

# Stimulant Use Disorder

# **Practice Update**

June 2022

# LAND ACKNOWLEDGEMENT

We would like to respectfully acknowledge that the land on which we work is the unceded territory of the Coast Salish Peoples, including the territories of the x<sup>w</sup>məθkwəỳəm (Musqueam), Skwxwú7mesh (Squamish), and səlililwəta?/ (Tsleil-Waututh) Nations.

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# **OVERVIEW**

Stimulants—including cocaine, methamphetamine, and other amphetamine-type substances are among 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<sup>1</sup>; this was an increase from 47% in 2015.<sup>2</sup> While cocaine use has reportedly been decreasing in BC,<sup>1</sup> it is increasing across Canada, with 2.5% of Canadians over 15 reporting cocaine use in the past year in 2017 compared to 0.9% in 2013.<sup>3</sup>

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 2021, post-mortem toxicology detected cocaine in 48% of illicit drug toxicity deaths and amphetamine or methamphetamine in 39% of illicit drug toxicity deaths.<sup>4</sup> Notably, the detection of methamphetamine in illicit drug toxicity deaths has increased from 14% in 2012 to 39% in 2021.<sup>4,5</sup> 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, 4.1% of expected crack cocaine samples, and 6.5% of expected methamphetamine samples were adulterated with fentanyl from September 2020 to January 2021).<sup>6</sup>

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 Public Health Emergencies*, 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. People who use drugs faced increased risks including overdose 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.

#### **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, facilitating transfer of prescription to a new pharmacy, or engaging other health care providers to support medication management. Prescribers are encouraged to consult the <u>24/7 Line</u> or <u>RACE app</u> if needing support to adapt care plans in response to states of emergency or other disruptive events. Exceptions to standard clinical care should be documented, including the rationale, patient discussion, and patient consent.

# About This Document

This practice update is composed of two parts. It is meant to highlight practical tips and introduce new evidence and approaches relevant for those providing care for individuals who use illicit stimulants. This does not represent a comprehensive guideline on management of stimulant use disorder and associated conditions.

The first section provides an overview of evidence-based treatment options for individuals with stimulant use disorder, as well as information on managing related conditions (e.g., stimulant withdrawal) and when to consult or refer to a specialist. Screening for substance use is part of comprehensive primary care. Information on screening for substance use is available in Module 2 of the BCCSU's <u>Addiction Care and Treatment Online Course</u>. Stimulant-specific screening and a discussion of validated screening tools is outside the scope of this brief update. Information on sexualized stimulant use (also called "chemsex" or "party 'n' play") can be found in Module 6 of the BCCSU's <u>Addiction Care and Treatment Online Course</u>. Clinicians are encouraged to consult a specialist perinatal addiction specialist when providing care for a pregnant person who uses illicit stimulants.

The second part provides an overview of clinical experience and preliminary data from a year of Risk Mitigation prescribing, and introduces a potential practice option to help reduce individuals' reliance on the illicit stimulant supply and associated risks outside of the context of risk of COVID-19.<sup>a</sup> These practice options, including trialing methylphenidate or dextroamphetamine to reduce

<sup>&</sup>lt;sup>a</sup> This practice update helps enact recent government policy, <u>Access to Prescribed Safer Supply in British Columbia</u>. As part of the development process of this practice update, broad consultation was sought, including health systems partners, opioid agonist treatment prescribers in BC, and people with lived and living experience. Given the direction of government, review focused on the clinical guidance contained in this document, rather than the concept of prescribing to reduce risks associated with and the toxic illicit drug supply.

reliance on the illicit stimulant supply, do not constitute treatment for stimulant use disorder. They are, instead, positioned as a harm reduction approach, based on limited signals of efficacy in the research evidence and limited clinical experience, that may be trialed, based on thorough assessment and clinical judgment, in order to reduce the harms associated with illicit stimulant use for those individuals who are not interested in evidence-based psychosocial treatment and for those who continue to be at high risk due to ongoing stimulant use despite engaging in evidencebased psychosocial treatment. As detailed in Part 2, a thorough assessment of potential risks and benefits for both individual patients and the community should inform this practice.

# PART 1: CURRENT TREATMENT OPTIONS

# Acute Stimulant Intoxication

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

- Mania
- Psychosis
- Paranoia
- Severe delirium
- Elevated blood pressure
- Chest pain
- 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.<sup>7</sup>

Agitation has been defined by the Internal Experts' Meeting on Agitation as characterized by hyperresponsiveness, racing thoughts, emotional tension, motor and verbal hyperactivity, communication impairment, and an inability to remain still or calm.<sup>8</sup> Distinguishing stimulant intoxication and/or stimulant-induced agitation from stimulant-induced psychosis is key when determining an approach to management. Individuals who are exhibiting features of stimulant intoxication and/or agitation can be treated with a low stimulus environment and benzodiazepines as needed, according to regional or institutional protocols. Those with features of psychosis including hallucinations, delusions, delirium, or other significant features of mental illness may require consultation from psychiatry in order to determine management. See <u>Stimulant-induced</u> <u>Psychosis</u>, below, for an overview of symptoms and prevalence as well as when to consult a specialist or refer out.

"When someone is in the 'freak-out stage'—paranoia, heart racing, scared—what they're feeling is very real to them. One of the best things you can do is talk to them in a calm voice. Talking is huge. Reassure them over and over. Help them feel safe. Ask them what they need to feel safe. Rub their back if they're comfortable with it. Offer them a cool cloth.

Make the space as safe as possible so they don't hurt themselves bouncing or thrashing around. When they come out of it, they're going to be freaked out. It's not uncommon for someone to come out of it really scared and not knowing what just happened, where they are, or who you are. Reassure them that they're okay. Tell them what just happened."

