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A scoping review and concept analysis to inform Canada's safe(r) opioid supply research agenda

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ABSTRACT

Background: Providing pharmaceutical opioid medications as alternatives to the unregulated drug market, commonly referred to as safe supply or safer supply (hereafter "safe(r) supply"), has emerged as a harm reduction strategy in Canada, with wide variation in principles and implementation. We aimed to clarify the concept of safe (r) opioid supply across harm-reduction and clinical contexts.

Methods: We conducted a scoping review and concept analysis. We systematically searched six major electronic databases and the grey literature to identify articles published between 2010 and 2024. Informed by Walker and Avant's concept analysis methodology, we extracted definitions and descriptions of programs and interventions, organizing key characteristics into thematic dimensions to develop a framework distinguishing various care approaches.

Results: Our review included 95 articles. Safe(r) supply operationalizes under two broad approaches: a medicalized/prescribed approach ('safer supply') and a non-medicalized/community-based approach ('safe supply'). We outlined three illustrative cases that nest within these approaches: (1) Prescribed opioids with opioid agonist therapy (OAT) offered and/or co-prescribed, (2) Prescribed opioids without OAT, (3) Community-based distribution of unregulated drugs with known composition.

Conclusion: Safe(r) supply encompasses prescribed opioid alternatives interventions (safer supply) and non-medicalized (safe supply) approaches with shared antecedents but distinct attributes and consequences. This study highlights the need to better define and standardize the parameters of safer supply approaches, including population, dosing, and intended objectives, to enable a more precise assessment of their potential benefits and

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risks. This nuanced understanding is crucial for developing evidence-based strategies in response to Canada's drug poisoning crisis.

Introduction

Canada is grappling with an unprecedented and uncontrolled toxic drug crisis, with antecedents predating the COVID-19 pandemic (Government of Canada, 2024). A key factor driving this crisis has been changes in the drug supply, including overall reduced availability of prescription opioids over the past decade (Gomes et al., 2024; St-Martin & Lacroix, 2023). This shift has created a void that illicit operations have sought to fill (Canadian Centre on Substance Use and Addiction & Canadian Community Epidemiology Network on Drug Use, 2020; Government of Canada, 2022; Jones et al., 2021). Unregulated substances, such as fentanyl, fentanyl analogues, sedatives (e.g., benzodiazepines), animal tranquilizers, and other adulterants have proliferated, posing a significant health risk due to their high potency and unpredictable composition (Canadian Centre on Substance Use and Addiction, 2022; Government of Canada, 2024; Health Canada, 2018; Statistical Reports on Deaths in British Columbia, 2024; The Ontario Drug Policy Research Network, 2021). Since the onset of the COVID-19 pandemic, this crisis has worsened, driven by a multitude of factors, including increased volatility in the drug supply (Canadian Centre on Substance Use and Addiction & Canadian Community Epidemiology Network on Drug Use, 2020), pandemic-related disruptions to healthcare and harm reduction services (Health Canada, 2024; Jacka et al., 2021), and socioeconomic instability (Hutchinson et al., 2023). Addressing this complex and evolving challenge requires innovation in prevention and harm reduction strategies to better address the diverse needs of people who use drugs.

Among the treatment options for people with opioid use disorder (OUD), opioid agonist treatment (OAT) with buprenorphine-naloxone or methadone is recommended as the first-line intervention (Yakovenko et al., 2024). In recent years, slow-release oral morphine has demonstrated effectiveness when prescribed off-label as an alternative agonist medication for patients not responding to the first-line OAT medications and is now recommended as a second-line option in Canada (Ferri et al., 2013; Yakovenko et al., 2024). Accordingly, we define methadone, buprenorphine-naloxone, and slow-release oral morphine as conventional OAT medications. For individuals where conventional OAT therapies were not effective, injectable opioid agonist treatment (iOAT) has proven to be an effective alternative (Fairbairn et al., 2019; Oviedo-Joekes et al., 2009, 2016). Building on the successful implementation of diacetylmorphine-assisted treatment in European countries (Strang et al., 2012) and the positive outcomes of two randomized trials in Canada (Oviedo-Joekes et al., 2009, 2016), iOAT is now available in select Canadian cities (e.g., Vancouver, Calgary, Edmonton, Ottawa, Toronto, Fredericton) as an open-ended treatment approach. This involves the provision of injectable opioids (primarily hydromorphone, rarely diacetylmorphine) under clinical supervision along with other multidisciplinary services (Eydt et al., 2021). Additionally, adapted iOAT approaches, such as take-home iOAT dosing, have been developed to meet specific patient needs, including support during COVID-19 self-isolation (Bardwell, Bowles, et al., 2023; Meyer et al., 2022; Oviedo-Joekes et al., 2021, 2023; Weng et al., 2022).

While OAT primarily focus on individuals diagnosed with OUD, approximately one-third of people at risk of opioid toxicity do not meet the diagnostic criteria for OUD (Gomes, Murray, et al., 2022). Moreover, there are critical barriers to access to OAT in some Canadian settings (Duff et al., 2024; Pijl et al., 2022). As a result, only a small proportion of people using unregulated drugs, including those at high risk of opioid toxicity, are successfully initiated and retained in these treatments (Hu et al., 2023; Pilarinos, Fast, et al., 2022; Kurz et al., 2022; Nosyk et al., 2024; Gomes, McCormack, et al., 2022).

The concept of providing low-barrier dispensations of drugs of known type, quality, and composition to individuals who would otherwise use unregulated substances and who are at risk of drug toxicity, commonly referred to as "safe supply" or "safer supply", has gained traction in Canada (Government of Canada, 2021). These terms are often used interchangeably; however, they reflect distinct origins and paradigms. "Safe supply" emerged around 2017–2018 in advocacy and policy discourse as a human rights-based, community-led concept calling for legal access to non-toxic drugs without requiring medical oversight. In 2019, the Canadian Association of People who Use Drugs (CAPUD) formally conceptualized safe supply as a harm reduction measure involving the provision of a legal and regulated supply of mind/body-altering drugs that are traditionally available only through the unregulated market (Canadian Association of People who Use Drugs, 2019). "Safer supply" has been used in clinical settings as early as 2016 to describe the prescribing of pharmaceutical-grade substances by healthcare providers to reduce overdose risk. The first of such program was implemented in 2016, by the London Intercommunity Health Centre (LIHC), which launched the Safer Opioid Supply Program to offer prescribed pharmaceutical alternatives to street-acquired substances (Gomes, Kolla, et al., 2022). "Safer Supply" implementation has evolved, particularly during the COVID-19 pandemic, with Risk Mitigation Guidance (RMG) facilitating its integration into OUD clinical and other treatment settings (Health Canada, 2019; Office of the Provincial Health Officer, 2024). For the purpose of this paper, "safe(r) supply" is used as an umbrella term to encompass the range of terminologies used in the literature and practice. We use "safer supply" for the medicalized/prescribed approach, and "safe supply" for the non-medicalized/community-based approach.

Despite growing interest in the clinical and social impacts of these programs, a significant gap remains in clarifying the ambiguity surrounding "safe(r) supply", which often conflates distinct approaches and oversimplifies differences in their goals, implementation, oversight, effectiveness, and potential benefits and harms (Ledlie et al., 2024). Grouping these conceptually diverse interventions under a single concept can obscure important distinctions and limit the ability to assess specific benefits, harms and relative effectiveness. As safe(r) supply programs evolve, there is a need to revisit the concept and its practical applications. This paper seeks to address this gap by clarifying conceptual boundaries of "safe(r) supply" and exploring the distinct paradigms from which they emerged.

Since safe(r) supply spans community, harm-reduction and clinical contexts, and a growing literature reports diverse implementations under various labels, we conducted a scoping review to identify uses and definitions across sources and a concept analysis informed by Walker and Avant to assess the current state of knowledge and clarify boundaries between various approaches of safe(r) supply for opioid use or OUD (Walker & Avant, 2018). Our specific objectives are to: (1) identify uses and defining attributes of safe(r) opioid supply interventions and (2) develop illustrative cases that highlight different approaches in practice and clarify the concept(s) underlying safe(r) supply as part of a response to the drug toxicity public health emergency in Canada.

Methods

The scoping review was conducted following the JBI Manual for Evidence Synthesis for Scoping Reviews (Peters et al., 2024) and the concept analysis was informed by Walker and Avant's eight-step framework (Walker & Avant, 2018). Shun's methodology (Lam Wai Shun et al., 2022), which integrates scoping review and concept analysis approaches, was used to guide the overall integration of these two

methodologies in our work (Table 1). Scoping review methodology was used to collect definitions and descriptions of safe(r) supply interventions. Concept analysis was employed to describe attributes of these interventions and develop illustrative cases that clarify internal boundaries within the umbrella concept and highlight different approaches in practice. Our scoping review protocol was registered *a priori* (https://osf.io/j37hm/), and a list of protocol amendments is available in Supplementary Methods 2.

Scoping review

Literature search

Six electronic databases (Embase, Medline, PsycINFO, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and Web of Science) were searched on February 24, 2023, to identify articles published between 2010 and 2023. Articles published before 2010 were not included as any use of the phrase "safe supply" or "safer supply" would be coincidental or refer to a different concept than safe(r) supply as it has been conceptualized in response to the drug toxicity crisis. To ensure literature saturation, we also searched trial registries, dissertations, health technology assessment resources, and the grey literature (i.e., a list of websites identified by the review team, including people with lived/living experience, based on expert knowledge and preliminary web searches) to identify articles outside of the peer-reviewed literature, including emerging guidelines, concept documents, and program descriptions and evaluations by community-based organizations of people who use drugs. No language restrictions were applied. Modifications (Supplementary Methods 3) were made to the strategies following an initial analysis of results, and all strategies were rerun on March 29, 2023. The database searches were rerun on April 11, 2024 and the grey literature search was rerun on February 12, 2025 to retrieve any new relevant publications prior to article submission. The search strategies (Supplementary Methods 3) were designed by a senior librarian (AB) and peer reviewed by another senior librarian prior to execution using the PRESS Checklist (McGowan et al., 2016). The retrieved articles were collected in a combined library created using the Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia) (*Covidence - Better Systematic Review Management*, n.d.), and duplicates were removed. Reference lists of included articles, as well articles that cited these inclusions, were manually screened to identify additional references.

Table 1
Combining scoping review and concept analysis methodologies. Note: Adapted from "Combining Scoping Review and Concept Analysis Methodologies to Clarify the Meaning of Rehabilitation Potential After Acquired Brain Injury," by P. Lam Wai Shun, B. Swaine, & C. Bottari, 2022, Disability and Rehabilitation, 44(5), 817–825. https://doi.org/10.1080/09638288.2020.1779825. Copyright 2022 by Taylor & Francis.

Scoping review	**Concept analysis**	**Combined methodology**
Stage 1: Identifying the research question	Step 1: Select a concept	Selecting a concept and determining the aim of the analysis (reported in the introduction)
Stage 2: Identifying relevant studies	Step 2: Determine the aims or the purpose of the analysis	Identifying relevant publications
Stage 3: Study selection	Step 3: Identify all uses of the concept	Selecting publications
Stage 4: Charting the data	Step 4: Determine the defining attributes	Extracting data from included studies
Stage 5: Collating, summarizing and reporting the results	Step 5: Identify a model case	Concept analysis
• Descriptive numerical analysis	Step 6: Identify additional cases	• Identifying uses of the concept, defining attributes, model case, additional cases, antecedents and consequences, empirical referents
• Qualitative thematic analysis	Step 7: Identify antecedents and consequences	
	Step 8: Define empirical referents	

Eligibility criteria

We included studies that assessed the feasibility, acceptability, accessibility, and/or effectiveness of prescribing pharmaceutical-grade opioid medications or providing drugs of known dose and composition as alternatives to the unregulated drug supply to people who use drugs. These criteria were informed by Proctor et al.'s implementation outcomes framework, which evaluates interventions in real-world settings (Proctor et al., 2011). We also included reports that provided details on the development of safe(r) supply intervention or programs. Studies examining the provision of safe(r) supply medications/drugs alone or with treatments for OUD (e.g., OAT) were eligible. These could be provided through prescriber-based (i.e., healthcare practitioners prescribing medications) or non-prescriber-based (e.g., compassion clubs, grassroots supply) approaches (Health Canada, 2019). Additionally, studies on risk mitigation guidance (RMG) or changes to prescribing policies during public health emergencies (e.g., COVID-19, opioid crisis) were eligible. To be included in the concept analysis, studies had to include any of the following: a description of the philosophy for providing the intervention, target population, indications for prescribing or distributing, details of the intervention (e.g., medications and supervision of medication consumption), accessibility (i.e., service delivery design), and/or other aspects of the intervention such as wrap-around services. Given the exploratory nature of this review, we included a range of methodological designs, including qualitative studies, case reports, cross-sectional surveys, case-control studies, cohort studies, randomized controlled trials, systematic reviews, and meta-analyses. We also included relevant program evaluation reports, clinical protocols, guidance reports, and concept documents from the grey literature search that described developmental aspects. We included only PDF uploaded or shared documents from the grey literature and did not include HTML-based webpages as they might be edited often.

