McMaster University | HEALTH FORUM

Rapid Synthesis

Impacts, monitoring, and mitigation of diversion of prescription medications provided through safe supply prescriptions

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Context

- In March 2020, British Columbia (B.C.) became the first jurisdiction to launch a province-wide Prescribed Alternatives policy to allow individuals at risk of overdose to receive pharmaceutical-grade opioids prescribed by a physician or nurse practitioner.(1)
- Although research on the Prescribed Alternatives programs is still growing, initial research has pointed to the potential for these programs to provide benefits, including by reducing overdose and all-cause mortality. (2; 3)
- Still, concerns have been raised regarding the potential for harm from these programs, including potential population-level harms occurring through diversion, which can inadvertently lead to increased access and availability of opioids.(4)
- Diversion, broadly, can be understood as redirecting prescribed medications to others either voluntarily (e.g., for illicit use, diplacement or unintended use, or to sell or share medications) or involuntarily.
- In addition to the Prescribed Safer Supply Policy Direction and other Prescribed Alternatives programs in B.C., programs in other jurisdictions can also provide insights about the potential impacts, monitoring activities, and mitigation strategies for diversion of prescribed medication.
- Taking stock of diversion impacts, monitoring, and mitigation strategies across these programs can help inform policy action related to the safer opioid supply policy, as well as other approaches to reduce the potential harms of prescribed medication diversion.

Box 1: Evidence and other types of information

+ Global evidence drawn upon

Evidence syntheses selected based on relevance, quality, and recency of search

+ Forms of domestic evidence used (🍁 = Canadian)

Evaluation

Qualitative insights

+ Other types of information used

Jurisdictional scan (six countries: BE, CA (BC, ON, NS), CH, DE, ES, NL, UK)

*** Additional notable features**

Prepared in 30 business days

Questions

- What are the impacts of diversion of prescription medications for use by others (e.g., through sharing or selling to others) that were provided through safer supply prescriptions for people who use substances and at high risk for overdose?
- How is the diversion of prescription medications provided through safer supply prescriptions measured and monitored over time?

- What is known about how to mitigate the diversion of prescription medications provided through safer supply prescriptions?

High-level summary of key findings

Key findings from research evidence

- We identified six evidence syntheses and 10 primary studies, most of which were identified as being of medium or low relevance to the research questions.
- Overall, the included evidence is mixed and very few of the included evidence documents directly examine the impacts of diversion of prescribed opioids.
- No direct benefits from diversion of prescription medications for use by others were identified from the literature, but it was found that diversion may lead to increased risks such as overdose, viral infections, criminal activity, costs, and hospitalizations, but the impacts directly attributable to diversion are unclear and not all of this evidence is specific to safer opioid supply or Prescribed Alternatives programs.
- The extent of diversion of prescription medications provided through safe supply prescriptions is largely unknown, with methods like prescription monitoring, pill counts, and behavioural observation most often used to evaluate diversion in other programs, but their applicability for safer opioid supply programs may be limited.
- Mitigation measures for the diversion of prescription medications can include providing adequate dosing, offering preferred medication options, involving people who use drugs in program design, implementing secure storage/monitoring protocols, and providing community education.

Key findings from jurisdictional scans

- We identified jurisdictional experiences by hand searching government and stakeholder websites for information relevant to the question from six countries including Belgium, Germany, Netherlands, Spain, Switzerland, and the United Kingdom, as well as three Canadian provinces (British Columbia, Ontario, and Nova Scotia).

Box 2: Approach and supporting materials

At the beginning of each rapid synthesis and through its development, we engage subject matter experts who help us to scope the question and ensure relevant context is taken into account in the summary of the evidence.

We identified evidence addressing the question by searching Health Systems Evidence, as well as Medline and Embase via Ovid, to identify evidence syntheses, protocols for evidence syntheses, and primary studies. All searches were conducted on 3 May 2024. The search strategies used are included in Appendix 1. We identified jurisdictional experiences by hand searching government and stakeholder websites for information relevant to the question from six countries including Belgium, Germany, Netherlands, Spain, Switzerland, and the United Kingdom, as well as three Canadian provinces (British Columbia, Ontario, and Nova Scotia).

