments or interventions

Patient Education and Informed Consent

The informed consent process should include a discussion and documentation of the potential risks and benefits of this intervention, as well as a discussion of continuing care (see Appendix 2). This should include a discussion of patient goals, as well as which clinical and psychosocial parameters would indicate that the patient is benefitting from the intervention, and which clinical and psychosocial parameters

would indicate that the patient is not benefitting from the intervention, and how the treatment plan would change if the patient is not benefitting.

When counselling on routes of administration, oral ingestion of the prescribed stimulant medication is recommended, as this is the lowest risk route of ingestion. However, education on harm reduction should be provided, as many patients will choose other routes of use. See Safer Tablet Injection: A Resource for Clinicians Providing Care to Patients Who May Inject Oral Formulations for more information.

Increased Flexibility

Events over the past year, including the COVID-19 pandemic and climate change-related phenomena (e.g., wildfire evacuations, weather warnings due to extreme heat), have demonstrated the necessity and feasibility of clinical flexibility that prioritizes patient safety and continuity of care. Patient care should be adapted, as needed, during local or global emergencies and disruptions, to ensure that patients can continue to access life-saving treatment without putting their health at risk (e.g., waiting in extreme heat) or facing unreasonable barriers. Examples of adaptations may include extended carries, reduced urine drug testing, reduced clinic appointments or shifting toward virtual care, and facilitating transfer of prescription to a new pharmacy. Prescribers are encouraged to consult the 24/7 Line or RACE app if needing support to adapt care plans in response to states of emergency or other disruptive events.

Appendix 1: DSM-5 Clinical Diagnostic Criteria for Substance Use Disorder

DSM-5 Criteria for Stimulant Use Disorder[j]

1. Stimulants are often taken in larger amounts or over a longer period than was intended	The presence of at least 2 of these symptoms indicates a stimulant use disorder. The severity of the stimulant use disorder is defined as: MILD: The presence of 2 to 3 symptoms MODERATE: The presence of 4 to 5 symptoms SEVERE: The presence of 6 or more symptoms
2. There is a persistent desire or unsuccessful efforts to cut down or control stimulant use	
3. A great deal of time is spent in activities necessary to obtain the stimulant, use the stimulant, or recover from its effects	
4. Craving or a strong desire to use stimulants	
5. Recurrent stimulant use resulting in a failure to fulfill major role obligations at work, school, or home	
6. Continued stimulant use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of stimulants	
7. Important social, occupational, or recreational activities are given up or reduced because of stimulant use	
8. Recurrent stimulant use in situations in which it is physically hazardous	
9. Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by stimulants	
10. Tolerance, as defined by either of the following: a) Need for markedly increased amounts of stimulants to achieve intoxication or desired effect b) Markedly diminished effect with continued use of the same amount of stimulant	
11. Withdrawal, as manifested by either of the following: a) Characteristic stimulant withdrawal syndrome b) Same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms	

[j] Adapted from the American Psychiatric Association.[49]

Appendix 2: Informed Consent

Seeking informed consent to trial an intervention requires disclosing the relevant information that will allow the patient to make a voluntary choice to accept and consent or decline the intervention. More information on informed consent is available through the Canadian Medical Protective Association's *Consent: A Guide for Canadian Physicians*. This appendix provides a brief overview of the informed consent process, and a template that may be used to guide and document the process.

The informed consent process should include a description of the proposed intervention, including potential risks and benefits; a description of eligibility; a description of engagement with care during the intervention; and a description of what indicators would indicate that the patient is benefitting from the intervention and should continue to receive it, as well as what indications would indicate that the patient is not benefitting from the intervention and alternative harm reduction, treatment, and recovery options should be explored instead. This conversation should be thoroughly documented in the patient's medical record.

Informed Consent Template

1. Provide a description of the intervention
   The specific intervention (e.g., prescription of dextroamphetamine to reduce reliance on toxic drug supply and overdose risk) should be described, including the limited evidence base supporting it, and potential benefits (e.g., reduced reliance on toxic drug supply, reduced overdose risk,) and risks (e.g., emergence of or worsening mental health symptoms in patients with known or diagnosed psychosis or bipolar disorder) should be described.

