SFU

CENTRE FOR APPLIED
RESEARCH IN MENTAL HEALTH
AND ADDICTION (CARMHA)

PUBLIC SUPPLY OF ADDICTIVE DRUGS:
A RAPID REVIEW

SELECT KEY FINDINGS

Nineteen studies met our inclusion criteria by: 1. reporting original research findings; 2. advocating for safe supply; and 3. appearing in peer-reviewed journals.

None of the identified studies were systematic reviews, economic analyses, or randomized controlled trials.

None of the identified studies investigated outcomes associated with providing addictive drugs for personal use outside the context of a structured program.

The results most commonly reported confirmed extremely high rates of homelessness, unemployment, food insecurity, and other indicators of poverty and social exclusion among people at high risk for poisoning.

Only one of the included studies recommended specific evidence-based interventions to address the risk factors for addiction reported in their results.

Most of the identified studies (n=15) were conducted in British Columbia by teams with primary expertise in infectious diseases (e.g., HIV).

[1]All authors contributed equally and are listed alphabetically

REVIEW TEAM MEMBERS[1]

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Stefanie N Rezansoff MSc, PhD has earned national and international awards for her research addressing practices that divert people who experience addiction and mental illness from the criminal justice system and toward wellness. Dr Rezansoff is a research scientist at CARMHA.

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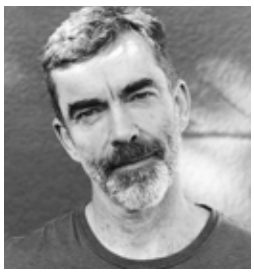


DR. JULIAN M SOMERS

Julian M Somers, MSc, PhD, RPsych is a clinical psychologist and specialist in addiction since 1987. His body of research includes theoretical, clinical, and empirical advances addressing harm reduction and recovery from addiction. He has led numerous large studies investigating ways of helping people who experience addiction, mental illness, homelessness, and involvement with corrections. He is a Distinguished SFU Professor and the Director of CARMHA.

[1]Report developed collaboratively and by consensus. Authors are listed alphabetically.

ABOUT THIS RAPID REVIEW

Researchers and clinicians at Simon Fraser University provide time-sensitive expert support to branches of government, including reviews of evidence. The scope of rapid reviews includes the identification of systematic reviews and economic evaluations, and the inclusion of relevant primary research when systematic reviews are scarce. Rapid reviews are expected to summarize key findings from relevant peer reviewed publications, appraise the quality of available evidence, and assess the generalizability of the available research to other contexts.

The current rapid review incorporates the Alberta Legislature's Select Special Committee to Examine Safe Supply's concept of *safe supply*.[2] The intervention and target population are defined as follows:

The provision of pharmaceutical opioids, heroin, crystal methamphetamine, cocaine, or other substances;

To people who are addicted to or dependent on these substances and who are at high risk for poisoning;

For witnessed or unwitnessed consumption.

Specific outcomes of interest were:

Fatal and non-fatal poisoning;

The health and safety of individuals or communities (e.g., crime, drug diversion);

Any other benefits or consequences.

Alberta's Ministry of Health specified that the current review should discuss the findings in the context of relevant evidence concerning alternative approaches for addressing fatal and non-fatal overdoses and associated impacts, including current standards of care for promoting recovery from addiction.

The term safe supply may suggest to some readers that research already establishes the safety and effectiveness of the practices defined previously. For the purposes of this report we have adopted terminology that does not presume the outcome of our review and refer to the Public Supply of Addictive Drugs (PSAD), which avoids implying safety and effectiveness while accurately describing the practice of interest.

The methodology used in this review is inclusive of peer reviewed publications indexed on MEDLINE. We also included articles provided directly by advocates for PSAD. Our findings are discussed in the broader context of evidence based practices related to the prevention of poisonings and other harms among people who are at high risk.

[2] Alberta Legislature's Special Select Committee to Examine Safe Supply, Mandate, available online: www.assembly.ab.ca/assembly-business/committees/ESS

INTRODUCTION

Over recent decades Canada and the United States have experienced catastrophic increases in addiction and related consequences, including fatal poisonings. The extraordinary rise in fatal poisonings in North America coincides with the fact that per-person consumption of opioids in Canada and the US exceeds that of other high income countries (International Narcotics Control Board, 2013). However, factors other than opioid prescribing are strongly associated with the rise in fatalities. British Columbia has by far the highest per capita poisoning mortality rate in Canada, claiming the lives of an estimated 2,224 people in 2021. The drugs identified among decedents in BC have varied considerably in recent years, and in 2021 included synthetic opioids such as fentanyl (91%), stimulants (74%) benzodiazepines (44%) and various other drugs (BC Coroners Service, 2022). These findings are indicative of a poly-substance use crisis rather than one that narrowly implicates opioids.

In response to the current crisis many have called for a Public Supply of Addictive Drugs (PSAD), referred to by advocates as *safe supply*. Commentators have called for "…a large-scale public health model of safe supply" (Ryan et al., 2020), arguing that "the only pragmatic and ethical way forward is to offer a regulated, safer supply" (Tyndall, 2020). In order to successfully reduce harms among people who are most at risk for poisoning, PSAD aims to provide drugs that would otherwise be obtained from illicit sources, in forms that match drug users' preferred route(s) of administration, and for use independently. PSAD is specifically described as "non-treatment based" (Ivsins, Boyd, Beletsky, et al., 2020) in order to reach individuals who are currently not engaged by health or other services. The Government of Canada states (Government of Canada, n.d.-a) that "safer supply services may offer:

- a range of medication options
- accessible locations
- flexible eligibility requirements
- flexible dosing conditions and carrying rules (for example, clients may be able to pick up their supply and use as needed)
- flexible client goals (for example, focusing on improving health and not requiring that clients stop using illegal drugs)"

FORERUNNING RESEARCH

Some proponents of PSAD claim support from two Canadian studies that examined the administration of otherwise illicit substances (Oviedo-Joekes et al., 2009, 2016). These two studies are briefly discussed here as background to PSAD.

The North American Opioid Medication Initiative (Oviedo-Joekes et al., 2009) was a randomized trial comparing oral methadone with twice daily injected diacetylmorphine (DAM; the active ingredient in heroin). Participants in the trial were homeless (73%), had been charged with crimes (94%), were hepatitis positive (63%), and 24% were Indigenous, more than four times the provincial prevalence of Indigenous peoples. The investigators report that "All patients were offered a comprehensive range of psychosocial and primary care services", but do not indicate whether evidence-based housing, employment support, or addiction treatment were among the comprehensive offerings.

The comparison between groups is described by the investigators: "The first primary outcome was retention in addiction treatment at 12 months (defined as receipt of the study medication on at least 10 of the 14 days before the 12-month assessment or confirmation of retention in any other treatment program or abstinence from opioids during this interval)". A second primary outcome was reduction in illegal activities, ascertained by self-report. Over 12 months of follow up more than half of the people randomized to receive methadone "discontinued the intervention" compared to about one-third of the diacetylmorphine group. Participants in both groups reported marked decreases in their use of "street heroin", with a comparatively greater decrease in the DAM group. Both groups reported using cocaine roughly 15 days per month throughout the study. Remarkably, the authors report that no one in either study group acknowledged any suicidal ideation throughout the trial. The authors conclude from their results that "Injectable diacetylmorphine was more effective than methadone". In a subsequent manuscript addressing needs among Indigenous participants, the authors conclude: "Offering medically prescribed diacetylmorphine or hydromorphone to Aboriginal people with severe long-term opioid dependence could be an effective means of attracting and retaining them in treatment" (Oviedo-Joekes et al., 2010). Alternative interventions that might be attractive to Indigenous people experiencing homelessness and opioid dependence aren't discussed.

The Study to Assess Longer-term Opioid Medication Effectiveness (Oviedo-Joekes et al., 2016) recruited 202 people who were randomly assigned to receive injections of either hydromorphone or diacetylmorphine. The goal of the study was "To test if injectable hydromorphone hydrochloride is noninferior to injectable diacetylmorphine in reducing illicit heroin use for chronic injection opioid users after 6 months of intervention." About 1/3 of the study participants were Indigenous and about 2/3 were unstably housed. The presence of concurrent mental illnesses is not reported, nor are the goals of study participants.

From the manuscript: "The primary outcome measure was street heroin use, defined as the number of days of use in the prior 30 days by means of self-report." The investigators identified Serious Adverse Events among nearly one-quarter of study participants (47/202), the most common of which was acute poisoning or overdose. The authors report that "the primary outcome did not show noninferiority", but nevertheless conclude that "these results suggest that injectable hydromorphone is as effective as injectable diacetylmorphine for long-term injection street opioid users not currently benefiting from available treatments."

The extent to which people are "benefitting from available treatments" is necessarily a function of the effectiveness of those treatments that are available. The authors do not discuss evidence-based interventions addressing homelessness, unemployment, or addiction treatment. Nor do they refer to the importance of reconciliation[3] as it relates to the reduction of addiction among the high proportion of Indigenous people who participated in their trials. As above, a subsequent paper concentrates on Indigenous participants (Oviedo-Joekes et al., 2018) and concludes that: "…injectable hydromorphone (and DAM when available) offers an opportunity to integrate additional wholistic and culturally safe approaches to treatment to meet the needs of Indigenous patients."

Both of the aforementioned trials focus on differences associated with specific formulations of opioids among people who experience profound addictions while living in poverty. In contrast to PSAD, neither trial provided people with their choices of addictive drugs for independent use. And by definition, both trials included people who were willing to participate in a structured program, in contrast to those who are the intended targets for PSAD. Last, neither trial addressed social determinants of addiction, which we briefly discuss below.

[3]Reconciliation is a guiding construct that seeks to supplant the legacy of colonization with partnership and respect for all relations, and was introduced in the Government of Canada's 1998 report Gathering Strength: Canada's Aboriginal Action Plan.

PSYCHOLOGICAL AND SOCIAL DETERMINANTS OF POISONING

The likelihood of both fatal and non-fatal poisoning is strongly associated with evidence of social and psychological distress. At the community level, poisonings are related to the Area Deprivation Index (Kurani et al., 2020), a validated measure that integrates poverty, education, housing, and employment (Singh, 2003). Fatal poisonings are significantly more likely in lower-income communities (Pear et al., 2019) and among people living in poverty (Monnat, 2018). The term *deaths of despair* refers to mortality attributed to poisoning, suicide and liver disease (Case & Deaton, 2017). At the individual level, those at highest risk for *deaths of despair* are people with disabilities, Indigenous peoples, and those who are unemployed (Olfson et al., 2021).

A considerable body of research investigates the psychological wellbeing of people who meet criteria for opioid use disorder (OUD) and who experience drug poisonings. More than half of those who survive drug poisonings report suicidal intent (i.e., wanted to die, didn't care about the risks), and the likelihood of suicidal ideation increases with the number of non-fatal poisonings that a person has experienced (Gicquelais et al., 2020). In a large (n=36,309) representative US sample of adults, those with OUD experienced significantly impaired health-related quality of life and were half as likely to be employed compared to those without OUD (Rhee & Rosenheck, 2019). Consistent with research identifying suicide and despair among victims of poisoning, concurrent mental illness is significantly associated with the likelihood of overdose (Dilokthornsakul et al., 2016).

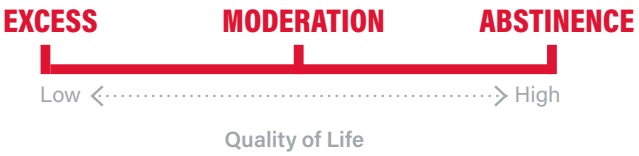
HARM REDUCTION, SUBSTANCE USE, QUALITY OF LIFE

Principles of *harm reduction* are summarized in Figure 1 (Marlatt, Somers, Tapert, 1993). The figure acknowledges the close relationship between personal risk and the extent of substance use, and the ethos that *harm reduction* promotes movement toward decreased risk.

Figure 1: Original Illustration of Harm Reduction (Marlatt, Somers, Tapert, 1993)

The term recovery has gained strength in the addiction field after having been refined in relation to mental illnesses and refers to the experience of substantially improved quality of life (QoL) following illness (e.g., Leamy et al., 2011). The relationship between harm reduction and recovery-oriented approaches is illustrated by adding a third axis to Figure 1 ranging from low to high QoL, revealing that the overall goal of both harm reduction and recovery-oriented approaches is to promote "steps in the right direction" (please see Figure 2).

Figure 2: Overlap between Harm Reduction and Recovery-Oriented Approaches



In the years since harm reduction was introduced there have been substantial developments in the identification of practices that reduce drug-related risks. The second edition of the influential text Harm Reduction observes: "From its grassroots and activist beginnings, harm reduction has expanded to become an even more inclusive and globally applied platform for a broad range of approaches that are focused toward reducing harm and increasing QoL among individuals engaging in high-risk behaviors and their communities" (Collins et al., 2012, p. 26). In practice, one of the major advances in the science of harm reduction has been the identification of connections between individual-level risk and community-level characteristics, as illustrated in the preceding section and discussed later.

HARM REDUCTION GOALS OF PEOPLE AT RISK FOR POISONING

The practice of harm reduction embraces human agency, or self-determination, as a fundamental aspect of wellness. This focus has resulted in a body of research detailing the preferences and goals of people who are at risk.

People who have experienced an overdose articulate different priorities than those who haven't. A sample of 440 people with OUD was recruited from a detox facility in Massachusetts and asked: "If you had unlimited treatment options and all were free, which one would work best for you when you leave here?" Options included medication, informal treatment (12-step programs), and residential treatment. People who had experienced a poisoning episode in the past year were nearly 7 times more likely than those with no prior poisonings to select residential treatment (Stein et al., 2017).

The goals of people diagnosed with OUD are often neglected or ignored by public addiction service providers and researchers. Measures that are commonly used to assess the success of public addiction programs are impacts on illicit opioid use and retention in a prescribing program (Dennis et al., 2020). However, these outcomes bear little resemblance to the goals articulated by people who seek help for addiction.

