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EVIDENCE BRIEF

Understanding Factors Associated with Fatal and Non-Fatal Drug Overdoses

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Key Messages

- Rates of both fatal and non-fatal overdoses have increased dramatically across Ontario.
- Individual risk factors for experiencing fatal and non-fatal overdoses include socio-demographics (e.g., age, gender, and race), medical history (e.g., medication-assisted treatment, and mental and physical health conditions), healthcare and service utilization (e.g., physician, hospital, and harm reduction site visits), and substance-use patterns (e.g., poly-substance use, co-prescription, dosage).
- Structural risk factors for experiencing fatal and non-fatal overdoses include income, employment, and housing insecurity, experiences of poverty, and experiences of racism.
- Protective factors against experiencing fatal and non-fatal overdoses include access to school-based education programs (among youth), not being diagnosed with a substance use disorder, access to harm reduction, not being diagnosed with mental illness (e.g. depression, anxiety), opioid agonist treatment, medication assisted treatment, and higher levels of educational attainment (among adults).

Issue and Research Question

Prescribed or non-prescription opioids can result in non-fatal or fatal overdose (also referred to as opioid poisoning or toxicity), particularly when unregulated opioids vary unpredictably and raise the risk of overdose and death.[1] Other drug exposures along with opioids can be dangerous, whether they are combined intentionally or are unknown to the user.[1]

The COVID-19 pandemic contributed to the severity of the national public health overdose crisis, impacting people who use drugs, their families, and communities.[2,3] Over 40,000 opioid toxicity deaths have occurred across Canada since 2016, with a 91% increase in apparent opioid toxicity deaths in the first two years of the pandemic (April 2020 – September 2023, 15,134 deaths),[4] compared to the two years prior (April 2018 – March 2020, 7,906 deaths).[2] The escalation of the opioid crisis since the pandemic may be due to factors such as an increasingly toxic drug supply, increased isolation, stress and anxiety, and changes in the availability or accessibility of services for people who use drugs.[3]

Existing conceptual frameworks (e.g., Bay Area Regional Health Inequities framework) demonstrate a range of factors which constitute as 'risk' both on individual and broader societal levels. There is currently no consistent national standard for reporting individual-level risks for opioid overdose deaths,

making it difficult to characterize and address these factors. Adopting uniform standards would improve the range of the data used by those who develop public health responses to opioid-related deaths.[5]

This evidence brief synthesized literature on risk and protective factors that are associated with fatal and non-fatal drug toxicity. The scope expanded beyond an individual-level approach by drawing on a socio-ecological framework to map out multi-level risk and protective factors and their connection with substance use-related overdoses. This framework encompasses individual, relationship, organizational, community, policy, and societal levels of influence. Moving beyond individual level factors to a more multi-dimensional lens aligns with a broad public health approach and can shed light on the multi-layer complexity of the drug toxicity crisis. This synthesis extends its review beyond the coroner's data (e.g., age, sex) and explores additional data sources and fields within Canadian contexts.

In addition to expanding the scope of analysis, this Evidence Brief suggests implications for policy and practice. By considering a broader range of factors and outcomes, the Evidence Brief aims to re-iterate the multi-faceted reality of the drug toxicity crisis and highlight the numerous intersecting factors that need to be considered to mitigate substance-use related harms. This synthesis can consequently be part of efforts to improve reporting and engage in public health action.

The objectives of the Evidence Brief are to:

- Synthesize published literature examining the association between risk and protective factors, and drug-related overdoses (fatal and non-fatal)
- Categorize and characterize these factors by the levels at which they exist (e.g. levels outlined), and their definitions and data sources
- Describe these factors among sub-groups, based on the population studied (e.g., people recently incarcerated), and outcomes included (e.g., fatal and non-fatal drug-related overdose)

Methods

Public Health Ontario (PHO) Library Services conducted a published literature search on September 27, 2022 of peer-review and grey literature from inception to date of search (i.e., Ovid MEDLINE, Embase, PsycINFO, and CINAHL) for English-language articles. The original search focused on fatal outcomes of drug-related overdoses. The original 2022 searches were then updated on February 13th, 2024 to include both fatal and non-fatal outcomes of drug-related overdoses, using the same peer-review and grey literature sources. Grey literature searches were conducted in 5 search engines and using 8 search strings identified by Public Health Ontario Library Services and results for each search strategy were screened to a maximum of 100 results (e.g. first 10 pages of results in Google with results sorted by relevance, for each search string) by one reviewer. Searches were not limited by study design or outcomes.