— Katt Cadieux

# Stimulant-induced Psychosis

Available data suggest that stimulant-induced psychosis is relatively common. A 2021 systematic review and meta-analysis (N=17, n=5,286) found that 68% of people who reported life-time cocaine use had experienced cocaine-induced psychotic symptoms.<sup>9</sup> While estimates of the epidemiology of transient methamphetamine-induced psychosis vary widely in the literature (23–76%),<sup>10,11</sup> a 2018 systematic review and meta-analysis of 17 observational studies (n=4,095) estimated the prevalence of psychotic disorders<sup>b</sup> attributed to methamphetamine use to be 42.7%.<sup>12</sup>

A significant number of individuals who experience stimulant-induced psychosis will develop persistent or ongoing psychotic symptoms, including schizophrenia, or bipolar disorder. According to a 2019 systematic review of the trajectory of methamphetamine-induced psychosis (N=94; n=7,387), persistent or chronic psychotic symptoms (duration >1 month) may develop in approximately 25% of participants across all studies.<sup>13</sup> Additionally, studies have found that approximately 15–30% of those initially diagnosed with amphetamine-induced psychosis<sup>14-16</sup> and 20% of those initially diagnosed with cocaine-induced psychosis<sup>17</sup> eventually receive a diagnosis of schizophrenia or bipolar disorder. Several predictors of developing persistent psychosis following methamphetamine-induced psychosis have been identified. The strongest identified factors are longer use of methamphetamines, more severe psychotic symptoms, and sustained depressive symptoms.<sup>18</sup>

The majority of investigations into the risk factors of developing stimulant-induced psychosis focus on methamphetamine use and identify methamphetamine use patterns (e.g., frequency and amount of use) and diagnosis and severity of stimulant use disorder as key risk factors for psychosis.<sup>19-21</sup> One study also found some correlation between participants' anxiety scores, based on the Hamilton Anxiety Scale, and the risk of psychosis.<sup>19</sup>

Common symptoms of psychosis include<sup>13,22</sup>:

- Delusions of persecution
- Agitation and anxiety
- Auditory and visual hallucination
- Hostility and violence
- Compulsive thoughts

Management of stimulant-induced psychosis is beyond the scope of this document. If a patient presents with symptoms of psychosis, psychiatry should be consulted, which may include a psychiatrist, mental health nurse, or the Rapid Access to Consultative Excellence (RACE) line (M-F 0800-1700; 604-696-2131 or 1-877-696-2131).

<sup>&</sup>lt;sup>b</sup> Epidemiological reports often do not distinguish between stimulant-induced psychosis and persistent or chronic psychosis related to stimulant use. This inconsistent or pooled reporting has, in part, resulted in broad variations in reported prevalence data for the two diagnoses.

# 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.<sup>23,24</sup> Symptoms of stimulant withdrawal may include:

- Craving
- Depressed mood
- Vivid, unpleasant dreams
- Fatigue
- Pain
- Anxiety
- 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 care, which may include providing adequate nutrition, supporting sleep hygiene, mental health assessment, and working with the patient to identify their goals and the supports that would help them achieve them. For example, for individuals trying to reduce or stop illicit stimulant use, developing a plan to prevent return to use and providing linkage or referral to psychosocial interventions such as counselling or contingency management. In addition, some individuals may benefit from support with cognitive behavioural therapy (CBT) to manage their withdrawal symptoms.<sup>7</sup>

# Stimulant Use Disorder

Stimulant use disorder, as defined by DSM-5 criteria (see <u>Appendix 1</u>), is associated with an increased risk of a number of health complications, including:

- Cardiovascular disease (e.g., myocardial infarction, renal insult, and stroke)<sup>25</sup>
- Psychiatric conditions (including psychosis, depression, mania and suicidal ideation)<sup>26-28</sup>
- Blood-borne virus transmission (such as HIV or Hepatitis C)<sup>29</sup>

Health equity issues such as housing, income, race/ethnicity, and laws targeting people who use drugs play a significant role in mediating substance use outcomes and impacting individuals' drug use trajectories and access to treatment and recovery-oriented care.<sup>30,31</sup> In addition, structural and systemic issues such as violence, stigma, racism, homelessness, and the chronicity of stress have been implicated in the prevalence and impact of stimulant use disorders and the development of secondary health conditions that are more prevalent in individuals with stimulant use disorders (e.g., cardiovascular disease, HIV, and hepatis C).<sup>32-35</sup> Further, communities that experience greater social and economic disparities experience higher rates of overdose deaths.<sup>34,36</sup> This is especially

important to consider in the context of stimulant use, as cocaine and methamphetamines were detected in 48% and 39%, respectively, of overdose deaths between 2018 and 2021.<sup>4</sup>

To date, the evidence on pharmacotherapy for the treatment of stimulant use disorders is limited and inconclusive. Recent trials of several non-psychostimulant pharmacotherapy options, including extended-release injectable naltrexone plus oral extended-release bupropion<sup>37</sup> as well as mirtazapine,<sup>38</sup> have shown some promise in reducing methamphetamine use compared to treatment with placebo, but require further study. Limited signals of efficacy (e.g., prolonging abstinence) and a generally good safety profile in the absence of contraindications (including a history of psychosis) have also prompted calls for further investigation into the use of prescribed psychostimulants as replacement for illicit stimulants (see <u>Pharmacotherapy for Stimulant Use</u> <u>Disorder</u>, below).

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,<sup>c</sup> CBT, the Matrix Model, and self-help groups based on the 12-step program have been recommended. There is a lack of guidance on which of these interventions should be considered first.<sup>39</sup>

# Psychosocial Treatment for Stimulant Use Disorder

The efficacy of contingency management in the treatment of stimulant use disorders is supported by a large body of evidence.<sup>40-44</sup> 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<sup>d</sup> and other psychosocial interventions (alone or in combination).<sup>39</sup> In particular, contingency management in combination with community reinforcement approach was found to be superior for abstinence during treatment (number needed to treat [NNT]=2.1), at the end of treatment (NNT=4.1), and at the longest followup after treatment completion (NNT=3.7). This combination of interventions was also superior in retaining participants (NNT=3.3).<sup>39</sup>

Contingency management has had relatively poor uptake, due to a variety of barriers including cost, practical concerns, and philosophical objections,<sup>45-47</sup> making it inaccessible for many individuals with stimulant use disorder. Recently, 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.<sup>48</sup> 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 in reducing cocaine use post-treatment<sup>49</sup> as well as methamphetamine

<sup>&</sup>lt;sup>c</sup> Community reinforcement includes a combination of interventions such as coping skills training and social, familial, recreational, and vocational reinforcements.