Over one thousand clients spanning 33 addiction agencies in Scotland were interviewed about their goals for treatment (McKeganey et al., 2004). More than half (56.6%) of the sample (n=1,007) reported that achieving "abstinence" was the only change they were seeking from treatment. By contrast, few reported the goal of "reduced drug use" (7.1%) and fewer than 1% identified the goal of "safer drug use".

In Ontario over 2,000 people receiving Opioid Agonist Therapy (OAT) for OUD were asked the question "What are your goals in treatment?" (Rosic et al., 2021). The most frequent response by far was to "Stop or taper off treatment" (68.3%), indicating that one of the measures used to define OAT success (i.e., program retention) is diametrically opposed to the goals of clients. The second most common treatment goal was to "Stay or get clean" (36.6%), reinforcing that the avoidance of drug use, rather than ongoing use via an alternative supply, is a priority among those currently receiving opiate agonist therapies.

Harms associated with drug use are among the most commonly reported sources of motivation for changing addictions. Pettersen and colleagues (Pettersen et al., 2018) interviewed people who had been diagnosed with substance use disorder and who had been abstinent for at least five years, finding that: "Their main reasons for quitting were experiencing the harmful consequences of substance use, concerns and pressure from close family members, countering doubt, having hope, and being aware of available treatment options." Among people who formerly identified as problematic heroin users, the factors cited most often as contributing to abstinence were being tired of the lifestyle and motivation to improve their psychological health (Best et al., 2008). In the same study, factors associated with sustained abstinence involved "moving away from drug-using friends and support from non-using friends" and improvements in "accommodation and employment" (Best et al., 2008).

Research on the preferences of people who meet criteria for SUD has extended to include the topics of drug legalization and decriminalization, revealing: "The majority of our participants were not in favor of legalizing nor decriminalizing heroin and cocaine, even if they or someone they knew had suffered legal consequences related to substance use, or if they themselves met criteria for a SUD. These findings suggest that this population would not support policy changes related to heroin and cocaine legalization/decriminalization, which may reflect their own experiences, making them more cautious about increasing availability of these drugs." (Hammond et al., 2020).

Numerous randomized controlled trials demonstrate the feasibility and effectiveness of providing people who experience addictions and homelessness with supports that address their chosen priorities involving improved housing, employment, and overall wellbeing. Individual Placement and Support is a structured employment program that was originally developed for people with serious mental illness (Mueser et al., 2016) and is similarly effective among people diagnosed with concurrent addictions (LePage et al., 2016). Canada's seminal At Home/Chez Soi study (Goering et al., 2011) demonstrated that recovery-oriented housing for people with severe addictions and mental illness results in extremely high housing stability (Palepu et al., 2013) and substantial reductions in both crime (Somers et al., 2013) and medical emergencies (Russolillo et al., 2014) compared to standard care in the same communities. Importantly, these results are derived from a randomized trial design and use of administrative data sources (e.g., Provincial Corrections, Emergency Department records) rather than client self-report. In addition to responding to the stated goals of people living in extreme vulnerability, recovery-oriented housing has been shown to be highly cost-effective (Latimer et al., 2020).

REVIEWS ADDRESSING PSAD

A limited number of literature reviews have focused on PSAD. A rapid review conducted by the Ontario HIV Treatment Network (2020) addressed the question: "What are possible benefits of providing a safe supply of substances to people who use drugs during public health emergencies such as the COVID-19 pandemic?" The reviewers concluded: "We found no peer-reviewed literature on the potential benefits or harms of safe supply programs."

A scoping review (Bonn et al., 2020) included opioid agonist therapies (OAT) in the definition of *safe supply*. The review, which was co-led by people who use drugs, focussed on barriers and facilitators of accessing addictive drugs during COVID-19. The review identified "restrictive drug laws or policies" among the most frequently cited barriers to securing safe supply or OAT. The review concludes by recommending "an immediate scale up of a safe supply of pharmaceutical-grade drugs and substances", to be followed by research. The review did not discuss other services that people who use drugs may desire apart from improvements to the way they access drugs.

A review conducted as part of the respected Cochrane Library examined supervised versus take-home opioid substitution treatment: "The objective of this systematic review is to compare the effectiveness of opioid substitution treatment (OST) with supervised dosing relative to dispensing of medication for off-site consumption" (Saulle et al., 2017). When discussing the results of their review and Implications for Practice the authors state: "Evidence on the use of supervised dosing in the context of opioid substitution treatment (OST) for the management of opioid dependence was limited to six studies, some of them we considered at high risk of bias. At present, there is uncertainty about the effects of supervised dosing compared to unsupervised medication due to the low and very low quality of the evidence." Importantly, none of the studies included in their review involved the dispensing of addictive drugs other than those used in OST (e.g., methadone, buprenorphine). And none of the reviewed articles presented findings outside the context of addiction treatment. With one exception, the authors report: "we did not identify any studies combining OST and psychosocial measures such as supportive counselling, psychotherapy, assistance with social needs such as housing, employment, education, welfare and legal problems." (Saulle et al., 2017).

Very recently a Stanford-Lancet Commission report (Humphreys et al., 2022) was published, responding to "soaring opioid-related mortality in the USA and Canada over the past 25 years" and "with the goals of understanding the opioid crisis, proposing solutions domestically, and attempting to stop its spread internationally" (Humphreys et al., 2022, p. 1). Their report describes the genesis of the current crisis and details the magnitude of the gap between best practices in the field of addiction and the services that are available publicly. The Commission identifies critical failings in both the Canadian and US public systems of care for people diagnosed with Opioid Use Disorder (OUD), and discusses the destructive influence of commercial interests that seek to profit from publicly funded services. They caution that: "Opioid medications can be powerful and effective in the treatment of OUD, but should not be used as an informal system of pharmacological sedation of poverty" (Humphreys et al., 2022, p. 24).

Reflecting the Commissioners' grounding in the literature on addiction, their report emphasizes that "many patients with OUD have serious, unaddressed psychiatric, medical, family, employment, and housing issues that medication alone will not solve" (Humphreys et al., 2022 p.24). Alongside their recommendations to improve the prevention and treatment of OUD, the authors issue the following caution: "Policies that should attract skepticism include the dispensing of hydromorphone from vending machines and prescribing a range of potent opioids and other drugs (e.g., benzodiazepines, stimulants) to individuals with OUD in hopes of creating a safe addictive-drug supply" (Humphreys et al., 2022, p. 24).

The current review differs from those referred to above by investigating peer-reviewed studies that report original research findings which the authors interpret as indicating the need for *safe supply*.

METHODS

The rapid review search strategy was guided by the PICOTS framework: **P**opulation; **I**ntervention; **C**omparator; **O**utcome; **T**imeframe; and **S**etting. PICOTS provides guidance to systematic reviewers in the formulation of research questions, analysis of published research and discussion with stakeholders (Samson & Schoelles, 2012).

The quality and robustness of evidence were assessed following the guidance of the Oxford Centre for Evidence Based Medicine (OCEBM) Levels of Evidence (2011). In general, systematic reviews of randomized trials represent the most robust level of evidence, followed by individual randomized controlled trials. Less robust levels of evidence include non-randomized cohort studies followed by case series. Per the OCEBM: "Level may be graded down on the basis of study quality, imprecision, indirectness".

Search parameters were selected to identify published, peer-reviewed research that examined the Public Supply of Addictive Drugs (Intervention); on beneficial or adverse outcomes (Outcomes); among socially marginalized people who use illicit drugs (Population). In order to include as much relevant research as possible, the parameters of Timeframe and Setting were not restricted and Comparators were not included (see Table 1).

The literature search was performed using MEDLINE (via the PubMed interface) in order to address the time demands of the rapid review. MEDLINE is considered to be the most comprehensive database for health-related topics (Lal & Adair, 2014) and a validated source of peer-reviewed literature addressing health services and public health (Wilczynski et al., 2013). The search focused on English, peer-reviewed, full text articles using all available time, and undertaken with a 30-day deadline. A librarian (Simon Fraser University) with specific expertise in search methods was consulted prior to the search and provided advice to optimize the rigour and soundness of rapid reviews. The research team was comprised of senior (PhD, MD, or both) researchers and licensed clinicians with primary expertise in addiction, drug safety and effectiveness, pharmacoepidemiology, and statistics. We also reviewed and included papers submitted directly by advocates for PSAD.

Search terms were used to identify included articles. Titles and abstracts were examined by at least two team members working independently, followed by more detailed relevance review by at least three reviewers. Consensus was reached remotely using Zoom.

The final search was completed on January 28, 2022 and included manuscripts published and indexed on or before January 15, 2022.

RESULTS

Results of the search procedure are presented in Table 1 and are available here:
www.ncbi.nlm.nih.gov/sites/myncbi/akm.moniruzzaman.1/collections/61613950/public/

TABLE 1: SEARCH HISTORY OF MEDLINE DATABASE

Search using PICO method	Query/Key words	Results
Population	drug user* OR "drug user*" OR substance user* OR "substance user*" OR opioid crisis OR overdose OR addiction OR addict* OR PWUD OR PWID OR "toxic drug supply" OR illicit drug user* OR "marginalized people" OR opioid user* OR depressant* OR stimulant* OR analgesic OR narcotic* OR psychotropic* OR psychoactive OR benzodiazepine* OR prescription drug* OR opioid* OR methamphetamine OR cocaine OR fentanyl OR morphine OR hydromorphone OR diacetylmorphine OR oxycontin OR oxycodone	**1,311,483**
Safe supply as Intervention	safe supply OR safer supply OR "safe supply" OR "safer supply" OR "substance supply" OR safer opioid distribution OR "safer opioid prescribing" OR "safer opioid*" OR "pharmaceutical opioid*"	**69,085**
Outcome	overdose OR poisoning OR "drug diversion" OR recovery OR adverse events OR retention OR harm* OR abstinence OR employment OR unemployment OR quality of life OR homeless* OR reunification OR social integration OR community integration OR jail OR incarceration OR crim*	**2,367,510**
Combined search (intervention and population and outcome)	((safe supply OR safer supply OR "safe supply" OR "safer supply" OR "substance supply" OR safer opioid distribution OR "safer opioid prescribing" OR "safer opioid*" OR "pharmaceutical opioid*") AND (drug user* OR "drug user*" OR substance user* OR "substance user*" OR opioid crisis OR overdose OR addiction OR addict* OR PWUD OR PWID OR "toxic drug supply" OR illicit drug user* OR "marginalized people" OR opioid user* OR depressant* OR stimulant* OR analgesic OR narcotic* OR psychotropic* OR psychoactive OR benzodiazepine* OR prescription drug* OR opioid* OR methamphetamine OR cocaine OR fentanyl OR morphine OR hydromorphone OR diacetylmorphine OR oxycontin OR oxycodone)) AND (overdose OR poisoning OR "drug diversion" OR recovery OR adverse events OR retention OR harm* OR abstinence OR employment OR unemployment OR quality of life OR homeless* OR reunification OR social integration OR community integration OR jail OR incarceration OR crim*) Filters: from 1950/1/1 - 2022/1/15	**840** **839**

There were no meta-analyses, systematic reviews, randomized controlled trials, or quasi experimental studies that met our inclusion criteria. Nineteen peer-reviewed publications were identified that both: presented original research findings; and advocated for "safe supply".

All of the included studies employed interviews or surveys among cohorts or case series, and twelve included between 9 and 91 participants. Studies that reported the characteristics of participants identified high rates of homelessness, unemployment, food insecurity, and poverty. Indigenous ethnicity was as high as 42% among respondents. None of the included studies reported results associated with the provision of addictive drugs (i.e., fentanyl, cocaine, heroin, crystal methamphetamine) for personal use outside the context of treatment. The overall level of evidence was low, affected by both the indirectness of evidence and imprecision of key terms (e.g., *safe supply*).

None of the included studies presented diagnostic details regarding the type(s) of Substance Use Disorders experienced by their study participants, the prevalence and type(s) of concurrent mental illness(es), the presence and severity of suicidal ideation, or participants' preferences for addiction treatment, housing or other forms of social support.

Fifteen of the included papers (79%) were conducted in BC and only one was conducted outside Canada. All of the BC-based papers were led (i.e., first or senior author) by researchers with expertise in HIV/AIDS.

Papers that described a "root cause" of the poisoning crisis specified that the cause was a "toxic drug supply". None referred to causes of addiction involving psychological or social factors.

THE 19 INCLUDED PUBLICATIONS ARE LISTED BELOW ACCOMPANIED BY A SUMMARY OF THEIR RELEVANT FEATURES

1 Ali F, Russell C, Nafeh F, Rehm J, LeBlanc S, Elton-Marshall T. Changes in substance supply and use characteristics among people who use drugs (PWUD) during the COVID-19 global pandemic: A national qualitative assessment in Canada. Int J Drug Policy. 2021 Jul;93:103237. doi: 10.1016/j.drugpo.2021.103237. Epub 2021 Apr 20. PMID: 33893026.

This study (Ali et al., 2021) reports "changes in substance use frequency, substance use characteristics, and substance supply", based on the results of questionnaires administered by phone to 200 people across Canada who either use illicit drugs or receive methadone. Most respondents identified as poly-substance users and stimulants were reported as the most commonly used class of drugs (74% of the sample).

The authors interpret their results as demonstrating that "Supply disruptions have had further unintended consequences such as 'substitution' effects, where PWUD have had to supplement their preferred substance for other – potentially more dangerous – products because of accessibility and affordability issues. This has created an unprecedented vulnerability…"

The living situations among respondents from BC were categorized as "Homeless/street" (37.5%), "Shelter" (9.5%), or "Transient" (12.5%). When asked about the current pandemic's impact on the likelihood of poisoning, a minority (38%) expressed the belief that "their level of risk had increased since COVID-19". The results do not indicate the prevalence of non-fatal poisonings in the sample.