We excluded studies focused on the use of unprocessed or traditional opioid preparations (e.g., opium gum, opium tincture), laboratory-based studies (e.g., pharmacokinetics, pharmacodynamics, genetic profiling, brain imaging studies) or animal studies. Studies where opioid medications were prescribed solely for pain management (chronic or acute/surgical pain) or for palliative care were also excluded. Commentaries and editorials were excluded. Conference abstracts without full-text access were excluded unless they provided sufficient details on the intervention. We reviewed studies on iOAT as this intervention also provide pharmaceutical-grade medications as alternatives to the unregulated drug supply; however, we excluded iOAT as a safer supply intervention as it primarily operates under the conventional approach for OUD treatment and have been rigorously evaluated in comparison to standard OAT treatments. *A priori*, we identified a key distinction that iOAT is typically administered and consumed under supervision while safer supply is not. We did however include studies detailing adaptations to iOAT (e.g., tablet iOAT).

Study selection

An abstract screening decision table was created to guide decision-making (Supplementary Methods 4). Following the removal of duplicate studies, two reviewers (UD and MDR) pilot-tested the eligibility criteria on a random sample of 30 abstracts identified by the search. Potential issues with the criteria were discussed in a meeting with the team, and modifications to the eligibility criteria were made as needed. To standardize the screening process, reviewers participated in a training session and conducted pilot screening of a minimum of 20 consecutive abstracts to identify any areas needing clarification. Subsequent abstracts were independently screened by pairs of reviewers (UD, CZ, SG, MDR, IM) and discrepancies were resolved by SL. After abstract screening, full-text versions of the potential articles for inclusion were evaluated against the eligibility criteria by pairs of reviewers (UD, CZ, IM, MDR, SL, MLD, SG) (Supplementary Methods 4). Eligibility disagreements were resolved via discussion until consensus was

reached, or by consulting an adjudicator (SL or JB) if consensus could not be reached.

Data extraction

A customized data charting form (Supplementary Methods 5) was constructed and integrated into the Covidence software to extract data (e.g., study design, country, year, patients, interventions, and outcomes) from each study. After attending a training session, data extraction was conducted independently, in duplicate, by pairs of reviewers (UD, IM, CZ, SG, MJ, CS). The extracted data was cross-referenced for discrepancies, which were resolved through discussion between the reviewers or by consulting an adjudicator (SL or JB).

Concept analysis

Informed by Walker and Avant's method (Walker & Avant, 2018), we extracted definitions, descriptions, and applications of the concept from the included studies by identifying explicit statements or descriptions related to the concept as stated by the authors. Additionally, we comprehensively reviewed the intervention features and contextual details provided in the studies. From these extracted definitions and contextual uses, we identified the concept's defining attributes, organized these into overarching themes, and developed a conceptual framework to clarify the boundaries between various cases of providing pharmaceutical alternatives to the unregulated drug supply. The delineation of different approaches was guided by the expert-led framework

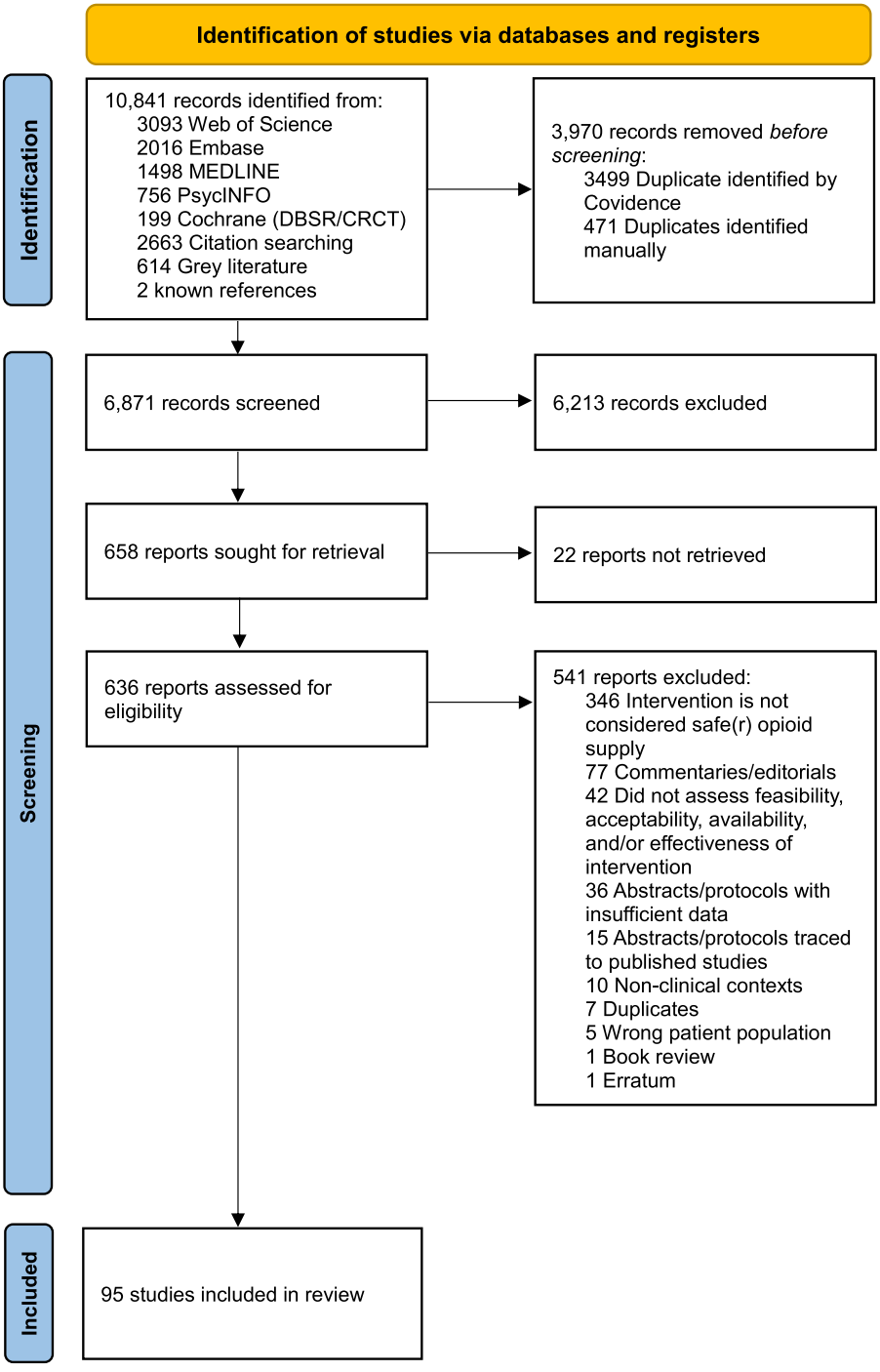

Fig. 1. PRISMA flow diagram.

previously outlined by Health Canada (2019), with modifications informed by evidence from the literature search. Next, we constructed a model case to illustrate how these defining attributes may manifest in practice, incorporating all the critical attributes extracted from the literature. We outlined alternative cases that reflects variations in the implementation of the concept, sharing the majority of defining attributes with the model case but differing in one or more key aspects. Each of these cases provide unique insights into the application and variation of the concept currently in practice. Importantly, and in keeping with concept analysis methods, these typologies are not intended to be hierarchical or to represent an ideal practice. Rather, they serve as illustrative examples that highlight different approaches, each with its own strengths, limitations, and contextual considerations. More specifically, a model case is an illustrative example of what is the most representative

Dimensions	Medicalized approach	
	Prescribed opioids **with** OAT offered or co-prescribed*	Prescribed opioids **without** OAT
Philosophy of care	Mitigating substance-related harms including health risks, social stigma, and criminalization	
	Acknowledging the limitations of traditional treatments in meeting the needs of all people who use drugs	
	Broadening the continuum of care and expanding the use of medications for OUD	
	Offering a harm reduction-focused approach that prioritizes access to care without mandating abstinence or engagement in treatment	
	Offering accessible and low-barrier substance use care	
	Offering a crisis-responsive, temporary measure, harm reduction approach to mitigate substance-related harms and facilitating retention in care during COVID-19**	
	Offering a medicalized harm reduction approach that promotes primary care and treatment for substance use disorders	
	Promoting engagement in substance use treatment and health services	
		Respecting and upholding the autonomy, dignity, and human rights of people who use drugs
		Offering safer options for people who want to use drugs
Population	People who use drugs at high risk of substance-related harms	
	People who use drugs with additional inclusion criteria/required characteristics (COVID-19 infection, medical issues, recent overdose, homelessness, and minority status)	
	People with OUD who is ready to engage in treatment	
Indications	High risk of overdose	
	Regular illegal drug use	
	OUD and opioid use consistent with OUD	
	Previous unsuccessful attempts with OAT	
	History of overdose and other drug-related harms, comorbid mental and physical health conditions	
	Confirmed COVID-19 infection and required to quarantine**	
	High tolerance to opioids and chronic pain***	
	Previous unsuccessful injectable or tablet hydromorphone treatment***	
		Currently not interested in attempting OAT
Intervention protocol	Prescribed short-acting opioids (e.g., hydromorphone) or direct substitute to fentanyl (e.g., fentanyl patches, tablets, powder, injectables)	
	Witnessed consumption of prescribed pharmaceutical alternatives is not required	
	Various formulations can be prescribed	
	Flexible route of consumption	
	Not required to remain on OAT concurrently	
	Witnessed consumption of prescribed pharmaceutical alternatives required*	
	Provision of OAT alongside prescribed pharmaceutical alternatives	
Accessibility points	Primary care/community health centres	
	Substance use treatment clinics	
	Permanent supportive housing/shelters	
	Harm reduction programs	
	Comprehensive and dedicated programs in stand-alone facilities	
	Temporary COVID-19 isolation sites (shelters, isolation unit in hospital)**	
		Vending machine dispensing
Continuity of care	Access to harm reduction resources and equipment	
	Access to peer workers/connections	
	Access to primary care	
	Access to social services	
	Access to substance use treatment services	
	Access to psychosocial services	

Dimensions	Non-medicalized approach
	Community-based distribution of unregulated drugs with known composition
Risk environment management	Reducing reliance on unregulated markets
	Reducing overdose risk and risks associated with unpredictable substances
	Offering alternatives to medicalized or criminalized approaches
	Addressing economic and legal barriers
	Reducing stigma and isolation
Integration with broader policy reforms	Advocating for decriminalization and drug policy reforms
	Advocating for structural changes beyond health (i.e., housing unaffordability, organized crime, drug poisoning)
	Aligning with human rights frameworks
	Providing structural alternatives to prohibition
	Advocating for legal and regulatory exemptions
Recognition of people's autonomy and rights	Supporting autonomy in drug choice and dosing
	Supporting participants' autonomy by allowing them to choose and access drugs without medical supervision
	Supporting autonomy and anonymity in drug purchasing
	Democratic participating and voluntary membership
Source and quality assurance of substances	Substances sourced from regulated and/or illicit vendors
	Rigorous testing protocols
	Secured storage and packaging
	Non-distribution until confirmed safe
Operational flexibility	Diverse models with varying target client populations, range, and types of medications, and operating policies
	Fulfillment centre for acquisition and testing and compassion club for distribution and follow-up
	Flexible operational hours and locations
	On-site overdose prevention site
	Could be available from a range of low-barrier addiction services
	Could be established alongside easily accessible and free addiction treatment and trauma-informed recovery services for those with an interest in OAT or other addiction treatment
Mutual aid and peer support	Leading programs through peer governance
	Creating space for share lived experiences
	Training volunteers in overdose prevention and response
	Training members in harm reduction education
	Drugs sharing among peers to increase access
	Emphasizing peer involvement and community guidance
	Fostering social cohesion and support

*Including tablet injectable opioid agonist therapy (TiOAT) interventions.
**Under risk mitigation guidance prescribing.
***For interventions with fentanyl patch.
OAT=opioid agonist therapy; OUD=opioid use disorder

Fig. 2. Key attributes and dimensions.
OAT=opioid agonist therapy; OUD=opioid use disorder *Including tablet injectable opioid agonist therapy (TiOAT) interventions. **Under risk mitigation guidance prescribing. ***For interventions with fentanyl patch.

configuration identified from the literature, not necessarily an ideal or "best" form of implementation. We also identified antecedents (i.e., conditions that lead to the concept's manifestation) and consequences (i.e., outcomes that result from the concept's implementation) to contextualize the concept's occurrence. Finally, we defined empirical referents or consequences of the concept (i.e., criteria to assess the presence, effectiveness, or impact of the concept) to facilitate assessment and operationalization. The construction of cases was conducted in collaboration with people with lived/living experience, ensuring that the framework reflected real-world applications and perspectives.

Results

A total of 6871 unique references were identified following the removal of duplicates, of which 636 underwent full-text screening, and 95 studies were included (Fig. 1).

Concept analysis

Figs. 2 and 3 visualises the concept analysis based on all 95 reports (100 %). Three illustrative cases, two referring to "safer supply" and one to "safe supply" were identified in our analysis: (1) Prescribed opioids with the conventional OAT medications offered or co-prescribed, (2) Prescribed opioids without the recommended OAT medications, and (3) Community-based distribution of unregulated drugs with known composition. A complete list of included publications and a summary of the study characteristics can be found in Supplementary Results 1–4.