Results were screened at title and abstract level against relevance criteria by two reviewers (417 papers reviewed by one and 1121 reviewed by another). All potentially relevant papers were retrieved and screened against the same criteria by the same reviewer (MP) in full document form. Screening at the full document level was validated by a team member (KW) and the lead author (PL) and any questions reconciled for a final decision. For inclusion, papers needed to focus on people who use drugs (occasional or regular use), must have included outcomes at the individual, relationship (interpersonal), community, and or society level, and must have evaluated fatal or non-fatal overdoses in OECD

countries. Papers excluded were from developing countries; focused solely on treatment or management for people who use drugs, economic evaluations, genetics, and biochemistry; and those without any factors related to death from drug toxicity. Case reports, editorials, letters, news, commentaries, and congress reports were also excluded. Given that this was an updated literature review, all papers published before 2022 focused on fatal-overdose outcomes were excluded.

Data were extracted by a single reviewer (MP) and validated by a team member (KW) and the content lead (PL). Extracted data included bibliographic citation, dates of the literature search, number of papers included in the review, country in which review conducted, sample description (age range, inclusion/exclusion, number randomized, exposure(s)/risk factor(s) reported, outcomes, results, risk factors, protective factors, and contextual factors. Presented risk factors were characterized across categories of individual, relationship, community, and societal level risk factors. When available, information was gathered on the data sources used in the included studies.

Main Findings

A total of 10 articles were included in this review: four systematic reviews,[6-9]and six meta-analyses,[10-1415] Most studies took place in North America, with others from Europe, Australia, Asia, the Western Pacific Region, and African regions. Exposure factors discussed in these articles included substance use practices (i.e., injection), poly-substance use, medical conditions, opioid-use, crystal methamphetamine use, heroin injection, benzodiazepine use, social cultural determinants of health (e.g., housing insecurity).

Several risk factors identified in the literature were classified into categories: individual level (e.g., socio-demographics), relationship level (e.g., interactions), community level (e.g., healthcare and service utilization and accessibility), and society level (e.g., racial segregation). Data sources incorporated across the articles included retrospective cohort studies, observational studies, coroners reports, past reviews of the literature, and chart reviews. Protective factors against fatal and non-fatal overdoses were minimally discussed.

Fatal Overdose Events

INDIVIDUAL LEVEL RISK FACTORS

Diverse risk factors were reported based on individuals' sex and age. A systematic review documented an increased risk of females experiencing a fatal drug overdose.[7] Increased risk of experiencing a fatal overdose was also reported among individuals aged between 25 and 64.[7] People who use drugs less than 30 years of age had a higher odds [OR = 1.61, 95%CI = 1.42-1.84, p=0.01] of fatal drug overdose in the past 12 months compared to those over 30 years of age.[26] Another systematic review and meta-analysis found that among people who use prescribed opioids, opioid agonist therapy or unregulated opioids, older adults (30 years of age or older) had a higher crude mortality rate (CMR) from opioid poisoning [pooled CMR Ratio = 2.84, 95%CI = 2.50-3.23] than younger adults (younger than 30 years).[23] Race, mental health status, and substance use disorders were also reported to be associated with risk of fatal overdose. Racialized populations are also more highly represented in low-income opioid overdose fatality rates than non-racialized populations.[19] Comparatively, a systematic review highlighted increased risk of drug-related overdose fatalities among white populations.[7] Drug overdose death was associated with diagnoses of substance use disorders such as: polysubstance disorders [OR = 3.56, 95%CI = 2.36-5.38],[26] cocaine disorders [OR = 1.9, 95%CI = 1.13-3.8],[26] psychostimulant disorders [OR =

2.71, 95%CI = 2.01-3.65],[26] benzodiazepines disorder [OR = 2.74, 95%CI = 1.67-4.5],[26,27] heroin dependence [OR = 1 .68, 95%CI = 1.36-2.07],[26] alcohol use disorders [OR = 1.92, 95%CI = 1.02-3.63)].[26]