The authors advocate for the provision of take-home naloxone, telemedicine, sterile supplies, and drug testing kits, adding "Although these interventions are necessary to address increased risk for overdoses and health concerns which have been exacerbated during the pandemic, they do not address the root cause of these issues, which is primarily related to the contaminated drug supply. As such, there need to be options for PWUD who are at risk of overdose to have access to an uncontaminated supply of pharmaceutical-grade substances (e.g., opioids or stimulants), alternatively knowns as 'Safe Supply'." The authors do not discuss criteria for identifying who is at risk of overdose, or define the elements of "safe supply" such as the range of included drugs, potencies, and amounts to be provided. The manuscript does not discuss any recommendations regarding addiction treatment, housing or homelessness.

2 Ferguson M, Parmar A, Papamihali K, Weng A, Lock K, Buxton JA. Investigating opioid preference to inform safe supply services: A cross sectional study. Int J Drug Policy. 2022 Jan 7;101:103574. doi: 10.1016/j.drugpo.2021.103574. Epub ahead of print. PMID: 35007878.

The authors (Ferguson et al., 2022) report: "The aim of this study was to identify opioid preferences and associated variables". Participants (n=367) were recruited from "a network of sites which distribute supplies for safer sex and substance use" in BC. A paper-based questionnaire was administered to a convenience sample, taking roughly 10 minutes to complete. "Participants received $10 CAD for participation and the sites received $5 per participant recruited".

Less than 30% of the sample reported being "stably housed" (28.3%) and less than one in five were "currently employed (19.9%). Indigenous ethnicity comprised 42% of the sample. Nearly three-quarters (74%) reported use of crystal methamphetamine.

There is no mention of evidence based interventions that address homelessness, unemployment, the treatment of addiction, or reconciliation in the interpretation of results. In contrast, the term "safe supply" appears fifteen times in the short Discussion without being clearly defined (e.g., drug types, doses, amounts, any contraindications, etc.). The authors recommend that drug users should determine the types of drugs that are made available to them: "Providing choice will result in most equitable and accessible safe supply programs".

3 Salters KA, Parent S, Nicholson V, Wang L, Sereda P, Pakhomova TE, Kibel M, Chau W, Closson K, Parashar S, Barrios R, Montaner JSG, Hogg RS. The opioid crisis is driving mortality among under-served people living with HIV in British Columbia, Canada. BMC Public Health. 2021 Apr 8;21(1):680. doi: 10.1186/s12889-021-10714-y. PMID: 33832472; PMCID: PMC8028792.

Salters and colleagues (2021) report results from an ongoing study involving people living with HIV (PLWH) who received antiretroviral therapy (ART) and were also enrolled in a drug treatment database (n=1,000). The overall study objective was "to evaluate the impact of health care engagement and social determinants of health on PLWH who have accessed ART in BC". The current study examined mortality within the cohort "to inform our public health approaches and reorganize our efforts to provide comprehensive and responsive care for all PLWH".

Poisoning ("Drug use/Overdose") was the most common cause of death among decedents (57 out of 208 deaths). Nearly half (47.9%) of decedents lacked stable housing and over three-quarters (76.2%) reported food insecurity.

Despite their stated focus on improving social determinants of health, the authors do not cite any evidence-based practices addressing homelessness, food insecurity, or addiction treatment. Instead, they conclude that these findings highlight the dire need for life-saving interventions, including increased safe supply options. A definition of "safe supply" is not provided.

4 Olding M, Werb D, Guise A, Small W, McNeil R. Navigating social norms of injection initiation assistance during an overdose crisis: A qualitative study of the perspectives of people who inject drugs (PWID) in Vancouver, Canada. Int J Drug Policy. 2019 Jul;69:24-33. doi: 10.1016/j.drugpo.2019.04.004. Epub 2019 Apr 28. PMID: 31029914; PMCID: PMC7059802.

This study (Olding et al., 2019) reports results from 19 individuals "who reported helping someone inject for the first time". The authors discuss moral conflicts described by participants, including their "legal and moral culpability" in the context of increasingly potent drugs.

The authors interpret their findings as support for "enacting policies conducive to a safer supply of opioids, including those that end drug prohibition and facilitate distribution of pharmaceutical-grade opioids". The majority of the 19 participants reported using cocaine, crystal methamphetamine, and other drugs alongside opioids, yet the authors do not discuss the potentially fatal contributions of other substances when advocating for safe supply.

5 Parent S, Papamihali K, Graham B, Buxton JA. Examining prevalence and correlates of smoking opioids in British Columbia: opioids are more often smoked than injected. Subst Abuse Treat Prev Policy. 2021 Oct 18;16(1):79. doi: 10.1186/s13011-021-00414-6. PMID: 34663374; PMCID: PMC8522853.

The authors (Parent et al., 2021) state that "the objectives of this study are to identify the prevalence and correlates associated with smoking opioids", and report results derived from a questionnaire administered in 22 BC sites as described above (see Study #2).

The study sample consisted of 369 people who reported using opioids in the past 3 days and results are presented comparing those who smoked opioids with those who ingested opioids via other means (e.g., snorting, injecting). The overall sample reported very high prevalence of unemployment (77.2%) and lack of "regular housing" (35.2%), both of which were more prevalent among opioid smokers. Opioid smokers were also more likely than other opioid users to report using crystal methamphetamine. Among the entire sample (n=369) the use of multiple drugs was reported including: methamphetamine (77.8%); cocaine (25.2%); and crack (19.2%). In addition, 30.9% reported receiving opiate agonist therapy in the past 3 days.

The authors do not cite any specific evidence-based interventions addressing homelessness, unemployment, or addiction treatment. Instead they conclude: "Our findings highlight important correlates associated with smoking opioids, particularly the concurrent use of methamphetamines. These findings can support concrete actions to better respond to the overdose crisis, such as targeting harm reduction approaches, educating on the risks of smoking opioids, advocating for consumption sites where people can smoke drugs, as well as providing a safer opioid supply with known content that can be smoked." Despite the high prevalence of poly-substance use in their sample, the authors do not include drugs other than opioids in their description of "safe supply".

6 Bardwell G, Ivsins A, Socías ME, Kerr T. Examining factors that shape use and access to diverted prescription opioids during an overdose crisis: A qualitative study in Vancouver, Canada. J Subst Abuse Treat. 2021 Nov;130:108418. doi: 10.1016/j.jsat.2021.108418. Epub 2021 Apr 20. PMID: 34118706.

This study (Bardwell, Ivsins, et al., 2021) presents results from interviews with 24 people in Vancouver who reported using prescription opioids (PO) that were not prescribed to them. The authors' stated objective is to explore "the rationale and perceived benefits of using a variety of diverted POs."

Nearly all participants (22/24) reported that income assistance was their primary source of income. Use of multiple types of drugs was common, including fentanyl (n=16), heroin (n=13), crystal methamphetamine (n=11), and crack cocaine (n=10) among others. A substantial proportion of the sample also received drugs by prescription including methadone (n=11) and morphine (n=7).

The authors conclude: "In summary, many participants preferred using POs because of their perceived known contents and lower overdose risk profile". Potentially dangerous interactions between diverted POs and other drugs reportedly used by participants are not discussed. The authors acknowledge the apparently high prevalence of "economic deprivation" in their sample, but do not refer to specific evidence-based practices that reduce poverty among marginalized drug users, concluding that: "These findings emphasize the need for the continued implementation and evaluation of safer drug supply initiatives, including those providing access to a variety of drug types."

7 Milaney K, Passi J, Zaretsky L, Liu T, O'Gorman CM, Hill L, Dutton D. Drug use, homelessness and health: responding to the opioid overdose crisis with housing and harm reduction services. Harm Reduct J. 2021 Aug 26;18(1):92. doi: 10.1186/s12954-021-00539-8. PMID: 34446034; PMCID: PMC8394031.

The authors (Milaney et al., 2021) state: "The main purpose of this study was to explore if there was an association between unstable housing and hospital use for people who use opioids". They present self-reported results collected from surveys of 432 Albertans who all reported use of opioids.

The majority of respondents (55.6%) reported having unstable housing. One-third of respondents (32.6%) identified as Indigenous, and nearly one-third reported experiencing an overdose (31.7%).

"Results revealed that being unstably housed was associated with receiving hospital care even after accounting for the additional variables".

The authors state: "Our findings support the growing evidence base highlighting the importance of housing and recovery-oriented models such as Housing First". They explain: "Housing First models are rooted in the belief that housing, not compliance or sobriety, is the foundation for improved health and wellbeing and once housing has been secured a person can successfully address other areas in their life such as physical health, mental health, substance use, employment, and education".

The authors conclude: "Results highlight the importance of concurrently addressing housing instability alongside the provision of harm reduction services such as safe supply and supervised consumption sites", specifying that: "Implementation of safe supply initiatives including regulated and safe opioid distribution are necessary." They do not provide a definition of "safe supply" and do not list any non-opioids (e.g., cocaine, crystal meth, benzodiazepines) in their recommendation.

8 Socias ME, Grant C, Hayashi K, Bardwell G, Kennedy MC, Milloy MJ, Kerr T. The use of diverted pharmaceutical opioids is associated with reduced risk of fentanyl exposure among people using unregulated drugs in Vancouver, Canada. Drug Alcohol Depend. 2021 Nov 1;228:109109. doi: 10.1016/j.drugalcdep.2021.109109. Epub 2021 Sep 25. PMID: 34601278; PMCID: PMC8595770.

"[T]he aim of this study was to assess the effects of using diverted POs [prescription opioids] on fentanyl exposure among people who use drugs (PWUD)".

A sample was identified from among two longitudinal cohort studies, consisting of 1150 people who reported using drugs in the previous six months and who had results from a urine drug test. Of the total sample, 241 (21.0%) reported using diverted prescription opioids "defined as reporting having used oxycodone, codeine, morphine, methadone, buprenorphine, hydromorphone, hydrocodone, or meperidine from any of the following sources: illegitimate prescription, given/ taken from family member, partner of friend, or bought on the street in the previous six months."

Employment was low among those who reported using POs (24.9%) as well as among the remainder of the sample (26.5%). Homelessness was significantly more prevalent among those who reported using diverted POs. Among those who reported using diverted POs the results of urine drug testing (UDT) were positive for: morphine (70.8%), methadone (45.6%); cocaine (51.9%); amphetamine (54.1%); and benzodiazepine (20.0%). Alongside these extremely high rates of polysubstance use, the authors focus on a particular relationship in their findings: "…the effect of using diverted POs on fentanyl exposure differed in relation to distinct patterns of opioid use. Specifically, among PWUO [defined by the authors as "people who use opiates"] in our sample, use of diverted POs was associated with approximately half the odds of fentanyl exposure, but this protective effect was not observed among participants with negative morphine UDT."

The authors do not discuss any specific evidence-based interventions addressing treatments for poly-substance addiction or addressing unemployment and homelessness. The prevalence of severe mental illness (e.g., schizophrenia, bipolar disorder) in their sample is unreported. The authors interpret the results as evidence of possible public health benefits associated with the diversion of prescription opioids, and conclude: "These findings suggest the potential positive benefits of PO diversion during an opioid epidemic as well as the potential of having access to a regulated supply of pharmaceutical grade opioids as a way to reduce fentanyl related harms".

9 Pauly B, Wallace B, Pagan F, Phillips J, Wilson M, Hobbs H, Connolly J. Impact of overdose prevention sites during a public health emergency in Victoria, Canada. PLoS One. 2020 May 21;15(5):e0229208. doi: 10.1371/journal.pone.0229208. PMID: 32438390; PMCID: PMC7242015.

Pauly and colleagues (2020) present the results of interviews with service users (n=12) and staff (n=15) employed at three sites in BC. The sites are described as "overdose prevention sites" (OPS) and are contrasted with "supervised consumption sites" on the bases that they are "staffed by experiential (people with living experience of drug use) and non-experiential harm reduction workers and are provincially rather than federally-sanctioned as a temporary emergency measure". "The overall focus of our research was to explore the early implementation and impacts of OPSs through a rapid case study design".

Participants were described as overwhelmingly without housing (50% no fixed address; 33% shelter; 17% supported housing) and only 17% reported any employment income. The authors interpret their findings as having strong implications for reducing poisonings: "From the perspective of all participants, the most agreed-upon positive impact across all three sites was the fact that zero deaths had occurred in any OPS. When asked directly about successes, one staff person stated "we're saving lives, that's successful"".

The authors do not identify any evidence-based practices to address employment, homelessness, or treat addiction. They interpret their results as addressing "the importance of moving from safer supplies to safer spaces", and argue that "the next step has to be a safer source of substances".

10 Aronowitz SV, Engel-Rebitzer E, Lowenstein M, Meisel Z, Anderson E, South E. "We have to be uncomfortable and creative": Reflections on the impacts of the COVID-19 pandemic on overdose prevention, harm reduction & homelessness advocacy in Philadelphia. SSM Qual Res Health. 2021 Dec;1:100013. doi: 10.1016/j.ssmqr.2021.100013. Epub 2021 Sep 28. PMID: 34870265; PMCID: PMC8485140.

This study (Aronowitz et al., 2021) reports results from 30 one-on-one, semi-structured, in-depth interviews to assess how Philadelphia's harm reduction advocates, community organizers, and substance use disorder treatment clinicians have responded to the overdose and homelessness crises during COVID-19".

Results are discussed thematically and attest to the deterioration of services for people who are homeless and who use drugs. No specific evidence-based interventions addressing homelessness or addiction treatment are discussed. The authors observed that "participants in our study discussed using the heightened need and increased attention caused by the pandemic to push for more radical measures like universal housing, sanctioned encampments, and safe supply of substances". The authors do not define "safe supply".

11 Papamihali K, Yoon M, Graham B, Karamouzian M, Slaunwhite AK, Tsang V, Young S, Buxton JA. Convenience and comfort: reasons reported for using drugs alone among clients of harm reduction sites in British Columbia, Canada. Harm Reduct J. 2020 Nov 23;17(1):90. doi: 10.1186/s12954-020-00436-6. PMID: 33228676; PMCID: PMC7682134.

