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# The opioid crisis in North America: facts and future lessons for Europe

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**Abstract**

Over the past two decades, opioid-related hospitalizations and deaths in North America have reached the level of a public health emergency. Initially, the epidemic of opioid misuse was largely driven by pharmaceutical companies and initiated by their spread of misinformation, which led physicians to engage in overzealous prescribing behaviour. This was followed by significant harms as deaths related to overdoses on prescription and illicit opioids rose steadily throughout the 1990s and early 2000s. This review examines the historical context of the opioid crisis in the United States and Canada, the role of physicians, the contributions of the pharmaceutical industry and the evolution of the epidemic in response to the introduction of highly potent synthetic opioids now recognized as the main culprits in opioid overdose and death. This article further explores the evidence surrounding the effectiveness of various treatment strategies and harm-reduction interventions designed to curtail the morbidity and mortality associated with opioid use. Finally, the magnitude of the opioid epidemic in North America is compared to that in European countries. This paper describes the differences in North American and European experiences with opioid overdose and the evidence-based approaches that can be implemented to reduce the mortality and morbidity linked to opioids while simultaneously ensuring adequate pain control for patients.

**Key words:** overdose, harm reduction, oxycodone, opioid epidemic, opioid misuse, opioid agonist therapy.

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## THE OPIOID CRISIS IN THE UNITED STATES, CANADA, AND EUROPE

In 2018 alone, approximately 68,500 Americans lost their lives due to opioid overdoses involving prescription pain relievers, heroin and illicit synthetic opioids such as fentanyl [1]. With an estimated cost of over $150 billion USD in 2015, the misuse of, and addiction to opioids has become a national crisis affecting the public health and economic welfare of the United States [2]. This epidemic is widespread throughout North America including Canada, which is currently in the grip of a public health emergency. Second only to the United States in per-capita consumption of prescription opioids, the similar trend of increasing deaths involving opioid medications in Canada comes as no surprise. According to the Public Health Agency of Canada, 3,987 opioid-related deaths occurred in 2017 and an estimated 17 Canadians are hospitalized daily due to opioid poisoning or overdose [3]. More alarming is that 92% of these deaths were unintentional and, compared to 55% in 2016, 72% involved fentanyl or one of its highly potent synthetic derivatives [3]. To date, the opioid epidemic has primarily been a phenomenon of Western society, causing significant mortality and morbidity in the white middle-aged population [4]. Driven by a multitude of factors such as health-care commercialization, the culture surrounding pain management, and the influence from the pharmaceutical industry, the extent to which this crisis has affected North America remains unmatched by other regions across the globe.

Opioid misuse, however, has been recognized by the World Health Organization (WHO) as an international issue and like North America, Europe has seen an increase in the nonmedical use of prescription and illicit opioids over the past two decades [5]. In 2017, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) estimated that the European Union (EU) had about 1.3 million high-risk opioid users and that about 81% of fatal overdoses in the EU involved opioids [6]. Analysis of treatment facility data also reveals that opioid users constitute the largest group of entrants in specialized treat-

ment programmes and are the greatest consumers of available treatment resources, primarily Opioid Agonist Therapy (OAT) combined with psychosocial interventions [6]. In addition to prescription opioids such as morphine, codeine and oxycodone, treatment entrants have reported the misuse of heroin, tramadol, methadone and buprenorphine [6]. While the misuse of prescription and illicit opioids is common to both Europe and North America, the mortality and morbidity associated with opioid use in Europe does not come close to that of the United States and Canada. According to the 2019 European Drug Report, approximately 8,200 overdose deaths involving opioids occurred in Europe in 2017 – this was almost 10 times lower than overdose deaths in the United States [6].

This review aims to describe the alarming prevalence of opioid-related overdose deaths that continue to plague North America with the potential to spread to Europe. Based on an analysis of current interventions, we describe the issues surrounding one-sided solutions that focus exclusively on limiting opioid supply without addressing the needs of opioid-dependent patients. The recent spike in mortality involving illicit opioids is evidence that the constraints placed on legal opioid prescriptions has created a vacuum that is being filled by drug traffickers importing low-cost fentanyl and its potent derivatives [7]. Opioid-dependent patients have increasingly turned to illicit markets to treat symptoms of withdrawal and to satisfy intense cravings that are characteristic of opioid use disorder [7]. Currently, illicit opioids, primarily heroin and fentanyl in Europe and North America respectively, are the main culprits in opioid-related morbidity and mortality. This shift underscores the importance of implementing balanced policies and public health strategies that address the key drivers of opioid abuse and increase access to evidence-based therapies for individuals with existing opioid use disorders.