Antecedents to the concept

Although the term "safe supply" was formally introduced by CAPUD in 2019, community-led advocacy for legal, regulated access to drugs predates the current overdose crisis. These calls, grounded in demands for autonomy, dignity, human rights, and overdose prevention, emerged from longstanding efforts by people who use drugs to challenge the harms of prohibition, criminalization, and the toxic unregulated drug market (Canadian Association of People who Use Drugs, 2019). The original vision of safe supply emphasized providing low-barrier access to substances of known quality and quantity to people who use drugs, with goals of promoting autonomy and liberation while challenging punitive drug policies (Foreman-Mackey et al., 2022). The escalating overdose emergency first declared a public health crisis in British Columbia in 2016, and the public health disruptions caused by the COVID-19 pandemic created conditions for the rapid expansion of these initiatives. In parallel to community-led advocacy, healthcare providers began implementing "safer opioid supply" programs as early as 2016, prescribing pharmaceutical alternatives to replace toxic, street-acquired opioids (Gomes, Kolla, et al., 2022). In practice, implementation of safer opioid supply has been influenced by prescriber hesitancy and fear of regulatory audit, a lack of explicit guidance from professional Colleges, and the precarity of harm reduction services due to stigma and political ideology (Foreman-Mackey et al., 2022). While both "safe supply" and "safer supply" aim to address drug-related harms, "safe supply" reflects a human rights-based, non-medicalized paradigm rooted in drug user liberation, whereas "safer supply" describes clinical interventions delivered under medical supervision.

The emergence and expansion of "safe(r) supply" initiatives in Canada can be further understood through several key antecedents (Fig. 3). First, the escalating drug poisoning crisis, exacerbated by an increasingly toxic unregulated supply and then the COVID-19 pandemic, created a sense of urgency that fueled the development of these interventions, which had previously been a marginal phenomenon (Canadian Association of People who Use Drugs, 2019; Glegg et al.,

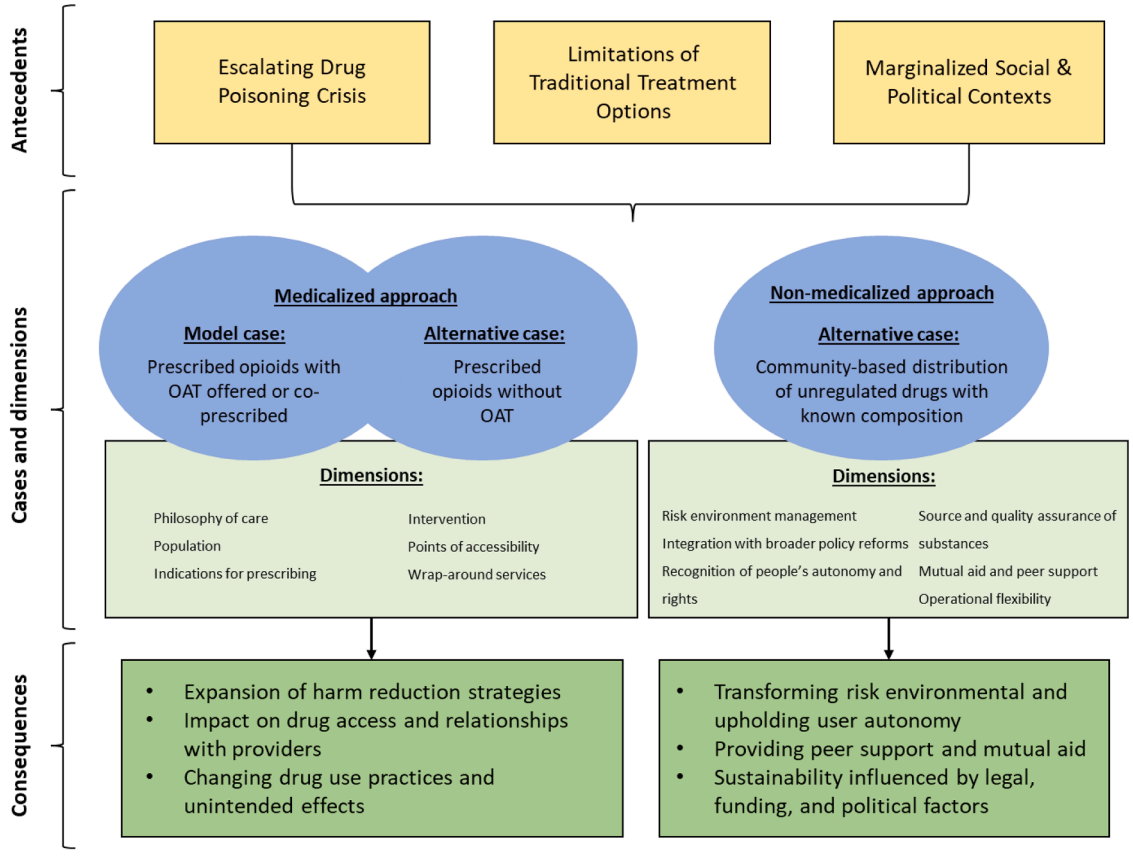

Fig. 3. Illustration of antecedents, cases, dimensions, and consequences from concept analysis
OAT=opioid agonist therapy.

2022; Government of Canada, 2021). Second, limitations of conventional treatment options, such as poor retention in OAT modalities such as methadone or buprenorphine/naloxone, underscored the need for additional strategies (Bardwell et al., 2019; Timko et al., 2016). Rigid dosing schedules, strict eligibility criteria, and a lack of patient-centered care have been shown to negatively impact both retention and client experience in OAT (Bojko et al., 2016; Pilarinos, Kwa, et al., 2022). Similarly, iOAT is often too structured for many individuals who are unwilling to attend clinics three to four times daily (Metcalfe et al., 2024) and its implementation has been limited across Canada by expense and need for a physical structure (Eydt et al., 2021). Third, Canada's housing crisis and broader social and political contexts, including structural disadvantages faced by marginalized populations, such as criminalization, homelessness, poverty, and mental health challenges, have shaped vulnerability to overdose (Drug User Liberation Front & Vancouver Area Network of Drug Users, 2023; Hales et al., 2020). Unstable housing contributes to overdose risk and limited healthcare access by exposing people to trauma and mental-health challenges while increasing their reliance on unregulated drug supplies (Milaney et al., 2021). Poverty and mental health challenges further compound these risks, creating a cycle of marginalization and overdose vulnerability. Together, these antecedents frame and highlight the complex social healthcare environments in which safe(r) supply initiatives were implemented (Fig. 3).

Definitions, scope and applications of the concept

Definitions of the "safe(r) supply" concept vary depending on the actor and context. CAPUD defines safe supply as "a legal and regulated supply of drugs with mind/body altering properties that traditionally have been accessible only through the illicit drug market", emphasizing liberation, autonomy, and the right to access safe substances (Canadian Association of People who Use Drugs, 2019). Canada's federal Department of Health defines safer supply as "providing prescribed medications as a safer alternative to the toxic illegal drug supply to people who are at high risk of overdose", reflecting a medicalized, treatment-adjacent approach (Canada, 2021). "Safer supply" has become the dominant term in Canadian policy and research, reflecting both the expansion and formalization of these prescribing practices (Glegg et al., 2022; Olding et al., 2024; Young et al., 2022)

Key attributes and dimensions

Attributes extracted from included papers were fundamentally distinct between medicalized and non-medicalized approaches. Key dimensions derived from medicalized approaches were: 1) Philosophy of care (i.e., underlying principles guiding the intervention), 2) Population (i.e., intended population for the intervention), 3) Indications (i.e., specific criteria for eligibility), 4) Intervention (i.e., details of the pharmaceutical alternatives or drugs provided), 5) Accessibility (i.e., distribution setting), and 6) Wrap-around services (i.e., additional supports integrated with the intervention) (Fig. 2). Key dimensions derived from non-medicalized approaches were: 1) Risk environment management (i.e., how the intervention alters legal, social, economic, and health conditions that contribute to drug-related harms), 2) Integration with broader policy reforms (i.e., alignment with movements for decriminalization, human rights, and public health transformation), 3) Recognition of autonomy and rights (i.e., the degree to which participants exercise agency over drug use decisions without medical oversight), 4) Source and quality assurance of substances (i.e., methods of sourcing, testing, and verifying substances for safety and known composition), 5) Mutual aid and peer support (i.e., the role of lived experience, peer governance, and horizontal care structures in program design and delivery), and 6) Operational flexibility (i.e., membership eligibility, access models, and distribution mechanisms (Fig. 2). A complete list of extracted attributes can be found in Supplementary Results 5 and 6.

Model case

Prescribed opioids with recommended OAT medications offered or co-prescribed

Our model case is nested within the medicalized approach and represents the most frequently "safer supply" reported practice in providing pharmaceutical alternatives, primarily through the prescribing of short-acting opioids – most commonly hydromorphone tablets as daily take-home doses – with the optional co-prescription of OAT medications, such as slow-release oral morphine or methadone (Fig. 2, Supplementary Results 7) (Haines et al., 2022; Hales et al., 2020; Nafeh et al., 2023; Olding et al., 2020; Waraksa et al., 2022). While hydromorphone tablets are commonly prescribed, some programs also offer fentanyl patches and fentanyl tablets as alternative medications (British Columbia Centre on Substance Use, 2022, 2023; Victoria Safer Initiative, 2022). In many instances, the OAT component is prescribed at doses primarily intended to prevent withdrawal (Hales et al., 2020). This model case, along with alternative cases outlined below, is grounded in a harm reduction philosophy that seeks to mitigate substance-related harms by reducing health risks, social stigma, and criminalization, while acknowledging the limitations of conventional substance use treatments in meeting the needs of all people who use drugs and broadening the continuum of care through innovative, low-barrier strategies (Supplementary Results 7). Notably, many individuals find that conventional OAT does not fully address their withdrawal symptoms or find that these treatments lack the euphoric effects associated with unregulated opioid use (McNeil et al., 2022; Schmidt et al., 2023). For these individuals, supplementing OAT with short-acting opioids can help manage withdrawal and provide the desired effects, thereby maintaining the functional aspects of their drug use within a safer, regulated framework. The philosophy of care specific to this model case is to reduce the risks associated with unregulated drug use, while offering a medicalized strategy that encourages engagement with addiction and primary care and other support services, including harm reduction supplies, outreach, psychosocial services, and peer support. The intended population for all cases, including this model case, consists of people who use drugs and are at high risk of substance-related harms. Additional inclusion criteria have included COVID-19 infection, medical issues, recent overdose, homelessness, and minority status. The model case is suited for people with OUD who are ready to engage in care and other support services. Some examples include the London InterCommunity Health Centre Safer Opioid Supply program guidance (Kolla & Fajber, 2023), which describes an organized program incorporating primary care, and the British Columbia Centre on Substance Use Risk Mitigation Guidance, which includes prescribing guidance without reference to an organized program (Ahamad et al., 2020). Indications for prescribing include being at high risk of overdose, regular unregulated opioid use, a confirmed diagnosis of OUD or opioid use consistent with OUD, previous unsuccessful attempts with OAT, a history of overdose or other drug-related harms, and comorbid mental and physical health conditions (Hales et al., 2020; Gomes, Kolla, et al., 2022; Mansoor et al., 2023). During the COVID-19 pandemic, additional prescribing criteria included a confirmed COVID-19 infection or the need to quarantine (Ahamad et al., 2020). For individuals with a high opioid tolerance and chronic pain who have not benefited from injectable or tablet hydromorphone treatments, fentanyl tablets are prescribed as an alternative (British Columbia Centre on Substance Use, 2023). Most programs within the model case provide short-acting opioids as take-home doses to allow for a flexible route of consumption, though a few programs require witnessed consumption of the prescribed short-acting opioids (Bardwell, Bowles, et al., 2023; British Columbia Centre on Substance Use, 2023; Ivsins et al., 2021; Olding et al., 2020). The prescribing strategy under the model case is accessible via various healthcare and community-based settings, including primary care and community health centers, addiction treatment clinics, permanent supportive housing and shelters, harm reduction programs, and comprehensive, dedicated programs in stand-alone facilities. Wrap-around,

patient-oriented services are often offered, providing access to primary care, outreach support, drug use equipment, and connections to psychosocial services and peer workers, ensuring tailored and comprehensive care that extends beyond medications alone.

Alternative cases

Prescribed pharmaceutical-grade opioids without recommended OAT medications (hydromorphone and fentanyl tablets). Prescribing short-acting pharmaceutical-grade opioids, such as hydromorphone tablets or fentanyl tablets, without recommended OAT medication is an alternative "safer supply" case, nested within the medicalized approach. This case is grounded in harm reduction principles and prioritizes access to care without mandating abstinence or engagement in treatment (Fig. 2, Supplementary Results 7) (Bardwell et al., 2024; Bardwell, Ivsins, et al., 2023; British Columbia Centre on Substance Use, 2022; Mansoor et al., 2023). Prescribing under this alternative case does not require individuals to participate in formal medical programs or wraparound supports, acknowledging that not all people who use drugs seek abstinence or structured medical intervention. Indications for prescribing short-acting medications are similar to those in the model case (Hales et al., 2020; Gomes, Kolla, et al., 2022; Mansoor et al., 2023). Hydromorphone tablets have been made accessible via biometric dispensing machines placed near harm reduction services or within supportive housing, providing flexible, 24-hour access to take-home doses of prescribed medications.

Prescribed pharmaceutical-grade opioids without recommended OAT medications (fentanyl patches). Fentanyl patches have also been prescribed as pharmaceutical-grade alternatives and offer a long-acting formulation designed to maintain stable opioid levels over multiple days for individuals with higher opioid tolerances (British Columbia Centre on Substance Use, 2022). Co-prescribing of fentanyl patches and OAT is not recommended, due to overlapping indications. The patches are applied transdermally and replaced at scheduled intervals under clinical supervision. Participants in the SAFER fentanyl patch program reported that the program's flexible structure (e.g., extended missed-dose protocols and no daily dispensing requirements) enhanced autonomy and engagement, while also improving withdrawal management, reducing reliance on unregulated substances, and contributing to better health, quality of life, and economic stability (Norton et al., 2024). Skin irritation and adhesion difficulties were identified as barriers to retention. While patches remain the most documented fentanyl formulation to date, other forms, such as sublingual or buccal fentanyl, are mentioned in some programs but remain under evaluated. Wraparound services in these alternative cases, including primary care, social support, and supervised consumption services, are similarly available as they are in the model case (Fig. 2, Supplementary Results 7).