<sup>&</sup>lt;sup>d</sup> Treatment as usual was defined in this study as non-specific therapy including case management and any unstructured, non-manualized psychosocial intervention.

use.<sup>44</sup> Individuals may experience positive outcomes from CBT even from short periods of treatment (as few as 2–4 sessions).<sup>44</sup> However, while CBT was found to be superior to treatment as usual for treatment retention, it was not superior for abstinence.<sup>39</sup> 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, abstinence, reductions in use and high-risk behaviour, and improvements in craving management and control.<sup>50</sup> Participants in this program receive a combination of CBT, family education, individual counselling, 12-step fellowship participation, and drug testing over a 16week intensive treatment protocol.<sup>51</sup>

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.<sup>39</sup> A 2013 multi-site randomized controlled trial (n=471) evaluating 12-step facilitation compared to treatment as usual<sup>52</sup> 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.<sup>53,54</sup> Additionally, individuals who obtained sponsors<sup>e</sup> through their 12-step program were more likely to have maintained abstinence at follow-up.<sup>56</sup> 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 and those who express interest in 12-step programs.

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 from this approach, particularly those who previously attended bed-based programs and experienced beneficial outcomes, unstably housed patients, or those in dangerous living situations.<sup>7</sup>

# Psychosocial Treatment Programs for Stimulant Use Disorder

Examples of programs and services providing psychosocial treatment for stimulant use disorder follows. For community-specific resources, contact the relevant regional health authority.

#### Cognitive Behavioural Therapy

- Specialist-led approach
- May be available in many communities
  - o Red Fish Healing Centre for Mental Health and Addiction

<sup>&</sup>lt;sup>e</sup> 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.55

#### **Contingency Management**

- Pender Community Health Centre (Vancouver)
- Downtown Community Health Centre (Vancouver)
- St. Paul's Hospital Rapid Access Addiction Clinic (Vancouver)
- Rewarding Recovery
  - o Fraser North Day Evening Weekend Program (New Westminster)
  - o Fraser South Day Evening Weekend Program (Surrey)
- Red Fish Healing Centre for Mental Health and Addiction

#### Matrix Model

- Three Bridges Community Health Centre (Vancouver)
- Red Fish Healing Centre for Mental Health and Addiction

# Harm Reduction and Safer Use Strategies

In taking up a client-centred, trauma- and evidence-informed approach, discussing safer use strategies with clients is recommended. For many people, abstinence may not be a possible or a preferable goal. Working alongside the client with their goals will support trust building and breaking down shame and stigma that is prevalent among people who use stimulants, and may impact individuals' decisions to access care and, thus, morbidity and mortality.

Clinicians should ask patients how they keep themselves safe and offer tailored education and services based on that conversation. Factors that may inform provision of harm reduction supplies and referrals include primary drug, route of administration, patient goals (e.g., abstinence vs. safer use or reduced use), and patient support system. For patients who are looking to reduce or cease illicit stimulant use, a plan can be developed based on what has helped them reduce their use in the past, their current supports, and the supports they identify wanting or needing.

As appropriate, patients should be informed of the risk of fentanyl contamination of illicit stimulants and encouraged to use drug checking services (including fentanyl test strips), where available, and to avoid using alone. Patients can be referred to safe consumption and overdose prevention sites, and counselled on other strategies to avoid using alone, such as using the Lifeguard App or a buddy system (for example, where a neighbour knocks on their door or a friend stays on the phone while the patient uses). In addition, as appropriate, patients should be provided with or directed to services that can provide harm reduction supplies such as sterile syringes, cookers, water, pipes, and mouthpieces, and should receive counselling about not sharing pipes, mouth pieces, and syringes. Toward the Heart has a variety of stimulant-specific harm reduction educational resources, including <u>Safer Smoking Supplies</u>, <u>Overdose Awareness: Stimulants</u>, <u>Safer Smoking guidance</u>, and <u>Safer Injecting guidance</u>. Toward the Heart's <u>Site Finder</u> can be used to find local harm reduction services.

# Evidence Regarding Pharmacotherapy for Stimulant Use Disorder

Multiple meta-analyses have found no evidence of efficacy for any forms of pharmacotherapy for stimulant use disorder; however, prescribed stimulants are often highlighted for further study. <sup>41,57-64</sup> Recent trials of several non-psychostimulant pharmacotherapy options, including extended-release injectable naltrexone plus oral extended-release bupropion<sup>37</sup> as well as mirtazapine,<sup>38</sup> have shown some promise in reducing methamphetamine use compared to treatment with placebo, but require further study. In addition, a 2020 systematic review and metaanalysis that restricted analysis to trials of medications deemed most analogous to cocaine or amphetamine-type substances, with similar behavioural effects, found that prescription psychostimulants likely promote sustained abstinence (defined as 2–3 weeks of no use) from illicit stimulant use (number needed to treat = 16) and may reduce use throughout the trial and extend the duration of abstinence. The overall effect was primarily influenced by studies that used prescription amphetamines (mostly dextroamphetamine) for treatment of cocaine use disorder specifically (number needed to treat individuals with cocaine use disorder = 12). The meta-analysis provides preliminary evidence that may support the use of medications with a more "potent" agonist effect (e.g., dextroamphetamine) vs. medications with a less "potent" effect (e.g., modafinil), and suggests that higher doses may be more effective than lower doses.<sup>60</sup> 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.60