2. Describe eligibility
   Eligibility considerations for this intervention include:
   Ongoing active stimulant use
   AND
   At high risk of illicit drug toxicity death or other harms related to illicit stimulant use

3. Describe engagement with care during intervention
   Specific follow up will depend on clinical judgment and the individual patient.
   Items for discussion should include:
   a. *Frequency of follow-up,*
   b. *Frequency of dispensation of medications (e.g., daily dispensation vs. take-home doses)*
   c. *Frequency of urine drug testing*
   d. *Expectation that patient will work together with prescriber on agreed upon plan for amount of engagement around care that would help ensure continuation of prescriptions, and what will happen if agreed upon plan is not met (e.g., consistently missed doses, missed follow up appointments may result in prescription being cancelled)*

4. Describe indications that patient is benefitting or not benefitting from intervention
   Clinical and psychosocial indications of benefit such as reduction or cessation of illicit substance use, reduced risk of overdose, and reduced need to engage in high-risk and criminalized activities should be described. Clinical and psychosocial indications of a lack of benefit such as no change or increased intensity of illicit substance use, no change or increased overdose risk, and no improvement in employment, volunteering, or housing should also be described.

Indications of benefit should be tailored to the individual patient; the patient should be invited to describe ways that they would know they are benefitting from the intervention (e.g., less engagement in marginalized income-generating activities, experiencing less withdrawal), which should be documented in the patient's medical record and revisited on follow up.

5. Describe options if patient does not benefit from intervention
   If thorough assessment of patient-identified goals and indicators of clinical and psychosocial stability indicate that the patient is not benefitting from the intervention despite attempts at optimizing dosing and psychosocial supports, it may be appropriate to discontinue the intervention and explore alternative harm reduction, treatment, and recovery options.

   Alternative options may include referral to psychosocial treatment (such as contingency management, CBT, or bed-based treatment options), providing patient education and referral to harm reduction services and supplies, referral to psychosocial and community supports, or a combination.

6. Ensure patient understands the above information, and seek consent or refusal of care

References

1. Canadian Centre on Substance Use and Addiction. Changes in stimulant use and related harms: Focus on methamphetamine and cocaine. *CCENDU Bulletin.* 2019.
2. Davis A, Amlani A, Buxton J. *Substance use trends in bc: A survey of harm reduction clients. Overall results for british columbia: 2015.* Vancouver, BC: BC Centre for Disease Control; 2016.
3. Canadian Centre on Substance Use and Addiction. *Cocaine.* 2019.
4. BC Coroners Service. Illicit drug overdose deaths in bc: January 1, 2010 - may 31, 2021. In: Ministry of Public Safety and Solicitor General, ed. Burnaby, BC: Office of the Chief Coroner; 2021. http://www2.gov.bc.ca/assets/gov/public-safety-and-emergency-services/death-investigation/statistical/illicit-drug.pdf.
5. BC Coroners Service. Illicit drug overdose deaths in bc: January 1, 2010-august 31, 2020. In: Ministry of Public Safety and Solicitor General, ed. Burnaby, BC: Office of the Chief Coroner; 2020. http://www2.gov.bc.ca/assets/gov/public-safety-and-emergency-services/death-investigation/statistical/illicit-drug.pdf.
6. BC Coroners Service. Illicit drug overdose deaths in bc: January 1, 2010 - february 28, 2021. In: Ministry of Public Safety and Solicitor General, ed. Burnaby, BC: Office of the Chief Coroner; 2021. http://www2.gov.bc.ca/assets/gov/public-safety-and-emergency-services/death-investigation/statistical/illicit-drug.pdf.
7. BC Centre on Substance Use. Unpublished drug checking data. 2020.
8. UBC Continuing Professional Development. Addiction care and treatment online course—chapter 6, stimulant use disorder.
9. Sofuoglu M, Dudish-Populson S, Polling J, Mooney M, Hatsukami D. The effect of individual cocaine withdrawal symptoms on outcomes in cocaine users. *Addiction Behaviour.* 2005; 30(6):1125–1134.
10. Pennay A, Lee N. Putting the call out for more research: The poor evidence base for treating methamphetamine withdrawal. *Drug and Alcohol Review.* 2011; 30(2):216–222.
11. Trivedi M, Walker R, Weng X, et al. Bupropion and naltrexone in methamphetamine use disorder. *New England Journal of Medicine.* 2021; 384:140–153. 10.1056/NEJMoa2020214
12. Coffin PO, Santos GM, Hern J, et al. Effects of mirtazapine for methamphetamine use disorder among cisgender men and transgender women who have sex with men: A placebo-controlled randomized clinical trial. *JAMA Psychiatry.* 2020; 77(3):246-255. 10.1001/jamapsychiatry.2019.3655
13. Crescenzo FD, Ciabattini M, D'Alò GL, et al. Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: A systematic review and network meta-analysis. *PLOS Medicine.* 2018; 15(12):e1002715. 10.1371/journal.pmed.1002715
14. De Crescenzo F, Ciabattini M, D'Alò GL, et al. Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: A systematic review and network meta-analysis. *PLoS Med.* 2018; 15(12):e1002715. 10.1371/journal.pmed.1002715
15. Ronsley C, Nolan S, Knight R, et al. Treatment of stimulant use disorder: A systematic review of reviews. *PLoS One.* 2020; 15(6):e0234809. 10.1371/journal.pone.0234809
16. De Giorgi R, Cassar C, Loreto D'alò G, et al. Psychosocial interventions in stimulant use disorders: A systematic review and qualitative synthesis of randomized controlled trials. *Riv Psichiatr.* 2018; 53(5):233-255. 10.1708/3000.30003
17. Farronato NS, Dürsteler-Macfarland KM, Wiesbeck GA, Petitjean SA. A systematic review comparing cognitive-behavioral therapy and contingency management for cocaine dependence. *J Addict Dis.* 2013; 32(3):274-287. 10.1080/10550887.2013.824328
18. Lee NK, Rawson RA. A systematic review of cognitive and behavioural therapies for methamphetamine dependence. *Drug and alcohol review.* 2008; 27(3):309-317. 10.1080/09595230801919494