COMMUNITY LEVEL RISK FACTORS

Cano et al. 2023 indicated that high opioid prescription rate increases risk of experiencing a fatal drug overdose. Fatal drug overdoses were also associated with opioid related emergency department visit rates, receiving naloxone through emergency medical services, and high percentages of Medicare claims for benzodiazepines.[7] Higher dosages of prescription opioids (e.g., between 20 and <50MME/d and 50 to <100 MME/d) were associated with an increased risk of opioid overdose death compared with the lowest-risk group category (typically 1 to <20MME/d).[16,18,22] Further, among adults prescribed opioids for chronic non-cancer pain, those with recent opioid prescriptions versus no recent prescription had a higher risk of fatal opioid overdose [adjusted HR = 8.4, 95%CI = 2.5-28.0].[22] In addition, there was an established association between having 3 or more opioid prescribers OR 4.68, 95% CI 3.57-6.12], 4 or more dispensing pharmacies [OR 4.92, 95% CI 4.35-5.57], and prescription of fentanyl [OR 2.8, 95% CI 2.3-3.41] and experiencing a fatal opioid overdose.[14]

SOCIETAL LEVEL RISK FACTORS

Being unhoused was associated with opioid overdose death [OR = 2.84, 95%CI = 2.1-3.84] and unmarried was associated with fatal drug overdose [OR 3.34, 95%CI = 2.82-3.97] among people who use drugs.[26] Further risk factors for fatal drug overdoses associated with housing status include high eviction rate, increase percentage of vacant housing units, rental stress, residential segregation, and geographic elevation.[7] A review specific to socioeconomic marginalization found that most literature on employment status and housing did not find a significant association with fatal opioid overdose.[19] In comparison, a systematic review which focused on data from the United States highlighted how high unemployment and poverty rates in addition to economic distress represent risk factors for fatal drug overdoses.[7] Furthermore, an increased risk of fatal drug overdose was associated with delayed use of visiting physicians due to cost.[7] Occupation groups with higher injury/illness, higher job insecurity, and less paid sick leave were also associated with opioid-related overdose deaths.[29]

Non-Fatal Overdose Events

INDIVIDUAL LEVEL RISK FACTORS

A meta-analysis reported that there was a higher risk of a non-fatal drug overdose among males [OR = 1.92, 95% CI = 1.80–2.05].[15] In contrast, a systematic review and meta-analysis highlighted that females who used illicit opioids had a 1.66 times increased likelihood to report experiencing a non-fatal opioid overdose when compared to males [OR=1.66, 95%CI=1.01-2.73].[10] This same systematic review and meta-analysis also documented a significant association among those aged less than 30 who used illicit opioids and experienced a non-fatal opioid overdose compared to those aged greater than 30 who used illicit opioids [OR OR=1.31, 95%CI=1.16-1.48].[10] Risk factors were also identified for individuals' mental health status and experiences of substance use patterns. A systematic review highlighted how specific mental health illnesses such as depression [OR = 1.78, 95% CI = 1.39–2.28], anxiety [OR = 1.45, 95% CI = 1.25–1.68], or suicidal ideation or attempt [OR = 2.80, 95% CI = 1.94–4.03] increased risk of experiencing a non-fatal drug overdose.[15] Similar outcomes were reported by Wang et al. who identified an association between depression (OR 2.22 95% CI 1.57-3.14), bi-polar disorder (OR 2.07, 95% CI 1.77-2.41) and experiences of non-fatal opioid overdose.[14] For substance-use patterns, there was a highlighted increased risk of non-fatal drug overdoses among those who need help injecting [OR = 1.54, 95% CI = 1.40–1.71] or share needles during injection [OR = 2.13, 95% CI = 1.54–2.95].[15] Armoon and colleagues also reported that people who use illicit opioids who have a high injecting frequency (more

than two times daily) had a 2.66 times likelihood of experiencing a non-fatal opioid overdose in the last year when compared to those who did not inject as frequently [OR=2.66, 95%CI=1.80-3.92].[10] Findings also suggested that high prevalence of non-fatal drug overdose was associated with increased and frequent injection over an individual's life course [β = 0.19, 95%CI: 0.05–0.33 p = 0.010].[13]