## TRENDS IN OPIOID USE AND OPIOID-RELATED MORBIDITY AND MORTALITY

Prior to the 1990s, the approach to pain management was largely conservative. Clinicians across North America were reluctant to use strong opioid medications due to risks of misuse and addiction. This changed following a push for more liberal use of opioids in patients with chronic non-cancer pain by prominent pain specialists who cited low incidence of addictive behaviour [8]. These claims were based on two publications: (i) a one-paragraph letter to the editor of the New England Journal of Medicine describing low addiction rates (0.03%) in acute pain patients receiving opioids, and (ii) a retrospective evaluation of 38 chronic pain patients in which only 2 patients developed substance abuse issues after receiving opioids [9, 10]. This effort to change the existing norms surrounding pain management was largely supported by opioid manufacturers, who embarked on a 20-year campaign to convince physicians that opioids could be prescribed more liberally and without worry of addiction [8]. Support for opioid use in pain management continued to grow amongst specialists and professional societies throughout the 1990s, causing many clinicians to be torn between improving their patients' quality of life and the fear that treatment would lead to a substance abuse disorder [8]. This movement, commonly dubbed the "war against pain", was endorsed by the Federation of State Medical Boards in their 1998 model guidelines, and the use of opioid medications in chronic non-cancer pain became the new standard of care [11]. An important milestone in the development of widespread opioid misuse was the introduction of oxycodone in a sustained-release opioid formulation capable of providing pain relief for 8-12 hours [12]. Its high affinity for the μ-opioid receptor made it a very effective pain reliever and a potent euphoric agent. The sustained release oxycodone, marketed as OxyContin, was particularly enticing because it only required one or two administrations daily, unlike other opioids at the time that needed to be taken every 2-4 hours for continued analgesia [12]. Reasoning that immediate reward is necessary to reinforce behaviour, the Food and Drug Administration (FDA) concluded that the slow-release formulation would dissuade abuse by imposing a delay on reinforcement [12]. Consequently, manufacturers gained permission to write claims on product labels that the abuse potential for OxyContin was low [12]. However, users quickly discovered that by crushing or dissolving the pills, large amounts of oxycodone could be administered immediately intranasally or through intravenous injection. The misbranding of OxyContin as an abuse-resistant drug later became the subject of a $300 million USD settlement with $34 million USD paid by the top 3 executives at Purdue, who also admitted to misleading patients and physicians with regards to the addictive profile of OxyContin [13].

In an era that recognized pain as a "fifth vital sign", physicians in the United States and Canada were encouraged to proactively identify and treat chronic pain [12]. This mandate to provide adequate pain control and the push from the pharmaceutical industry to use opioids created an ideal environment for overzealous opioid use in pain management. What followed at the turn of the millennium was an unprecedented increase in opioid prescriptions – over 400% from 1999 to 2010 [14]. OxyContin prescriptions in the United States in-

creased almost 10-fold from 670,000 to 6.2 million yearly prescriptions from 1997 to 2002 [15]. The International Narcotics Control Board (INCB) and the National Institute of Drug Abuse (NIDA) estimate that between 1995 and 2015, there was a three to 14-fold increase in prescription opioid use in the United States and Canada [16]. Corresponding with this increase in prescriptions was an increase in overdose deaths in individuals receiving opioid medications from healthcare professionals as well as those who obtained medications through diversion. From 1999 to 2015 the number of overdoses in the United States involving any opioid increased more than three-fold from 2.9 to 10.4 deaths per 100,000 persons [17]. Likewise, in Ontario, Canada's most populous province, opioid-related deaths increased nearly three-fold from 1.9 to 5.3 deaths per 100,000 persons in 2000 and 2015 respectively [18].