"This study (Papamihali et al., 2020) aims to identify prevalence and reasons people report for using drugs alone, and to identify barriers to safer drug use practices in a population who access harm reduction supply distribution sites across BC." The sample was drawn from 22 sites in BC as described above (see Study #2).

No measures were included addressing mental illness, housing/homelessness, unemployment, social isolation or suicidal ideation.

Discussing their findings, the authors report: "In this study, we found that comfort and convenience was the most commonly reported reason for using alone".

Specific recommendations made by the authors are: "Public health messaging that urges individuals to avoid using drugs alone and to use in observed consumption spaces is important and provides options for PWUD to be safer in their drug use." And "it is also important to implement interventions that do not rely solely on individual behaviour changes but rather address the source of the opioid overdose epidemic—the toxic illicit drug supply." They conclude that "providing a safer supply of drugs and eliminating stigma, are paramount to mitigate harms".

12 Goodyear T, Mniszak C, Jenkins E, Fast D, Knight R. "Am I gonna get in trouble for acknowledging my will to be safe?": Identifying the experiences of young sexual minority men and substance use in the context of an opioid overdose crisis. Harm Reduct J. 2020 Mar 30;17(1):23. doi: 10.1186/s12954-020-00365-4. PMID: 32228646; PMCID: PMC7106659.

The authors (Goodyear et al., 2020) report results from 50 semi-structured interviews with "sexual minority men ages 15–30 who use substances and live in Vancouver, Canada, to identify how patterns and contexts of substance use are occurring in the context of the opioid overdose crisis."

Alcohol (94%) and cannabis (82%) were the substances used most prevalently in the past 12 months, while relatively few members of the sample consumed heroin (10%), fentanyl (8%), or other opioids (8%). Results include descriptions of drug procurement practices that "attempt to mitigate overdose risk by procuring substances from sources they perceive as trustworthy (e.g., online drug markets, trusted drug dealers)."

The authors conclude that "our findings illustrate the need for a safe and regulated drug supply", adding "we argue for urgent and significant structural intervention that includes the decriminalization of drug use and the introduction of an accessible, regulated, and safe drug supply."

13 Kolla G, Strike C. 'It's too much, I'm getting really tired of it': Overdose response and structural vulnerabilities among harm reduction workers in community settings. Int J Drug Policy. 2019 Dec;74:127-135. doi: 10.1016/j.drugpo.2019.09.012. Epub 2019 Oct 4. PMID: 31590088.

This study (Kolla & Strike, 2019) presents results related to "satellite sites" in Toronto, described as "a program where PWUD are employed by a community health center to operate satellite harm reduction programs within their homes." Results were derived from direct observation in seven sites, interviews with five site workers, and a focus group with four site workers and the satellite site program coordinator.

Themes of homelessness and eviction were described as pervasive challenges among satellite site users, and housing precarity was also described as a substantial concern among site operators.

The authors conclude that their findings support the need for "decriminalization and an expansion of safer supply interventions". The term "safe supply" is not defined (e.g., types of drugs, doses, screening/assessment, contraindications, cost, etc.).

14 Bardwell G, Small W, Lavalley J, McNeil R, Kerr T. "People need them or else they're going to take fentanyl and die": A qualitative study examining the 'problem' of prescription opioid diversion during an overdose epidemic. Soc Sci Med. 2021 Jun;279:113986. doi: 10.1016/j.socscimed.2021.113986. Epub 2021 May 3. PMID: 33971445; PMCID: PMC8559599.

This study (Bardwell, Small, et al., 2021) examines "the perspectives of people who divert" prescription opioids (POs) including hydromorphone and morphine. The sample (n=21) was drawn from two cohorts examining AIDS care and injection drug use.

All 21 recruited participants reported receipt of social assistance. "The majority of participants (n = 19) diverted their own prescriptions".

The authors conclude that "participants identified a variety of benefits to diversion such as providing a safer drug supply to others to prevent overdose and other harms, helping people who are dope sick, and getting money to pay for other expenses (e.g., food, other drugs)."

No evidence-based interventions addressing unemployment, homelessness, food insecurity, or addiction are discussed.

15 Ivsins A, Boyd J, Mayer S, Collins A, Sutherland C, Kerr T, McNeil R. Barriers and facilitators to a novel low-barrier hydromorphone distribution program in Vancouver, Canada: a qualitative study. Drug Alcohol Depend. 2020 Nov 1;216:108202. doi: 10.1016/j.drugalcdep.2020.108202. Epub 2020 Sep 15. PMID: 32948372; PMCID: PMC7490624.

The authors "examine barriers and facilitators to uptake of, and engagement with, a novel opioid distribution program operating in Vancouver, Canada's Downtown Eastside neighborhood involving the distribution of physician-prescribed hydromorphone (HDM) tablets".

Results are based on interviews with 42 service users and observations conducted on the premises of the program.

The most common sources of income among participants in the past 30 days were: social assistance (n=39); reselling goods (n=24); panhandling (n=17); recycling/binning (n=17); and drug selling (n=12). Housing was most commonly described as single room accommodation (n=18); apartment (n=10); and unhoused/outside (n=9). Of the 42 participants the rates of reported use of drugs in the past 30 days was: heroin (n=30); fentanyl (n=38); crystal meth (n=32); and "other opiates" (n=27).

The authors identify structural barriers experienced by program clients: "For example, participants with unstable housing or mobility issues described difficulty fully engaging with the program because of its restrictive schedule and operating hours."

No specific evidence-based interventions are mentioned addressing precarious housing, homelessness, unemployment, or treatment of addictions.

The authors conclude: "That the program is so well received among program participants (given enrollment and waitlist numbers) points to the crucial need for immediate scale-up of safe supply programs across North America." The authors do not specify whether their support for "safe supply" includes all of the drugs types used by the participants in their study.

16 Wallace B, van Roode T, Pagan F, Hore D, Pauly B. The potential impacts of community drug checking within the overdose crisis: qualitative study exploring the perspective of prospective service users. BMC Public Health. 2021 Jun 16;21(1):1156. doi: 10.1186/s12889-021-11243-4. PMID: 34134698; PMCID: PMC8207696.

The authors (Wallace et al., 2021) describe the goals of this study as follows: "In this study, we explore how community drug checking may have different impacts beyond individual behaviour change, when examined through a socioecological model. We drew on critical perspectives of harm reduction and social justice to reconceptualise effectiveness of drug checking services within the context of an illicit drug overdose crisis, and the ongoing criminalization and stigmatization of people who use substances."

Results are drawn from 27 interviews "conducted with people who use or have used substances, family or friends of people who use substances, and/or people who make or distribute substances." Participants were recruited from "sites that were proposed as locations for the pilot project's drug checking services." The interview script was developed "to seek perspectives on how best to deliver drug checking services".

The results include no objective measures of harm reduction associated with drug checking, and do not address any form of drug supply. However, the authors conclude: "Community drug checking may operate as a meaningful harm reduction response with impacts at and beyond the individual level. These include increasing power and accountability within the illicit drug market, improving the health of communities, and supporting safer supply initiatives and regulation of substances at the policy level."

17 Ivsins A, Boyd J, Mayer S, Collins A, Sutherland C, Kerr T, McNeil R. "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. J Urban Health. 2021 Feb;98(1):59-69. doi: 10.1007/s11524-020-00489-9. Epub 2020 Oct 28. PMID: 33118145; PMCID: PMC7592642.

The authors report: "In this paper we present outcomes from a qualitative evaluation of the Molson hydromorphone tablet distribution program" (Ivsins et al., 2021; also see study #15 above). Results are based on 42 interviews and observations conducted on the premises of the program.

The characteristics of program participants are the same as those reported under Study #15. Most of the participants (n=42) lived outside (n=9), in shelters (n=5) or in single room accommodations (n=18). Nearly all (n=39) received income from social assistance. While receiving hydromorphone, the past month use of additional illicit drugs was

identical to the distribution reported in study #15. Participants identified several limitations with the program including:

Demands on their time:
"So for me to come here five times a day, that means either I come down here and I wait for the five hours, or I go home for ten minutes and then come back, go home for ten minutes and come back, go home for ten minutes and come back, right?";

Conflicting with their objective to stop using drugs:
"You have to deal with people using drugs that you're trying to get off and it's not good";

Not effectively supplanting their preferred drugs:
"It's a good idea, but it's... like they say it's supposed to replace the fentanyl, right? That's what it's supposed to be, is for a clean supply, right? Whereas I'm still using fentanyl, because of the hydromorphone pills that they're getting are shit, I think."

No evidence-based interventions are cited that address the "high levels of poverty, homelessness, and drug use" identified in their sample. Instead, the authors conclude that: "Our findings provide evidence of the need for, and feasibility of, safer supply programs". Details of the intended model of "safe supply" are not provided.

18 Mayer S, Fowler A, Brohman I, Fairbairn N, Boyd J, Kerr T, McNeil R. Motivations to initiate injectable hydromorphone and diacetylmorphine treatment: A qualitative study of patient experiences in Vancouver, Canada. Int J Drug Policy. 2020 Nov;85:102930. doi: 10.1016/j.drugpo.2020.102930. Epub 2020 Sep 16. PMID: 32949832; PMCID: PMC7901590.

This study (Mayer et al., 2020) presents the results of 52 interviews with people who receive either injectable hydromorphone or diacetylmorphine (HDM/DAM). Questions addressed participants experiences initiating injectable HDM/DAM "(e.g. Can you tell me about when you first started the injectable opioid agonist treatment program?)" and "the impacts of structural vulnerabilities (e.g. housing vulnerability, poverty) on treatment experiences".

Participants were disproportionately Indigenous (40%), living in Single Room Occupancy (SRO) hotels (46%), shelters (14%), or unsheltered/outside (15%); and receiving income in the past 30 days from social assistance (90%), drug selling (33%), recycling (31%), "vending (e.g., selling items on the street)" (27%), part time employment (27%), panhandling (23%) and "Boosting (e.g., Shoplifting, theft)" (23%).

The authors' thematic analysis identifies that structural and poverty-related risks were significant sources of motivation leading people to access injectable HDM/DAM. The authors acknowledge the importance of dangerous drug use and "economic precarity linked to food and housing insecurity" in their sample. No specific evidence-based practices that address homelessness, unemployment, or addiction treatment are mentioned.

19 Olding M, Ivsins A, Mayer S, Betsos A, Boyd J, Sutherland C, Culbertson C, Kerr T, McNeil R. A Low-Barrier and Comprehensive Community-Based Harm-Reduction Site in Vancouver, Canada. Am J Public Health. 2020 Jun;110(6):833-835. doi: 10.2105/AJPH.2020.305612. Epub 2020 Apr 16. PMID: 32298171; PMCID: PMC7204455.

This brief (2-page) manuscript (Olding et al., 2020) presents an evaluation of a supervised consumption site (also described as an overdose prevention site [OPS]) based on "91 interviews with people about their experiences using services, five interviews with peer staff regarding program operations, and 200 hours of ethnographic observation." The authors conclude that "This evaluation indicates benefits" of their service and "suggest that OPSs are promising sites for colocated iOAT, drug checking, and "safe supply" programs that distribute pharmaceutical drug". The authors do not define "safe supply".

DISCUSSION

This rapid review replicates the results obtained by previous reviewers (Ontario HIV Treatment Network, 2020) who concluded: "We found no peer-reviewed literature on the potential benefits or harms of safe supply programs."

The manuscripts that met our inclusion criteria reported the characteristics of people who are at high risk for poisoning and in a few cases also described the experiences of family members and carers acting in peer-based as well as professional roles. The results confirm that people at greatest risk of poisoning are overwhelmingly likely to experience homelessness or inadequate housing, unemployment, food insecurity, and consequences of colonization. Carers and drug users alike report the dearth of assistance and widespread experiences of stigma when seeking help. The primary results presented in each of the included manuscripts are based on either interviews or questionnaires, many involving relatively small sample sizes or overlapping cohorts.

Only one of the included papers acknowledged the relationship between social exclusion and addiction, and was conducted in Alberta (Milaney et al., 2021). The overwhelming majority of manuscripts included in this review were conducted in British Columbia and none interpreted their results as indicative of the need for evidence-based housing, employment assistance, or addiction treatment.

Authors from BC were particularly clear in their advocacy for the Public Supply of Addictive Drugs (PSAD), as illustrated by the following selection of quotes:

"These findings warrant the need for increased accessibility of safe supply programs" [Study # 1] (Ali et al., 2021)

"…these findings highlight the dire need for life-saving interventions, including increased safe supply options" [Study # 3] (Salters et al., 2021)

"Implementation of safe supply initiatives including regulated and safe opioid distribution are necessary." [Study # 7] (Milaney et al., 2021)

"…the next step has to be a safer source of substances" [Study # 9] (Socias et al., 2021)

"…our findings illustrate the need for a safe and regulated drug supply" [Study # 12] (Goodyear et al., 2020)

"…participants identified a variety of benefits to diversion such as providing a safer drug supply to others to prevent overdose and other harms, helping people who are dope sick, and getting money to pay for other expenses (e.g., food, other drugs)." [Study # 14] (Bardwell, Small, et al., 2021)

"That the program is so well received among program participants (given enrollment and waitlist numbers) points to *the crucial need for immediate scale-up of safe supply programs across North America." [Study # 15] (Ivsins, Boyd, Mayer, et al., 2020)*

"Our findings provide evidence of the need for, and feasibility of, safer supply programs". [Study # 17] (Ivsins et al., 2021)

None of the manuscripts defined their use of the term "safe supply" (see Ethical and Legal Considerations below). Several refer to the provision of opioids only, despite the fact that self-reported use of stimulants and other drugs was pervasive in their samples (e.g., Olding et al., 2020). None of the BC-based papers discuss evidence implicating the importance of mental illness and suicidal ideation among people who experience poisonings related to addiction, the long-term harms of using addictive drugs, or the interventions that respond effectively to the expressed needs of people living with addictions (see Standard of Care below).