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 to date is largely focused on cocaine use. A 2016 meta-analysis (N=17 RCTs) examining the safety and efficacy of psychostimulants (methylphenidate, N=6; dextroamphetamine, N=2) and psychoanaleptics with mild stimulant effects (bupropion, N=6; modafinil, N=3) for the management of amphetamine and methamphetamine use disorders found no significant difference between treatment and placebo groups in terms of end-of-study abstinence, treatment retention, or serious adverse events.<sup>57</sup> 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 psychostimulants (dexamphetamine and methylphenidate), naltrexone, and topiramate.<sup>64</sup>

In light of the limited evidence showing benefit for pharmacotherapy for stimulant use disorder, it may be appropriate, based on through assessment, clinical judgment, and patient preference, to trial mirtazapine<sup>38</sup> for individuals who are not interested in psychosocial treatment or who continue to use illicit stimulants to manage cravings and withdrawal symptoms despite participating in evidence-based psychosocial treatment. While extended-release injectable naltrexone is not currently available in Canada, should it become available in the future, it may, similarly, be appropriate to trial this in combination with oral extended-release bupropion.<sup>37</sup>

For a further review of the evidence regarding stimulant replacement to reduce harms associated

with illicit stimulant use, see <u>Evidence Regarding Stimulant Replacement to Reduce Harms</u> <u>Associated with Illicit Stimulant Use</u> in Part 2 of this document.

# PART 2: PRESCRIBING STIMULANTS TO REDUCE ILLICIT STIMULANT-RELATED HARMS

This section of the document describes both clinical experience and preliminary data from over a year of prescribing according to the *Risk Mitigation* interim clinical guidance and helps enact the provincial <u>Prescribed Safer Supply Policy</u>. As such, this intervention can be understood as a form of safer supply; however, this document's scope is limited to the prescription of methylphenidate and dextroamphetamine as a harm reduction approach to reduce individuals' reliance on the illicit drug supply and associated harms. Prescribed safer supply beyond these two medications is out of scope of this document. Prescribers should consult the provincial <u>Prescribed Safer Supply Policy</u> and their local regional health authority for information on facilitating access to prescribed safer supply beyond the scope of this document.

The emerging practice options described in this section do not constitute treatment for stimulant use disorder and should not be considered evidence-based practice. They should, instead, be understood as a harm reduction approach that may, with careful assessment, be trialed in order to help reduce individuals' reliance on the illicit drug supply and related harms. While all individuals with stimulant use disorder should be offered evidence-based psychosocial treatment, it is understood that some individuals are not interested in psychosocial treatment, while other individuals may continue to experiencing cravings and withdrawal symptoms despite receiving psychosocial treatment. Using a harm reduction approach to "meet patients where they are at" may help reduce overdose deaths, other drug-related harms, and engage individuals in care (e.g., primary care, psychosocial supports).

When considering a trial of prescribed stimulants to reduce overdose risk and other harms, a thorough risk/benefit assessment should be performed and document. Potential risks (e.g., diversion, stimulant-induced psychosis, new-onset stimulant use disorder) and benefits (e.g., reduced overdose risk, reduced reliance on high-risk and criminalized income-generating activities, reduced exposure to the toxic drug supply) for both individual patients and the community should be considered.

# Evidence Regarding Stimulant Replacement to Reduce Harms Associated with Illicit Stimulant Use

As outlined above, a 2020 systematic review and meta-analysis of psychostimulants for the treatment of stimulant use disorder showed a significant effect on abstinence, driven primarily by studies looking at dextroamphetamine for the treatment of cocaine use disorder. This meta-analysis is the first to provide preliminary evidence that may support the use of medications with a more "potent" agonist effect compared to medications with a less "potent" effect, and suggests that higher doses may be more effective than lower doses.<sup>60</sup>

Most of the studies included in the available 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)<sup>60-64</sup>; thus, the relative safety of stimulant prescribing for individuals with a history of or active psychiatric disease is unknown. However, data from individuals prescribed stimulants for ADHD either following hospitalization for psychosis or mania<sup>26</sup> or with concurrent bipolar disorder<sup>27</sup> shows an association between prescribed stimulants and psychosis or mania (see Cautions, below, for more information on psychosis and stimulant prescribing).

There have been additional methodological limitations in the existing literature that have made it difficult to synthesize the existing data with any certainty. For example, a wide range of outcomes have been measured, with abstinence the most commonly reported outcome.<sup>64</sup> However, abstinence may not be a possible or preferable 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.<sup>64</sup> Regarding outcomes other than abstinence, some individual studies have found statistically significant reductions in mostly secondary outcomes including cravings, positive urine drug tests, and depressive symptoms, in the context of ongoing illicit stimulant use.<sup>64</sup>

Additional stimulant medications continue to be explored, including oral lisdexamfetamine (brand name Vyvanse, among others). A 2021 phase-2, open-label, single-group study (n=16) of oral lisdexamfetamine for treatment of methamphetamine use disorder found that doses up to 250mg/day were safe and well tolerated.<sup>65</sup> 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, as well as eligibility criteria, which excluded individuals who had used dexamphetamine in the previous 4 weeks, those with a known sensitivity or previous adverse reaction, and those with known contraindications, including active psychosis, severe agitation, and high suicide risk. 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.

# Clinical Experience from Risk Mitigation Prescribing

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 <u>Current Treatment</u> <u>Options</u>, above). Prescribing stimulants per the *Risk Mitigation* interim clinical guidance represents the first wide-spread prescribing of stimulants to reduce the use of illicit stimulants. Clinical experience, as outlined below, indicates that some patients reported being able to reduce their reliance on illicit stimulants and, thus, lower their risk of overdose and other harms associated with the illicit drug supply; however, most patients did not significantly benefit from this prescribing. As the COVID-19 pandemic resolves and more individuals are fully vaccinated, the need for prescribing to support quarantine and self-isolation will decrease significantly.