Compared to other Western countries, healthcare providers in North America have historically relied more heavily on treating pain and illnesses using pharmacotherapy. At a time when adequate pain control was given precedence above all else, and the demand for medical care greatly outweighed its supply, the use of pills, by physicians operating under a fee-for-service model, often became the most feasible and incentivized option and the solution expected by many patients as a form of satisfactory care [19]. This is in contrast to the European experience where direct-to-consumer advertising by pharmaceutical companies is not permitted and healthcare providers have been more judicious in providing patients with opioids – likely due to the presence of regulatory schemes designed to safeguard against inappropriate prescribing [19, 20]. In 2010, the per-capita consumption, in defined daily doses (DDD – average maintenance dose per day of a drug used for its main indication in adults), of prescription opioids in the US (47,809 DDD) and Canada (26,380 DDD) exceeded that of any other country, and was far above the EU average [19]. The large circulating quantities of prescription opioids correlate with both increased diversion and with increased opioid-related mortality and morbidity. In his description of a 'triple wave opioid epidemic', Ciccarone argues that the opioid epidemic in North America can be divided into three phases driven by, in order, prescription opioid pills, heroin, and non-methadone synthetic opioids [20, 21]. Compared to Europe, the greater prevalence of opioid-related harms in North America is likely the product of many different factors, some of which stem from the initial phase of problematic opioid use that was the result of easy access to, and encouraged prescription of, opioids in North American medical systems.

## SUPPLY-SIDE INTERVENTIONS ADDRESSING OPIOID OVER-PRESCRIPTION

Multiple avenues have been explored by North American governments and health officials to reduce opioid-related deaths. Given its complexity, arriving at an effective solution that addresses the underlying drivers of this public health crisis will require concerted efforts from legislators, health policymakers and healthcare providers. Recognizing the relationship between opioid dispensing and overdose harms, the implementation of upstream measures to reduce opioid prescriptions has been an area of focus throughout the past decade. In response to the increasing death tolls, government agencies and professional societies in Canada and the United States responded with changes in pain management guidelines encouraging healthcare providers to be more judicious when prescribing opioids. The Centers for Disease Control and Prevention (CDC) guidelines, published in April 2016, have recommended the use of non-pharmacologic and non-opioid pharmacologic therapies in chronic pain patients [22]. These guidelines also support prescription of the lowest effective dose to treat "pain severe enough to require opioids" as well as the use of immediate-release opioids in place of long-acting extended-release opioids [22]. In 2015, the American Medical Association (AMA) established an opioid task force to address legislation pertaining to effective prescription drug monitoring programmes, guidelines for treatment of opioid use disorder, continuing medical education, as well as naloxone access and Good Samaritan overdose protection [23].

In line with the goal of minimizing the incidence of opioid-related substance use disorders, the guidelines for opioid use in treating chronic non-cancer pain in Canada and the United States have been revised [22, 24]. These guidelines recommend that, in all cases of chronic non-cancer pain, before considering opioids, clinicians explore non-pharmacological therapies such as physical and exercise therapy for chronic low back pain and osteoarthritis of the knee and cognitive behaviour therapy for catastrophic thinking [25, 26]. This is in line with the current recognition that the use of opioids as a panacea for all types of pain is inappropriate as this practice fails to address the complex physiological and psychological aspects of chronic pain. This approach is further supported by studies demonstrating that multimodal and multidisciplinary therapies are more effective than single modalities in reducing pain and improving daily function [22]. These guidelines also suggest that a trial of non-opioid pharmacologic therapies is recommended prior to initiating opioid therapy. These

include acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) for musculoskeletal pain as well as anticonvulsants, tricyclic antidepressants, and serotonin-norepinephrine reuptake inhibitors (SNRIs) as first line treatments for neuropathic pain [25, 26]. The revised guidelines also take into consideration the interplay between psychiatric illness and opioid misuse. When treating individuals with an active psychiatric disorder, stabilization of the psychiatric disorder is recommended before opioids are prescribed [25, 26]. Throughout the course of treatment, the guidelines advocate for a patient-provider partnership where realistic treatment goals for pain and function are established and opioid therapy is continued only if there is meaningful improvement that outweighs risks to patient safety. In cases where patients continue to experience persistent problematic pain while non-opioid therapy is optimized, opioid treatment is indicated [25, 26]. Both CDC and Canadian guidelines support urine drug testing prior to initiation of therapy and encourage prescribers to review the patient's history of controlled substance use with prescription drug monitoring programmes to assess their risk of overdose [25, 26].

