

# North America's fentanyl death crisis: Selected lessons for Europe's future?

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For the past decade, North America ([NA]; i.e., Canada and the United States) has been experiencing an unprecedented public health crisis from drug-related toxicity deaths (DTDs) (Ciccarone, 2021; Fischer, 2023). After 2000, this crisis has claimed in excess of 1 million lives; this death toll is similar to that from the COVID-19 pandemic, but involves mostly younger ages, thus incurring a comparably higher burden of disease. In 2022, there were 109,680 (rate: 32.4/100,000) DTDs in the United States and 7525 (21.2/100,000) DTDs in Canada, representing the leading cause of death for many age groups (Ciccarone, 2021; Fischer, 2023). Importantly, the vast majority of recent DTDs in both countries have been caused by illicit, synthetic opioid (fentanyl/fentanyl-analogues [F/FA]) products. F/FA substances are highly potent and toxic, commonly mixed or contaminated with other drugs, resulting in extremely high risk for overdose fatalities (Cheema et al., 2020; Hayashi et al., 2021).

The European Union's (EU) recent DTD levels are substantially lower in magnitude (i.e., 6166 or 1.38/100,000 in 2021) compared with NA's exceptionally high DTD toll (EMCDDA, 2023). While there has been recurring speculation whether a similar F/FA-related crisis may unfold in the EU, there is conflicting evidence towards the possibility of such a scenario. On the one hand, recent epidemiological data show that approximately three-quarters (74%) of DTDs in Europe were opioid-related. Although a minority of EU countries report that most of these DTDs were heroin-related, these deaths feature increasing involvement of both (pharmaceutical and non-pharmaceutical) opioids, including a small (<3%) – but mostly prescription-related – proportion of fentanyl-related DTDs recorded mostly in Germany and Northern Europe (EMCDDA, 2023). On the other hand, Europe overall has not experienced the markedly oscillatory patterns in prescription opioid dispensing that occurred in and contributed to vast supply reductions for medical and non-medical opioid use in NA, and therefore presumably facilitated the onset

and rapid proliferation of F/FA availability (Fischer & Robinson, 2024; Manchikanti et al., 2022). At the same time, the availability of heroin in Europe depends on imports from volatile global, illicit drug markets – a source that may quickly change or dry up, and so lead to supply gaps that may facilitate the proliferation of widespread F/FA availability and use.

The arguably quintessential lesson from NA's persistent F/FA crisis is that, despite extensive expansions of standard and implementation of new intervention strategies, these efforts have overall not effectively succeeded in reducing the related DTD toll (BCCDC, 2024; Fischer, 2023; Irvine et al., 2019). For example, in the province of British Columbia (BC), Canada's epicenter of the DTD crisis, a widely diversified menu of opiate agonist treatment (OAT; e.g., including different medication and/or administration options) has been made available. While up to approximately 25% of the population at risk for overdose are estimated to be OAT-engaged, especially long-term retention is low and/or co-use of other (opioid and non-opioid, including F/FA) drugs is common (Krebs et al., 2021; Piske et al., 2020). For targeted prevention, approximately 50 government-sanctioned (and more unofficial) supervised consumption/overdose prevention service sites (SCS/OPS) have been established. While illicit substance use at these facilities is considered DTD-protective, the existing SCS/OPS contingent cover only a marginal proportion of overall drug consumption episodes on the population level; moreover, most SCS/OPS do not accommodate non-injection (e.g., inhalation) use, the most common mode of use implicated in recent DTDs, therefore further limiting utilisation and protective impacts (Panagiotoglou, 2022; Parent et al., 2021). Similarly, point-of-care and take-away versions of "drug checking" services (e.g., for F/FA content) are available; however, their utilisation is considered sporadic, and effects on risk behaviors unclear (Ti et al., 2020; Tilhou et al., 2023). Finally, naloxone (antidote-based overdose reversal) is widely disseminated and frequently applied; yet, its mode of action is only reactive to

overdose, and its applied efficacy is increasingly compromised by both common solitary/isolated drug consumption and increasing F/FA potency and/or contamination with other drugs (Fischer et al., 2024; Lei et al., 2022; Pergolizzi Jr et al., 2021).

In consequence, while each of the interventions described provides substantive elements of protection, this, on the overall population level, has been insufficient to curtail BC's excessive and persistent DTD toll. These adverse circumstances raise fundamentally important questions as to the appropriateness, but especially inherent limitations of the intervention strategies presently available and relied on for a DTD-related public health crisis (EMCDDA, 2023; Fischer, 2023; Irvine et al., 2019). These questions are hypothetically while equally pertinent for Europe, where a reasonably good availability and coverage of related interventions, in conjunction with elaborate 'early warning' systems exist; however, in case of an acute F/FA-related crisis as recently experienced in NA, these may prove to be similarly insufficient to effectively address and halt the to-be-expected DTD toll.

A recent Canada-based innovation to reduce F/FA-related DTDs have been "safer opioid supply" (SOS) programs where, to date, a small proportion of at-risk users are provided with pharmaceutical-grade opioids (e.g., morphine, hydromorphone, fentanyl) to reduce illicit/toxic F/FA exposure and related overdose (Fischer & Robinson, 2023; Ledlie et al., 2024). While the SOS concept is controversial and concerns exist regarding possible diversion, initial results have shown notable improvements for drug use, overdose risk and health outcomes among participants, and so warrant further evaluation and evidence-informed ramp-up.

In conclusion, the odds of a F/FA-driven DTD crisis in Europe similar to NA's are hard to gauge. If it unfolds, the armory of existing intervention strategies, based on experiences described, may be expected to be insufficient, underscoring the need for anticipatory strategic

preparedness and advanced intervention development and establishment.

## Data availability

All data in this manuscript are accessible in the public domain (e.g., in the form of journal articles, reports, websites).

## Declaration of conflicting interests

The authors declared the following potential conflict of interest with respect to the research, authorship, and/or publication of this article: Dr. Fischer and Dr. Jutras-Aswad have held research grants and contracts in the areas of substance use, health, policy from public funding and government organisations (i.e., public-only sources) in the last 5 years; Dr. Fischer was temporarily employed by Health Canada (2021–2022). Dr. Jutras-Aswad has received study materials from Cardiol Therapeutics and Exka for clinical trials. Dr. LeFoll has obtained research support (i.e., research funding/in-kind supports or expert consultancy) from Pfizer, Inc. (GRAND Awards & medications), Indivior (clinical trial funding & consultancy), Aurora Cannabis Enterprises Inc., Bioprojet Pharma, Brainsway (Transcranial magnetic stimulation [TMS] study), Canopy Growth Corporation (research grants), Alcohol Countermeasure Systems (ACS), Alkermes, Universal Ibogaine, and Shinogi. Mrs. Robinson has no competing interests.

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