19. Rash CJ, Stitzer M, Weinstock J. Contingency management: New directions and remaining challenges for an evidence-based intervention. *Journal of substance abuse treatment.* 2017; 72:10-18. 10.1016/j.jsat.2016.09.008

20. Carroll KM. Lost in translation? Moving contingency management and cognitive behavioral therapy into clinical practice. *Ann N Y Acad Sci.* 2014; 1327(1):94-111. 10.1111/nyas.12501

21. Kirby KC, Benishek LA, Dugosh KL, Kerwin ME. Substance abuse treatment providers' beliefs and objections regarding contingency management: Implications for dissemination. *Drug Alcohol Depend.* 2006; 85(1):19-27. 10.1016/j.drugalcdep.2006.03.010

22. Zastepa E, Sun JC, Clune J, Mathew N. Adaptation of contingency management for stimulant use disorder during the covid-19 pandemic. *J Subst Abuse Treat.* 2020; 118:e108102.

23. Farronato N, Dürsteler-MacFarland, KM, Wiesbeck, GA, Petitjean, SA. A systematic review comparing cognitive-behavioral therapy and contingency management for cocaine dependence. *Journal of addictive diseases.* 2013; 32(3):274-287. 10.1080/10550887.2013.824328

24. Reif S, George P, Braude L. Residential treatment for individuals with substance use disorders: Assessing the evidence. *Psychiatric Services.* 2014; 65(3):301–312.

25. Donovan DM, Daley DC, Brigham GS, et al. Stimulant abuser groups to engage in 12-step: A multisite trial in the national institute on drug abuse clinical trials network. *J Subst Abuse Treat.* 2013; 44(1):103-114. 10.1016/j.jsat.2012.04.004

26. Hatch-Maillette M, Wells E, Doyle S, et al. Predictors of 12-step attendance and participation for individuals with stimulant use disorders. *J Subst Abuse Treat.* 2016; 68:74–82.

27. Wells EA, Donovan DM, Daley DC, et al. Is level of exposure to a 12-step facilitation therapy associated with treatment outcome? *J Subst Abuse Treat.* 2014; 47(4):265–274.

28. Kelly J, Greene M, Bergman B, Hoeppner B, Slaymaker V. The sponsor alliance inventory: Assessing the therapeutic bond between 12-step attendees and their sponsors. *Alcohol and Alcoholism.* 2016; 51:32–39.

29. Wendt DC, Hallgren KA, Daley DC, Donovan DM. Predictors and outcomes of twelve-step sponsorship of stimulant users: Secondary analyses of a multisite randomized clinical trial. *Journal of Studies on Alcohol and Drugs.* 2017; 78(2):287–295.