One potential explanation for the consistencies across the BC-based papers may be that all were conducted by authors with primary expertise in infectious diseases (e.g., HIV/AIDS). Infectious diseases are understood to involve vector-borne pathways of transmission and require treatments that are overwhelmingly pharmacological. Applied to the phenomenon of addiction it may seem reasonable to assume the presence of a vector (e.g., a "toxic drug supply") and the need for a pharmacological intervention that disrupts the vector (i.e., PSAD). To illustrate, the Canadian AIDS Treatment Information Exchange (CATIE; nd) describes itself as "Canada's source for HIV and hepatitis C information", and features an article advocating for safe supply. The first sentence of the article states the purported cause of poisonings: "Canada is experiencing an overdose crisis caused by a toxic illicit drug supply." The article emphasizes that "..a "safe supply" of drugs is urgently needed to address the toxic illicit supply", adding that: "The goal of safe supply is to enable people who use drugs to access regulated substances from a legal source", including "heroin, fentanyl, cocaine, methamphetamines, and MDMA". All of CATIE's top tier donors are pharmaceutical companies.

The metaphor of an infectious disease fits extremely poorly with the phenomenon of addiction. Rather than focusing on vectors associated with the "supply" of drugs, the clinical science of addiction has articulated the conditions that create "demand" for drugs. Nearly every adult in North America has access to drugs, including alcohol, cannabis, and others. However, as summarized in our Introduction, problems of addiction and poisonings are concentrated among people who are psychologically and socially excluded. The relationship between social and psychological integration and addiction has been demonstrated in seminal animal studies (e.g., Alexander et al., 1978), in large natural experiments such as the return of Vietnam Veterans who were addicted to heroin (Robins et al., 1974), in the pioneering methadone programs that stimulated the massive expansion of Opioid Agonist Therapy (OAT) by President Nixon in the 1970s (Dole et al., 1968), and in the dramatic reversal of poisonings accomplished by the Portuguese Drug Strategy (Portuguese Government, 1999). In practical terms, the overwhelming majority of factors that contribute to harm reduction, or the prevention and treatment of addiction, involve relationships and are social.

PSAD OUTSTANDING ISSUES

Several crucial implications of PSAD have not been addressed by advocates. These include: the relationship between PSAD and the standard of care for treating persons with addictions; the clinical importance of medical and psychiatric comorbidities in populations that have been prioritized by advocates to receive PSAD; the size of the eligible population and per person costs of implementing PSAD; impacts of PSAD on drug shortages; and medico-legal and ethical ramifications. We address these points briefly below to illustrate their importance.

STANDARD OF CARE (SOC)

Evidence regarding biomedical and psychosocial interventions for treating substance use disorders is diverse and the care provided by a physician or psychologist addiction specialist assumes a broader and more informed perspective than that of generalists or specialists in other areas. Certain populations routinely receive a higher SoC and achieve markedly better outcomes. Physicians who experience addictions are supported by highly effective and well-established programs referred to as Physician Health Programs (PHP) (Brewster et al., 2008; Gary et al., 2017). Based on their record of success, the PHP model has been extended to an array of healthcare professionals (e.g., nurses and paramedics), lawyers, persons employed in safety sensitive occupations, and public servants. The same standard informs care provided in major private programs (e.g., Betty Ford).

The PHP approach incorporates several key elements:

- Early identification with comprehensive evaluation.
- Rapid offer of comprehensive treatment for a broad array of potentially impairing medical and psychiatric illnesses.[3]
- An alternative to a disciplinary process.
- Comprehensive continuing care, monitoring, and support within an intensive psychosocial and contingency managed approach.
- Extensive use of evidence based non-professional mutual help (Kelly, Abry, et al., 2020; Kelly, Humphreys, et al., 2020) and professional evidence based interventions (e.g., Cognitive-behavioural Therapy, Motivational Enhancement Therapy, Contingency Management) and limited of use of medications.
- Orientation toward sustained long-term recovery versus acute care responses to short-term harms.
- An integrated continuum of community-based supports for recovering individuals and their families.

The psychosocial emphasis of PHP's was evident in the SoC used in North America's original methadone programs, which reported achieving a "high rate of social productivity, as defined by stable employment and responsible behavior" (Dole et al., 1968, p. 2711), and "94% success in ending the criminal activity of former heroin addicts" (Dole et al., 1968, p. 2708). The researchers explained that their results "of course, cannot be attributed to the medication, which merely blocks drug hunger" (Dole et al., 1968, p. 2711), and instead credited their prolonged and intensive relationships with clients, including weeks of inpatient care and months or years of community-based support.

Heterogeneity between people experiencing addiction is not an indication that this SoC should be abandoned. Rather, evidence-based, theoretically sound interventions must be adapted to each individual's circumstances, as illustrated by the success of recovery-oriented housing and the transformative reduction in poisonings achieved in Portugal. From the Portuguese National Strategy: "Strictly speaking, there is no such thing as treatment without social reintegration" (Portuguese Government, 1999, Chapters IX, Pt 74).

In relation to this SoC, the scale-up of PSAD to people who are physically and mentally unwell, at high risk for poisoning with minimal access to social determinants of health (SDoH; Government of Canada, n.d. b) is strongly contraindicated.

[3]In Canada this includes access to highly comprehensive inpatient and outpatient programs for addiction and complex comorbid mental health and medical issues (Homewood Traumatic Stress Injury and Concurrent Disorders Program and others and Bellwood Concurrent Trauma & Addiction Program and others) which initiate remission and facilitate transfer to comprehensive aftercare programs.

Alternatively, adapting addiction best practices to populations experiencing deficits in SDoH requires:

- An expectation that complex psychosocial, medical, psychiatric and health needs interact with polydrug use.
- Recognizing that the population will often live in environments that perpetuate ill health and act as a barrier to wellness.
- Implementing single-source teams that provide evidence-based recovery oriented housing (Palepu et al., 2013; Patterson et al., 2013), Individualized Placement and Support (Bond et al., 2019; Wallstroem et al., 2021), peer-support and coaching, and professional specialists.
- Employing contingency management and community reinforcement to create an expectation of wellness and increased agency, both being integral to effective harm reduction and to recovery.

The influence of the above SoC is reflected at the jurisdictional level in policies addressing addiction. The term *recovery-oriented systems of care* (ROSC) has been defined by the US Substance Abuse and Mental Health Services Administration (Substance Abuse and Mental Health Administration (SAMHSA), 2010) as: "a coordinated network of community-based services and supports that is person-centered and builds on the strengths and resiliencies of individuals, families, and communities to achieve improved health, wellness, and quality of life for those with or at risk for mental health and substance use problems." The guiding influence of ROSC determines funding for addiction services in the US (Substance Abuse and Mental Health Administration (SAMHSA), 2012), and defines the orientation of governments in England (HM Government, 2017), Scotland (Scottish Government, 2018), Belgium and the Netherlands (Bellaert et al., 2021), and other jurisdictions at the national, state, or provincial levels. The vision of an all-of-society approach to addressing addiction is prominent in Portugal's National Strategy, which introduces itself as "a reveille that will mobilise all elements of Portuguese society: institutions, families and, above all, the younger generations" (Portuguese Government, 1999 Introduction).

Opioid Agonist Therapy (OAT) employing recognized best practices should be offered to individuals meeting criteria for OUD and for a duration determined by the individual in consultation with their care providers and other supports. However, as a component of the SoC to treat opioid addiction, OAT must be accompanied by social and psychological services, including those related to independent housing and employment. Summarizing evidence from the field of addiction, recent systematic reviewers emphasized that: "Studies show that employment is one of the strongest predictors of positive outcomes for persons with SUD, including more frequent treatment completion, lower incidence of relapse, less criminality and parole violations, and improved quality of life" (Magura & Marshall, 2020). Current publicly-funded OAT services ignore this evidence. In a year-long Vancouver study participants received injectable opioids up to three times a day and "only 2 (1%) participants were employed at all 5 timepoints" (Nikoo et al., 2018, p. 20). In 2017 130,300 people received prescriptions for opiate use disorder across the United States and fully 75% were unemployed (Krawczyk et al., 2021). In Ontario's provincial OAT program, each year on methadone "was associated with a 7% increase in the odds of women engaging with criminal activity" (van Reekum et al., 2020, p. 1). The failure of public OAT programs to promote employment and reduce crime will not be improved by providing more and stronger addictive drugs.

POTENTIAL FOR ADVERSE OUTCOMES

Numerous prescription drugs are associated with adverse events including mortality. A review of fatal drug poisonings concluded that "Overdoses involving prescription drugs in the United States have reached epidemic proportions", involving various classes of drugs including sleep aids (e.g., zolpidem), muscle relaxants (e.g., carisoprodol), and anxiolytics (e.g., alprazolam, diazepam) alongside opioids (Paulozzi, 2012). Nine different prescription opioids contributed to Australian emergency hospitalizations over a ten-year period (Lam et al., 2022), revealing that "In contrast to most opioids, fentanyl and methadone were relatively more likely to be involved in non-intentional poisonings" (p633). Some advocates for PSAD appear dangerously ignorant of this evidence, writing writing in Canada's Globe & Mail that: "People who use psychoactive drugs from a known source, with a known potency, free of contaminants, will not overdose and die." (Dodd et al., 2022). Populations prioritized by advocates to receive PSAD include many who currently receive OAT, and are known to experience significant medical and psychiatric comorbidities that exacerbate risks associated with pharmaceuticals (NIMH (National Institute of Mental Health), n.d.; Strain, n.d.).

The lifetime risk of developing a co-occurring mental disorder among individuals with opiate use disorder is about 50%. Chronic non-cancer pain is exceedingly common in OAT populations, estimated at more than 60% (Dunn et al., 2014; Peles et al., 2011; Rosenblum et al., 2003). The prevalence of traumatic brain injury among OUD patients has increased markedly due to anoxia associated with acute poisoning (Winstanley et al., 2021) and has in turn been postulated to perpetuate OUD (Corrigan & Adams, 2019). Given the history of prolonged use of illicit opioids and OAT including methadone and buprenorphine in this population, the likelihood of experiencing altered pain perception including Opioid-Induced Hyperalgesia (OIH) is substantial if not ubiquitous (Compton et al., 2012; Dunn et al., 2014; Higgins et al., 2019; Zahari et al., 2016). This results in the individual experiencing a paradoxical heightened sensitivity to pain and pain's emotional consequences and experiencing pain at lower thresholds. As a consequence, individuals that use opioids tend to experience more disability from pain as well as more prolonged recovery from injuries (Rivat & Ballantyne, 2016). Additionally, evolving medical literature supports the long-held suspicion that opioid induced pain sensitivity changes are permanent (Wachholtz & Gonzalez, 2014). OIH is clearly dose-dependent.

Fatal poisonings are overwhelmingly associated with polydrug use. The Government of Alberta reports: "In 2020, 82 per cent of unintentional fentanyl related deaths listed at least one other substance as contributing to death, the most frequent being methamphetamine (58 per cent) and cocaine (30 per cent)."(Government of Alberta - Health, 2020, p. 5). In BC the Coroners Service (2022) reports that the top four detected drugs among poisoning victims between 2018-21 were fentanyl (86.7%), cocaine (48%), methamphetamines/amphetamines (39.7%) and other opioids (29.1%). Alcohol (28%) and benzodiazepines (7.9%) were also part of the polysubstance use profiles of poisonings in BC. Medical comorbidities involving cardiac and respiratory disease are substantial. Also notable is the correlation between poor retention rates in populations receiving OAT and lack of access to SDoH. These are among the populations most often prioritized to receive PSAD.

Acute and chronic use of opioids, including typical opioids such as fentanyl and hydromorphone and medications such as methadone cause a broad range of cognitive and psychomotor impairments, endocrine dysfunction (Chou et al., 2015; Hallinan et al., 2009), sleep disorders (Dunn et al., 2018), increased likelihood of falls (Bond et al., 2019), and immune system dysfunction (Baldacchino et al., 2012). The medical literature consistently identifies deficits in verbal working memory, risk-taking and cognitive flexibility.

Ongoing use of opioids by depressed individuals

can perpetuate a vicious cycle, further negatively impacting mood and pain perception (Scherrer et al., 2016). Pain and depression are known to mutually perpetuate each other; pain negatively affects the recognition and treatment of depression and is associated with more severe depressive symptoms. Additionally, depressed individuals with pain complain more of pain and have greater impairment (Bair et al., 2003). Lastly, OUD is strongly associated with fatal and non-fatal poisoning (Hser et al., 2015, 2017).

As indicated above, non-fatal poisoning with brain anoxia is a proxy for traumatic brain injury. Traumatic brain injury results in cognitive impairments, increased risk of depression and decreased occupational functioning (Drake et al., 2000).

Chronic cocaine and methamphetamine use result in neurocognitive deficits (Potvin et al., 2014; Scott et al., 2007) and multiple psychiatric adverse events including psychotic disorders, mood, and anxiety disorders. Although the literature concerning benzodiazepines is less robust, this drug class is known to cause neurocognitive deficits that persist following withdrawal (Crowe & Stranks, 2018). The detected prevalence of benzodiazepines among decedents in BC has surged in recent years to 50% (BC Coroners Service, 2022).

In performing a risk-benefit analysis we weighed the potential adverse outcomes of PSAD against established, evidence based interventions for OUD and other substance use disorders. The population that is most likely to receive PSAD is a population with the highest likelihood of experiencing the above mentioned medical and psychiatric comorbidities. It is probable, if not certain that high-dose, oral or intravenous opioids provided within a PSAD context will perpetuate and aggravate pre-existing cognitive or psychomotor deficits, OIH, endocrine, sleep and mood disorders, and may precipitate these events among vulnerable individuals. Guidelines to manage adverse events associated with opioid prescribing uniformly do not recommend dose increase. Similarly, provision of prescription stimulants (methylphenidate, dextroamphetamine) or illicit stimulants (cocaine, methamphetamine) can reasonably be assumed to exacerbate existing psychotic, mood and anxiety symptoms in a stimulant-dependent population. Lastly, we are aware of no high quality evidence indicating that prescribing benzodiazepines in a polydrug dependent population is either safe or would mitigate adverse consequences associated with this drug class.