RELATIONSHIP LEVEL RISK FACTORS

Non-fatal opioid overdoses were associated with witnessing an overdose (2.22 times more likely to experience a non-fatal opioid overdose) [OR=2.22, 95%CI=1.61-3.08].[10] People who use illicit opioids who inject in public spaces were 1.61 times more likely to experience a non-fatal opioid overdose [OR=1.61, %CI=1.37-1.89].[10] A literature review reported that having a larger social network of individuals who use drugs increased the risk of non-fatal opioid overdoses.[6]

COMMUNITY LEVEL RISK FACTORS

There was a documented increased risk for non-fatal drug overdose in relation to experiences of inpatient detoxification [OR = 2.56, 95% CI = 1.39–4.72], emergency department visits or hospitalization [OR = 1.63, 95% CI = 1.32–2.02].[15] There was an association between increasing prescription opioid dose and risk of experiencing a non-fatal opioid overdose.[8] Wang and colleagues documented an absolute risk of 5.1 per 1000 for experiencing a non-fatal opioid overdose while receiving 90-mg of morphine equivalent per day.[14] Kennedy et al assessed risk factors associated with using an established supervised consumption site and experiencing a non-fatal drug overdose.[9] They documented how engagement with a supervised consumption site frequently does not increase risk of experiencing a non-fatal drug overdose within the site.[9]

SOCIETAL LEVEL RISK FACTORS

Experiences of incarceration were deemed to be risk factors for non-fatal drug overdoses [OR = 1.79, 95%CI = 1.43–2.23].[11] Similarly, experiencing homelessness increased risk of experiencing a non-fatal opioid overdose [OR = 1.64, 95%CI = 1.45- 1.84].[10] Colledge and colleagues also documented an association between experiences of homelessness and risk of experiencing a non-fatal drug overdose [β = 0.30, 95%CI: 0.14–0.46, p = 0.001].[13] Increased risk of experiencing a non-fatal opioid overdose was also associated with receiving money, goods or drugs in exchange for sex [OR=1.77, 95%CI1.46-2.15].[10]

Protective Factors

There were some protective factors identified in the reviews that focused on receiving treatment for opioid use disorder. In this section, we use the terms used in the studies cited, such as opioid agonist treatment (OAT) and medication-assisted treatment (MAT), which often refer to first-line treatments such as methadone and buprenorphine/naloxone, and may include other pharmacotherapy.

From a systematic review on treatment among people in correctional facilities, participants who received methadone maintenance treatment (MMT) or buprenorphine (BPN)/naloxone (NLX) while incarcerated had fewer non-fatal overdoses and lower all-cause mortality (in prison and post-release) and drug related death (after release).[17] The best results were seen for opioid related treatment during a continuum of treatment that was administered prior to, during, and after incarceration. Another systematic review and meta-analysis found opioid agonist treatment (OAT) lowered the risk of opioid poisoning mortality [pooled RR = 0.34, 95%CI = 0.27-0.42], with the strongest association seen for unintentional drug related death [pooled RR = 0.41, 95%CI = 0.33-0.52].[25] Similarly, medication-assisted treatment (MAT) had the lowest pooled overdose crude mortality rate (CMR) of 0.24 (95%CI = 0.20–0.28) during in-treatment period, where CMR increased to 0.68 (95%CI = 0.55–0.80) after treatment

discharge, and there was an even higher CMR of 2.43 (95%CI = 1.72–3.15) for those who had not received treatment.[24]

Among adults who use opioids, higher levels of educational attainment were associated with lower rates of opioid-related fatal overdose.[19]

Discussion

At a time when rates of both fatal and non-fatal overdoses are increasing across Ontario, a range of individual and structural risk factors, as well as protective factors can be considered in addressing the drug toxicity crisis. This evidence brief used a socio-ecological framework and drew from review-level literature. Risk and protective factors associated with fatal and non-fatal outcomes were categorized at each level.

Individual-level risks included mental health and substance use disorder. Various structural level risk factors were also associated with experiences of fatal and non-fatal overdoses (e.g., unhoused, unemployment). Established protective factors against fatal and non-fatal overdoses included opioid agonist treatment.

These results point to opportunities for informing public health actions including: the tailoring of interventions (e.g., age, gender); interventions and their continuity (e.g., OAT, OAT/incarceration); comprehensive care (e.g., mental health, poly-substance use); harm reduction services (e.g., needle distribution); social care (e.g., housing); and equity/ intersectionality (e.g., race and income); as well as social networks (e.g., engaging people who use drugs).

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