It is unknown at this point whether individuals will benefit from prescribed stimulants outside of the context of COVID-19 risk. However, the increasing toxicity of the illicit drug supply requires

additional practice options in order to reduce overdose and other harms for individuals who are not interested in psychosocial treatment or those who are unable to stop or reduce their use despite psychosocial treatment and remain at high risk of harms from illicit stimulant use; limited clinical experience with *Risk Mitigation* prescribing and limited signals of efficacy in the research evidence suggest that a limited trial of prescribed stimulants as a harm reduction measure, with thorough assessment of potential benefits, harms, or lack of effect once started, may be an appropriate practice option in some situations (see <u>Assessment</u>, below, for information on eligibility, cautions, contraindications, and assessment, and <u>Assessment</u> of <u>Benefit and Continuing Care</u> for information on assessing for benefit and decision-making regarding continuing or stopping a trial of prescribed stimulants as a harm reduction measure).

According to PharmaNet<sup>66</sup> and other Ministry of Health<sup>67-69</sup> data available through the BCCDC COVID-19 Cohort (BCC19C), an estimated 1,220 people were dispensed stimulant medications from March 27, 2020, to February 28, 2021.<sup>f</sup>

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, 9 (11%) were prescribed stimulants or stimulants and opioids. The rest (89%) were prescribed other medications under the *Risk Mitigation* interim clinical guidance.

Of the 82 persons who died, 7 had an active dispensation on the day they died<sup>9</sup> (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. 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 (median 25) days for stimulant medications. In addition, a mortality rate of 8.9 deaths per 1,000 person years has been reported for individuals prescribed stimulants.

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.

<sup>&</sup>lt;sup>f</sup> 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.

<sup>&</sup>lt;sup>9</sup> To date, there is incomplete cause-of-death data for the Risk Mitigation cohort. In addition, the small number of deaths reported who had an active dispensation on the day of death precludes release of specific causes of death due to privacy considerations.

# Prescribing Stimulants to Reduce Reliance on the Illicit Drug Supply

Evidence-based psychosocial treatment remains the standard of care and should be offered to all individuals with stimulant use disorder. However, the increasing toxicity of the illicit drug supply, limited signals of efficacy, overall safety in the absence of contraindications, and lack of any other effective pharmaceutical treatment for stimulant use disorder<sup>h</sup> has led to the emergence of a trial of prescribed stimulants to reduce the risks associated with the illicit drug supply 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. However, it should be understood that this potential harm reduction measure is based on limited clinical experience and a body of literature that shows limited signals of efficacy, and has the potential to do harm to both individuals prescribed stimulants (e.g., stimulant-induced psychosis) and the community (e.g., diversion, new-onset stimulant use). The potential benefits and risks to both individual and community should be weighed when considering trialing this intervention for individuals who are not interested in psychosocial treatment or are unable to stop or reduce their use despite evidence-based psychosocial treatment and remain at high risk of harms from illicit stimulant use. 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 provincial protocols are available to guide the provision of stimulants through the <u>Prescribed</u> <u>Safer Supply Policy</u>, it is the opinion of the authors of this practice update that clinicians should use clinical judgment paired with documented thorough assessment and consideration of patient preference, patient goals, and patient and community safety to determine whether trialing prescription dextroamphetamine or methylphenidate in combination with psychosocial supports is a reasonable approach for individuals who use stimulants who decline psychosocial treatment or those who continue to experience cravings and withdrawal necessitating accessing the illicit stimulant supply despite accessing psychosocial and other treatment interventions.

*"Food, stability, safety, housing, offering CBT, counselling, support. All of these need to be part of the plan. It can't just be the stimulant prescription.* 

Stimulant prescribing should be looked at as a harm reduction piece—giving those options to someone, especially with the toxicity in the drug supply, is huge. But it's not the end-all, be-all."

— Katt Cadieux

<sup>&</sup>lt;sup>h</sup> See <u>Evidence Regarding Pharmacotherapy for Stimulant Use Disorder</u> in Part 1 of this document, for an overview of pharmacotherapy for stimulant use disorder.

The assessment, rationale, offer of referral to evidence-based psychotherapy, discussion of potential risks and benefits, and informed consent should be documented in the patient's medical record. If dextroamphetamine or methylphenidate is trialed for this purpose, an evaluation of the benefit of this intervention to the patient should be performed (see <u>Assessment and Continuing Care</u>).

Trialing prescription stimulants to reduce reliance on the illicit drug supply and related harms does not constitute treatment, and has the potential to do harm to both patient (e.g., stimulantinduced psychosis, cardiac disease) and community (e.g., diversion, potential for new-onset stimulant use disorder). A thorough risk/benefit analysis should guide clinical decision-making (see <u>Assessment</u>, below).

# Assessment

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

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

The assessment and informed consent process should include a discussion and documentation of the potential risks and benefits of prescribing stimulants as a harm reduction intervention, 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 that the patient is not benefitting from the intervention, and how the treatment plan would change if the patient is not benefitting. See <u>Appendix 2: Informed Consent</u> for an example of how to discuss the intervention and seek informed consent.

Documented assessment for eligibility should include the following:

- Active substance use assessment (i.e., type of substance, quantity used, frequency of use, route of administration, withdrawal symptoms, and cravings)
  - o 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
  - o 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?
    - What does this substance help or provide you with?