In contrast to our rapid evidence profiles, which provide an overview and insights from relevant documents, this rapid synthesis provides an in-depth understanding of the evidence.

We appraised the methodological quality of evidence syntheses that were deemed to be highly relevant using the first version of the AMSTAR tool. AMSTAR rates overall quality on a scale of 0 to 11, where 11/11 represents a review of the highest quality, medium-quality evidence syntheses are those with scores between four and seven, and low-quality evidence syntheses are those with scores less than four. The AMSTAR tool was developed to assess reviews focused on clinical interventions, so not all criteria apply to evidence syntheses pertaining to delivery, financial, or governance arrangements within health systems or implementation strategies.

A separate appendix document includes:
1) methodological details (Appendix 1)
2) a summary table of key findings from included evidence documents (Appendix 2)
3) a summary table of experiences from other countries and select Canadian provinces and territories (Appendix 3)
4) details from each included evidence synthesis (Appendix 4) and single study (Appendix 5)
5) details about the experiences from other countries and from Canadian provinces (Appendix 6)
6) documents excluded at the final stages of reviewing (Appendix 7).

- Although all of these jurisdictions reported programs to provide safe supply for take-home, unobserved dosing and/or other approaches that may have insights for diversion from take-home, unobserved dosing (e.g., opioid agonist treatment, injectable opioid agonist treatment), the impacts of programs are generally examined at a population-level and were not sensitive enough to identify impacts of diversion compared to the program operating as intended.
- In B.C., there is currently limited evidence on the scale of hydromorphone diversion occurring among clients of the prescribed safer supply program, and while there are anecdotal reports suggesting youth involvement, population-level data does not indicate an increase in opioid use disorder among youth.
- Jurisdictions generally employ registries to monitor prescription trends for potential diversion, with examples including Belgium's opioid substitution treatment registry and the Narcotics Monitoring System in Ontario.
- Monitoring efforts also include protocols in B.C. instructing prescribers to tag safer supply prescriptions with an identifying code in PharmaNet and the U.K.'s Yellow Card Scheme to monitor adverse drug dependence outcomes, including those that may be linked to diversion.
- To help prevent diversion, Ontario and B.C. both have patch-for-patch programs that require the return of fentanyl patches before new ones are issued.
- A key motivation for diversion appears to be insufficient access to appropriate medication and dosing through safer supply programs, suggesting that diversion can be mitigated by addressing dissatisfaction with prescribed medication efficacy.

Framework to organize what we looked for

We organized our findings using the framework below.

- Type of substances that could be diverted for use by others
  - Opioids
    - Fentanyl patches, tablets, and inhalable compounded options (e.g., Duragesic®, Fentora®)
    - Hydromorphone tablets, injectables, and inhalable compounded options (e.g., Dilaudid®)
    - Morphine injectable, and immediate or sustained release tablets/capsules, except when prescribed for OAT (e,g., M-Eslon®, Kadian®)
    - Oxycodone immediate and sustained release formulations (e.g., Oxycontin®)
    - Sufentanil injection
    - Diacetylmorphine (DAM)
  - Stimulants
    - Dextroamphetamine (e.g., Dexadrine®)
    - Methylphenidate (e.g., Ritalin®, Concerta®)
    - Other stimulants prescribed for harm reduction (e.g., Adderall®)
  - Benzodiazepines
    - Diazepam (e.g., Valium®)
    - Clonazepam
    - Any other benzodiazepines prescribed for harm reduction (e.g., Ativan®)
- Features of safe supply prescription program
  - Type of safe supply prescriptions
    - Safe supply for take-home, unobserved dosing
    - Other approaches that may have insights for diversion from take-home, unobserved dosing
      - Injectable opioid agonist treatment programs (iOAT)
      - Supervised tablet injectable opioid agonist therapy (TiOAT)
  - Where are safe supply prescriptions are provided
    - Hospitals (inpatient)
    - Hospitals (outpatient)
    - Community pharmacies
    - Community-based health organizations

