

# Possible benefits of providing safe supply of substances to people who use drugs during public health emergencies such as the COVID-19 pandemic

## ? Questions

- What are possible benefits of providing a safe supply of substances to people who use drugs during public health emergencies such as the COVID-19 pandemic?

## 🔑 Key Take-Home Messages

- Safe supply is an approach that focuses on saving lives by prescribing pharmaceutical grade substances such as opioids and stimulants to individuals at risk of overdose (1) and does not include substitution or opioid agonist treatments, such as methadone, buprenorphine/suboxone, or slow release oral morphine, as these therapies do not contain the mind/body altering properties that people seek in recreational drugs (2).
- Safe supply initiatives have begun in Canadian cities including Toronto (3), London and Ottawa without any overdose related deaths (4, 5), and Vancouver has begun a pilot program that dispenses prescribed hydromorphone (Dilaudid) tablets (6).
- We found no peer-reviewed literature regarding the potential benefits or harms of safe supply programs. However, we did find some evidence related to substitution treatments. Clinical trials that compared slow release oral morphine to methadone found that those in the slow release oral morphine group had: fewer heroin cravings (7, 8), a statistically significant improvement in mental symptoms and treatment satisfaction (9), and similar retention rates and safety outcomes as the methadone treatment group (10).
- Canadian clinical trials have found that among severe opioid dependent users, injectable diacetylmorphine (pharmaceutical heroin) was more effective in retaining participants and reducing rates of illicit drug use or other illegal activity than methadone (11). Hydromorphone is as

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effective as diacetylmorphine for subgroups of individuals with severe opioid use disorder (12), indicating that these treatments may be effective for patients who are resistant to or unsuccessful with other types of treatment.

- There is a call for efforts to address safe supply needs through pharmacological stimulant-based interventions that provide larger doses with greater frequency with methylphenidate and extended-release amphetamines as potential treatment candidates (13).

## The Issue and Why it's Important

Between 2016 and 2018, over 10,000 individuals have died due to an opioid-related overdose in Canada (1). Between January and September of 2018, 73% of accidental opioid-related deaths involved fentanyl or fentanyl analogues (1), a powerful opioid that can cause overdose and death, even when used in small amounts (14). The growing number of overdose deaths has increased concerns about people buying street drugs not knowing what is in them. Safe supply is defined as “an approach that focuses on saving lives by using existing pharmaceutical-grade medications as an alternative to highly toxic street drugs for people at risk of overdose” (1).

The current coronavirus (COVID-19) pandemic has increased the health risks for people who use drugs, such as experiencing withdrawal because of a disruption to the supply chain of illicit drugs and/or using alone while in self-isolation or quarantined to prevent community spread of the virus (15). Individuals who use drugs may also have co-morbidities such as heart, lung conditions, or compromised immune systems that put them at a higher risk of contracting the coronavirus (16).

In response to these dual public health emergencies, temporary exemptions have been made to the *Controlled Substances Act* as of March 19, 2020 (17). These temporary exemptions have:

- Authorized prescribers to refill or extend verbally (e.g. over the phone) prescriptions for controlled substances such as hydromorphone, stimulants, benzodiazepines (17).
- Permitted pharmacists to extend prescriptions as well as transfer prescriptions to another pharmacy.
- Allowed pharmacy employees to deliver these controlled substances to patient homes or other locations (1).

With these exemptions in place, the British Columbia Centre on Substance Use has developed new guidelines to simultaneously support people who use drugs and to prevent the spread of

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11. Oviedo-Joekes E, Brissette S, Marsh DC, Lauzon P, Guh D, Anis A, et al. Diacetylmorphine versus methadone for the treatment of opioid addiction. *New England Journal of Medicine*. 2009;361(8):777–86.

COVID-19 (15). As street drugs may become more limited and toxic due to the COVID-19 pandemic, the guidelines suggest providing eligible people who use drugs with prescribed substances such as stimulants or opioids to help them maintain social distancing and avoid the illicit street market (17). In Ontario, an open letter signed by 111 organizations and 693 individuals was sent to the Deputy Premier and Minister of Health and the Associate Minister, Mental Health and Addictions in April 2020, calling for expanded access to emergency safe supply in the province (18).

The purpose of this rapid response is to describe the benefits of providing a safe supply to people who use drugs with a focus on depressants (opioids) and stimulants. This includes examining what safe supply is, the effectiveness of various substances that can be used as safe supply, and examples where safe supply programs have been initiated in Canada.

## What We Found

### Safe supply

The Canadian Association of People who Use Drugs (CAPUD) states that “safe supply refers to a legal and regulated supply of drugs with mind/body altering properties that traditionally have been accessible only through the illicit drug market” (2). Safe supply does not include substitution or agonist treatments, such as methadone, buprenorphine/suboxone, or slow release oral morphine, as these therapies do not contain the mind/body altering properties that people seek in recreational drugs (2). Safe supply involves providing individuals with prescribed medications to take home (also known as “carries”); individuals may receive a day’s or up to a week’s supply of tablets at a time (19). Supervision of consumption is not required, although prescribers often encourage patients to take their pills at a supervised consumption site (19).