- Substance use and treatment history (including experience with *Risk Mitigation* prescribing of stimulants)
- 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)
- Patient goals (e.g., reduce use, safer use, manage cravings and withdrawal symptoms)
- Potential indicators of benefit (see <u>Assessment of Benefit and Continuing Care</u> below, which may help guide discussion indicators that patient is benefitting from the intervention)
- Stimulant use disorder diagnosis
  - o If patient has not previously received a stimulant use disorder diagnosis, assess using <u>DSM-5 criteria</u>
- Overall physical health including blood pressure
- Cardiac assessment, including hypertension and history of any cardiac conditions (see contraindications below)
- Patient goals (e.g., reduce use, safer use, manage cravings and withdrawal symptoms)
- Potential indicators of benefit (see <u>Assessment of Benefit and Continuing Care</u> below, which may help guide discussion indicators that patient is benefitting from the intervention)

# Cautions

- Use extreme caution if there is a known diagnosis or indications of psychosis or bipolar disorder or history of stimulant-induced psychosis. Prescribing stimulants may worsen mental health symptoms for individuals with these conditions. Consider consultation with a psychiatrist or addiction psychiatrist, if available
  - O A population-based case crossover study among young people (<25) receiving social assistance in Ontario who received their first prescription for a stimulant in the 180 days preceding hospitalization for psychosis or mania found that initiation of prescribed stimulants (for ADHD) was associated with an increased risk of hospitalization for psychosis or mania in the first 60 days of treatment (odds ratio: 1.86; 95%CI: 1.39 to 2.56).<sup>26</sup> Almost half of individuals (45%) who received a subsequent stimulant prescription following discharge from the hospital for psychosis or mania were readmitted for psychosis or mania (median 18 days following subsequent prescription). Note, however, that this data represents individuals' first exposure to prescribed psychostimulants. The relevance for individuals with stimulant tolerance is unknown
  - ASwedishstudyusinglinked national registries found that patients with concurrent ADHD and bipolar disorder who initiated treatment with methylphenidate had an increased risk of manic episodes within 3 months of initiation (hazard ratio: 6.7, 95%CI: 2.0 to 22.4) if they were not also taking mood stabilizers; for patients taking mood stabilizers at treatment initiation, the risk of mania in the first 3

months of treatment was reduced (hazard ratio: 0.6; 95%CI: 0.4 to 0.9)27

- A study of commercial insurance claims of youth (age 12–25) who started treatment with methylphenidate or amphetamine for ADHD (n=221,846) found that new onset psychosis occurred in approximately 1 in 660 patients,<sup>28</sup> with a higher risk of psychosis associated with amphetamines compared to methylphenidate (see <u>Medication Selection, Dosing, and Dispensation</u>, below), while a combination of outcomes across multiple trials of different stimulant medications arrived at an estimate of 1 in 400 children developing psychotic-like or manic-like symptoms<sup>70</sup>
- It should also be noted that most of the studies examining stimulant replacement excluded individuals with severe psychiatric comorbidities (e.g., psychotic or bipolar disorders, suicidal ideation, and prescription of antipsychotic medication) and/or did not assess for other common comorbidities such as ADHD<sup>60-64</sup>; thus, the relative safety of stimulant prescribing for individuals using illicit stimulants with a history of or active psychiatric disease is unknown
- o Patients with psychosis or bipolar disorder should be receiving treatment or offered or referred to treatment for these conditions when prescription psychostimulants are offered
- o 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
- o If clinical judgment indicates that the risk of overdose or anticipated benefit outweighs all other risks of harm for these patients, and psychostimulants are prescribed as a trial, close follow up is indicated
- o Treatment decision and rationale, including weighing of risks and benefits, and any consultation should be documented
- Pregnancy
  - o Extreme caution should be used
  - o Care should be provided in collaboration with the patient's obstetrician, where possible
  - o A perinatal addiction specialist should be consulted
  - o A thorough discussion of alternatives, risks, and benefits should be had with the patient, including potential risks to the fetus
  - o Safe use of dextroamphetamine in pregnancy has not been established. If considering prescribing this medication to a pregnant patient, the potential benefit must be weight against the potential harm to parent and fetus<sup>71</sup>
  - There is limited experience with use of methylphenidate in pregnant people; however, cases of neonatal cardiorespiratory toxicity have been reported. Methylphenidate should not be prescribed to pregnant people unless the potential benefit outweighs the risk to the fetus<sup>72</sup>

# Contraindications

- Do not prescribe stimulants for a person with unstable angina or moderate to severe hypertension. Prescribe with extreme caution in those with a cardiac history and document rationale. Consultation with cardiology is recommended, where available
- Dextroamphetamine:
  - o 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 patient with a cardiac condition, ensure ongoing documentation that the benefits continue to outweigh any risks
- Methylphenidate:
  - o Marked anxiety, agitation, glaucoma, motor tics, a personal or family history of Tourette's, and concurrent use of MAOIs or within 14 days of MAOI administration since hypertensive crisis may result, serious cardiac conditions (as above for dexamphetamine), allergy or intolerance to the medication or any ingredients

# 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<sup>i</sup>:
  - Dextroamphetamine SR (Dexedrine) 10–20mg PO BID provided daily with a maximum total daily dose of 40mg BID per day<sup>j</sup>

#### AND/OR

- Dextroamphetamine IR 10-20mg PO BID-TID with a maximum total daily dose of 80mg dextroamphetamine per day
  - Contraindications: 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 patient with a cardiac condition, ensure ongoing documentation that the benefits continue to outweigh any risks

OR

<sup>&</sup>lt;sup>i</sup> Dexedrine is <u>FDA Pregnancy Category 3</u>.

<sup>&</sup>lt;sup>1</sup> In some clinical practices, doses of 60mg BID are being used; however, there is limited data to support this practice.