    - Who provides the safe supply prescription
        - Physician
        - Pharmacist
        - Nurse or nurse practitioner
- Monitoring and evaluation approaches
    - Analysis of substances seized through drug enforcement (e.g., if distinguishing features available for medications made available through safer prescribing)
    - Drug testing (e.g., urine drug screening, through autopsies) for chemical identifiers in safe supply prescriptions
    - Self-report
        - Interview
        - Survey
    - Public reporting of monitoring and evaluation
- Strategies to mitigate diversion
    - Making safe supply visually distinct (e.g., unique shapes, colours, and packaging)
    - Incorporating chemical identifiers
    - Prescription monitoring
    - Drug return programs
    - Witnessed dosing and/or consumption
- Impacts of diversion
    - Re-sale of substances provided through safe supply prescriptions
    - Safety of street drug supply
    - Overdose mortality among people using diverted prescription opioids
    - Public acceptance of safe supply prescription programs
    - Crime
    - Other

What we found

We identified 16 evidence documents relevant to the question, of which we deemed two to be highly relevant and eight of medium relevance. The highly relevant evidence documents include the following two medium- and low-quality evidence syntheses:

- Primary prevention of prescription opioid diversion: A systematic review of medication disposal interventions (AMSTAR rating 7/10; search last conducted 2019)
- The impact of misuse and diversion of opioid substitution treatment medicines: Evidence review and expert consensus (AMSTAR rating 3/9; search last conducted 2014).

We outline in narrative form below our key findings related to the question from highly relevant evidence documents and based on experiences from the jurisdictional scan of six countries (Belgium, Germany, Netherlands, Spain, Switzerland, and the United Kingdom), as well as three Canadian provinces (British Columbia, Ontario, and Nova Scotia) (see Box 2 for more details).

A summary of the evidence organized by three framework elements (monitoring and evaluation approaches, strategies to mitigate diversion, and impacts of diversion) is provided in Appendix 2, while a summary of the experiences from other countries and from Canadian provinces is provided in Appendix 3. Detailed data extractions from each of the included evidence documents is provided in Appendices 4 and 5 and greater details about the experiences from other countries and from Canadian provinces is provided in Appendix 6. Hyperlinks for documents excluded at the final stage of reviewing in Appendix 7.

Key findings from relevant evidence sources

Q1: What are the impacts of diversion of prescription medications for use by others (e.g., through sharing or selling to others) that were provided through safer supply prescriptions for people who use substances and at high risk for overdose?

Overall, the included evidence is mixed and very few studies directly examine the impacts of diversion of prescribed opioids. Some research on safer opioid supply programs highlight that diversion generally occurs between networks of persons who use drugs for compassionate reasons. For example, in a qualitative program evaluation, a number of Safer Opioid Supply participants in Ottawa, Canada, acknowledged that diversion of medication does occur, and often occurs because people wanted to trade their hydromorphone (Dilaudid) for fentanyl, as the hydromorphone provided was not enough to meet their needs, or because they wanted to support and share with other persons who use drugs. Participants (clients) generally did not feel that diversion was a central issue, as diversion was done between people already using the substances.(5) Similarly, a medium-quality rapid review on safer opioid supply programs found that reasons for diversion often include 'compassionate sharing' with others unable to access treatment, inadequate access to opioids at doses that met their needs, and financial needs. The same review also found that despite concerns regarding the diversion of drugs, in particular hydromorphone, population-level analyses of mortality data have not found increases in hydromorphone-related deaths in Ontario and B.C. These studies suggest that while diversion does occur, its impacts on opioid-naïve populations may be limited.(6)

However, other research emphasizes the importance of addressing diversion, as the potential impacts to both the individual diverting and others around them warrant cause for concern. A low-quality evidence synthesis and expert consensus on the misuse and diversion of opioid antagonist treatment (OAT) medicines found that direct impacts to the individual include failure to progress in recovery (which can in turn lead to negative effects on health such as overdose and health risks associated with injecting behaviour), while potential impacts on others include unsupervised use, unintended exposure of children to diverted medication, and drug-related criminal behaviour. Across studies evaluating the diversion of OAT medications, reported rates of selling, giving away or swapping OAT medications range from 16% in Portugal and Greece (where 21% and 78% of dosing is supervised, respectively), to 39% in France (where 26% of dosing is supervised). The evidence review and expert consensus highlights the importance of mitigating these potential impacts by reducing misuse and diversion while ensuring the best possible care during the treatment for opioid dependence, which is essential and must be supported.(7) Although the focus of safer opioid supply programs is on harm mitigation (i.e., by reducing overdose), rather than as a treatment with the goal of recovery, these findings from OAT programs provide potentially relevant additional considerations for opioid supply programs.