COST ESTIMATION

To our knowledge no comprehensive cost analysis for PSAD has been performed. Establishing a cost estimate for the provision of cocaine or methamphetamine within a PSAD context is currently not possible due to lack of drug price data from licit sources.

We are able to provide a limited cost estimate for use of intravenous fentanyl. Consistent with advocacy for providing drug users with their preferred drugs and formulations, we estimated costs involving IV fentanyl because hydromorphone or morphine are insufficient to replace the drugs sought by many drug users.

To estimate daily IV fentanyl requirements we focused primarily on clinical experience. Individuals with OUD stabilized on Kadian (long acting oral morphine) and who are not receiving other long-acting opioids such as methadone generally require 800 mg - 1200 mg of Kadian per day. Use of additional illicit opiates is precluded as evidenced by opioid negative biological testing. We note that 800 mg to 1200 mg is substantially more than the recommended dose of 480 mg of long-acting morphine per the January 2022 BC Center on Substance Use Guideline (BC Centre on Substance Use, 2022, p. 31).

Kadian 800 mg to 1200 mg daily use converts to a range of IV fentanyl 1865 μg - 4000 μg to 2800 μg – 6000 μg (ClinCalc, n.d.).

This assumes no reduction for cross tolerance and no additional long-acting opioids.

The cost of 50 μg of IV fentanyl is $2.7290 (Alberta Government, n.d.). As such, the daily cost to maintain an individual receiving Kadian 800 mg to 1200 mg per day with IV fentanyl would range from $101.79 to $327.48 per day (1865 ÷ 50 = 37.3 x $2.729 to 6000 ÷ 50 = 120 x $2.729). This would equate to a drug cost of between $37,153.34 to $119,530.20 per person per year. Our cost estimate is solely for one opioid and does not assume additional costs for startup, pharmacist and other associated staffing costs, IT, billing, prescription monitoring, lease, and security.

None of the reviewed manuscripts discussed the estimated cost of "safe supply". Moreover, details that are ordinarily essential to the financing, planning and implementation of health and social services are notably absent from advocacy for PSAD, including:

- The criteria that would be used to establish eligibility;
- The estimated size of the eligible population;
- The specific medications, doses, and formulations that would be included;
- The estimated annual public cost of PSAD;
- Demonstration that the costs of PSAD compare favourably to established interventions that reduce harms among people who experience addiction, mental illness, and poverty;
- Criteria signifying that PSAD should be stopped.

Canada has experienced significant drug shortages and notably, shortages of anesthetic drugs including fentanyl (Hall et al., 2013). PSAD would deplete current provincial formularies of IV fentanyl and other drugs with implications for surgical procedures and other hospital-based pain management services.

ETHICAL AND LEGAL CONSIDERATIONS

The results of our review indicate that polydrug dependent and marginalized populations with low access to SDoH are most often described as potential beneficiaries of PSAD. We recognize that the SoC for addiction is not well implemented for this population in Canada's publicly-funded system. Nevertheless, the provision of PSAD deviates markedly from existing SoC for addiction treatment, and no high quality scientific research (e.g., RCTs, meta-analyses) addresses fundamental questions about the proposed approach, including: Does PSAD decrease or increase illicit opioid or polydrug use and drug use consequences such as fatal and non-fatal poisonings?; Will PSAD lead to increased diversion creating an expanded illicit market and more cases of OUD and other substance use disorders?; Is PSAD cost-effective compared to well established (and costed) interventions that reduce criminal justice involvement, medical emergencies, and housing instability among people living with profound addictions?

The absence of any careful articulation of these details raises serious ethical concerns. Provision of PSAD is associated with highly probable adverse effects while diverging from the SoC that guides effective addiction treatment. Consent to an ill-defined high-risk intervention may not be reasonably obtained among prospective recipients of PSAD, particularly if established evidence-based interventions are not offered as alternatives. In this context, PSAD represents a human experiment that conflicts with the ethical principles of physicians, clinical psychologists and other regulated health professionals.

The recent Stanford–*Lancet* Commission emphasized the role of commercial, particularly pharmaceutical, interests and a multi-system regulatory failure as contributors to the current drug poisoning crisis (Humphreys et al., 2022). The Commission detailed an urgent need to prevent profit driven clinicians and industries from influencing addiction policies and practices. Among their recommendations to reduce the influence of profit, the Commission recommends: "Bodies with legal or regulatory power to shape prescribing should not accept industry funding or include people with direct financial ties to the pharmaceutical industry" (Humphreys et al., 2022, p. 16). The Commission details the destructive consequences of pharmaceutical industry funding on medical education and research, skewing practice toward prescribing addictive drugs at the expense of psychosocial services that define the SoC for addiction. Successful legal actions brought against tobacco and opioid manufacturers and distributors underscore the potentially massive medico-legal risks associated with PSAD. Decision-makers and insurers should carefully scrutinize relationships between advocates for PSAD and related financial interests involving pharmaceuticals or devices.

CONCLUSION

We found no evidence demonstrating benefits of PSAD, replicating the results of previous reviewers. Nevertheless, we found numerous publications that advocated for "safe supply", often forcefully, but without defining the term or addressing fundamental details such as eligibility, estimated costs, and responsibility for adverse consequences. At the same time, these publications detail stunning evidence of poverty and social exclusion among the people at greatest risk for poisoning. Nearly 80% of the publications that advocated for PSAD were conducted in BC, and none of these recommended evidence-based interventions addressing homelessness, unemployment, addiction treatment, concurrent mental illness, or discussed implications for reconciliation with First Peoples. Regardless of the intentions of each of the contributing teams of investigators, these studies are now cited uncritically as the scientific basis for PSAD.

The term *safe supply*, as used by most advocates, might reasonably be assumed to indicate that evidence is already available demonstrating the safety and effectiveness of an established model of practice. Our review found no evidence supporting either of these assumptions, suggesting that at present, *safe supply* represents a loosely defined slogan to increase the distribution of publicly-funded addictive drugs to people whose life circumstances perpetuate profound addictions.

In order for PSAD to potentially reduce the current rate of poisonings two things are required. First, a system would need to be created that attracts highly marginalized people who are excluded from existing services and provides them with an ongoing array of addictive drugs that are manufactured by pharmaceutical companies, distributed by regulated professionals, and paid for by the public.

The second requirement for the "success" of PSAD is that policy makers must ignore high-quality evidence detailing the preferences of marginalized people experiencing profound addictions, the evidence-based interventions that effectively support their goals, and evidence of the abundant adverse consequences associated with continued exposure to opioids and other addictive drugs. Only by ignoring this evidence can advocates hope to demonstrate potential benefits of PSAD, while perpetuating what the Stanford-Lancet Commission describes as "an informal system of pharmacological sedation of poverty" (Humphreys et al., 2022, p. 24).

An alternative approach is exemplified by the standard of care used to successfully treat addictions among physicians, public servants and other groups, and that is reflected in the growing number of jurisdictions that have embraced recovery-oriented addiction policies. This standard of care recognizes that nearly all of the modifiable factors associated with addictions are social and psychological. Poisonings and addictions flourish in settings where large numbers of people are socially excluded and live in poverty. Reversing these harms has been demonstrated in Canadian randomized trials and through large scale national reforms such as Portugal's National Strategy, which recognize that "Strictly speaking, there is no such thing as treatment without social reintegration" (Portuguese Government, 1999, Chapters IX, Pt 74).

BIBLIOGRAPHY

Alberta Government. (n.d.). Alberta Drug Benefit List - Effective April 1, 2021. Retrieved March 10, 2022, from www.ab.bluecross.ca/dbl/pdfs/dbl_full_list.pdf

Alexander, B. K., Coambs, R. B., & Hadaway, P. F. (1978). The effect of housing and gender on morphine self-administration in rats. Psychopharmacology, 58(2), 175–179. doi.org/10.1007/BF00426903

Ali, F., Russell, C., Nafeh, F., Rehm, J., LeBlanc, S., & Elton-Marshall, T. (2021). Changes in substance supply and use characteristics among people who use drugs (PWUD) during the COVID-19 global pandemic: A national qualitative assessment in Canada. The International Journal on Drug Policy, 93, 103237. doi.org/10.1016/j.drugpo.2021.103237

Aronowitz, S. V, Engel-Rebitzer, E., Lowenstein, M., Meisel, Z., Anderson, E., & South, E. (2021). "We have to be uncomfortable and creative": Reflections on the impacts of the COVID-19 pandemic on overdose prevention, harm reduction & homelessness advocacy in Philadelphia. SSM. Qualitative Research in Health, 1, 100013. doi.org/10.1016/j.ssmqr.2021.100013

Bair, M. J., Robinson, R. L., Katon, W., & Kroenke, K. (2003). Depression and pain comorbidity: a literature review. Archives of Internal Medicine, 163(20), 2433–2445. doi.org/10.1001/archinte.163.20.2433

Baldacchino, A., Balfour, D. J. K., Passetti, F., Humphris, G., & Matthews, K. (2012). Neuropsychological consequences of chronic opioid use: a quantitative review and meta-analysis. Neuroscience and Biobehavioral Reviews, 36(9), 2056–2068. doi.org/10.1016/j.neubiorev.2012.06.006

Bardwell, G., Ivsins, A., Socías, M. E., & Kerr, T. (2021). Examining factors that shape use and access to diverted prescription opioids during an overdose crisis: A qualitative study in Vancouver, Canada. Journal of Substance Abuse Treatment, 130, 108418. doi.org/10.1016/j.jsat.2021.108418

Bardwell, G., Small, W., Lavalley, J., McNeil, R., & Kerr, T. (2021). "People need them or else they're going to take fentanyl and die": A qualitative study examining the 'problem' of prescription opioid diversion during an overdose epidemic. Social Science & Medicine (1982), 279, 113986. doi.org/10.1016/j.socscimed.2021.113986

BC Centre on Substance Use. (2022). Risk Mitigation in the Context of Dual Public Health Emergencies. www.bccsu.ca/wp-content/uploads/2022/02/Risk-Mitigation-Guidance-Update-February-2022.pdf

BC Coroners Service. (2022). Illicit Drug Toxicity Type of Drug - Data to December 31, 2021. www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/deaths/coroners-service/statistical/illicit-drug-type.pdf

Bellaert, L., Martinelli, T. F., Vanderplasschen, W., Best, D., van de Mheen, D., & Laenen, F. Vander. (2021). Chasing a pot of gold: an analysis of emerging recovery-oriented addiction policies in Flanders (Belgium) and The Netherlands. Drugs: Education, Prevention and Policy, 28(5), 399–410. doi.org/10.1080/09687637.2021.1915250

Best, D. W., Ghufran, S., Day, E., Ray, R., & Loaring, J. (2008). Breaking the habit: a retrospective analysis of desistance factors among formerly problematic heroin users. Drug and Alcohol Review, 27(6), 619–624. doi.org/10.1080/09595230802392808

Bond, G. R., Drake, R. E., & Pogue, J. A. (2019). Expanding Individual Placement and Support to Populations With Conditions and Disorders Other Than Serious Mental Illness. Psychiatric Services (Washington, D.C.), 70(6), 488–498. doi.org/10.1176/appi.ps.201800464

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

Brewster, J. M., Kaufmann, I. M., Hutchison, S., & MacWilliam, C. (2008). Characteristics and outcomes of doctors in a substance dependence monitoring programme in Canada: prospective descriptive study. BMJ (Clinical Research Ed.), 337, a2098. doi.org/10.1136/bmj.a2098

Canadian AIDS Treatment Information Exchange (CATIE). (n.d.). Safe Supply: What is it and what is happening in Canada? Retrieved March 9, 2022, from www.catie.ca/prevention-in-focus/safe-supply-what-is-it-and-what-is-happening-in-canada

Case, A., & Deaton, A. (2017). Mortality and morbidity in the 21(st) century. Brookings Papers on Economic Activity, 2017, 397–476. doi.org/10.1353/eca.2017.0005

Chou, R., Turner, J. A., Devine, E. B., Hansen, R. N., Sullivan, S. D., Blazina, I., Dana, T., Bougatsos, C., & Deyo, R. A. (2015). The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. Annals of Internal Medicine, 162(4), 276–286. doi.org/10.7326/M14-2559

ClinCalc. (n.d.). Equivalent Opioid Calculator. Retrieved March 10, 2022, from clincalc.com/Opioids/

Collins, S. E., Clifasefi, S. L., Logan, D. E., Samples, L. S., Somers, J. M., & Marlatt, G. A. (2012). Current status, historical highlights, and basic principles of Harm Reduction. In G. A. Marlatt, M. E. Larimer, & K. Witkiewitz (Eds.), Harm Reduction: Pragmatic Strategies for Managing High-Risk Behaviors, Second Edition. Guilford Publications.