Community-based distribution of unregulated drugs with known composition. Community-based distribution of unregulated drugs with known composition is an alternative "safe supply" case that falls under a non-medicalized harm reduction approach that seeks to prevent overdose and promote safe drug use through peer-led distribution of tested substances (Bowles et al., 2024; British Columbia Centre on Substance Use, 2019; Drug User Liberation Front & Vancouver Area Network of Drug Users, 2023; Kalicum et al., 2024; Nyx & Kalicum, 2024). In Canada, the Drug Users Liberation Front (DULF) was the only identified instance of this approach in the peer-reviewed literature, though it has ceased operating since 2023 following drug trafficking charges against the compassion club leaders. Other efforts to implement non-medical models of safe supply, such as dispensaries, have similarly been met with law enforcement responses and shut down (Yousif, 2023). Although people who use drugs are often in favour of non-medical safe supply (Palayew et al., 2024; Palis et al., 2024), there is considerable political, law enforcement, and general public opposition. Attributes and derived dimensions that characterize the non-medicalized approach are fundamentally distinct from the above medicalized approach and are not intended to be in correspondence with the goals, structures, or outcomes of clinical safer supply approaches. The non-medicalized approach to providing alternatives to the toxic unregulated drugs reflects a community-rooted strategy grounded in harm reduction, autonomy, and drug user liberation. One of the guiding principles of this approach is to manage risk environments, including legal, social, health, and economic, that contribute to drug-related harms. By distributing rigorously tested substances outside the criminalized drug market, the approach aims to mitigate the harms of contamination, policing, incarceration, and fatal overdose, while actively challenging punitive legal frameworks surrounding drug use (British Columbia Centre on Substance Use, 2019; Drug User Liberation Front & Vancouver Area Network of Drug Users, 2023). This approach also serves as a form of activist intervention aligned with broader movements for decriminalization, human rights, and public health-oriented policy reform (Nyx & Kalicum, 2024). Central to this approach is the affirmation of autonomy and agency for people who use drugs; participants are not required to pursue abstinence, obtain medical approval, or submit to surveillance. Individuals are granted meaningful control over the substances they want and need, not only to mitigate withdrawal symptoms but also to support well-being, euphoria, and pleasure sought by people who use drugs (Bowles et al., 2024). Substances available for sale, such as heroin, cocaine, and methamphetamine, are sourced from regulated producers and/or illegal markets and undergo rigorous testing using mass spectrometry, nuclear magnetic resonance spectrometry, high-performance liquid chromatography, FTIR spectrometry, and immunoassay testing before being packaged and sold (Drug User Liberation Front & Vancouver Area Network of Drug Users, 2023; Kalicum et al., 2024). Compassion clubs are typically organized and operated by drug-user-led collectives and non-profit organizations, supported by mutual aid, peer support, and community governance (Bowles et al., 2024; Nyx & Kalicum, 2024). The programs are designed with operational flexibility, reflected in the range of substances and formulations offered, adaptable access schedules, options for on-site use or take-home supply, and inclusive membership criteria (Drug User Liberation Front & Vancouver Area Network of Drug Users, 2023). Eligibility is based on membership in a drug-user-led collective, ensuring accessibility for those who may not be eligible from or interested in conventional treatment programs. The availability and function of wrap-around services within non-medicalized models differ from those associated with medicalized approaches. Support is often provided by peers and volunteers who are trained in overdose response. While the core model does not include formal addiction treatment, these initiatives have been proposed as complementary to accessible, low-barrier, and trauma-informed recovery services, including OAT and other treatment options, for participants who seek them (Drug User Liberation Front & Vancouver Area Network of Drug Users, 2023; Nyx & Kalicum, 2024).

Consequences of the concept

Medicalized approach: prescribed pharmaceutical alternatives. The implementation of prescribed pharmaceutical alternatives has led to several intended and unintended effects (Fig. 3). One primary consequence is the expansion of prescription-based harm reduction approaches in healthcare settings (Foreman-Mackey et al., 2022; Glegg et al., 2022; McCrae et al., 2022). These programs have contributed to changes in the way opioid agonist prescription programs are conceptualized and deployed, with some approaches operating alongside conventional OAT or primary care services, and others existing independently (Ahamad et al., 2020; Mansoor et al., 2023; Schmidt et al., 2024). Another key consequence is the impact on drug access and relationships between people who use drugs and healthcare providers. By integrating pharmaceutical alternatives, these programs have created

new pathways for engagement between patients and providers and have increased access to addiction and primary care, mental health services, and social supports, particularly for individuals previously disconnected from the healthcare system (Bonn et al., 2020; Gomes, Kolla, et al., 2022; Ivsins et al., 2022; Klaire et al., 2022; McMurchy & Palmer, 2022). For example, some hospitals have expanded and improved care options for patients with OUD to meet the needs of people with safer supply prescriptions (Bahji et al., 2024; Kleinman & Thakrar, 2023). However, challenges remain, including program accessibility service delivery limitations and prescriber hesitancy given the limited and evolving evidence base (Bardwell, Bowles, et al., 2023; Comeau et al., 2023; McCall et al., 2024; McNeil et al., 2022; Palis et al., 2024; Xavier et al., 2024). Finally, prescribed pharmaceutical alternatives have been associated with changes in drug use practices, including shifts in consumption patterns and concerns about diversion. Some studies have reported that participants transition from injection drug use to other routes of administration, such as oral consumption, potentially reducing injection-related harms (Ferguson et al., 2022; Gagnon et al., 2023; Ledlie et al., 2024). Others described self-reported reductions in fentanyl use or decreased reliance on the unregulated drug market (Cool Aid Community Health Centre, 2021; Haines et al., 2024; Hardill & King, 2024; Ivsins et al., 2021, 2022; Kolla & Fajber, 2023; Schmidt et al., 2023). However, diversion of prescribed medications has also been observed in certain contexts, with the available scientific literature highlighting that some clients view it as an informal harm reduction strategy to share standardized doses with peers who lack access (Haines & O'Byrne, 2023; Kalicum et al., 2024). However, the extent and impact of diversion remain uncertain due to limited empirical data and its potential implications, ranging from increased overall availability of opioids, which may lead to a higher risk of opioid initiation, misuse, and overdose to potentially improved access for underserved populations—continue to be debated in public health and policy discussions (Fischer & Robinson, 2023; Macevicius et al., 2023; Wilson et al., 2024). The impacts of prescribed alternatives programs on local illegal drug markets are still not completely understood (Pauly et al., 2022).

Non-medicalized approach: community-based distribution of tested drugs. Non-medicalized approaches, such as compassion clubs and peer-led distribution of tested substances, have produced a distinct set of consequences centered on risk environment transformation, autonomy, and mutual aid. These initiatives have provided participants with access to unregulated substances of known composition, contributing to perceived reductions in overdose risk, improved predictability of drug effects, and enhanced personal safety (Bowles et al., 2024; Kalicum et al., 2024). Participants reported reduced reliance on toxic street drugs and greater confidence in dosing, which contributed to changes in drug use patterns, including reductions in fentanyl consumption and decreased frequency of use (Kalicum et al., 2024; Nyx & Kalicum, 2024). The peer-led, non-clinical nature of these programs was also associated with increased trust, a sense of dignity, and community solidarity among participants, particularly those who had experienced discrimination in medicalized care settings (Bowles et al., 2024; Nyx & Kalicum, 2024). However, these models face legal, logistical, and sustainability challenges. The criminalized status of the substances distributed, lack of funding, and political opposition significantly constrain program scalability and continuity (Bowles et al., 2024). Despite these limitations, some participants shared or redistributed substances within their networks, framing such practices as a form of community-based harm reduction for those without access to safer supply (Kalicum et al., 2024). These practices, while legally risky, reflect underlying principles of mutual aid and the ethical commitment to keeping peers safe (Nyx & Kalicum, 2024). Overall, the impacts of non-medicalized models extend beyond individual-level risk reduction, highlighting broader efforts to contest drug prohibition, reshape drug policy, and assert collective rights to safe drug use.

Characteristics of studies informing the concept analysis. The distribution of reports according to location, publication year, literature source, and study design is summarized in Table 2. Overall, the majority of studies were conducted in Canada (98 %, $n = 93$), published between 2021 and 2025 (94 %, $n = 89$), and sourced from journal publications (61 %, $n = 58$). Qualitative research designs accounted for the largest proportion of studies (33 %, $n = 31$).

Discussion

Overview

Safe(r) supply has emerged as a Canadian-led innovation in response to a crisis of toxic drugs and has attracted significant attention and controversy. However, the concept lacks a clear operational definition and well-defined parameters, hindering robust evidence-generation to guide policy decisions. Our scoping review and concept analysis examined current approaches for providing pharmaceutical-grade opioids as alternatives to the toxic unregulated drug supply, including prescribed medications through healthcare systems and community-based distribution of tested unregulated drugs. While these two categories of approaches share the overarching goal of reducing drug-related harm, they diverge significantly in implementation, governance, and philosophy. Our findings indicate that there is no single set of defining attributes or consequences for safe(r) supply; rather, these vary by approach. Instead of artificially trying to reconcile attributes into a single set, our analysis supports distinguishing two clearly defined categories. We propose transitioning away from using the language of "safer supply" in reference to medical models and adopting the terminology of "prescribed opioid alternative interventions" to reflect the range models of care situated along the continuum from harm reduction to treatment. The term "safe supply" would then retain its original meaning: a human rights-based, community-led concept advocating legal access to non-toxic drugs without requiring medical oversight. Establishing distinct cases and specifying key attributes of programs would facilitate the development of reproductible, scalable, and evaluable interventions across settings. Evaluation, synthesis, and policy should therefore specify the relevant approach and use approach-aligned indicators.

Table 2
Characteristics of all included studies.

	Total
Number of studies, n	**95**
Study location, n (%)	
Canada	93 (98 %)
United States	2 (2 %)
Publication year, n (%)	
2016–2020	6 (6 %)
2021–2025	89 (94 %)
Literature source, n (%)	
Journal publication	58 (61 %)
Grey literature	37 (39 %)
Primary studies, n (%)	
Qualitative research	31 (33 %)
Retrospective observational cohorts	8 (8 %)
Cross-sectional studies	10 (11 %)
Case studies[†]	6 (6 %)
Mixed-methods studies	10 (11 %)
Prospective observational cohorts	2 (2 %)
Quasi-experimental studies	1 (1 %)
Secondary studies, n (%)	
Environmental scans	3 (3 %)
Scoping reviews	2 (2 %)
Rapid reviews	3 (3 %)
Ethical analysis	2 (2 %)
Other types of reports, n (%)	
Program descriptions	2 (2 %)
Resource documents	7 (7 %)
Clinical recommendations	3 (3 %)
Clinical protocols	6 (6 %)

[†] Case studies category includes case series, case report, and case studies.

Cases and implementation

Our concept analysis presents a model case as an illustrative example of how prescribed alternatives commonly function in practice, not as an ideal case as originally conceptualized but as one of several strategies addressing an urgent public health need. In this case, pharmaceutical sources (e.g., prescription hydromorphone tablets) are co-prescribed with conventional OAT medications (e.g., slow-release oral morphine, methadone) integrating harm reduction and patient-centered care within OUD treatment, supporting OAT initiation while providing an element of euphoria to substitute the unregulated supply (Brothers et al., 2022a; Eydt et al., 2021; Glegg et al., 2022; Selfridge et al., 2022). However, the case does not reflect all policy changes overtime since earlier program proposals had to comply with existing regulatory frameworks without necessitating legislative changes (Health Canada, 2019). The COVID-19 pandemic later prompted a shift in some regulatory policies, introducing greater flexibility that enabled the implementation of additional cases currently in practice (Glegg et al., 2022; McCrae et al., 2022). Albeit this model case could act as a bridge to substance use treatment and social services for individuals who are ready to engage.

A more harm reduction-centric alternative case emerged, still prescription-based but reduces requirements to engage in medical intervention (Bardwell, Ivsins, et al., 2023). Co-located with harm reduction services or supportive housing, biometric vending machines offer 24-hour access to prescribed doses and reduce the need for daily in-person visits. While prescriptions are still issued by clinicians, this alternative case does not impose conventional OAT medication, lowers provider-mediated access barriers, and blends clinical infrastructure with flexible, user-centered access. This case straddles the boundary between the medicalized and non-medicalized approaches and raises important questions around surveillance, access criteria, and alignment with harm reduction values. Lastly, the alternative case of community-based distribution of tested drugs operating under the non-medicalized approach, emphasizes a harm reduction philosophy and prioritizes reduced reliance on the toxic unregulated supply rather than reducing drug use (Drug User Liberation Front & Vancouver Area Network of Drug Users, 2023; Kalicum et al., 2024).