In addition, a cohort study on the Safer Opioid Supply policy in British Columbia suggested that safer opioid supply policies were associated with an increase in provincial rates of opioid-related hospitalizations after two years, but this ecological analysis was not able to determine what proportion of hospitalizations were related to Safer Opioid Supply diversion as opposed to other reasons (e.g., increased substance use, toxicity of street drug supply). As a result, it is difficult for the findings to directly evaluate population-level impacts of safer supply medication diversion.(8) However, a separate population-based cohort study on opioid and stimulant Risk Mitigation Guidance (RMG) using individual-level data found a reduction in all-cause mortality and overdose-related mortality.(3) Similarly, a shelter-based safer supply program evaluation highlighted beneficial effects through contributing to decreased non-fatal overdoses within shelter settings.(9) Again, the specific impact of diversion was unclear. Overall, little data exists to adequately understand the amount of diversion that has occurred or is likely to occur in safer opioid supply programs and attempts to understand the impacts of diversion are limited and indirectly evaluated. However, the limited evidence available from OAT programs seems to suggest that diversion is likely prevalent (ranging between 16% and 39% in a low-quality review) and may occur more often among networks of persons who use drugs (rather than people with limited drug experience). While it is important to note that diversion rates among OAT programs may not translate to safer opioid supply programs, they nonetheless may provide some insights about what range safer opioid supply medication diversion may fall into.

Q2: How is the diversion of prescription medications provided through safe supply prescriptions measured and monitored over time?

The reviewed studies indicated that measuring the full extent of diversion from safer supply programs over time remains a challenge. Multiple studies acknowledged that the full extent of diversion occurring is largely unknown.(5; 6) Some methods employed to attempt to detect and track diversion include prescription drug monitoring programs that collect dispensing data,(10) routine pill counts and drug screening by health providers, and observing concerning behaviours of patients or family members.(11) However, the reviewed studies indicate a need for more comprehensive and standardized approaches to reliably quantify diversion rates across different safer supply program models. Additionally, the applicability of these approaches may be limited for safer opioid supply programs, given that these programs dispense daily.

Q3: What is known about how to mitigate the diversion of prescription medications provided through safe supply prescriptions?

Included studies identified several potential strategies to help mitigate and reduce diversion of medications provided via safer supply prescriptions. A qualitative program evaluation and medium-quality rapid review found that ensuring adequate dosing levels through the programs was highlighted as important, as inadequate doses can increase motivations to divert drugs out of desperation to meet their needs to address withdrawal.(5; 6) A retrospective case series study and a thematic analysis using interviews found that involving people who use drugs directly in the design and delivery of safer supply initiatives was also noted as helping to tailor programs to meet participants' needs and preferred medication options such as fentanyl patches.(12; 13) Implementing secure storage requirements, staff training on diversion, and monitoring protocols within healthcare facilities can also prevent insider diversion.(14; 15) A medium-quality systematic review on non-medical use of prescription stimulants found that community-based education campaigns on the risks and harms of diversion were also noted as potentially being valuable.(16) Finally, a medium-quality systematic review found that providing medication disposal bags was found to be more effective than education alone for proper disposal of unused medications.(17) Experiences with hospital-based diversion prevention practices such as disposal bags may not be able to provide relevant insights for safer opioid supply diversion prevention, given that they are generally dispensed daily, highlighting the need for a comprehensive approach specific to safer opioid supply. Given this, a multi-pronged approach addressing dosing, medication options, program design, secure handling, and education may be required.

Key findings from jurisdictional scans

Q1: What are the impacts of diversion of prescription medications for use by others (e.g., through sharing or selling to others) that were provided through safer supply prescriptions for people who use substances and at high risk for overdose?