- Prescribe methylphenidate<sup>k</sup>:
  - o Methylphenidate SR 20-40mg PO OD with maximum total daily dose of 100mg/24hrs

AND/OR

- o Methylphenidate IR 10–20mg PO BID daily to maximum total daily dose of 100mg methylphenidate per day
  - Contraindications: 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

# Medication Selection, Dosing, and Dispensation

- 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<sup>60</sup>
  - o It is unknown if risk of psychosis increases with dose; however, higher average methamphetamine dose has been associated with increased risk of stimulant-induced psychosis<sup>19</sup>
- A study of commercial insurance claims of youth (age 12–25) who started treatment with methylphenidate or amphetamine for ADHD (n=221,846) found that new onset psychosis occurred significantly more often in individuals prescribed amphetamines (hazard ratio: 1.65, 95%CI 1.31 to 2.09). It is unknown whether these findings can be extrapolated to adults with substance use disorders; however, the potential lower risk of psychosis may inform medication selection<sup>28</sup>
- The selected medication and dose should be documented in the patient's health record
- Frequency of dispensation should be guided by clinical judgment, prioritizing patient and community safety. Generally, daily dispensing should be prescribed. Exceptions should be documented

# Patient Education

The following discussion should be documented in the patient chart:

- Patients with concurrent psychotic or bipolar disorder should be warned of the potential worsening of symptoms with prescribed stimulant medications. Patients should be monitored closely and advised to stop or reduce dose and present for medical help early should this occur
- Patients should be educated on potential side effects (e.g., heart palpitations,

<sup>&</sup>lt;sup>k</sup> Methylphenidate is <u>FDA Pregnancy Category C</u>.

sleeplessness, anxiety, psychotic or manic symptoms) and advised that medication effects may be different than usually experienced with illicit stimulants

- Patients should receive consultation on safe storage (e.g., if living in an SRO or supportive housing, medication could be stored and dispensed by staff)
- Patients should receive education on harm reduction and safer use strategies (see <u>Harm Reduction</u>, in this document)

# Monitoring and Follow up

- Provide close monitoring during initiation
- Prescription length should be based on individual patients' follow-up requirements
- See Assessment of Benefit and Continuing Care, below

# Assessment of Benefit and Continuing Care

If the above assessment indicates that a trial of stimulant prescribing is appropriate, an initial trial period (i.e., 2–4 weeks) should be followed by a thorough assessment of clinical and psychosocial indicators, as well as patient goals, to determine whether the patient is benefitting from the intervention. This assessment should be documented. With patient consent, other care team members (e.g., outreach workers, social workers, primary care providers) may also provide information relevant for decision making. Patient report, clinical observation, collateral information (where possible), and objective measures should inform assessment. 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. Clear indication of patient benefit, supported by clinical judgment and aligned with patient goals, supports the continuation of this intervention. It should be noted, however, that not all of the potential benefits listed below may emerge in the initial 2- to 4-week period following initiation; it may take some time for clinician and patient to determine an optimal dose, to access relevant psychosocial supports, and for the patient to begin to stabilize. Clinical discretion should be used to determine whether a continued trial is appropriate, with appropriate documentation.

#### INDICATIONS THAT THE PATIENT IS BENEFITTING

#### Clinical

- Reduced (or cessation of) illicit stimulant use
- Reduced risk and incidence of overdose due to reduction or cessation of illicit stimulant use
- Reduced cravings
- Reduced potential communicable disease exposure and infection
- Reduced emergency department or acute care usage
- Increased engagement in primary care and other health services
- Management of withdrawal symptoms
- Patient report of improved overall well-being
- Functional outcomes such as increased focus and executive function
- Consistent urine drug tests<sup>1</sup> positive for prescribed medication(s)<sup>m</sup> and reduced number of UDT positive for illicit stimulants

#### **Psychosocial**<sup>n</sup>

- Reduced need to engage in high-risk and criminalized activities (e.g., sex work) to support substance use
- Maintaining, seeking, or gaining employment or volunteer activities
- Improved attitude toward self
- Ability to set and meet goals in major areas (e.g., personal health, career)
- Enrolled in education or training programs
- Integrating new activities
- Reconnecting with family and friends (e.g., improved social functioning)
- Attaining safe housing and accessing other social services

<sup>&</sup>lt;sup>1</sup> Information regarding detection windows and potential causes of false positives for methamphetamine and cocaine urine drug tests can be found in the BCCSU's <u>Urine Drug Testing—Breakout Resource</u>.

<sup>&</sup>lt;sup>m</sup> 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 taken instead of illicit stimulants reduces risk of overdose and other harms from the illicit drug supply. <sup>n</sup> 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.

#### 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)
  - Note that methylphenidate cannot be identified through immunoassay. Samples must be sent for confirmatory testing for "methamphetamine." The clinician should then contact the clinical biochemist, who can analyze the data and attach an appropriate comment to the report regarding the presence or absence of methylphenidate in the sample
- No change in well-being or social functioning
- Consistently missed doses
- Development or worsening of mental health issues, for example psychosis, bipolar disorder, suicidal ideation, aggression, or engaging in hazardous behaviour
- Development of physical health conditions such as new-onset angina or hypertension
- The patient not taking the medication as prescribed or selling the medication to provide increased access to illicit stimulants

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, Matrix Model, or bed-based treatment options), providing patient education and referral to harm reduction services and supplies, referral to psychosocial and community supports, trialing a different stimulant medication, 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 <u>24/7 Line</u> for assistance in determining whether the intervention is or is not beneficial, and next steps.

# Evaluation

Clinicians prescribing stimulants for individuals as a harm reduction intervention must become part of the provincial evaluation outlined in the <u>Prescribed Safer Supply</u> policy, through two avenues:

- 1. All safer supply prescribing will be captured in the health administrative data from PharmaNet
  - Dispensation of prescribed safer supply to individuals at pharmacies or clinic settings will be recorded in PharmaNet, which will be used to support provincial evaluation and monitoring efforts
  - Prescribers must indicate on the prescription that the drug is prescribed safer

supply, so that pharmacists or other practitioners are able to provide appropriate and informed care and record the prescription in different information systems. More information will be forthcoming from the Province on how to correctly record prescriptions in appropriate data systems

2. As the provincial evaluation is initiated, prescribers will be invited to engage in additional types of evaluation as appropriate

See the provincial <u>Prescribed Safer Supply</u> policy for more information on evaluation.

# Prescriber and Pharmacist Procedures for Prescribed Harm Reduction Drugs: Risk Mitigation or Prescribed Safer Supply

The safety and sustainability of the prescribed harm reduction drug options outlined in the <u>Risk</u> <u>Mitigation Interim Clinical Guidance</u>, this document, and the <u>Prescribed Safer Supply Policy</u> are predicated on ongoing fulsome monitoring and evaluation to inform program effectiveness and identify any unintended risks or harms. Accurately capturing these prescriptions in PharmaNet is essential to enable comprehensive and rigorous evaluation.