Compton, P., Canamar, C. P., Hillhouse, M., & Ling, W. (2012). Hyperalgesia in heroin dependent patients and the effects of opioid substitution therapy. The Journal of Pain, 13(4), 401–409. doi.org/10.1016/j.jpain.2012.01.001

Corrigan, J. D., & Adams, R. S. (2019). The intersection of lifetime history of traumatic brain injury and the opioid epidemic. Addictive Behaviors, 90, 143–145. doi.org/10.1016/j.addbeh.2018.10.030

Crowe, S. F., & Stranks, E. K. (2018). The Residual Medium and Long-term Cognitive Effects of Benzodiazepine Use: An Updated Meta-analysis. Archives of Clinical Neuropsychology : The Official Journal of the National Academy of Neuropsychologists, 33(7), 901–911. doi.org/10.1093/arclin/acx120

Dennis, B. B., Sanger, N., Bawor, M., Naji, L., Plater, C., Worster, A., Woo, J., Bhalerao, A., Baptist-Mohseni, N., Hillmer, A., Rice, D., Corace, K., Hutton, B., Tugwell, P., Thabane, L., & Samaan, Z. (2020). A call for consensus in defining efficacy in clinical trials for opioid addiction: combined results from a systematic review and qualitative study in patients receiving pharmacological assisted therapy for opioid use disorder. Trials, 21(1), 30. doi.org/10.1186/s13063-019-3995-y

Dilokthornsakul, P., Moore, G., Campbell, J. D., Lodge, R., Traugott, C., Zerzan, J., Allen, R., & Page, R. L. 2nd. (2016). Risk Factors of Prescription Opioid Overdose Among Colorado Medicaid Beneficiaries. The Journal of Pain, 17(4), 436–443. doi.org/10.1016/j.jpain.2015.12.006

Dodd, Z., Nyx, E., Ranger, C., & Tyndall, M. (2022). Alberta's safe-supply committee is missing an opportunity to protect people from harm. Opinion. Contributed to the Globe and Mail. www.theglobeandmail.com/opinion/article-albertas-safe-supply-committee-is-missing-an-opportunity-to-protect/

Dole, V. P., Nyswander, M. E., & Warner, A. (1968). Successful treatment of 750 criminal addicts. JAMA, 206(12), 2708–2711. www.ncbi.nlm.nih.gov/pubmed/5754883

Drake, A. I., Gray, N., Yoder, S., Pramuka, M., & Llewellyn, M. (2000). Factors predicting return to work following mild traumatic brain injury: a discriminant analysis. The Journal of Head Trauma Rehabilitation, 15(5), 1103–1112. doi.org/10.1097/00001199-200010000-00004

Dunn, K. E., Brooner, R. K., & Clark, M. R. (2014). Severity and interference of chronic pain in methadone-maintained outpatients. Pain Medicine (Malden, Mass.), 15(9), 1540–1548. doi.org/10.1111/pme.12430

Dunn, K. E., Finan, P. H., Andrew Tompkins, D., & Strain, E. C. (2018). Frequency and correlates of sleep disturbance in methadone and buprenorphine-maintained patients. Addictive Behaviors, 76, 8–14. doi.org/10.1016/j.addbeh.2017.07.016

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. The International Journal on Drug Policy, 101, 103574. doi.org/10.1016/j.drugpo.2021.103574

Gary, D., Carr, P., Hall, B., Finlayson, A., & DuPont, R. (2017). Chapter 12: Physician Health Programs: The US Model. In Physician Mental Health and Well-Being (pp. 265–294). Springer. doi.org/10.1007/978-3-319-55583-6

Gicquelais, R. E., Jannausch, M., Bohnert, A. S. B., Thomas, L., Sen, S., & Fernandez, A. C. (2020). Links between suicidal intent, polysubstance use, and medical treatment after non-fatal opioid overdose. Drug and Alcohol Dependence, 212, 108041. doi.org/10.1016/j.drugalcdep.2020.108041

Goering, P. N., Streiner, D. L., Adair, C., Aubry, T., Barker, J., Distasio, J., Hwang, S. W., Komaroff, J., Latimer, E., Somers, J., & Zabkiewicz, D. M. (2011). The At Home/Chez Soi trial protocol: a pragmatic, multi-site, randomised controlled trial of a Housing First intervention for homeless individuals with mental illness in five Canadian cities. BMJ Open, 1(2), e000323. doi.org/10.1136/bmjopen-2011-000323

Goodyear, T., Mniszak, C., Jenkins, E., Fast, D., & Knight, R. (2020). "Am I gonna get in trouble for acknowledging my will to be safe?": Identifying the experiences of young sexual minority men and substance use in the context of an opioid overdose crisis. Harm Reduction Journal, 17(1), 23. doi.org/10.1186/s12954-020-00365-4

Government of Alberta - Health. (2020). Alberta COVID-19 Opioid Response Surveillance Report: Q2 2020. open.alberta.ca/publications/alberta-opioid-response-surveillance-report#summary

Government of Canada. (n.d.-a). Safer Supply. Retrieved March 10, 2022, from www.canada.ca/en/health-canada/services/opioids/responding-canada-opioid-crisis/safer-supply.html

Government of Canada. (n.d.-b). Social determinants of health and health inequalities - Canada.ca. Retrieved March 2, 2022, from www.canada.ca/en/public-health/services/health-promotion/population-health/what-determines-health.html

Hall, R., Bryson, G. L., Flowerdew, G., Neilipovitz, D., Grabowski-Comeau, A., & Turgeon, A. F. (2013). Drug shortages in Canadian anesthesia: a national survey. Canadian Journal of Anaesthesia = Journal Canadien d'anesthesie, 60(6), 539–551. doi.org/10.1007/s12630-013-9920-z

Hallinan, R., Byrne, A., Agho, K., McMahon, C. G., Tynan, P., & Attia, J. (2009). Hypogonadism in men receiving methadone and buprenorphine maintenance treatment. International Journal of Andrology, 32(2), 131–139. doi.org/10.1111/j.1365-2605.2007.00824.x

Hammond, A. S., Dunn, K. E., & Strain, E. C. (2020). Drug Legalization and Decriminalization Beliefs Among Substance-using and Nonusing Individuals. Journal of Addiction Medicine, 14(1), 56–62. doi.org/10.1097/ADM.0000000000000542

Higgins, C., Smith, B. H., & Matthews, K. (2019). Evidence of opioid-induced hyperalgesia in clinical populations after chronic opioid exposure: a systematic review and meta-analysis. British Journal of Anaesthesia, 122(6), e114–e126. doi.org/10.1016/j.bja.2018.09.019

HM Government. (2017). 2017 Drug Strategy. assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/628148/Drug_strategy_2017.PDF

Hser, Y.-I., Evans, E., Grella, C., Ling, W., & Anglin, D. (2015). Long-term course of opioid addiction. Harvard Review of Psychiatry, 23(2), 76–89. doi.org/10.1097/HRP.0000000000000052

Hser, Y.-I., Mooney, L. J., Saxon, A. J., Miotto, K., Bell, D. S., Zhu, Y., Liang, D., & Huang, D. (2017). High Mortality Among Patients With Opioid Use Disorder in a Large Healthcare System. Journal of Addiction Medicine, 11(4), 315–319. doi.org/10.1097/ADM.0000000000000312

Humphreys, K., Shover, C. L., Andrews, C. M., Bohnert, A. S. B., Brandeau, M. L., Caulkins, J. P., Chen, J. H., Cuéllar, M.-F., Hurd, Y. L., Juurlink, D. N., Koh, H. K., Krebs, E. E., Lembke, A., Mackey, S. C., Larrimore Ouellette, L., Suffoletto, B., & Timko, C. (2022). Responding to the opioid crisis in North America and beyond: recommendations of the Stanford-Lancet Commission. Lancet (London, England), 399(10324), 555–604. doi.org/10.1016/S0140-6736(21)02252-2

International Narcotics Control Board. (2013). Narcotic Drugs 2013. www.incb.org/documents/Narcotic-Drugs/Technical-Publications/2013/Narcotic_Drugs_Report_2013.pdf

Ivsins, A., Boyd, J., Beletsky, L., & McNeil, R. (2020). Tackling the overdose crisis: The role of safe supply. The International Journal on Drug Policy, 80, 102769. doi.org/10.1016/j.drugpo.2020.102769

Ivsins, A., Boyd, J., Mayer, S., Collins, A., Sutherland, C., Kerr, T., & McNeil, R. (2020). Barriers and facilitators to a novel low-barrier hydromorphone distribution program in Vancouver, Canada: a qualitative study. Drug and Alcohol Dependence, 216, 108202. doi.org/10.1016/j.drugalcdep.2020.108202

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. doi.org/10.1007/s11524-020-00489-9

Kelly, J. F., Abry, A., Ferri, M., & Humphreys, K. (2020). Alcoholics Anonymous and 12-Step Facilitation Treatments for Alcohol Use Disorder: A Distillation of a 2020 Cochrane Review for Clinicians and Policy Makers. Alcohol and Alcoholism (Oxford, Oxfordshire), 55(6), 641–651. https://doi.org/10.1093/alcalc/agaa050

Kelly, J. F., Humphreys, K., & Ferri, M. (2020). Alcoholics Anonymous and other 12-step programs for alcohol use disorder. The Cochrane Database of Systematic Reviews, 3(3), CD012880. doi.org/10.1002/14651858.CD012880.pub2

Kolla, G., & Strike, C. (2019). "It's too much, I'm getting really tired of it": Overdose response and structural vulnerabilities among harm reduction workers in community settings. The International Journal on Drug Policy, 74, 127–135. doi.org/10.1016/j.drugpo.2019.09.012

Krawczyk, N., Fawole, A., Yang, J., & Tofighi, B. (2021). Early innovations in opioid use disorder treatment and harm reduction during the COVID-19 pandemic: a scoping review. Addiction Science & Clinical Practice, 16(1), 68. doi.org/10.1186/s13722-021-00275-1

Kurani, S., McCoy, R. G., Inselman, J., Jeffery, M. M., Chawla, S., Finney Rutten, L. J., Giblon, R., & Shah, N. D. (2020). Place, poverty and prescriptions: a cross-sectional study using Area Deprivation Index to assess opioid use and drug-poisoning mortality in the USA from 2012 to 2017. BMJ Open, 10(5), e035376. doi.org/10.1136/bmjopen-2019-035376

Lal, S., & Adair, C. E. (2014). E-mental health: a rapid review of the literature. Psychiatric Services (Washington, D.C.), 65(1), 24–32. doi.org/10.1176/appi.ps.201300009

Lam, T., Hayman, J., Berecki-Gisolf, J., Sanfilippo, P., Lubman, D. I., & Nielsen, S. (2022). Pharmaceutical opioid poisonings in Victoria, Australia: Rates and characteristics of a decade of emergency department presentations among nine pharmaceutical opioids. Addiction (Abingdon, England), 117(3), 623–636. doi.org/10.1111/add.15653

Latimer, E. A., Rabouin, D., Cao, Z., Ly, A., Powell, G., Aubry, T., Distasio, J., Hwang, S. W., Somers, J. M., Bayoumi, A. M., Mitton, C., Moodie, E. E. M., & Goering, P. N. (2020). Cost-Effectiveness of Housing First With Assertive Community Treatment: Results From the Canadian At Home/Chez Soi Trial. Psychiatric Services (Washington, D.C.), 71(10), 1020–1030. doi.org/10.1176/appi.ps.202000029

Leamy, M., Bird, V., Le Boutillier, C., Williams, J., & Slade, M. (2011). Conceptual framework for personal recovery in mental health: systematic review and narrative synthesis. The British Journal of Psychiatry : The Journal of Mental Science, 199(6), 445–452. doi.org/10.1192/bjp.bp.110.083733

LePage, J. P., Lewis, A. A., Crawford, A. M., Parish, J. A., Ottomanelli, L., Washington, E. L., & Cipher, D. J. (2016). Incorporating Individualized Placement and Support Principles Into Vocational Rehabilitation for Formerly Incarcerated Veterans. Psychiatric Services (Washington, D.C.), 67(7), 735–742. doi.org/10.1176/appi.ps.201500058

Magura, S., & Marshall, T. (2020). The Effectiveness of Interventions Intended to Improve Employment Outcomes for Persons with Substance Use Disorder: An Updated Systematic Review. Substance Use & Misuse, 55(13), 2230–2236. doi.org/10.1080/10826084.2020.1797810

Marlatt, G. A., Somers, J. M., & Tapert, S. F. (1993). Harm Reduction: Application to Alcohol Abuse Problems. In L. S. Onken, J. D. Blaine, & J. J. Boren (Eds.), Behavioral Treatments for Drug Abuse and Dependence. US Department of Health and Human Services. Rockville MD.