Although all jurisdictions were found to have programs to provide safe supply for take-home, unobserved dosing and/or other approaches that may have insights for diversion from take-home, unobserved dosing (e.g., injectable opioid antagonist treatment), most jurisdictions did not provide evidence or reports about the potential impacts of diversion for these programs. The impacts of programs are generally examined at a population-level and were not sensitive enough to identify impacts of diversion compared to the program operating as intended. For example, in the U.K., efforts are being made to establish pilot Safer Drug Consumption Facilities, which are thought to contribute to improvements in street drug safety and crime by reducing public injection and injection-related litter. Some programs such as Heroin Assisted Treatment in Switzerland have been successful in reducing crime rates associated with drug procurement, but do not provide insights about these outcomes specifically in relation to diversion.

In Canada, a report from B.C. highlighting that clients of the prescribed safer supply program reported diverting hydromorphone to obtain other substances that better meet their needs or to support others who may not be able to access safer supply. Additionally, while some anecdotal reports suggest that youth may increasingly be accessing diverted hydromorphone, current B.C. data does not indicate an increase in opioid use disorder among youth. In addition, the B.C. Coroners Service found no additional increase in deaths among youth related to unregulated drug toxicity (which includes controlled drugs as well as medications not prescribed to the user).

Q2: How is the diversion of prescription medications provided through safe supply prescriptions measured and monitored over time?

Across jurisdictions, we found that measurement and monitoring of the diversion of prescription medications over time is generally conducted using registries that allow for the analysis of prescription trends to identify activities potentially indicative of diversion. For example, in 2006, The Belgian Institute for Pharmaco-Epidemiology implemented an opioid substitution treatment registry for all reimbursed prescriptions of methadone and buprenorphine in an attempt to prevent doctor shopping from patients and subsequently mitigate some forms of diversion. It appears the registry is no longer in operation, but a 2022 report entitled The Drug Situation in Belgium references an Opioid Agonist Treatment registry. However, in the context of safer opioid supply programs, the applicability of these methods may be limited given that early refills or 'double doctoring' may not be relevant.

In B.C., Canada, the Ministry of Health and Ministry of Mental Health and Addictions in collaboration with the Office of the Provincial Health Officer, as well as key research and health system partners in B.C., oversee monitoring of the Safer Opioid Supply policy. Monitoring and evaluation efforts include protocols with direction for prescribers to include "SA" in prescriptions, telling the dispensing pharmacist to tag the prescription with an identifying code for evaluating purposes in PharmaNet. In Ontario, a Narcotics Monitoring System collects and stores information on prescribing and dispensing activities of narcotics and other controlled substance medications, recording a unique number from the individual receiving the prescription's ID on their prescription to identify trends, detect unusual behaviour, and develop harm reduction strategies. Again, these approaches may be limited in terms of their applicability for monitoring diversion in the context of safer opioid supply programs.

Finally, one program in the U.K. attempts to monitor potential diversion by registering adverse outcomes related to drug dependence in the community. Specifically, both healthcare professionals and patients can report adverse effects and incidents of drug dependence using the Yellow Card Scheme by the Medicines and Healthcare products Regulatory Agency, which can help in monitoring and identifying trends in opioid misuse and diversion. Similar to other approaches for monitoring, these programs are more suited to monitoring potential diversion of opioids for pain, rather than in the context of safer opioid supply.

Q3: What is known about how to mitigate the diversion of prescription medications provided through safe supply prescriptions?

Few approaches to mitigate the diversion of prescription medications provided through safe supply prescriptions were identified in jurisdictions included in this rapid synthesis. In B.C., Prescribed Safer Supply protocols include measures to avoid diversion, such as requiring patients to return fentanyl patches before receiving additional patches, and agreeing to only receive opioids or other sedative prescriptions from their primary prescriber. Similarly, in Ontario, the Patch-For-Patch Fentanyl return program requires patients receiving prescription fentanyl to return their patches to a pharmacy before receiving new ones to help combat abuse, misuse, and diversion of prescription fentanyl. However, the Patch-for-Patch program in Ontario is only for pain, rather than safer opioid supply programs. Additionally, the Office of the Provincial Health Officer in B.C. released a report in December 2023 that reviewed the Prescribed Safer Supply programs, which highlighted that motivation for diversion is often related to prescribed medications not being the correct dose, leading the client to prefer to sell the prescribed medication and instead buy something that better meets their needs (e.g., selling Dilaudid to obtain fentanyl). This finding indicates that a key deterrent to diversion is likely ensuring that clients obtain the correct prescribed medication and dosing for their unique situation.

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