In both North American and European settings, the majority of prescription opioids that land in the hands of unprescribed users originate from legitimate sources. This can occur in cases where medications are overprescribed or when prescribed medications are not taken as indicated [27]. Prescription drug monitoring programmes (PDMPs) collect, review and analyse data on prescribed controlled substances from pharmacies, and report these data to prescribers. Studies assessing the effectiveness of these programmes have found that they reduce doctor shopping, inappropriate opioid prescriptions, opioid diversion and treatment facility admissions. A recent review of programmes across the United States further illustrated that the implementation of PDMPs was associated with a reduction in opioid-related overdose deaths and an increase in clinicians' ability to monitor treatment for opioid dependence [28].

These initiatives, designed to control opioid supply, have been quite effective, as evidenced by the 22% decrease in opioid prescriptions from 2013 to 2017 and a 9% decrease from 2016 to 2017 alone [23]. Recent data from the CDC show an annual 4.9% decrease in the number of opioid prescriptions in the United States between 2012 and 2016 [17]. Similarly, when comparing 2012 and 2016 data, the Canadian Institute of Health Information (CIHI) reported a 4.9% reduction in the total number of opioids dispensed despite a 6.8% increase in the total number of opioid prescriptions [29]. Despite these reductions in opioid prescriptions and dispensing, opioid-related fatalities continue to rise – highlighting that although supply-side interventions are necessary, a complementary approach targeting the demand-side of the equation is critical to understanding and addressing the reasons individuals continue to use opioids. While preventing the initiation of opioid use is the only safeguard that is 100% effective against addiction, millions of patients across North America remain addicted to opioids and will require holistic management that may involve the use of medication-assisted treatment (MAT) when necessary and ensures that patients are evaluated and treated for comorbid psychiatric illnesses [30].

## THE RISE OF FENTANYL AND THE SHIFT FROM PRESCRIPTION OPIOIDS TO ILLICIT SUBSTANCES

Despite a decline in the non-medical use of prescription opioids and lethal overdoses, the treatment demand for opioid use disorder continues to increase [15]. With reductions in the supply of legally prescribed opioids, consumers have turned to heroin, illicit fentanyl and fentanyl derivatives, which have become the primary drivers of opioid-related overdose deaths [15]. These illicit fentanyl products are primarily manufactured in China and Mexico and mixed with heroin before they are smuggled into the United States [7]. Similarly, according to the European drug monitoring agency, the majority of illicit fentanyl products available in Europe are sourced from companies based in China [6]. Fentanyl visually resembles white-powder heroin and thus users are typically unaware that their heroin is contaminated with fentanyl [7]. The variability in dosing and very high potency of illicit fentanyl make it particularly dangerous, with a greater risk for lethal overdose as it removes the user's ability to know the potency of the drug for appropriate dosing that is consistent with established tolerance levels. United States data from the CDC's "Morbidity and Mortality Weekly Report" highlight this alarming trend. While the number of fentanyl prescriptions continued to decrease from 2013 to 2016, the number of deaths involving synthetic opioids, excluding methadone, increased from 3,105 in 2013 to approximately 20,000 in 2016 [25]. Likewise, the CIHI reports that despite a 7% decrease in the number of fentanyl prescriptions from 2012 to 2016, the percentage of lethal opioid overdoses involving fentanyl, or its derivatives, continued to rise [29]. These trends from the United States and Canadian data point to illicit, and not prescription, fentanyl and fentanyl analogues as the agents behind the recent spike in opioid-related overdose deaths. Likewise in Europe, while heroin continues to be the most commonly used illicit opi-

oid, the use of potent synthetic opioids appears to be on the rise as evidenced by a growing number of non-fatal overdoses and deaths [6]. Since 2009, 25 new opioids have been detected in the European drug market, 18 of which were fentanyl derivatives [6]. In 2015, fentanyl derivatives accounted for 60% of the seizures of new synthetic opioids and individuals requiring MAT for non-heroin opioid use are a continuously growing cohort [6]. Among those seeking treatment for problematic opioid use, the fraction of individuals seeking specialized treatment for non-heroin opioid use has grown from 10% in 2013 to 22% in 2017 [21, 31]. While the opioid most commonly implicated in overdoses and deaths differs in North American and European settings, the common observation is that in both these regions, synthetic opioids are on the rise. Given the unprecedented potencies of these substances, and the harms they represent to users, future efforts by health organizations and policymakers need to focus on establishing protective measures for those who continue to use opioids in addition to efforts aimed at controlling supply.