Mayer, S., Fowler, A., Brohman, I., Fairbairn, N., Boyd, J., Kerr, T., & McNeil, R. (2020). Motivations to initiate injectable hydromorphone and diacetylmorphine treatment: A qualitative study of patient experiences in Vancouver, Canada. The International Journal on Drug Policy, 85, 102930. doi.org/10.1016/j.drugpo.2020.102930

McKeganey, N., Morris, Z., Neale, J., & Robertson, M. (2004). What are drug users looking for when they contact drug services: abstinence or harm reduction? Drugs: Education, Prevention and Policy, 11(5), 423–435. doi.org/10.1080/09687630410001723229

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), 92. doi.org/10.1186/s12954-021-00539-8

Monnat, S. M. (2018). Factors Associated With County-Level Differences in U.S. Drug-Related Mortality Rates. American Journal of Preventive Medicine, 54(5), 611–619. doi.org/10.1016/j.amepre.2018.01.040

Mueser, K. T., Drake, R. E., & Bond, G. R. (2016). Recent advances in supported employment for people with serious mental illness. Current Opinion in Psychiatry, 29(3), 196–201. doi.org/10.1097/YCO.0000000000000247

Nikoo, M., Vogel, M., Choi, F., Song, M. J., Burghardt, J., Zafari, Z., Tabi, K., Frank, A., Barbic, S., Schütz, C., Jang, K., & Krausz, M. (2018). Employment and paid work among participants in a randomized controlled trial comparing diacetylmorphine and hydromorphone. The International Journal on Drug Policy, 57, 18–24. doi.org/10.1016/j.drugpo.2018.03.021

NIMH (National Institute of Mental Health). (n.d.). Substance Use and Co-Occurring Mental Disorders. Retrieved March 2, 2022, from www.nimh.nih.gov/health/topics/substance-use-and-mental-health

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), 833–835. doi.org/10.2105/AJPH.2020.305612

Olding, M., Werb, D., Guise, A., Small, W., & McNeil, R. (2019). Navigating social norms of injection initiation assistance during an overdose crisis: A qualitative study of the perspectives of people who inject drugs (PWID) in Vancouver, Canada. The International Journal on Drug Policy, 69, 24–33. doi.org/10.1016/j.drugpo.2019.04.004

Olfson, M., Cosgrove, C., Altekruse, S. F., Wall, M. M., & Blanco, C. (2021). Deaths Of Despair: Adults At High Risk For Death By Suicide, Poisoning, Or Chronic Liver Disease In The US. Health Affairs (Project Hope), 40(3), 505–512. doi.org/10.1377/hlthaff.2020.01573

Ontario HIV Treatment Network. (2020). Possible benefits of providing safe supply of substances to people who use drugs during public health emergencies such as the COVID-19 pandemic. www.ohtn.on.ca/rapid-response-possible-benefits-of-providing-safe-supply-of-substances-to-people-who-use-drugs-during-public-health-emergencies-such-as-the-covid-19-pandemic/

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. doi.org/10.1056/NEJMoa0810635

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. doi.org/10.1001/jamapsychiatry.2016.0109

Oviedo-Joekes, E., Guh, D., Marsh, D. C., Brissette, S., Nosyk, B., Krausz, M., Anis, A., Christian, W. M., Spittal, P., & Schechter, M. T. (2010). Characteristics and response to treatment among Aboriginal people receiving heroin-assisted treatment. Canadian Journal of Public Health = Revue Canadienne de Sante Publique, 101(3), 210–212. doi.org/10.1007/BF03404375

Oviedo-Joekes, E., Palis, H., Guh, D., Marchand, K., Brissette, S., Lock, K., MacDonald, S., Harrison, S., Anis, A. H., Krausz, M., Marsh, D. C., & Schechter, M. T. (2018). Characteristics and response to treatment among Indigenous people receiving injectable diacetylmorphine or hydromorphone in a randomised controlled trial for the treatment of long-term opioid dependence. Drug and Alcohol Review, 37(1), 137–146. doi.org/10.1111/dar.12573

Oxford Centre for Evidence-Based Medicine. (2011). The Oxford 2011 Levels of Evidence. www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebm-levels-of-evidence

Palepu, A., Patterson, M. L., Moniruzzaman, A., Frankish, C. J., & Somers, J. (2013). Housing First improves residential stability in homeless adults with concurrent substance dependence and mental disorders. American Journal of Public Health, 103(SUPPL. 2). doi.org/10.2105/AJPH.2013.301628

Papamihali, K., Yoon, M., Graham, B., Karamouzian, M., Slaunwhite, A. K., Tsang, V., Young, S., & Buxton, J. A. (2020). Convenience and comfort: reasons reported for using drugs alone among clients of harm reduction sites in British Columbia, Canada. Harm Reduction Journal, 17(1), 90. doi.org/10.1186/s12954-020-00436-6

Parent, S., Papamihali, K., Graham, B., & Buxton, J. A. (2021). Examining prevalence and correlates of smoking opioids in British Columbia: opioids are more often smoked than injected. Substance Abuse Treatment, Prevention, and Policy, 16(1), 79. doi.org/10.1186/s13011-021-00414-6

Patterson, M. L., Rezansoff, S., Currie, L., & Somers, J. M. (2013). Trajectories of recovery among homeless adults with mental illness who participated in a randomised controlled trial of Housing First: a longitudinal, narrative analysis. BMJ Open, 3(9), e003442. doi.org/10.1136/bmjopen-2013-003442

Paulozzi, L. J. (2012). Prescription drug overdoses: a review. Journal of Safety Research, 43(4), 283–289. doi.org/10.1016/j.jsr.2012.08.009

Pauly, B., Wallace, B., Pagan, F., Phillips, J., Wilson, M., Hobbs, H., & Connolly, J. (2020). Impact of overdose prevention sites during a public health emergency in Victoria, Canada. PloS One, 15(5), e0229208. doi.org/10.1371/journal.pone.0229208

Pear, V. A., Ponicki, W. R., Gaidus, A., Keyes, K. M., Martins, S. S., Fink, D. S., Rivera-Aguirre, A., Gruenewald, P. J., & Cerdá, M. (2019). Urban-rural variation in the socioeconomic determinants of opioid overdose. Drug and Alcohol Dependence, 195, 66–73. doi.org/10.1016/j.drugalcdep.2018.11.024

Peles, E., Schreiber, S., Hetzroni, T., Adelson, M., & Defrin, R. (2011). The differential effect of methadone dose and of chronic pain on pain perception of former heroin addicts receiving methadone maintenance treatment. The Journal of Pain, 12(1), 41–50. doi.org/10.1016/j.jpain.2010.04.009

Pettersen, H., Landheim, A., Skeie, I., Biong, S., Brodahl, M., Benson, V., & Davidson, L. (2018). Why Do Those With Long-Term Substance Use Disorders Stop Abusing Substances? A Qualitative Study. Substance Abuse : Research and Treatment, 12, 1178221817752678. doi.org/10.1177/1178221817752678

Portuguese Government. (1999). Portugal's National Drug Strategy 1999 (English version). www.emcdda.europa.eu/drugs-library/portugals-national-drug-strategy-1999-english-version_en

Potvin, S., Stavro, K., Rizkallah, E., & Pelletier, J. (2014). Cocaine and cognition: a systematic quantitative review. Journal of Addiction Medicine, 8(5), 368–376. doi.org/10.1097/ADM.0000000000000066

Rhee, T. G., & Rosenheck, R. A. (2019). Association of current and past opioid use disorders with health-related quality of life and employment among US adults. Drug and Alcohol Dependence, 199, 122–128. doi.org/10.1016/j.drugalcdep.2019.03.004

Rivat, C., & Ballantyne, J. (2016). The dark side of opioids in pain management: basic science explains clinical observation. Pain Reports, 1(2), e570. doi.org/10.1097/PR9.0000000000000570

Robins, L. N., Davis, D. H., & Goodwin, D. W. (1974). Drug use by U.S. Army enlisted men in Vietnam: a follow-up on their return home. American Journal of Epidemiology, 99(4), 235–249. doi.org/10.1093/oxfordjournals.aje.a121608

Rosenblum, A., Joseph, H., Fong, C., Kipnis, S., Cleland, C., & Portenoy, R. K. (2003). Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. JAMA, 289(18), 2370–2378. doi.org/10.1001/jama.289.18.2370

Rosic, T., Naji, L., Panesar, B., Chai, D. B., Sanger, N., Dennis, B. B., Marsh, D. C., Rieb, L., Worster, A., Thabane, L., & Samaan, Z. (2021). Are patients' goals in treatment associated with expected treatment outcomes? Findings from a mixed-methods study on outpatient pharmacological treatment for opioid use disorder. BMJ Open, 11(1), e044017. doi.org/10.1136/bmjopen-2020-044017

Russolillo, A., Patterson, M., McCandless, L., Moniruzzaman, A., & Somers, J. (2014). Emergency department utilisation among formerly homeless adults with mental disorders after one year of Housing First interventions: A randomised controlled trial. International Journal of Housing Policy, 14(1). doi.org/10.1080/14616718.2014.884881

Ryan, A., Sereda, A., & Fairbairn, N. (2020). Measures to support a safer drug supply. In CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne (Vol. 192, Issue 49, p. E1731). doi.org/10.1503/cmaj.77303

Salters, K. A., Parent, S., Nicholson, V., Wang, L., Sereda, P., Pakhomova, T. E., Kibel, M., Chau, W., Closson, K., Parashar, S., Barrios, R., Montaner, J. S. G., & Hogg, R. S. (2021). The opioid crisis is driving mortality among under-served people living with HIV in British Columbia, Canada. BMC Public Health, 21(1), 680. doi.org/10.1186/s12889-021-10714-y

Samson, D., & Schoelles, K. M. (2012). Developing the Topic and Structuring Systematic Reviews of Medical Tests: Utility of PICOTS, Analytic Frameworks, Decision Trees, and Other Frameworks. (S. M. Chang, D. B. Matchar, G. W. Smetana, & C. A. Umscheid (eds.)).

Saulle, R., Vecchi, S., & Gowing, L. (2017). Supervised dosing with a long-acting opioid medication in the management of opioid dependence. The Cochrane Database of Systematic Reviews, 4(4), CD011983. doi.org/10.1002/14651858.CD011983.pub2

Scherrer, J. F., Salas, J., Copeland, L. A., Stock, E. M., Ahmedani, B. K., Sullivan, M. D., Burroughs, T., Schneider, F. D., Bucholz, K. K., & Lustman, P. J. (2016). Prescription Opioid Duration, Dose, and Increased Risk of Depression in 3 Large Patient Populations. Annals of Family Medicine, 14(1), 54–62. doi.org/10.1370/afm.1885

Scott, J. C., Woods, S. P., Matt, G. E., Meyer, R. A., Heaton, R. K., Atkinson, J. H., & Grant, I. (2007). Neurocognitive effects of methamphetamine: a critical review and meta-analysis. Neuropsychology Review, 17(3), 275–297. doi.org/10.1007/s11065-007-9031-0

Scottish Government. (2018). Rights, respect and recovery: alcohol and drug treatment strategy. www.gov.scot/publications/rights-respect-recovery/pages/1/

Singh, G. K. (2003). Area deprivation and widening inequalities in US mortality, 1969-1998. American Journal of Public Health, 93(7), 1137–1143. doi.org/10.2105/ajph.93.7.1137

Socias, M. E., Grant, C., Hayashi, K., Bardwell, G., Kennedy, M. C., Milloy, M.-J., & Kerr, T. (2021). The use of diverted pharmaceutical opioids is associated with reduced risk of fentanyl exposure among people using unregulated drugs in Vancouver, Canada. Drug and Alcohol Dependence, 228, 109109. doi.org/10.1016/j.drugalcdep.2021.109109

Somers, J. M., Rezansoff, S. N., Moniruzzaman, A., Palepu, A., & Patterson, M. (2013). Housing First Reduces Re-offending among Formerly Homeless Adults with Mental Disorders: Results of a Randomized Controlled Trial. PLoS ONE, 8(9). doi.org/10.1371/journal.pone.0072946

Stein, M. D., Flori, J. N., Risi, M. M., Conti, M. T., Anderson, B. J., & Bailey, G. L. (2017). Overdose history is associated with postdetoxification treatment preference for persons with opioid use disorder. Substance Abuse, 38(4), 389–393. doi.org/10.1080/08897077.2017.1353570

Strain, E. (n.d.). Opioid use disorder: Epidemiology, pharmacology, clinical manifestations, course, screening, assessment, and diagnosis - UpToDate. Retrieved March 2, 2022, from www.uptodate.com/contents/opioid-use-disorder-epidemiology-pharmacology-clinical-manifestations-course-screening-assessment-and-diagnosis

Substance Abuse and Mental Health Administration (SAMHSA). (2010). Recovery-Oriented System of Care (ROSC) Resource Guide. www.samhsa.gov/sites/default/files/rosc_resource_guide_book.pdf

Substance Abuse and Mental Health Administration (SAMHSA). (2012). SAMHSA's Working definition of recovery. store.samhsa.gov/sites/default/files/d7/priv/pep12-recdef.pdf

Tyndall, M. (2020). A safer drug supply: a pragmatic and ethical response to the overdose crisis. CMAJ : Canadian Medical Association Journal, 192(34), E986–E987. doi.org/10.1503/cmaj.201618

van Reekum, E. A., Rosic, T., Hudson, J., Sanger, N., Marsh, D. C., Worster, A., Thabane, L., & Samaan, Z. (2020). Social functioning outcomes in men and women receiving medication-assisted treatment for opioid use disorder. Biology of Sex Differences, 11(1), 20. doi.org/10.1186/s13293-020-00298-4

Wachholtz, A., & Gonzalez, G. (2014). Co-morbid pain and opioid addiction: long term effect of opioid maintenance on acute pain. Drug and Alcohol Dependence, 145, 143–149. doi.org/10.1016/j.drugalcdep.2014.10.010

Wallace, B., van Roode, T., Pagan, F., Hore, D., & Pauly, B. (2021). The potential impacts of community drug checking within the overdose crisis: qualitative study exploring the perspective of prospective service users. BMC Public Health, 21(1), 1156. doi.org/10.1186/s12889-021-11243-4

Wallstroem, I. G., Pedersen, P., Christensen, T. N., Hellström, L., Bojesen, A. B., Stenager, E., White, S., Mueser, K. T., Bejerholm, U., van Busschbach, J. T., Michon, H., & Eplov, L. F. (2021). A Systematic Review of Individual Placement and Support, Employment, and Personal and Clinical Recovery. Psychiatric Services (Washington, D.C.), 72(9), 1040–1047. doi.org/10.1176/appi.ps.202000070

Wilczynski, N. L., McKibbon, K. A., Walter, S. D., Garg, A. X., Haynes, R. B., Lal, S., & Adair, C. E. (2013). MEDLINE clinical queries are robust when searching in recent publishing years. Journal of the American Medical Informatics Association : JAMIA, 20(2), 363–368. /doi.org/10.1136/amiajnl-2012-001075

Winstanley, E. L., Mahoney, J. J. 3rd, Castillo, F., & Comer, S. D. (2021). Neurocognitive impairments and brain abnormalities resulting from opioid-related overdoses: A systematic review. Drug and Alcohol Dependence, 226, 108838. doi.org/10.1016/j.drugalcdep.2021.108838

Zahari, Z., Lee, C. S., Ibrahim, M. A., Musa, N., Mohd Yasin, M. A., Lee, Y. Y., Tan, S. C., Mohamad, N., & Ismail, R. (2016). Comparison of Pain Tolerance between Opioid Dependent Patients on Methadone Maintenance Therapy (MMT) and Opioid Naive Individuals. Journal of Pharmacy & Pharmaceutical Sciences : A Publication of the Canadian Society for Pharmaceutical Sciences, Societe Canadienne Des Sciences Pharmaceutiques, 19(1), 127–136. doi.org/10.18433/J3NS49

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