Balancing principles of medical ethics with the fundamental rights of people who use drugs can create moral tension (Duthie et al., 2022). Prescribing pharmaceutical opioid alternatives may pose risks, such as non-medical opioid initiation and dependency, which could contribute to iatrogenic adverse consequences in the community, including increased opioid availability through diversion and heightened overdose risk among opioid-naïve individuals (Howard et al., 2023). At the same time, withholding such prescriptions may leave people who use drugs with no alternatives to the highly toxic unregulated drug market, exacerbating harms. The model case, which encourages engagement in OUD treatment as a condition for accessing prescribed pharmaceutical alternatives, aligns with beneficence and non-maleficence principles but risks perpetuating stigma and marginalizing individuals unwilling or unable to engage in medical intervention. The alternative harm reduction-centric cases acknowledges that not all individuals who use drugs define recovery similarly and that survival and stability can outweigh engagement in medical intervention.

Most programs in Canada do not fit neatly into a single case; instead, they incorporate elements from multiple cases, highlighting the flexibility of these programs to adapt to diverse community needs and regulatory environments. For example, clients can receive both short- and long-acting opioid medications, or only short-acting opioids, within the same program (Kolla et al., 2021; Victoria Safer Initiative, 2022). Fentanyl patches could also be prescribed (British Columbia Centre on Substance Use, 2022; Victoria Safer Initiative, 2022), bridging harm reduction and OAT principles (e.g., through patch for patch exchanges and witnessed application) by reducing some risks associated with take-home short-acting opioids, such as diversion and the requirements that clients engage in frequent (often multiple times a day) clinical visits. Ultimately, "safe(r) supply" interventions span a spectrum and clarifying distinct cases may help evaluate and optimize strategies tailored to diverse needs and levels of engagement with treatment.

All cases identified in our concept analysis aim at individuals at high risk of overdose who regularly use illicit drugs, yet eligibility criteria vary across programs. Often, an OUD diagnosis is required, however, policies do not specify OUD severity (Ministry of Mental Health and Addictions Ministry of Health, 2021) and there are nuanced distinctions in how eligibility for off-label prescribed pharmaceutical alternatives is determined. Some programs accept participants regardless of formal OUD diagnosis (e.g., episodic unregulated opioid use, or active OUD among those not interested in or not benefitting from OAT (Bardwell, Ivsins, et al., 2023; Victoria Safer Initiative, 2022). Patient preferences also shape prescribing decisions (Haines & O'Byrne, 2023; McNeil et al., 2022). This lack of standardized prescribing guidance raises questions about the objectivity and clinical utility of OUD as a meaningful eligibility threshold and whether it acts as a barrier to accessing these programs (Bird et al., 2024; Boyd et al., 2020). Standardized eligibility criteria and prescription practices could strengthen the evidence and credibility of these novel interventions.

Summary of literature characteristics and outcomes

Most of the included sources in our study was published in Canada (98 %), highlighting that this concept remains predominantly a Canadian phenomenon in both practice and research. Despite some promising initial findings, our findings suggest that the evidence on prescribed pharmaceutical alternatives remains nascent. The available evidence relies mainly on observational studies (often including self-reported data and without control groups), and qualitative studies that provide valuable insights into patient and provider perspectives on mechanisms and outcomes but are less suited to providing robust causal inferences. While some population-based cohort studies suggest reductions in overdose-related events, healthcare utilization, and social harms (Gomes, Kolla, et al., 2022; Slaunwhite et al., 2024; Young et al., 2022, 2023). However, other studies have found no measurable benefits at the population level, sometimes due to limited analytic granularity or confounding variables (Nguyen et al., 2024). Long-term outcomes have not yet been evaluated as most programs are still relatively new, and several ongoing studies are expected to address these questions as data mature. Additionally, few studies have systematically examined unintended harms such as medication diversion or the impact of these programs on the broader community. This gap highlights the need for rigorous longitudinal research, including randomized or quasi-experimental designs, to capture these interventions' full range of outcomes and unintended consequences.

The potential for diversion also warrants attention, particularly with unwitnessed short-acting opioids (Ahamad et al., 2020; Hales et al., 2020; Victoria Safer Initiative, 2022). From the scoping review component of our study, only 1 quantitative study (Brothers et al., 2022b) assessed diversion, and seven qualitative studies discussed it (Giang et al., 2023; Haines et al., 2022, 2025; Haines & O'Byrne, 2023; Kalicum et al., 2024; Kolla et al., 2021; McMurchy & Palmer, 2022). Public health research on the impacts of take-home opioid analgesic pills in the community, preceding safe(r) supply programs, has highlighted concerns about the development of iatrogenic OUD (Hulme et al., 2018; Strang et al., 2020) and contribution to the unregulated prescription opioid market (Jones et al., 2014). While concerns persist regarding the possibility of iatrogenic OUD (Hulme et al., 2018; Strang et al., 2020) and the confounding of income-generating activities, it has been argued that diverted pharmaceuticals can also serve as an informal harm reduction mechanism, offering a safer option than unregulated fentanyl for those lacking access to prescribed medications (Kalicum et al., 2024). In settings where access to pharmaceutical alternatives is highly restricted, diversion may be driven not only by individual behavior but

by structural scarcity and punitive drug policies. Addressing root causes of diversion (e.g., insufficient wrap-around services, unmet survival and substance use needs) remain central to sustainability of safe(r) supply programs (Martignetti et al., 2025; Olding et al., 2024). Despite increasing concern about diversion, existing health system and administrative datasets are not designed to capture diversion-related behaviors or dynamics. Primary data collection is therefore critical, through community-based qualitative studies, anonymous self-reporting, ethnographic fieldwork, or peer-led research efforts, to develop a more accurate understanding of when, how, and why diversion occurs.

Future directions and recommendations

Our work contributes to the literature by clarifying approaches previously grouped under the broad concept of "safe(r) supply". Our findings help clarifying the concepts, set research priorities and define key indicators for research reporting and incremental evaluation (e.g., patient characteristics, eligibility criteria, medications prescribed, the extent of take-home dosing, treatment objectives, and integration of patient values and preferences). This distinction is crucial as existing interventions often group individuals who have not benefitted from conventional OAT with those who may decline OAT for other reasons, obscuring key differences in patient motivations and treatment pathways. There is a growing body of evidence for implementations following the model case (i.e., prescribed opioids with OAT offered or co-prescribed), positioning it for the development of clinical recommendations and integration into routine clinical practice. Continued research is needed to strengthen this evidence base and guide implementation. Other alternative cases, such as fentanyl patch prescribing, warrant further investigation to build a strong foundation for potential clinical integration. The non-medicalized approach remains underexplored in the literature, raising questions about the willingness and feasibility of pursuing this approach within the Canadian context. Core indicators, informed by the OPTIMUS group, which is developing international consensus for monitoring OUD treatment outcomes (Wiessing et al., 2023), could ensure consistency and comparability while allowing for adaptation to each program's domain. Moreover, given the multiple, variable, and context-specific components, it may be most helpful to conceptualize these interventions as "complex interventions" (Skivington et al., 2021). This framing offers a valuable roadmap for research by emphasizing the importance of identifying core vs. peripheral components, necessary vs. sufficient elements, and clarifying the mechanisms of impact and contextual conditions under which interventions are most effective.

Clinicians have been central to developing and implementing prescribed opioid alternatives interventions (McCall et al., 2024) Many of these initiatives have improved retention among individuals disengaged from healthcare services and are perceived as successful and acceptable for patients (Foreman-Mackey et al., 2022; Haines & O'Byrne, 2023; Ivsins et al., 2021; Schmidt et al., 2023). Evidence-based regulatory and policy frameworks could help further define and clarify physicians' role in prescribing pharmaceutical opioid alternatives and better distinguish access to these interventions in terms of clinical care and public health measures. Meanwhile, non-prescription-based approaches, such as peer-led or community-based safe supply programs, are a potential strategy for engaging individuals outside conventional healthcare settings, although these efforts often depend on policy and legislative changes. Ongoing collaboration is essential to determine how non-prescription-based interventions can effectively address the ongoing overdose crisis in Canada. Given the quickly changing evidence landscape, findings of this review would benefit from being updated regularly, through systematic reviews of outcomes as the literature becomes more populated and a living clinical practice guideline, to ensure recommendations reflect the latest research.

Limitations

A limitation of this review is the rapidly evolving nature of this field, with new studies being published frequently (Ivsins et al., 2024; Kalicum et al., 2025; Norton et al., 2024; Olding et al., 2024; Schmidt et al., 2024; Urbanoski et al., 2024). Additionally, the exclusion of studies focused specifically on stimulant substitution therapy, while appropriate given the focus on OUD, may have omitted some relevant conceptual insights. While the reports we reviewed on the non-medicalized case have fewer descriptions of wraparound services compared to the other approaches, this does not necessarily imply their absence. It is possible that these services are available but not well-documented in the reports we examined. Although this review did not explicitly limit its scope to Canada, the scarcity of studies from other countries reflects that "safe(r) supply" is predominantly a Canadian phenomenon, with fewer comparable interventions being implemented or documented elsewhere. Additionally, provincial variations in definitions and interpretations of safe vs. safer supply could offer important granularity to how the concept is understood and implemented across jurisdictions in Canada. Given the complexity of the landscape and the substantial work required (e.g., a comprehensive environmental scan), this level of analysis was beyond the scope of this paper.

Conclusion

Our findings highlighted boundaries and conceptual ambiguities in interventions that provide safer alternatives to the toxic unregulated drug supply, often grouped under an umbrella term of "safe(r) supply". The proposed framework can foster a more inclusive and effective strategy for addressing the ongoing opioid crisis. Collective agreement on appropriate terminology, distinguishing prescribed opioid alternatives interventions (currently referred to as safer supply) and safe supply, and a clearer research agenda are essential to evaluate the distinct benefits and harms of medicalized and non-medicalized approaches across the continuum of care. The sustainability and broader application of these approaches beyond the specific and current Canadian context will also require a robust evaluation and strong evidence of their benefits and harms. As these interventions continue to evolve in response to the ongoing drug toxicity crisis, future research should focus on addressing these knowledge gaps to inform and optimize evidence-based guidelines and policy frameworks.

Ethics approval

The authors declare that the work reported herein did not require ethics approval because it did not involve animal or human participation.

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CRediT authorship contribution statement

Uyen Do: Writing – review & editing, Writing – original draft, Visualization, Validation, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Sarah Larney:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Matthew Bonn:** Writing – review & editing, Validation, Formal analysis. **Ingrid Matei:** Writing – review & editing, Validation, Formal analysis, Data curation. **Camille Zolopa:** Writing – review & editing, Data curation. **Amy Bergeron:** Writing – review & editing, Validation, Methodology, Conceptualization. **Mohammad Karamouzian:** Writing – review & editing, Validation. **Elaine Hyshka:** Writing – review & editing, Validation. **Thomas D. Brothers:** Writing – review & editing, Validation. **Nikki Bozinoff:** Writing – review & editing, Validation. **Dan Werb:** Writing – review & editing, Validation. **Didier Jutras-Aswad:** Writing – review & editing, Validation. **Stine Høj:** Methodology, Conceptualization. **Isabelle Boisvert:** Writing – review & editing, Validation. **Igor Yakovenko:** Writing – review & editing, Validation. **Julie Bruneau:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

SL has received advisory board fees from Gilead Sciences. JB has received advisory board fees from Gilead Sciences and AbbVie, as well as a research grant from Gilead Sciences, outside the scope of this work. DJA received study materials from Cardiol Therapeutics for a clinical trial funded by a public organization (2022–2023), outside the scope of this work. EH served as Co-Chair of Health Canada's Expert Advisory Group on Safe(r) Supply between 2019 and 2023. DW is a co-founder of DoseCheck, a private entity developing drug checking technology. UD, IM, CZ, AB, MK, TDB, NB, IY, MB, SH, and IB have nothing to declare.

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References

Ahamad, K., Bach, P., Brar, R., Nancy, C., Coll, N., & Compton, M. (2020, March). *Risk mitigation in the context of dual health emergencies v1.5*. British Columbia Centre on Substance Use. https://www.bccsu.ca/wp-content/uploads/2020/04/Risk-Mitigation-in-the-Context-of-Dual-Public-Health-Emergencies-v1.5.pdf.

Bahji, A., Danilewitz, M., Sachdev, A., Mathew, N., Lamba, W., Rafizadeh, R., Chopra, N., Dhaliwal, A., George, T. P., Crockford, D., Primeau, V., Tibbo, P., Buckley, L., & Tanguay, R. (2024). What psychiatrists should know about prescribed safer opioid supply. *Canadian Journal of Psychiatry. Revue Canadienne De Psychiatrie, 69*(11), 806–808. https://doi.org/10.1177/07067437241289964

Bardwell, G., Bowles, J. M., Mansoor, M., Werb, D., & Kerr, T. (2023). Access to tablet injectable opioid agonist therapy in rural and smaller urban settings in British Columbia, Canada: A qualitative study. *Substance Abuse Treatment, Prevention, and Policy, 18*(1), 14. https://doi.org/10.1186/s13011-023-00525-2

Bardwell, G., Ivsins, A., Mansoor, M., Nolan, S., & Kerr, T. (2023). Safer opioid supply via a biometric dispensing machine: A qualitative study of barriers, facilitators and associated outcomes. *CMAJ: Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne, 195*(19), E668–E676. https://doi.org/10.1503/cmaj.221550

Bardwell, G., Ivsins, A., Wallace, J. R., Mansoor, M., & Kerr, T. (2024). "The machine doesn't judge": Counternarratives on surveillance among people accessing a safer opioid supply via biometric machines. *Social Science & Medicine, 345*, Article 116683. https://doi.org/10.1016/j.socscimed.2024.116683

Bardwell, G., Wood, E., & Brar, R. (2019). Fentanyl assisted treatment: A possible role in the opioid overdose epidemic? *Substance Abuse Treatment, Prevention, and Policy, 14*(1), 50. https://doi.org/10.1186/s13011-019-0241-2

Bird, K., Genuis, Q., & Ickowicz, S. (2024). Clinicians' Perspectives and an ethical analysis of safer supply opioid prescribing. *Journal of Bioethical Inquiry*. https://doi.org/10.1007/s11673-024-10387-3

Bojko, M. J., Mazhnaya, A., Marcus, R., Makarenko, I., Islam, Z., Filippovych, S., Dvoriak, S., & Altice, F. L. (2016). The future of opioid agonist therapies in Ukraine: A qualitative assessment of multilevel barriers and ways forward to promote retention in treatment. *Journal of Substance Abuse Treatment, 66*, 37–47. https://doi.org/10.1016/j.jsat.2016.03.003

Bonn, M., Touesnard, N., Cheng, B., Pugliese, M., Comeau, E., Bodkin, C., Brothers, T. D., Genge, L., Herder, M., Lepage, C., Scheime, A., Werb, D., & Wildeman, S. (2020). *Securing safe supply during COVID-19 and beyond: Scoping review and knowledge mobilization*. June 17. Canadian Institutes of Health Research https://cihr-irsc.gc.ca/e/52043.html.