## INTERVENTIONS TARGETING OPIOID ABUSE (SAFEGUARDING OPIOID USERS AGAINST OPIOID HARMS)

Another area that has gained significant interest in the effort to reduce opioid-related mortality is the development of countermeasures that minimize the harms associated with opioid use and overdose. These strategies include increasing accessibility to naloxone, the development of abuse-deterrent opioid formulations, and medication-assisted treatment (MAT) for those with opioid use disorders. In recent years, the distribution of the opioid antagonist naloxone to first responders and the general public has increased throughout the United States and Canada. In 2017 alone, the weekly naloxone prescriptions in the United States increased from 3500 to 8000 and continued to rise, reaching an all-time high in early 2018 [23]. Moreover, the use of naloxone by emergency physicians and first responders has evolved in response to the upward trend of intoxications involving illicit opioids and the introduction of substances with unprecedented potencies. While effective in intoxications with known substances, the rate and dose of administration in overdoses involving newer illicit opioids such as carfentanyl remain unknown and challenging to determine in acute situations [32]. In addition to increasing the availability of this antidote to opioid overdose, considerable effort has been directed towards the development of medications that are resistant to abuse. To receive FDA approval as an abuse-deterrent formulation (ADF), drug manufacturers are required to conduct pre- and post-market studies to confirm abuse deterrent properties. These include *in-vitro* laboratory evaluations of abuse potential through physical manipulation, chemical extraction and the ease with which the formulation can be drawn into and injected from a syringe [33]. In 2012, an abuse-deterrent formulation of extended-release oxycodone received FDA approval for its resistance to physical manipulation making it difficult to administer intranasally or inject intravenously. Likely due to availability and affordability, the entry of this abuse-deterrent medication into the market coincided with a shift towards increased use of buprenorphine and heroine instead of the original extended-release formulation of oxycodone [26]. Despite early promising signs of ADF effectiveness, critics have argued that the monetary costs of new branded products outweigh their benefits and that the removal of less expensive, non-abuse deterrent generics would require consumers to pay for costly drugs [26]. This can impede access to pain medications, and individuals who cannot afford these new formulations may look to black markets for unsafe alternatives to relieve their pain [26]. This argument loses its validity once ADFs are widely available and generic versions enter the market. Additionally, with the phasing out of non-abuse deterrent formulations, the inclusion of ADFs in covered formularies will likely reduce the financial burden on prescription opioid consumers [26]. While some still view ADFs as a financial burden, the evidence suggests that strategies to prevent opioid abuse can significantly reduce both individual and societal costs resulting from addiction and overdose. In the United States, reformulated oxycodone has been associated with annual medical cost savings of approximately $430 million USD [26]. Additional support stems from a budget impact model used to quantify potential cost savings linked to a hypothetical ADF. This hypothetical reformulation, designed to deter common forms of abuse, was associated with $1.6 billion USD per year in projected savings for third party payers [26]. Currently, a common limitation of ADFs is that they do not avert abuse involving oral administration of multiple drug doses [26]. Overall, ADFs preserve patient access to medication while simultaneously limiting abuse and its consequences. ADFs reduce the likelihood of prescription opioid users progressing to abuse, individuals with substance disorders developing new complications, and product manipulations which can result in morbidity and mortality.

Finally, individuals with substance use disorders should be offered evidence-based medication-assisted treatment (MAT) including buprenorphine or methadone alongside behavioural interventions.

MAT agents bind the μ-opioid receptor and confer protection against relapse and overdose through various mechanisms. Methadone acts as a full agonist with a long terminal half life (120 hrs) while buprenorphine acts as a partial agonist with a protective "ceiling" effect [34]. The reduced efficacy of buprenorphine at the μ-opioid receptor is beneficial in opioid-tolerant patients where, unlike methadone, it does not induce euphoria and prevents dose-dependant respiratory depression [34]. Buprenorphine can also be antagonistic in the presence of a full agonist and may precipitate withdrawal in this setting [34]. Both medications reduce cravings, suppress the stress response, prevent withdrawal and block the reinforcing effects of other opioids [34]. Compared to withdrawal as a strategy for detoxification, MAT demonstrates greater effectiveness with regard to treatment retention, reduced risk of mortality and morbidity, and sustained opioid abstinence [35]. Best practice guidelines in Canada and national practice guidelines from the American Society of Addiction Medicine support the use of buprenorphine/naloxone (suboxone) as the first line therapy in adults with moderate to severe opioid use disorder [35, 36]. Its effectiveness, however, depends heavily on individual compliance, as patients compliant with buprenorphine for at least 80% of a 4-week period benefit from a 10-fold increase in the odds of abstinence at 3 months [37].