Most of the drugs prescribed as alternatives to support people to reduce their reliance on the toxic illicit drug supply, both for risk mitigation and as a safer supply alternative, are used for additional indications; therefore, prescriptions for harm reduction and safer supply must be distinguished from other indications (e.g., ADHD). Prescribers and pharmacists are therefore being asked to assist as follows:

#### Instructions for Prescribers:

Any prescription written for a drug to be used as an alternative to the toxic street supply including prescriptions written for risk mitigation during the dual public health emergencies or as a safer supply option should clearly include "SA" in the Directions for Use or "comments" section of the prescription, BELOW the instructions written on the form. This code is not part of the official instructions but indicates to the dispensing pharmacist that the prescription is to be tagged with the non-public facing code that will allow the prescription to be identified in the PharmaNet database. An example follows.

	DR. WENDY OSLER 543 21st St. Any town BC V2K 2B6 Tel: 250-999-9911 Fax: 250-999-9119	
NAME: PHONE: PHN: DOB: ADDR: DATE:	SMITH, Jill         (250) 999-0000         01233 456 789         12-December-1982         123 45th St         Anytown BC V3T 929         1 Apr 2020         1) Methylphenidate Tab 10mg IR         Take one tablet PO twice daily         Dispense: 46 tablet(s)	
	Directions - For Pharmacist: Daily dispensed, not witnessed Rx: April 1 – 23/2020 (23 days) SA	
	Signature MSP: 00000 CPSID: 07811	

#### Instructions for the Pharmacist:

When a prescription for any drug that is identified as a safer alternative is processed (new or refill/part-fill prescription), it should be entered per usual prescription entry standards with the addition of an "SA" intervention code in the customary intervention code section of the software, not the Directions for Use ("sig") section. This code goes in the intervention code field and is simply a tag on the prescription that can be captured when monitoring and evaluating these harm reduction prescriptions for program evaluation. Entry of the intervention code with each prescription fill is the only action required on the pharmacist's part and has no monetary reimbursement attached.

#### Drugs to be Included

Any drug prescribed for risk mitigation to support self-isolation or quarantine due to COVID-19 or drugs prescribed for safer supply should be identified on the prescription and tagged with the "SA" intervention code upon entry into PharmaNet. The list below identifies the medications included in this practice update, but all drugs prescribed for prescribed safer supply should be identified as per above:

#### Stimulants

All those prescribed for risk mitigation or prescribed safer supply, which include:

- Dextroamphetamine IR or SR
- Methylphenidate IR or SR

#### 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 engagement 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)
- Providing non-judgmental support and social connection
- Accompanying patients to appointments, if requested
- Facilitating access to treatment, harm reduction, and primary care services (e.g., vaccination)
- Helping patients to navigate challenges accessing treatments or interventions

"The peer engagement part is actually where the success came from for me. I completed a 6-month treatment program but the community I moved back to lacked any aftercare. I learned of the Risk Mitigation guidance through doing peer work and got prescribed stimulants as a harm reduction approach for my use. Since then, there has been a huge decrease in my illicit substance use."

— Shawn W., Indigenous Peer Navigator

# Patient Education and Informed Consent

The informed consent process should include a discussion of the potential risks and benefits of this intervention, as well as a discussion of continuing care (see <u>Appendix 2</u>) and harm reduction education. 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. The discussion of patient education and informed consent should be documented.

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 <u>Safer Tablet Injection: A Resource for Clinicians Providing Care to Patients Who May Inject Oral Formulations</u> for more information. See <u>Harm Reduction</u>, in this document, for more information on safer smoking and injecting practices.

# APPENDIX 1: DSM-5 CLINICAL DIAGNOSTIC CRITERIA FOR SUBSTANCE USE DISORDER

DSM-5 Criteria for Stimulant Use Disorder <sup>o</sup>				
1.	Stimulants are often taken in larger amounts or over a longer period than was intended			
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	The presence of at least 2 of these symptoms		
6.	Continued stimulant use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of stimulants	The severity of the stimulant use disorder is defined as:		
7.	Important social, occupational, or recreational activities are given up or reduced because of stimulant use	MILD: The presence of 2 to 3 symptoms MODERATE: The presence of 4 to 5 symptoms		
8.	Recurrent stimulant use in situations in which it is physically hazardous	SEVERE: The presence of 6 or more symptoms		
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.	<ul> <li>Tolerance, as defined by either of the following:</li> <li>a. Need for markedly increased amounts of stimulants to achieve intoxication or desired effect</li> <li>b. Markedly diminished effect with continued use of the same amount of stimulant</li> </ul>			
11.	<ul><li>Withdrawal, as manifested by either of the following:</li><li>a. Characteristic stimulant withdrawal syndrome</li><li>b. Same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms</li></ul>			

<sup>°</sup> Adapted from the American Psychiatric Association.73

# **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 <u>Consent: A Guide for Canadian Physicians</u> and The Canadian Nurses Protective Society's <u>Consent to Treatment: The Role of the Nurse</u>. In addition, nurse practitioners must meet the BC College of Nurses and Midwives (BCCNM)'s <u>Consent Practice Standard</u>. 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 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., known risks associated with stimulant prescribing) should be described.

**Note:** If prescriber is participating in provincial evaluation, a discussion of the evaluation and use of patient data should be included in the consent process.

2. Describe eligibility

*Eligibility considerations for this intervention include:* 

Ongoing active stimulant use

AND

• At high risk of overdose or other harms related to 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. takehome 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

# **APPENDIX 3: AUTHORSHIP LIST**

This practice update was developed by the authorship committee listed below. As part of the development process, broad consultation was sought from key stakeholders, including health systems partners, prescribers and other clinicians across BC, the VCH Concurrent Disorders Technical Panel, and people with lived and living experience.

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