Bowles, J., Nyx, E., Kalicum, J., & Kerr, T. (2024). Qualitative findings from North America's first drug compassion club. *PLoS One, 19*(12), Article e0315804. https://doi.org/10.1371/journal.pone.0315804

Boyd, S., Ivsins, A., & Murray, D. (2020). Problematizing the DSM-5 criteria for opioid use disorder: A qualitative analysis. *International Journal of Drug Policy, 78*. https://doi.org/10.1016/j.drugpo.2020.102690 *(no pagination)*.

British Columbia Centre on Substance Use. (2019). *Heroin compassion clubs*. https://www.bccsu.ca/wp-content/uploads/2019/02/Report-Heroin-Compassion-Clubs.pdf.

British Columbia Centre on Substance Use. (2022). *Prescribed safer supply protocols: Fentanyl patch*. https://www.bccsu.ca/wp-content/uploads/2022/10/Prescribed-Safer-Supply-Protocols-Fentanyl-Patch.pdf.

British Columbia Centre on Substance Use. (2023). *Prescribed safer supply protocols: Fentanyl tablet (PRN and Maintenance) Clinical Summary*. https://www.bccsu.ca/wp-content/uploads/2023/08/Clinical-Summary-Fentanyl-Tablet.pdf.

Brothers, T. D., Leaman, M., Bonn, M., Lewer, D., Atkinson, J., Fraser, J., Gillis, A., Gniewek, M., Hawker, L., Hayman, H., Jorna, P., Martell, D., O'Donnell, T., Rivers-Bowerman, H., & Genge, L. (2022a). Evaluation of an emergency safe supply drugs and managed alcohol program in COVID-19 isolation hotel shelters for people experiencing homelessness. *Drug and Alcohol Dependence, 235*. https://doi.org/10.1016/j.drugalcdep.2022.109440 *(no pagination)*.

Brothers, T. D., Leaman, M., Bonn, M., Lewer, D., Atkinson, J., Fraser, J., Gillis, A., Gniewek, M., Hawker, L., Hayman, H., Jorna, P., Martell, D., O'Donnell, T., Rivers-Bowerman, H., & Genge, L. (2022b). Evaluation of an emergency safe supply drugs and managed alcohol program in COVID-19 isolation hotel shelters for people experiencing homelessness. *Drug and Alcohol Dependence, 235*. https://doi.org/10.1016/j.drugalcdep.2022.109440 *(no pagination)*. Embase.

Canada, H. (2021, July 22). *Safer supply: Prescribed medications as a safer alternative to toxic illegal drugs* [Service description]. https://www.canada.ca/en/health-canada/services/opioids/responding-canada-opioid-crisis/safer-supply.html.

Canadian Association of People who Use Drugs. (2019). *Safe supply: Concept document*. https://vancouver.ca/files/cov/capud-safe-supply-concept-document.pdf.

Canadian Centre on Substance Use and Addiction. (2022, March 18). *CCENDU drug alert—Nitazenes*. https://www.ccsa.ca/en/nitazenes-ccendu-drug-alert.

Canadian Centre on Substance Use and Addiction, & Canadian Community Epidemiology Network on Drug Use. (2020). *CCENDU alert—Changes related to COVID-19 in the illegal drug supply and access to services, and resulting health harms*. https://www.ccsa.ca/sites/default/files/2020-05/CCSA-COVID-19-CCENDU-Illegal-Drug-Supply-Alert-2020-en.pdf.

Comeau, E., Bonn, M., Wildeman, S., & Herder, M. (2023). 'More of the same, but worse than before': A qualitative study of the challenges encountered by people who use drugs in Nova Scotia, Canada during COVID-19. *PLoS One, 18*(4), Article e0283979. https://doi.org/10.1371/journal.pone.0283979

Cool Aid Community Health Centre. (2021). *Cool aid community health centre report on risk mitigation guidance prescriptions*. https://coolaid.org/wp-content/uploads/2021/03/CACHC_RMG_March-August2020Report.pdf.

Covidence—Better systematic review management. (n.d.). Covidence. Retrieved April 8, 2024, from https://www.covidence.org/.

Drug User Liberation Front, & Vancouver Area Network of Drug Users. (2023). *The D.U.L.F. and V.A.N.D.U. Evaluative compassion club and fulfillment centre framework: A strategic framework for preventing overdose deaths due to the unpredictable illicit drug supply*. Archived on the Wayback Machine July 30 2024. https://web.archive.org/web/20240730084142/https://www.dulf.ca/_files/ugd/fe034c_848afa78e1e947dfb03b5f962dd05a54.pdf?index=true.

Duff, E., Fehr, C., Shams, S., Wintoniw, S., Devenney, A., Ashfield, D., & O'Rourke, T. (2024). A cross-sectional study of opioid agonist therapy barriers and facilitators. *The Journal for Nurse Practitioners, 20*(4), Article 104914. https://doi.org/10.1016/j.nurpra.2023.104914

Duthie, K., Mathison, E., Eyford, H., & Ghosh, S. M. (2022). Prescribing safe supply: Ethical considerations for clinicians. *Journal of Medical Ethics, 19*. https://doi.org/10.1136/jme-2021-108087. Embase.

Eydt, E., Glegg, S., Sutherland, C., Meador, K., Trew, M., Perreault, M., Goyer, M.-È., Le Foll, B., Turnbull, J., & Fairbairn, N. (2021). Service delivery models for injectable opioid agonist treatment in Canada: 2 sequential environmental scans. *CMAJ Open, 9*(1), E115–E124. https://doi.org/10.9778/cmajo.20200021

Fairbairn, N., Ross, J., Trew, M., Meador, K., Turnbull, J., MacDonald, S., Oviedo-Joekes, E., Le Foll, B., Goyer, M. E., Perreault, M., & Sutherland, C. (2019). Injectable opioid agonist treatment for opioid use disorder: A national clinical guideline. *Canadian Medical Association Journal, 191*(38), E1049–E1056. https://doi.org/10.1503/cmaj.190344

Ferguson, M., Parmar, A., Papamihali, K., Weng, A., Lock, K., & Buxton, J. A. (2022). Investigating opioid preference to inform safe supply services: A cross sectional study. *International Journal of Drug Policy, 101*. https://doi.org/10.1016/j.drugpo.2021.103574 *(no pagination)*. Embase.

Ferri, M., Minozzi, S., Bo, A., & Amato, L. (2013). Slow-release oral morphine as maintenance therapy for opioid dependence. *The Cochrane Database of Systematic Reviews, 6*. https://doi.org/10.1002/14651858.CD009879.pub2. CD009879.

Fischer, B., & Robinson, T. (2023). Safer drug supply" measures in Canada to reduce the drug overdose fatality toll: Clarifying concepts, practices and evidence within a public health intervention framework. *Journal of Studies on Alcohol and Drugs, 84*(6), 801–807. https://doi.org/10.15288/jsad.23-00195

Foreman-Mackey, A., Pauly, B., Ivsins, A., Urbanoski, K., Mansoor, M., & Bardwell, G. (2022). Moving towards a continuum of safer supply options for people who use drugs: A qualitative study exploring national perspectives on safer supply among professional stakeholders in Canada. *Substance Abuse Treatment, Prevention, and Policy, 17*(1), 66. https://doi.org/10.1186/s13011-022-00494-y. Embase.

Gagnon, M., Rudzinski, K., Guta, A., Schmidt, R.A., Kryszajtys, D.T., Kolla, G., & Strike, C. (2023). Impact of safer supply programs on injection practices: Client and provider experiences in Ontario, Canada. *Harm Reduction Journal*, 20(1), 81. https://doi.org/10.1186/s12954-023-00817-7.

Giang, K., Charlesworth, R., Thulien, M., Mulholland, A., Barker, B., Brar, R., Pauly, B., & Fast, D. (2023). Risk mitigation guidance and safer supply prescribing among young people who use drugs in the context of COVID-19 and overdose emergencies. *International Journal of Drug Policy, 115*, Article 104023. https://doi.org/10.1016/j.drugpo.2023.104023

Glegg, S., McCrae, K., Kolla, G., Touesnard, N., Turnbull, J., Brothers, T. D., Brar, R., Sutherland, C., Le Foll, B., Sereda, A., Goyer, M. E., Rai, N., Bernstein, S., & Fairbairn, N. (2022). COVID just kind of opened a can of whoop-ass": The rapid growth of safer supply prescribing during the pandemic documented through an environmental scan of addiction and harm reduction services in Canada. *International Journal of Drug Policy, 106*. https://doi.org/10.1016/j.drugpo.2022.103742 *(no pagination)*. Embase.

Gomes, T., Hamzat, B., Holton, A., Shearer, D., Singh, S., Cormack, D.M., Yang, J., Eurich, D., Randall, R., Liu, Z., Missaoui, H., Kaboré, J.-L., Cheung, G., & Benigeri, M. (2024). *Trends in opioid prescribing in Canada, 2018-2022*.

Gomes, T., Kolla, G., McCormack, D., Sereda, A., Kitchen, S., & Antoniou, T. (2022). Clinical outcomes and health care costs among people entering a safer opioid supply program in Ontario. *CMAJ, Canadian Medical Association Journal, 194*(36), E1233–E1242. https://doi.org/10.1503/cmaj.220892. Embase.

Gomes, T., McCormack, D., Bozinoff, N., Tadrous, M., Antoniou, T., Munro, C., Campbell, T., Paterson, J. M., Mamdani, M., & Sproule, B. (2022). Duration of use and outcomes among people with opioid use disorder initiating methadone and buprenorphine in Ontario: A population-based propensity-score matched cohort study. *Addiction, 117*(7), 1972–1981. https://doi.org/10.1111/add.15862

Gomes, T., Murray, R., Kolla, G., Leece, P., Kitchen, S., Campbell, T., Besharah, J., Cahill, T., Garg, R., Iacono, A., Munro, C., Nunez, E., Robertson, L., Shearer, D., Singh, S., Toner, L., & Watford, J. (2022). *Patterns of medication and healthcare use among people who died of an opioid-related toxicity during the COVID-19 pandemic in Ontario*. https://odprn.ca/wp-content/uploads/2022/01/Opioid-Related-Toxicity-Deaths-and-Healthcare-Use-Report.pdf.

Government of Canada. (2021). *Safer supply*. July 22. Government of Canada [Service description] https://www.canada.ca/en/health-canada/services/opioids/responding-canada-opioid-crisis/safer-supply.html.

Government of Canada. (2022). Fourth law enforcement roundtable on drugs. *Public Safety Canada*. https://www.publicsafety.gc.ca/cnt/rsrcs/pblctns/2022-frth-lw-nfrcmnt-rndtbl-drgs/index-en.aspx.

Government of Canada. (2024). *Opioid- and stimulant-related harms in Canada*. Government of Canada. https://health-infobase.canada.ca/substance-related-harms/opioids-stimulants/.

Haines, M., Hill, E., & O'Byrne, P. (2025). Safer supply programs: Discussions on medication diversion, sharing, and selling. *International Journal of Drug Policy, 137*, Article 104731. https://doi.org/10.1016/j.drugpo.2025.104731

Haines, M., Kerwin, S., Drolet, J., Tefoglou, A., & O'Byrne, P. (2024). *Safer supply Ottawa evaluation: Summer 2024 report*. https://safersupplyottawa.com/research/.

Haines, M., & O'Byrne, P. (2023). Safer opioid supply: Qualitative program evaluation. *Harm Reduction Journal, 20*(1), 53. https://doi.org/10.1186/s12954-023-00776-z

Haines, M., Tefoglou, A., & O'Byrne, P. (2022). *Safer supply Ottawa evaluation*.

Hales, J., Kolla, G., Man, T., O'Reilly, E., Rai, N., & Sereda, A. (2020). *Emergency safer supply program: A harm reduction informed guiding document for primary care teams*.

Hardill, K., & King, C. (2024). *Embedding a safer supply program in a small urban community: Peterborough 360 degree safer supply program (SSP) Evaluation May 2022 through December 2023*. Peterborough 360 degree nurse practitioner-led clinic. https://www.360nursepractitionerledclinic.ca/documents/.

Health Canada. (2018, November 14). *Fentanyl* [Guidance]. https://www.canada.ca/en/health-canada/services/substance-use/controlled-illegal-drugs/fentanyl.html.

Health Canada. (2019). *Toolkit for substance use and addictions program applicants*. https://drive.google.com/file/d/1gOxsb6LNVmrEyeU3CBwr7XPYSPHG9S8L/view?usp=embed_facebook.