In addition to its role in successful addiction recovery, several studies have demonstrated an association between MAT and a reduction in the transmission of blood-borne diseases. Compared with no treatment, the use of maintenance MAT (methadone or buprenorphine) was associated with a greater than 60% reduction in HCV among 552 young adult intravenous drug users (IVDU) in the San Francisco area [38]. Additionally, in their meta-analysis which included 8 studies from 1996 to 2009, Hagen and colleagues report a pooled relative risk of 0.6 for new HCV infection associated with MAT (95% CI: 0.35-1.03) [36]. The lower risk of contracting HCV applies to a broader demographic as risk reductions of 40% to 60% have been reported with the use of MAT in the older adult population, as well as in prisoners [38]. This effect is also observed with other blood-borne viral infections, including HIV, where MAT is associated with a 54% reduction in the risk of infection [39].

## HARM REDUCTION

Although changes in policies governing prescription behaviour and the introduction of ADFs have respectively encouraged responsible prescribing and provided safer alternatives for pain relief, the overdose and overdose-related death rates are still too high [1]. Addressing the associated mortality and morbidity necessitates the adoption of harm reduction strategies that allow individuals who use drugs to do so safely. Built into the definition of addiction, as defined by the DSM-5, is an element of lost control. Harm reduction strategies recognize addiction as a disease and take a patient-centred approach to restoring individual autonomy at a pace that is comfortable for the individual. Introduced in response to the AIDS epidemic in the Netherlands, the United Kingdom and Australia, there are now almost four decades of data pointing to the effectiveness and cost-effectiveness of harm-reduction approaches [40–42]. In the realm of substance use, there is good evidence for vaccinations to protect against hepatitis B, provision of clean needles and syringes, safe injection facilities, psychosocial therapies and pharmacologic agents to treat addiction and dependence. Unlike traditional abstinence-based methods, this approach provides treatment to individuals who are not willing or ready to stop using illicit drugs. While continued drug use may lead to further health, psychological, and social harms, interventions such as MAT, needle and syringe exchange programmes and supervised injection facilities (SIFs) promote health and well-being by allowing for what is best for the patient within the confines of what they are ready for. In the literature, systematic reviews consistently highlight the effectiveness of SIFs in meeting the objectives of reducing harms related to blood-borne diseases, curtailing overdose harms, reducing public drug use and the number of publicly discarded syringes, and increasing referrals to health and social services. Furthermore, evidence supporting fears such as increased drug use and trafficking is scarce. Since its opening in 2003, North America's first legal SIF, called Insite, has been used by over 3.6 million persons [43]. As of 2019, over 6,000 overdoses had been reversed in the Vancouver area with no deaths [43]. In addition to providing a safe environment for opioid use, SIFs have integrated holistic addiction care that has not been readily accessible. The use of these facilities is associated with increased access to services including nursing care, social work, residential treatment or detoxification sites, to addiction medicine providers and MAT [44]. While often available at SIFs, sterile needles and syringes can be provided in other settings. In the prevention of intravenously transmitted blood-borne infections including HIV, hepatitis B (HBV) and C (HCV), and other complications including endocarditis, cellulitis and abscesses, needle-exchange programmes are supported by a vast body of international literature [45, 46]. Through these programmes, drug users exchange potentially contaminated syringes

for sterile ones, and in many cases, users can access other sterile equipment (i.e. cotton swabs, cookers, water and bleach) to facilitate safer drug use. Like SIFs, needle exchange programmes also act as potential entry points for access to addiction medicine and rehabilitation. Studies conducted as early as the mid 1980s suggest that due to fear of blood-borne disease transmission, needle exchange programmes reduce sharing of needles and increase the use of clean needles and cleaning of needles [47]. Through the adoption of safer injecting practices by intravenous drug users, needle-exchange programmes have demonstrated their effectiveness in various settings through reductions in the transmission of blood-borne illnesses.

