Overdose deaths and HIV infections among people who use drugs: shared determinants and integrated responses

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1. Introduction

The ongoing North American overdose (drug poisoning) crisis has been associated with an increase in the incidence of new HIV infections among people who inject drugs [1,2]. Risk for overdose deaths and HIV infections are not evenly distributed among people who use drugs. Both outcomes are concentrated among people who use drugs who are most intensely exposed to discrimination, criminalization, poverty, and housinglessness, and who have least access to harm reduction and treatment services when required [3,4]. Interventions that effectively reduce risks for overdose death and HIV infection take an equity-oriented approach, empower people who use drugs, and create safe(r) environments for drug use [3,5]. Here, we describe how social and structural factors concentrate risk for overdose death and HIV infection among people who inject drugs. We then review integrated social and clinical responses aiming to reduce risks of both outcomes.

2. Rising tides of overdose deaths and HIV infections among people who rely on the unregulated drug supply

People who use drugs in North America are facing a complex and devastating crisis of overdose deaths. This has been described as a ‘triple wave’ crisis, as rates of overdose deaths increased in stages reflecting transitions in the toxicity of the drug supply from pharmaceutical opioids, to heroin, and then unregulated (nonpharmaceutical) fentanyl and fentanyl analogues [6,7]. As overdose deaths rates rise even higher during the COVID-19 pandemic, this ‘fourth wave’ of deaths has been attributed to pandemic-associated social disruptions [7], to increasing use of unregulated stimulants and polysubstance use [6], and to the flooding of unregulated, nonpharmaceutical sedatives (e.g. benzodiazepines, xylazine) into the fentanyl supply [8]. More than 100,000 people are estimated to have died from drug overdose in the U.S. in 2021 [9]. The vast majority of overdose deaths in North America are now caused by drugs supplied from unregulated sources, which have become increasingly unpredictable [6,7].

Trends in new HIV diagnoses among people who inject drugs have changed in similar waves, as the previously-decreasing incidence of new HIV infections attributed to injection drug use began to level off, and since 2013 has begun to rise again [1]. The HIV epidemic had previously stabilized in areas where people who use drugs could effectively access evidence-based prevention services, including needle and syringe distribution programs, oral opioid agonist treatments (OAT; e.g. methadone, buprenorphine, or slow-release oral morphine), injectable OAT (e.g. diacetylmorphine, hydromorphone, or pharmaceutical fentanyl), HIV pre-exposure prophylaxis (PrEP), and supervised consumption sites (SCS). However, these have not been universally available, and people who use drugs in vulnerable regions have experienced new HIV outbreaks [2,10]. There were 2,465 new HIV infections attributed to injection drug use in the U.S. in 2018 (excluding men who have sex with men who also inject drugs) [1].

3. Discrimination concentrates risks and harms

Risks for overdose deaths and HIV infection follow a social gradient, and they are most concentrated among people who use drugs who face multiple forms of discrimination and social exclusion [3,11]. While there are different immediate (proximate) risk factors for overdose deaths (i.e. use of a toxic, unregulated drug supply) and HIV infection (i.e. receptive sharing of injecting equipment), both of these health harms are associated with poverty and with being unhoused or precariously housed [4,12], with criminalization (of drug possession/use and of HIV) [2,13], and with settler-colonialism and structural racism [3–5]. See Figure 1 for schematic with selected examples.

These social and structural factors shape risks for biological outcomes through multiple causal pathways, which are explored in theoretical and conceptual models such as ‘structural violence,’ Rhodes’ ‘risk environment’ framework, Krieger’s ‘ecosocial model of disease distribution,’ and Bronfenbrenner’s
Figure 1. Illustrative schematic of shared environmental determinants of overdose deaths and HIV infection among people who use drugs. Macroevironmental factors operate at the level of societies, while microenvironmental factors operate at the level of communities. Shared macro- and microenvironmental factors influence risk for overdose deaths and HIV infection by facilitating and constraining the options and choices available to people who use drugs. In this way, they act as determinants of the likelihood of individual behaviors and proximate risk factors. Harm reduction programs like needle and syringe distribution programs, supervised consumption sites, and drug user organizations can counteract environmental exposures by creating supportive relationships and spaces to improve access to other interventions (e.g. health care, HIV testing and pre-exposure prophylaxis [PrEP], income support, take-home naloxone, drug testing [e.g. fentanyl test strips], and mental health and addiction treatment when required. Most people who use drugs do not experience health harms associated with their use, but people who are exposed to multiple social and structural determinants are more likely to experience harms.