We found no peer-reviewed literature on the potential benefits or harms of safe supply programs. However, proponents of safe supply note several factors that support the approach, including:

- A significant population of opioid drug users are not ready to give up the high that comes with opioids (20).
- Medications such as methadone and buprenorphine, which are intended to reduce cravings and keep withdrawal symptoms in check, are not successful among all patients (5).
- Despite comprehensive systems of substance use disorder treatment, the rates of relapse are still high in North America, and many people who use drugs have little to no interest in seeking treatment (21).

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## Slow release oral morphine

One systematic review published in 2013 evaluated the efficacy of slow release oral morphine for opioid dependence compared to other maintenance treatments (22). Amounts of slow release oral morphine provided to participants in the included studies was as low as 60mg/day (23) and ranged up to 800mg/day (23, 24). The review found that slow release oral morphine performed just as well as other maintenance treatments in outcomes such as participants' mental health and social function but withdrawal symptoms were worse when compared to methadone (22). The slow release oral morphine was well tolerated and seemed to reduce cravings, depression symptomatology, physical complaints, and anxiety symptoms (22, 25).

A rapid response produced by the Canadian Agency for Drugs and Technologies in Health (CADTH) reported on five randomized controlled trials published prior to 2017 which examined the use of slow release oral morphine with methadone as a comparator (25). Three of the trials identified the average daily dose of slow release oral morphine which ranged from approximately 774–832mg/day (7, 8, 10). One of these trials, set in both Germany and Switzerland, allowed participants to take home up to a five-day supply (8). Two trials found that general cravings for heroin decreased among those in the slow release oral morphine treatment groups (7, 8) and one found that cravings for cocaine were not different between the two treatment groups (7). Another trial found a statistically significant improvement in mental symptoms and treatment satisfaction among the slow release oral morphine treatment group (9), another found that retention rates and safety outcomes were similar between the two treatment groups (10), and a third found no statistically significant differences between treatment groups in any of the outcomes examined (26).

## Hydromorphone and diacetylmorphine

The North American Opiate Medication Initiative (NAOMI) trial, conducted in Vancouver from 2005 to 2008, compared injectable diacetylmorphine (pharmaceutical heroin) with oral methadone maintenance therapy in patients with opioid dependence that did not respond to treatment (11). This study found that injectable diacetylmorphine was more effective in retaining participants and reducing rates of illicit drug use or other illegal activity (11). The NAOMI trial was later followed by the Study to Assess Longer-term Opioid Medication Effectiveness (SALOME) trial conducted from 2011 to 2013 (12). Since diacetylmorphine is difficult to access around the world due to political and regulatory barriers, SALOME tested whether an already available drug – hydromorphone (Dilaudid) – could perform as well as diacetylmorphine (12). Participants self-administered doses of either substance up to three times per day on site (400mg per dose, up to 1000mg per day) under supervision

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(12). Findings suggested that hydromorphone was as effective as diacetylmorphine as treatment for subgroups of individuals with severe opioid use disorder (12). In 2019, Canada was the first country to approve injectable hydromorphone as a treatment for severe opioid use disorder as studies indicate that injectable hydromorphone has been able to support some individuals with opioid use disorder and increase retention rates in treatment programs (1).

Pooled analyses of other trials examining injectable heroin have found that patients often stopped using street heroin within six months, showed improvements in health, and had a decrease in criminal activity (27, 28).

Three clinical trials that took place in Europe examined the use of pharmaceutical heroin compared to methadone (26, 29, 30). Treatments provided in the trials varied: an injectable solution of heroin-hydrochloride or as an inhalable mixture of heroin-base and caffeine in addition to continued methadone maintenance treatment (30); as injectable or inhalable diacetylmorphine (29); or as oral immediate release diacetylmorphine (26). Doses of heroin in two of the trials were 400mg per visit, up to 1000mg per day and were provided to participants in supervised treatment centres (29, 30). Due to the risks of overdose, diversion, and misuse of injectable diacetylmorphine or hydromorphone, clinical trials included supervised administration in order to safely mitigate and treat potential fatal overdoses (31, 32). Findings stated that patients on heroin assistance therapy who did not respond to other treatments had greater improvements in their mental and physical health (29), reported less use of illicit street heroin than those on the methadone treatment (29, 30), or found no statistically significant difference in clinical outcomes between treatment groups (26) – indicating that pharmaceutical heroin may be a successful treatment for these individuals.