Currently, as heroin continues to dominate in Europe, fentanyl products represent an emerging threat. Although fentanyl-related overdoses are expected to increase, interventions for harm reduction have been adopted in many EU countries [6]. These include the provision of naloxone kits to peers and families as well as the operation of supervised drug consumption rooms [6]. With these preventative strategies in place, the likelihood that opioid-related harms will approximate those observed in North America is low. However, like in North America, tackling the broader issue of problematic opioid use across Europe will require concerted efforts from law enforcement officers, government officials, and healthcare professionals to formulate innovative strategies to prevent opioid dependence and effectively rehabilitate those who require treatment.

## SUMMARY AND RECOMMENDATIONS

In summary, opioid use in the form of prescription medications and illicit drugs has led to significant harms and deaths in North American and to a lesser degree in European settings. While recognized as a global issue by the WHO, the scale to which this crisis has affected Canada and the United States surpasses that of any other region. The origin of this crisis is believed to be multifactorial, with differences in the organization and delivery of healthcare, the culture surrounding pain management, influence from the pharmaceutical industry and laws governing direct consumer advertisement offering potential explanations as to why opioid-related morbidity and mortality have been more pronounced in North America. At the turn of the century, the primary driver of widespread addiction and dependence was an excessive supply of prescription pain relievers. Pharmaceutical companies provided misleading information about the addiction potential of prescription opioids and physicians were encouraged to liberally prescribe opioid pain medications by prominent pain specialists and societies. After witnessing the harms that followed, interventions focussed on opioid supply were successful in reducing opioid prescriptions while the demand for pain relief and treatment of existing opioid use disorders were sidelined. Hence, individuals sought illicit opioids such as heroin, fentanyl and potent fentanyl derivatives, which represent the current primary source of opioid-related overdose and deaths. Addressing this complex public health issue requires a multifactorial approach that encourages responsible prescribing behaviours and the use of PDMPs on the part of healthcare providers, while simultaneously safeguarding against overdose through ADFs and harm reduction initiatives such as needle exchange programmes and supervised injection sites.

While the shift towards more conservative prescribing is an important step in mitigating widespread opioid overdose, opioid medications continue to play an important role in acute pain management. However, in the setting of long-term opioid use, it is difficult to ascertain whether the perceived benefits of continued therapy represent genuine pain relief rather than a desire to prevent withdrawal. The use of opioids in the management of chronic pain lacks strong evidence. In certain patients, it can hinder functional improvement, prolong recovery, and aggravate pain via opioid-induced hyperalgesia. In addition to accidental overdose, risks of long-term opioid use include constipation, depression, sedation, motor vehicle collisions, and reduced libido [48]. In keeping with current best practices in North America and Europe, the following recommendations surrounding opioid use in the healthcare setting are made:

1. When opioids are prescribed, goals of treatment should be established with a plan to taper opioids and avoid long-term exposure if treatment objectives are not met. Recognizing that adverse effects are linked to dose and the well-described dose-dependent increase in the risk of a fatal overdose, excessive dose escalation is cautioned against [48].
2. Monitoring for high risk behaviours such as obtaining prescriptions from multiple prescribers (doctor shopping), or opioid diversion is needed to reduce opioid-related harms. This can be achieved through PDMPs, which should be more widely adopted in healthcare systems.
3. When tapering is sometimes problematic, coordinated multidisciplinary care, involving primary care physicians, nurses, pharmacists, physical therapists, occupational therapists, psychiatrists and other allied health professionals, is recommended.
4. MAT should be considered in patients with opioid use disorder as it frequently enables patients

to resume normal social life including return to work. Medication diversion is an issue, however, that has hindered the success of MAT. In keeping with the evidence supporting a multidisciplinary approach to addictions care, guidelines advise that alongside MAT, patients should receive counselling, preventative primary care, referrals to relevant psychosocial treatments and specialist care, as well as substance use monitoring with regular assessments including urine drug tests.

As the import of new synthetic opioids to Europe and North America continues, good surveillance data will be indispensable when reassessing the state of this epidemic and evaluating the efficacy of both supply and demand-side interventions. Furthermore, these data can assist policymakers, public health organizations, and drug enforcement agencies in their pursuit of innovative strategies to limit morbidity and mortality and promote the safety and wellbeing of individuals using opioids.

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