‘ecological systems theory’ [3,5,10]. For example, people experiencing poverty and houselessness often need to sell ‘washes’ (leftover drug residue on cookers and filters after preparing and injecting drugs) for income generation to meet basic material needs, and other people with low incomes are most likely to buy them. If the person selling the wash develops HIV, and discrimination makes them afraid to disclose their HIV-positive status, this can increase risks of HIV transmission through their network among people who rely on their washes. If people who use drugs in these networks had more income or had regular access to their own supply of drugs, this might reduce or interrupt transmission.

Social and structural factors can also interact with each other [3]. For example, structural racism leads to disproportionate enforcement of drug criminalization and also lower access to evidence-based addiction treatment among racialized people who use drugs, compared to white people who use drugs [5]. There have been dramatic rises in overdose among minoritized and racialized groups in the United States and Canada [3,5,15]. A report by the First Nations Health Authority in British Columbia (BC), Canada, found that First Nations people were more than five times more likely to die of an overdose than non-First Nations people and explored causal pathways for this inequity [15]. The report highlighted Indigenous strengths in the face of experiences of racism and inter-generational trauma that contributed both to riskier substance use and acted as barriers to health care access. Criminalization may have particularly harmful effects on women who use drugs, who are more likely to be the primary caregiver for children; they may stay away from health-care services (and even harm reduction services) for fear of losing child custody [3]. Discrimination against lesbian, gay, bisexual, transgender, queer, two-spirit, and intersex (LGBTQ2SI+) -identified people contributes to higher rates of substance use disorders than non-LGBTQ2SI+-identified people, and also to barriers to accessing harm reduction and treatment.
support that are not often designed for LGBTQSI+ identified people [3,16].

4. Enabling equitable responses

Effective responses create equitable, just, and safe(r) environments for people who use drugs, promote autonomy, build capacity, and enable options that promote health (and reduce risk) for the drug-using community. For example, increasing coverage and availability of needle and syringe distribution programs enables people to avoid receptive sharing of drug use equipment. Establishing supervised consumption sites provides an environment free from policing enforcement where people who use drugs can take their time, test the substance they intend to consume, connect with community, and have someone respond with oxygen and/or naloxone in the event of an overdose. Oral OAT and injectable OAT (while also forms of addiction treatment) reduce reliance on the unregulated drug supply and enable people with more options about when and how to use drugs, once they are less worried about withdrawal. This is also true for the emerging practice of prescribing ‘safe supply’ medications as pharmaceutical alternatives to the unregulated drug supply [7]. Needle and syringe distribution programs and safe consumption sites can also integrate other services, including HIV screening, take-home naloxone kit distribution, primary care with PrEP and/or medications to address opioid use disorder (oral or injectable OAT), safe supply, and drug testing services [2,17].

For health professionals, several specific clinical practices can help reduce risks of HIV infection and drug poisoning deaths among people who inject drugs. See Table 1 for a list of education resources for health providers. This includes offering PrEP, oral or injectable OAT, and a safe supply of medications while integrating other harm reduction practices like needle and syringe distribution programs and safe consumption sites into every health-care setting. These services should be available wherever people who use drugs are, whether that be primary care; mobile outreach programs to homes, shelters, and encampment sites; in hospitals or emergency departments; and while people are incarcerated [11]. This requires flexibility in service delivery in terms of location and timing, and it may require policy and payment model changes to incorporate innovations like telehealth, low-threshold access to medications on demand, and office-based methadone prescribing with pharmacy dispensing. Long-acting injectable medications for opioid use disorder (e.g. buprenorphine, or injectable naltrexone [an opioid antagonist]) and for PrEP (i.e. cabotegravir) may also be of great benefit and convenience to some people who use drugs but may not be appropriate for or desired by everyone.