30. Bhatt M, Zielinski L, Baker-Beal L, et al. Efficacy and safety of psychostimulants for amphetamine and methamphetamine use disorders: A systematic review and meta-analysis. *Syst Rev.* 2016; 5(1):189. 10.1186/s13643-016-0370-x

31. Castells X, Cunill R, Perez-Mana C, Vidal X, Capella D. Psychostimulant drugs for cocaine dependence. *Cochrane Database Syst Rev.* 2016; 9:Cd007380. 10.1002/14651858.CD007380.pub4

32. Sangroula D, Motiwala F, Wagle B, Shah VC, Hagi K, Lippmann S. Modafinil treatment of cocaine dependence: A systematic review and meta-analysis. *Substance use & misuse.* 2017; 52(10):1292-1306. 10.1080/10826084.2016.1276597

33. Tardelli VS, Bisaga A, Arcadepani FB, Gerra G, Levin FR, Fidalgo TM. Prescription psychostimulants for the treatment of stimulant use disorder: A systematic review and meta-analysis. *Psychopharmacology (Berl).* 2020; 237(8):2233-2255. 10.1007/s00213-020-05563-3

34. Pérez-Mañá C, Castells X, Torrens M, Capellà D, Farre M. Efficacy of psychostimulant drugs for amphetamine abuse or dependence. *The Cochrane database of systematic reviews.* 2013; (9):Cd009695. 10.1002/14651858.CD009695.pub2

35. Chan B, Freeman M, Kondo K, et al. Pharmacotherapy for methamphetamine/amphetamine use disorder-a systematic review and meta-analysis. *Addiction.* 2019; 114(12):2122-2136. 10.1111/add.14755

36. Chan B, Kondo K, Freeman M, Ayers C, Montgomery J, Kansagara D. Pharmacotherapy for cocaine use disorder-a systematic review and meta-analysis. *J Gen Intern Med.* 2019; 34(12):2858-2873. 10.1007/s11606-019-05074-8

37. Siefried KJ, Acheson LS, Lintzeris N, Ezard N. Pharmacological treatment of methamphetamine/amphetamine dependence: A systematic review. *CNS Drugs.* 2020; 34(4):337-365. 10.1007/s40263-020-00711-x

38. Nuijten M, Blanken P, Wetering Bvd, Nuijen B, Brink Wvd, Hendriks V. Sustained-release dexamfetamine in the treatment of chronic cocaine-dependent patients on heroin-assisted treatment: A randomised, double-blind, placebo-controlled trial. *The Lancet.* 2016; 387:e10034.

39. Blanken P, Nuijten M, Brink Wvd, Hendricks V. Clinical effects beyond cocaine use of sustained-release dexamphetamine for the treatment of cocaine dependent patients with comorbid opioid dependence: Secondary analysis of a double-blind, placebo-controlled randomized trial. *Addiction.* 2020; 115(5):917–923. 10.1111/add.14874

40. Palis H, MacDonald S, Jun J, Oviedo-Joekes E. Use of sustained release dextroamphetamine for the treatment of stimulant use disorder in the setting of injectable opioid agonist treatment in canada: A case report. *Harm Reduction Journal.* 2021; 18(57).

41. Ezard N, Clifford B, Dunlop A, et al. Safety and tolerability of oral lisdexamfetamine in adults with methamphetamine dependence: A phase-2 dose-escalation study. *BMJ Open.* 2021; 11(5):e044696. 10.1136/bmjopen-2020-044696

42. BC Ministry of Health—Data Stewardship Committee. Pharmanet data extract. 2020. http://www2.gov.bc.ca/gov/content/health/conducting-health-research-evaluation/dataaccess-health-data-central.

43. BC Ministry of Health. Consolidation file (msp registration & premium billing) data extract. 2020. http://www2.gov.bc.ca/gov/content/health/conducting-health-research-evaluation/dataaccess-health-data-central.

44. British Columbia Ministry of Health. Vital statistics death events. (vital statistics bc). Data extract. 2020. http://www2.gov.bc.ca/gov/content/health/conducting-health-researchevaluation/data-access-health-data-central;.

45. British Columbia Ministry of Health. Medical services plan (msp) payment information file. Data extract 2020. http://www2.gov.bc.ca/gov/content/health/conducting-health-researchevaluation/data-access-health-data-central.

46. Moran L, Ongur D, Hsu J, Castro V, Perlis R, Schneeweiss S. Psychosis with methylphenidate or amphetamine in patients with adhd. *New England Journal of Medicine.* 2019; 380(12):1128–1138.

47. Brahm N, Yeager L, Fox M, Farmer K, Palmer T. Commonly prescribed medications and potential false-positive urine drug screens. *American Journal of Health-System Pharmacy.* 2010; 67(16).

48. Standridge J, Adams S, Zotos A. Urine drug screening: A valuable office procedure. *American Family Physician.* 2010; 81(5):635–640.

49. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders: Dsm-5.* 5th edition ed. Arlington, VA: American Psychiatric Publishing, Inc.