## Opioid safe supply

Currently there are various safe supply initiatives running in Canada with the use of pharmaceutical-grade opioids, including “Safer Supply”, a program at the London Intercommunity Health Centre in London, Ontario, run by Dr. Andrea Sereda (20). Safer Supply has prescribed hydromorphone tablets (an average of 116mg per person per day) and/or slow release oral morphine tablets (an average of 300mg per person per day) to over 100 high-risk individuals since 2016 (20, 33). Participants receive daily doses of hydromorphone and a select number of participants receive weekly carries (33). At intake, all enrolled participants used drugs via injection and 29% of participants had infectious complications such as endocarditis (33). Furthermore, 79% were living with HCV and 27% were living with HIV (47% of which had non-suppressed viremia) (33). As of 2019, there were no fatal overdoses in the group, and participants have

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made gains in health and social functioning (5). A chart review of participants in October 2019 found a reduction in harmful drug use with 25% of participants switching to oral drug use only and another 13% switching to a combination of oral and injection drug use (33). In the past four years, there were no new cases of endocarditis (33). Furthermore, 26% of those living with HCV were engaged in treatment and the rate of non-suppressed viremia among those living with HIV was reduced to 10% (33). Other social outcomes included decreases in the number of participants experiencing homelessness, participating in crime, or taking part in sex work (33). Three deaths occurred: one was unrelated to injection drug use; and the other two were related to infectious complications among participants who had uncontrolled health conditions and frequent hospital admissions for sepsis upon entering Safer Supply (33).

A similar program is run in Ottawa by Dr. Jeff Turnbull, who began the first residential Managed Opioid Program (MOP) in 2017 (4). The residential MOP provides 25 participants with housing as well as intravenous doses of hydromorphone or slow release oral morphine (Kadian) up to seven times per day, injected under the supervision of a nurse (34). There had not been any overdoses or deaths in its first year of operation, and there are currently more than 50 participants on the waitlist for this program (4). In Toronto, Dr. Nanky Rai began prescribing hydromorphone tablets in 2019 at the Parkdale Queen West Community Health Centre in Toronto to approximately 10 patients who have reportedly seen an improved quality of life (3). Dr. Mark Tyndall is the founder of an automated machine called MySafe, which dispenses prescribed hydromorphone tablets up to four times per day to high-risk opioid addicts in Vancouver's Downtown Eastside (6). MySafe uses a scanner to recognize the unique vein pattern of an individual's hand and can hold five days worth of drugs for up to 48 participants (6). One concern regarding dispensing drugs is that these substances will end up on the street, but Dr. Tyndall states that this would still be a better alternative than having individuals using a toxic street supply (6), as long as the dispensed drugs are not being diverted to "new" users.

## Stimulant safe supply

A 2020 commentary in the Harm Reduction Journal by Fleming *et al.* calls for a safe supply of stimulant substances and the meaningful involvement of people who use stimulants in planning such interventions (13). From 2016 to 2017 in British Columbia, cocaine was found in over 50% and methamphetamine in over 33% of illicit drug overdose deaths, respectively (35). There have not been any trials to date that have utilized doses which allow users to achieve the desired high associated with using stimulants such as cocaine or methamphetamine (13). The authors of the commentary call for efforts to address safe supply needs through pharmacological stimulant-based interventions that provide larger doses at higher

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frequency with methylphenidate and extended-release amphetamines as potential treatment candidates (13).

## Conclusion

Safe supply may be a viable option for eligible participants who do not tolerate, use, or desire substitution treatments as well as those who use street drugs in addition to substitution treatments. Further research is recommended to support evidence informed decision-making on safe supply substances, doses, and delivery methods as well as research to determine the cost-effectiveness, safety, benefits (19), and long-term outcomes of such programs.

## Factors That May Impact Local Applicability

It is important to note that the context of the studies included in the systematic reviews and the individual clinical trials differ from the current opioid overdose crisis and COVID-19 pandemic. Furthermore, the majority of these clinical trials were part of supervised treatment programs which aimed to reduce opioid drug use while safe supply differs in that it is focused on harm reduction with the goal of decreasing the risk of overdose as a result of using toxic street drugs (19).

## What We Did

We searched Medline, Embase and PsycInfo using a combination of text terms safe supply and/or safe supplies. Searches were conducted on April 1, 2020, and results limited to articles published since 2000. Reference lists of identified articles were also searched. Google (grey literature) searches using terms of safe supply, substance use, opioid, stimulant, heroin, diacetylmorphine, hydromorphone were also conducted. The search yielded 208 references from which 35 were included.

## Rapid Response: Evidence into Action

The OHTN Rapid Response Service offers quick access to research evidence to help inform decision making, service delivery and advocacy. In response to a question from the field, the Rapid Response Team reviews the scientific and grey literature, consults with experts, and prepares a review summarizing the current evidence and its implications for policy and practice.

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