In the face of oppressive social conditions that increase risks for overdose deaths and HIV infection and that also hinder prevention efforts, clinical and health system responses should take an equity-oriented approach [11]. People with lived (past) or living (present) experience with drug use should be involved in leading the planning and delivery of services to make them more accessible and effective. Indeed, organizations of people who use drugs have been leading overdose and HIV prevention efforts for many years, even while facing criminalization [18]. Health services should apply harm reduction principles including offering trauma-informed and culturally safe care for people who use drugs [11]. Patients, clients, and/or program participants who use drugs should have access to spaces that are equitable, just, and inclusive to access supports and help navigating health systems. Recognizing the specific harms of criminalization on health outcomes, health professionals have a role to play in advocating for drug policy reform including decriminalization and regulation.

While all health-care providers and health systems can take on these challenges and create safer environments for people who use drugs, further research is needed to understand the best care delivery models and to increase uptake. This includes outstanding questions like how to improve access and effectiveness of SCS (e.g. the effects of changes in SCS policies to become more inclusive and support assisted injecting or splitting/sharing of drugs [18]); how SCS can be best integrated with other HIV prevention services (e.g. strategies to incorporate oral or injectable PrEP into SCS settings); or how to improve access to emerging practices like prescribing a ‘safe supply’ of pharmaceutical alternatives to unregulated drugs [7]. Multiple factors (including discrimination, misunderstanding and lack of education, and prohibitionist laws and regulations) limit the uptake of some harm reduction approaches in health-care settings, and implementation research could focus on how to change these. People who use drugs should be supported to prioritize research questions and to lead research projects to make them most relevant and impactful.

Table 1. Recommended resources for health professionals to learn more about incorporating harm reduction principles and practices into health-care settings.

- Canadian Association of People who Use Drugs (CAPUD), ‘Hear Us, See Us, Respect Us: Respecting the Expertise of People who Use Drugs’ (Canada): https://doi.org/10.5281/zenodo.5514066
- Providers Clinical Support System (PCSS) education and training resources, including Substance Use Disorders 101 Core Curriculum (USA): https://pcssnow.org/education-training/sud-core-curriculum/
- Mentoring, Education, and clinical tools for Addiction: Partners in Health Integration (META.PHI) provider resources (Canada): http://www.metaphi.ca/provider-resources/
- California Bridge program (CA Bridge) resources (USA): https://cabridge.org/tools/resources/
- US Public Health Service, ‘Preexposure prophylaxis for the prevention of HIV infection in the United States – 2021 Update: A clinical practice guide’ (USA): https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf
- National Institute on Drug Abuse (NIDA), Resources for Your Professional Discipline and Specialty (USA): https://nida.nih.gov/nidamed-medical-health-professionals/resources-for-your-professional-discipline-specialty
- Centers for Disease Control and Prevention, ‘Syringe Services Programs (SSPs)’ (USA): https://www.cdc.gov/ssp/index.html
- Substance Abuse and Mental Health Services Administration (SAMHSA), ‘Medications for Opioid Use Disorder’ (USA): https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Full-Document/PEP21-02-01-002
5. Conclusions
People who use drugs in North America are facing concurrent crises of overdose (drug poisoning) deaths and HIV infections, which are shaped by social (e.g. racism, settler-colonialism, sexism, cis-heteronormativity) and structural (e.g. poverty, criminalization) factors that both increase risk and limit access to effective responses. Prevention efforts for overdose deaths and for HIV infections should create safe(r) environments for people who use drugs free from discrimination. Health professionals may need to think ‘outside the box’ and apply harm reduction and equity-oriented principles to better serve this community.

Notes on contributors
All authors substantially contributed to the conception and design of the commentary and interpreting the relevant literature, were involved in writing the review article, revised it for intellectual content, and approved the final version for submission. TD Brothers wrote the first full draft with critical conceptual input from N Touesnard.