Health Canada. (2024, January 26). *Supervised consumption sites pandemic impact survey: Results at a glance* [Surveys]. https://www.canada.ca/en/health-canada/services/publications/healthy-living/supervised-consumption-sites-pandemic-impact-survey.html.

Howard, R., Brown, C. S., Lai, Y.-L., Gunaseelan, V., Brummett, C. M., Englesbe, M., Waljee, J., & Bicket, M. C. (2023). Postoperative opioid prescribing and new persistent opioid use: The risk of excessive prescribing. *Annals of Surgery, 277*(6), e1225–e1231. https://doi.org/10.1097/SLA.0000000000005392

Hu, T., McCormack, D., Juurlink, D. N., Campbell, T. J., Bayoumi, A. M., Leece, P., Kent, J. T., & Gomes, T. (2023). Initiation of opioid agonist therapy after hospital visits for opioid poisonings in Ontario. *CMAJ: Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne, 195*(49), E1709–E1717. https://doi.org/10.1503/cmaj.231014

Hulme, S., Bright, D., & Nielsen, S. (2018). The source and diversion of pharmaceutical drugs for non-medical use: A systematic review and meta-analysis. *Drug and Alcohol Dependence, 186*, 242–256. https://doi.org/10.1016/j.drugalcdep.2018.02.010

Hutchinson, M., Lavigne, É., & Patterson, Z. (2023). Opioid use in the era of COVID-19: A multifaceted study of the opioid epidemic in Canada. *Frontiers in Pharmacology, 14*, Article 1122441. https://doi.org/10.3389/fphar.2023.1122441

Ivsins, A., Boyd, J., Mayer, S., Collins, A., Sutherland, C., Kerr, T., & McNeil, R. (2021). It's helped me a lot, just like to stay alive": A qualitative analysis of outcomes of a novel hydromorphone tablet distribution program in Vancouver, Canada. *Journal of Urban Health : Bulletin of the New York Academy of Medicine, 98*(1), 59–69. https://doi.org/10.1007/s11524-020-00489-9. Embase.

Ivsins, A., MacKinnon, L., Bowles, J. M., Slaunwhite, A., & Bardwell, G. (2022). Overdose prevention and housing: A qualitative study examining drug use, overdose risk, and access to safer supply in permanent supportive housing in Vancouver, Canada. *Journal of Urban Health : Bulletin of the New York Academy of Medicine, 99*(5), 855–864. https://doi.org/10.1007/s11524-022-00679-7. Embase.

Ivsins, A., Mansoor, M., Bowles, J., & Bardwell, G. (2024). Reasons for enrolling in safer supply programs: A longitudinal qualitative study on participant goals and related outcomes in the MySafe program. *Journal of Studies on Alcohol and Drugs, 85*(6), 845–855. https://doi.org/10.15288/jsad.23-00388

Jacka, B. P., Janssen, T., Garner, B. R., Yermash, J., Yap, K. R., Ball, E. L., Hartzler, B., & Becker, S. J. (2021). Impacts of the COVID-19 pandemic on healthcare access among patients receiving medication for opioid use disorder. *Drug and Alcohol Dependence, 221*, Article 108617. https://doi.org/10.1016/j.drugalcdep.2021.108617

Jones, C. M., Paulozzi, L. J., & Mack, K. A. (2014). Sources of prescription opioid pain relievers by frequency of past-year nonmedical use: United States, 2008-2011. *JAMA Internal Medicine, 174*(5), 802–803. https://doi.org/10.1001/jamainternmed.2013.12809

Jones, W., Kaoser, R., & Fischer, B. (2021). Patterns, trends and determinants of medical opioid utilization in Canada 2005–2020: Characterizing an era of intensive rise and fall. *Substance Abuse Treatment, Prevention, and Policy, 16*(1), 65. https://doi.org/10.1186/s13011-021-00396-5

Kalicum, J., Nyx, E., Kennedy, M. C., & Kerr, T. (2024). The impact of an unsanctioned compassion club on non-fatal overdose. *International Journal of Drug Policy*. , Article 104330. https://doi.org/10.1016/j.drugpo.2024.104330

Kalicum, J., Nyx, E., Kennedy, M. C., & Kerr, T. (2025). Perceived impacts of North Americas first de-medicalized safer supply program. *Substance Abuse Treatment, Prevention, and Policy, 20*(1), 11. https://doi.org/10.1186/s13011-025-00642-0

Klaire, S., Sutherland, C., Kerr, T., & Kennedy, M. C. (2022). A low-barrier, flexible safe supply program to prevent deaths from overdose. . [French] *CMAJ, Canadian Medical Association Journal, 194*(31), E1098–E1100. https://doi.org/10.1503/CMAJ.211515-F. Embase.

Kleinman, R. A., & Thakrar, A. P. (2023). Using short-acting opioids to relieve opioid withdrawal in hospital. *CMAJ: Canadian Medical Association Journal = Journal de l'Association Medicale Canadienne, 195*(49), E1718–E1720. https://doi.org/10.1503/cmaj.230968

Kolla, G., & Fajber, K. (2023). *Safer opioid supply program evaluation: A comparison of SOS client outcomes from 2022 to 2023*. London Intercommunity Health Center. https://www.substanceusehealth.ca/sites/default/files/resources/2023-LIHC-SOS-Evaluation.pdf.

Kolla, G., Long, C., Perri, M., Bowra, A., & Penn, R. (2021). *Safer opioid supply program: Preliminary report*. November 22. London InterCommunity Health Centre https://lihc.on.ca/wp-content/uploads/2022/01/2021-SOS-Evaluation-Full.pdf.

Kurz, M., Min, J. E., Dale, L. M., & Nosyk, B. (2022). Assessing the determinants of completing OAT induction and long-term retention: A population-based study in British Columbia, Canada. *Journal of Substance Abuse Treatment, 133*, Article 108647. https://doi.org/10.1016/j.jsat.2021.108647

Lam Wai Shun, P., Swaine, B., & Bottari, C. (2022). Combining scoping review and concept analysis methodologies to clarify the meaning of rehabilitation potential after acquired brain injury. *Disability and Rehabilitation, 44*(5), 817–825. https://doi.org/10.1080/09638288.2020.1779825

Ledlie, S., Garg, R., Cheng, C., Kolla, G., Antoniou, T., Bouck, Z., & Gomes, T. (2024). Prescribed safer opioid supply: A scoping review of the evidence. *The International Journal on Drug Policy, 125*, Article 104339. https://doi.org/10.1016/j.drugpo.2024.104339

Macevicius, C., Gudiño Pérez, D., Norton, A., Kolla, G., Beck-McGreevy, P., Selfridge, M., Kalicum, J., Hutchison, A., Urbanoski, K., Barker, B., Slaunwhite, A., Nosyk, B., & Pauly, B.(Bernie) (2023). Just have this come from their prescription pad: The

medicalization of safer supply from the perspectives of health planners in BC, Canada. *Drugs: Education, Prevention and Policy, 0*(0), 1–11. https://doi.org/10.1080/09687637.2023.2283383

Mansoor, M., Foreman-Mackey, A., Ivsins, A., & Bardwell, G. (2023). Community partner perspectives on the implementation of a novel safer supply program in Canada: A qualitative study of the MySafe project. *Harm Reduction Journal, 20*(1), 61. https://doi.org/10.1186/s12954-023-00789-8

Martignetti, L., Knight, R., Nafeh, F., Atkinson, K., Laurence, G., Johnson, C. H., Werb, D., & Karamouzian, M. (2025). Motivations for and perspectives of medication diversion among clients of a safer opioid supply program in Toronto, Canada. *International Journal of Drug Policy, 135*, Article 104665. https://doi.org/10.1016/j.drugpo.2024.104665

McCall, J., Hobbs, H., Ranger, C., Cameron, F., Stuart, H., Nelken, J., Majalahti, J., Urbanoski, K., Kolla, G., LeMaistre, J., Toombs, K., Herriot, R., & Pauly, B. (2024). Prescribed safer supply during dual public health emergencies: A qualitative study examining service providers perspectives on early implementation. *Substance Abuse Treatment, Prevention, and Policy, 19*(1), 19. https://doi.org/10.1186/s13011-024-00598-7

McCrae, K., Glegg, S., Goyer, M. E., Le Foll, B., Brar, R., Sutherland, C., & Fairbairn, N. (2022). The changing landscape of pharmaceutical alternatives to the unregulated drug supply during COVID-19. *Harm Reduction Journal, 19*(1). https://doi.org/10.1186/s12954-022-00657-x *(no pagination)*. Embase.

McGowan, J., Sampson, M., Salzwedel, D. M., Cogo, E., Foerster, V., & Lefebvre, C. (2016). PRESS Peer Review of Electronic Search Strategies: 2015 guideline statement. *Journal of Clinical Epidemiology, 75*, 40–46. https://doi.org/10.1016/j.jclinepi.2016.01.021

McMurchy, D., & Palmer, R. (2022). *Assessment of the implementation of safer supply pilot projects*. https://www.substanceusehealth.ca/sites/default/files/resources/2022-03-safer_supply_preliminary_assessment_report_en.pdf.

McNeil, R., Fleming, T., Mayer, S., Barker, A., Mansoor, M., Betsos, A., Austin, T., Parusel, S., Ivsins, A., & Boyd, J. (2022). Implementation of safe supply alternatives during intersecting COVID-19 and overdose health emergencies in British Columbia, Canada, 2021. *American Journal of Public Health, 112*(S2), S151–S158. https://doi.org/10.2105/AJPH.2021.306692. Embase.

Metcalfe, R. K., Dobischok, S., Bansback, N., MacDonald, S., Byres, D., Lajeunesse, J., Harrison, S., Koch, B., Topping, B., Brock, T., Foreman, J., Schechter, M., & Oviedo-Joekes, E. (2024). Client preferences for the design and delivery of injectable opioid agonist treatment services: Results from a best-worst scaling task. *Addiction, 119*(12), 2139–2150. https://doi.org/10.1111/add.16620

Meyer, M., Strasser, J., Kock, P., Walter, M., Vogel, M., & Dursteler, K. M. (2022). Experiences with take-home dosing in heroin-assisted treatment in Switzerland during the COVID-19 pandemic-Is an update of legal restrictions warranted? *International Journal of Drug Policy, 101*. https://doi.org/10.1016/j.drugpo.2021.103548 *(no pagination)*.

Milaney, K., Passi, J., Zaretsky, L., Liu, T., O'Gorman, C. M., Hill, L., & Dutton, D. (2021). Drug use, homelessness and health: Responding to the opioid overdose crisis with housing and harm reduction services. *Harm Reduction Journal, 18*(1). https://doi.org/10.1186/s12954-021-00539-8 *(no pagination)*. Embase.

Ministry of Mental Health and Addictions Ministry of Health. (2021). *Access to prescribed safer supply in British Columbia: Policy direction*. https://www2.gov.bc.ca/assets/gov/overdose-awareness/prescribed_safer_supply_in_bc.pdf.

Nafeh, F., Mbichila, T., Bouck, Z., Scheim, A., Mitra, S., Bonn, M., Morris, F., Atkinson, K., Mason, K., Eeuwes, J., Strike, C., Gomes, T., Werb, D., & Karamouzian, M. (2023). A preliminary assessment of short-term social and substance use-related outcomes among clients of integrated safer opioid supply pilot programs in Toronto, Canada. *International Journal of Mental Health and Addiction*. https://doi.org/10.1007/s11469-023-01219-3

Nguyen, H. V., Mital, S., Bugden, S., & McGinty, E. E. (2024). British Columbia's safer opioid supply policy and opioid outcomes. *JAMA Internal Medicine*. https://doi.org/10.1001/jamainternmed.2023.7570

Norton, A., Ivsins, A., Holliday, E., Sutherland, C., Kerr, T., & Kennedy, M. C. (2024). A qualitative evaluation of a fentanyl patch safer supply program in Vancouver, Canada. *International Journal of Drug Policy, 131*, Article 104547. https://doi.org/10.1016/j.drugpo.2024.104547

Nosyk, B., Min, J. E., Homayra, F., Kurz, M., Guerra-Alejos, B. C., Yan, R., Piske, M., Seaman, S. R., Bach, P., Greenland, S., Karim, M. E., Siebert, U., Bruneau, J., Gustafson, P., Kampman, K., Korthuis, P. T., Loughin, T., McCandless, L. C., Platt, R. W., & Socías, M. E. (2024). Buprenorphine/naloxone vs methadone for the treatment of opioid use disorder. *Journal of the American Medical Association, 332*(21), 1822–1831. https://doi.org/10.1001/jama.2024.16954

Nyx, E., & Kalicum, J. (2024). A case study of the DULF compassion club and fulfillment centre—A logical step forward in harm reduction. *International Journal of Drug Policy, 131*, Article 104537. https://doi.org/10.1016/j.drugpo.2024.104537

Office of the Provincial Health Officer. (2024). *Alternatives to unregulated drugs: Another step in saving lives*. The Office. https://www2.gov.bc.ca/assets/gov/health/about-bc-s-health-care-system/office-of-the-provincial-health-officer/reports-publications/special-reports/alternatives_to_unregulated_drugs.pdf.

Olding, M., Ivsins, A., Mayer, S., Betsos, A., Boyd, J., Sutherland, C., Culbertson, C., Kerr, T., & McNeil, R. (2020). A low-barrier and comprehensive community-based harm-reduction site in Vancouver, Canada. *American Journal of Public Health, 110*(6). https://doi.org/10.2105/AJPH.2020.305612. Article 6.