Declaration of interests
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References
Papers of special note have been highlighted as either of interest (+) or of considerable interest (+-) to readers.
1. Lyss SB, Zhang T, Oster AM. Brief report: HIV diagnoses among persons who inject drugs by the urban-rural classification—United States, 2010–2018. JAIDS J Acquir Immune Defic Syndr. 2021 Nov;188(3):238–242. doi:10.1097/QAI.0000000000002769.
2. Hoder SL, Feinberg J, Strathdee SA, et al. The opioid crisis and HIV in the USA: deadly synergies. Lancet. 2021 Mar 20;397(10279):1139–1150. doi:10.1016/S0140-6736(21)00391-3.
3. Collins AB, Boyd J, Cooper HLF, et al. The intersectional risk environ- ment of people who use drugs. Soc Sci Med. 2019 Aug 1;234:112384. doi:10.1016/j.socscimed.2019.112384.
4. Des Jarlais DC, Sypsa V, Feleemyer J, et al. HIV outbreaks among people who inject drugs in Europe, North America, and Israel. Lancet HIV. 2020 Jun;7(6):e434–42. doi:10.1016/s2352-3018(20)30082-5.
5. Bluthenthal RN. Structural racism and violence as social determinants of health: Conceptual, methodological and intervention challenges. Drug Alcohol Depend. 2021 May;222:108681.
6. Ciccarone D. The rise of illicit fentanyl, stimulants and the fourth wave of the opioid overdose crisis. Curr Opin Psychiatry. 2021 Jul;34(4):344–350. doi:10.1097/yco.0000000000001717.
7. Bonn M, Palayew A, Bartlett S, et al. Addressing the syndemic of HIV, hepatitis C, overdose, and COVID-19 among people who use drugs: the potential roles for decriminalization and safe supply. J Stud Alcohol Drugs. 2020 Sep 1;81(5):556–560. doi:10.15288/jsad.2020.81.556.
8. Friedman J, Castillo FM, Bourgois P, et al. Xylazine spreads across the us: a growing component of the increasingly synthetic and polysubstance overdose crisis. Drug Alcohol Depend. 2022 Feb 26;109380. 10.1016/j.drugalcdep.2022.109380.
9. Ahmad FB, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2021. Available from https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm. cited 2022 May 4.
10. Beletsky L, Thumath M, Haley DF, et al. HIV’s trajectory: biomedical triumph, structural failure. Am J Public Health. 2021 Jul;111 (7):1258–1260. doi:10.2105/ajph.2021.306354.
11. Wallace B, MacKinnon K, Strosher H, et al. Equity-oriented frame- works to inform responses to opioid overdoses: a scoping review. JBI Evid Synth. 2021 Aug;19(8):1760–1843. doi:10.11124/jbies-20-00304.
12. Stone J, Artenie A, Hickman M, et al. The contribution of unstable housing to HIV and hepatitis C virus transmission among people who inject drugs globally, regionally, and at country level: a modelling study. Lancet Public Health. 2022 Feb;7(2):e136–e145. doi:10.1016/s2468-2667(21)00258-9.
13. Baker P, Beletsky L, Avalos L, et al. Policing practices and risk of HIV infection among people who inject drugs. Epidemiol Rev. 2020 Jan 31;42(1):27–40. doi:10.1093/epirev/mxa010.
14. Brothers TD, Leger M, Bonn M, et al. Social and structural determinants of injecting-related bacterial and fungal infections among people who inject drugs: protocol for a mixed studies systematic review. BMJ Open. 2021 Aug 9;11(8):e049924. doi:10.1136/bmjopen-2021-049924.
15. First Nations Health Authority. First nations in BC and the toxic drug crisis: January – December 2020. 2021 May. Available from. cited 2022 May 4. https://www.fnha.ca/about/news-and-events/news/first-nations-toxic-drug-deaths-doubled-during-the-pandemic-in-2020
• Report from First Nations Health Authority (FNHA) in British Columbia, Canada, identifying that First Nations people died of toxic drug deaths at 5.3 times the rate of other BC residents in 2020. This report and an earlier FNHA report (available at
describe causal pathways for higher risks of overdose deaths among First Nations people compared to non-Indigenous people.

16. Girouard MP, Goldhammer H, Keuroghlian AS. Understanding and treating opioid use disorders in lesbian, gay, bisexual, transgender, and queer populations. Subst Abuse. 2019 Jul 3;40(3):335–339. doi:10.1080/08897077.2018.1544963.

17. Broz D, Carnes N, Chapin-Bardales J, et al. Syringe services programs’ role in ending the HIV epidemic in the U.S.: Why we cannot do it without them. Am J Prev Med. 2021 Nov;61(5):S118–29. doi:10.1016/j.amepre.2021.05.044.

18. McNeil R, Small W, Lampkin H, et al. "People knew they could come here to get help": an ethnographic study of assisted injection practices at a peer-run ‘unsanctioned’ supervised drug consumption room in a Canadian setting. AIDS Behav. 2014 Mar;18(3):473–485. doi:10.1007/s10461-013-0540-y.