Olding, M., Rudzinski, K., Schmidt, R., Kolla, G., German, D., Sereda, A., Strike, C., & Guta, A. (2024). Perspectives on diversion of medications from safer opioid supply programs. *JAMA Network Open, 7*(12), Article e2451988. https://doi.org/10.1001/jamanetworkopen.2024.51988

Oviedo-Joekes, E., Brissette, S., Marsh, D. C., Lauzon, P., Guh, D., Anis, A., & Schechter, M. T. (2009). Diacetylmorphine versus methadone for the treatment of opioid addiction. *The New England Journal of Medicine, 361*(8), 777–786. https://doi.org/10.1056/NEJMoa0810635

Oviedo-Joekes, E., Dobischok, S., Carvajal, J., MacDonald, S., McDermid, C., Klakowicz, P., Harrison, S., LaJeunesse, J., Chow, N., Brown, M., Gill, S., & Schechter, M. (2023). Clients' experiences on North America's first take-home injectable opioid agonist treatment (iOAT) program: A qualitative study. *BMC Health Services Research, 23*(1), 553. https://doi.org/10.1186/s12913-023-09558-6

Oviedo-Joekes, E., Guh, D., Brissette, S., Marchand, K., MacDonald, S., Lock, K., Harrison, S., Janmohamed, A., Anis, A. H., Krausz, M., Marsh, D. C., & Schechter, M. T. (2016). Hydromorphone compared with diacetylmorphine for long-term opioid dependence: A randomized clinical trial. *JAMA Psychiatry, 73*(5), 447–455. https://doi.org/10.1001/jamapsychiatry.2016.0109

Oviedo-Joekes, E., MacDonald, S., Boissonneault, C., & Harper, K. (2021). Take home injectable opioids for opioid use disorder during and after the COVID-19 Pandemic is in urgent need: A case study. *Substance Abuse Treatment, Prevention, and Policy, 16*(1), 22. https://doi.org/10.1186/s13011-021-00358-x

Palayew, A., Banta-Green, C. J., Lamont, M., Damper, D., Moreno, C., Goodreau, S. M., Mooney, S. J., & Glick, S. N. (2024). Acceptability and anticipated effectiveness of a safe supply of opioids, among people who inject opioids in King County, WA. *International Journal of Drug Policy, 127*, Article 104389. https://doi.org/10.1016/j.drugpo.2024.104389

Palis, H., Haywood, B., McDougall, J., Xavier, C. G., Desai, R., Tobias, S., Burgess, H., Ferguson, M., Liu, L., Kinniburgh, B., Slaunwhite, A. K., Crabtree, A., & Buxton, J. A. (2024). Factors associated with obtaining prescribed safer supply among people accessing harm reduction services: Findings from a cross-sectional survey. *Harm Reduction Journal, 21*(1), 5. https://doi.org/10.1186/s12954-024-00928-9

Pauly, B., McCall, J., Cameron, F., Stuart, H., Hobbs, H., Sullivan, G., Ranger, C., & Urbanoski, K. (2022). A concept mapping study of service user design of safer supply as an alternative to the illicit drug market. *International Journal of Drug Policy, 110*. https://doi.org/10.1016/j.drugpo.2022.103849 *(no pagination)*. Embase.

Peters, M. D. J., Godfrey, C., McInerney, P., Munn, Z., Tricco, A. C., & Khalil, H. (2024). Scoping reviews (2020). *JBI Manual for Evidence Synthesis*. https://doi.org/10.46658/JBIMES-24-09

Pijl, E. M., Alraja, A., Duff, E., Cooke, C., Dash, S., Nayak, N., Lamoureux, J., Poulin, G., Knight, E., & Fry, B. (2022). Barriers and facilitators to opioid agonist therapy in rural and remote communities in Canada: An integrative review. *Substance Abuse Treatment, Prevention, and Policy, 17*, 62. https://doi.org/10.1186/s13011-022-00463-5

Pilarinos, A., Fast, D., Nosova, E., Kwa, Y., Joe, R., Buxton, J. A., & DeBeck, K. (2022). Initiation of opioid agonist treatment and subsequent substance use and other patterns among adolescents and young adults in Vancouver, Canada. *Drug and Alcohol Dependence, 235*, Article 109441. https://doi.org/10.1016/j.drugalcdep.2022.109441

Pilarinos, A., Kwa, Y., Joe, R., Thulien, M., Buxton, J. A., DeBeck, K., & Fast, D. (2022). Navigating opioid agonist therapy among young people who use illicit opioids in Vancouver, Canada. *The International Journal on Drug Policy, 107*, Article 103773. https://doi.org/10.1016/j.drugpo.2022.103773

Proctor, E., Silmere, H., Raghavan, R., Hovmand, P., Aarons, G., Bunger, A., Griffey, R., & Hensley, M. (2011). Outcomes for implementation research: Conceptual distinctions, measurement challenges, and research agenda. *Administration and Policy in Mental Health, 38*(2), 65–76. https://doi.org/10.1007/s10488-010-0319-7

Schmidt, R. A., Guta, A., Rai, N., Sereda, A., O'Reilly, E., Hales, J., Kolla, G., & Strike, C. (2024). Safer Opioid supply programs: Hydromorphone prescribing in Ontario as a harm reduction intervention to combat the drug poisoning crisis. *Canadian Journal of Public Health*. https://doi.org/10.17269/s41997-024-00979-2

Schmidt, R. A., Kaminski, N., Kryszajtys, D. T., Rudzinski, K., Perri, M., Guta, A., Benoit, A. C., Bayoumi, A. M., Challacombe, L., Hales, J., Kenny, K., Kolla, G., O'Reilly, E., Sereda, A., Rai, N., & Strike, C. (2023). I don't chase drugs as much anymore, and I'm not dead": Client reported outcomes associated with safer opioid supply programs in Ontario, Canada. *Drug and Alcohol Review, 42*(7), 1825–1837. https://doi.org/10.1111/dar.13745

Selfridge, M., Card, K., Kandler, T., Flanagan, E., Lerhe, E., Heaslip, A., Nguyen, A., Moher, M., Pauly, B., Urbanoski, K., & Fraser, C. (2022). Factors associated with 60-day adherence to "safer supply" opioids prescribed under British Columbia's interim clinical guidance for health care providers to support people who use drugs during COVID-19 and the ongoing overdose emergency. *International Journal of Drug Policy, 105*. https://doi.org/10.1016/j.drugpo.2022.103709 *(no pagination)*. Embase.

Skivington, K., Matthews, L., Simpson, S. A., Craig, P., Baird, J., Blazeby, J. M., Boyd, K. A., Craig, N., French, D. P., McIntosh, E., Petticrew, M., Rycroft-Malone, J., White, M., & Moore, L. (2021). A new framework for developing and evaluating complex interventions: Update of Medical Research Council guidance. *British Medical Journal, 374*, n2061. https://doi.org/10.1136/bmj.n2061

Slaunwhite, A., Min, J. E., Palis, H., Urbanoski, K., Pauly, B., Barker, B., Crabtree, A., Bach, P., Krebs, E., Dale, L., Meilleur, L., & Nosyk, B. (2024). Effect of Risk Mitigation Guidance opioid and stimulant dispensations on mortality and acute care visits during dual public health emergencies: Retrospective cohort study. *British Medical Journal, 384*, Article e076336. https://doi.org/10.1136/bmj-2023-076336

Statistical Reports on Deaths in British Columbia. (2024, October 24). Province of British Columbia; Province of British Columbia. https://www2.gov.bc.ca/gov/content/life-events/death/coroners-service/statistical-reports.

St-Martin, P., & Lacroix, D. (2023). *Prescription Opioid Trends in Canada—An independent IQVIA report on measuring and understanding the use of prescription opioids dispensed from 2019 to 2022*. IQVIA. https://www.iqvia.com/-/media/iqvia/pdfs/canada/white-paper/2023_opioids_report_2019-2022_iqvia_en.pdf.

Strang, J., Groshkova, T., & Metrebian, N. (2012). *New heroin-assisted treatment—Recent evidence and current practices of supervised injectable heroin treatment in Europe and beyond.* European Union Drugs Agency. https://www.euda.europa.eu/publications/insights/heroin-assisted-treatment_en.

Strang, J., Volkow, N. D., Degenhardt, L., Hickman, M., Johnson, K., Koob, G. F., Marshall, B. D. L., Tyndall, M., & Walsh, S. L. (2020). Opioid use disorder. *Nature Reviews Disease Primers, 6*(1), 3. https://doi.org/10.1038/s41572-019-0137-5

The Ontario Drug Policy Research Network. (2021). May 19 *Changing circumstances surrounding opioid-related deaths in Ontario during the COVID-19 pandemic* https://odprn.ca/research/publications/opioid-related-deaths-in-ontario-during-covid/.

Timko, C., Schultz, N. R., Cucciare, M. A., Vittorio, L., & Garrison-Diehn, C. (2016). Retention in medication-assisted treatment for opiate dependence: A systematic review. *Journal of Addictive Diseases, 35*(1), 22–35. https://doi.org/10.1080/10550887.2016.1100960

Urbanoski, K.A., van Roode, T., Selfridge, M., Hogan, K.C., Fraser, J., Lock, K., McGreevy, P.B., Burmeister, C., Barker, B., Slaunwhite, A., Nosyk, B., & Pauly, B. (2024). Access and barriers to safer supply prescribing during a toxic drug emergency: A mixed methods study of implementation in British Columbia, Canada. *Substance Abuse Treatment, Prevention, and Policy*, 19(1), 44. https://doi.org/10.1186/s13011-024-00625-7.

Victoria Safer Initiative. (2022). *Safer supply protocols*. https://www.nss-aps.ca/sites/default/files/resources/2022-10-12-VictoriaSAFERInitiativeProtocols.pdf.

Walker, L., & Avant, K. (2018). *Strategies for Theory Construction in Nursing* (6th ed.). Pearson https://www.pearson.com/en-us/subject-catalog/p/strategies-for-theory-construction-in-nursing/P200000001997/9780137530373.

Waraksa, M., Bond, N., Laurence, G., & Atkinson, K. (2022). *Safer Opioid Supply Program Protocols Parkdale Queen West Community Health Centre Toronto, Ontario*. https://pqwchc.org/wp-content/uploads/Clinical-and-Operational-Protocols-Parkdale-Queen-West-Community-Health-Centre-June-23-2022.pdf.

Weng, J., Fairbairn, N., Sutherland, C., Johnson, C., & Nolan, S. (2022). Supervised tablet injectable opioid agonist therapy (TiOAT): A strategy to address safer supply for individuals with an opioid use disorder? *Journal of Addiction Medicine, 16*(3), 258–260. https://doi.org/10.1097/ADM.0000000000000887. Embase.

Wiessing, L., Banka-Cullen, P., Barbaglia, M. G., Belackova, V., Belbaisi, S. A. S., Blanken, P., Carrieri, P., Comiskey, C., Dacosta-Sánchez, D., Dom, G., Fabricius, V., Faria, H., Ignjatova, L., Inić, N., Jacobsen, B., Javakhishvili, J. D., Kamendy, Z., Kapitány-Fövény, M., Kiss, A., & … for the OPTIMUS study group. (2023). Opioid agonist maintenance treatment outcomes—The OPTIMUS international consensus towards evidence-based and patient-centred care, an interim report. *International Journal of Mental Health and Addiction*. https://doi.org/10.1007/s11469-023-01213-9

Wilson, P., Colizza, K., & Hyshka, E. (2024). Safer supply and political interference in medical practice: Alberta's Narcotics Transition Services. *International Journal of Drug Policy, 133*, Article 104600. https://doi.org/10.1016/j.drugpo.2024.104600

Xavier, C., Palis, H., Liu, L., Kinniburgh, B., & Crabtree, A. (2024). *Receipt and access of prescribed alternatives and opioid agonist treatment among respondents from the 2022 Harm Reduction Client Survey (Knowledge Update)*. BC Centre for Disease Control. http://www.bccdc.ca/Health-Professionals-Site/Documents/HRCS_PA%20Prescription%20Access_Reasons%20for%20Stopping_FINAL.pdf.

Yakovenko, I., Mukaneza, Y., Germé, K., Belliveau, J., Fraleigh, R., Bach, P., Poulin, G., Selby, P., Goyer, M.E., Brothers, T.D., Rehm, J., Hodgins, D.C., Stewart, S.H., Wood, E., & Bruneau, J. (2024). *Management of opioid use disorder: 2024 update to the national clinical practice guideline*. https://doi.org/10.1503/cmaj.241173.

Young, S., Gomes, T., Kolla, G., McCormack, D., Dodd, Z., Raboud, J., & Bayoumi, A. M. (2023). Initiations of safer supply hydromorphone increased during the COVID-19 pandemic in Ontario: An interrupted time series analysis. *PLoS One, 18*(12), Article e0295145. https://doi.org/10.1371/journal.pone.0295145

Young, S., Kolla, G., McCormack, D., Campbell, T., Leece, P., Strike, C., Srivastava, A., Antoniou, T., Bayoumi, A. M., & Gomes, T. (2022). Characterizing safer supply prescribing of immediate release hydromorphone for individuals with opioid use disorder across Ontario, Canada. *International Journal of Drug Policy, 102*, Article 103601. https://doi.org/10.1016/j.drugpo.2022.103601

Yousif (2023, May 5). *Police arrest man for opening store selling hard drugs in Canada*. https://www.bbc.com/news/world-us-canada-65487199.