The opioid epidemic in North America: Key lessons for Europe

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Table of contents

List of acronyms

CDC	Centers for Disease Control and Prevention
EMT	Emergency Medical Technician
EU	European Union
NA	North America
NPS	New Psychoactive Substances
NSP	Needle and syringe programs
OST	Opioid Substitution Treatment
SOs	Synthetic Opioids
SROM	Slow-Release Oral Morphine

UNODC	United Nations Office on Drugs and Crime
WP	Work Package

Summary

Synthetic opioids (SOs) are among the leading causes of death among people who use drugs and one of the most important challenges in drug policy in today's world. The rate of overdose and overdose mortality involving SOs in North America has been higher than in any other region in the world. The present study aimed to find key lessons learned from the experience of the US and Canada to mitigate the use and harms of SOs and prevent an opioid epidemic in Europe.

In the present qualitative study six North American experts (three from the US and three from Canada) were invited to participate in in-depth interviews. The interviewees were selected based on their professional background reflected in their scientific publications and on recommendations from SO-PREP partners. Using an interview guide, the participants were asked about their knowledge and opinions of the development of the opioid epidemic, advantages and disadvantages of the current strategies to prevent, control, and reduce the harms of SOs in their countries, as well as other lessons that the European countries can learn from their experience.

A set of policies and interventions implemented by the governments of the US and Canada to respond to the opioid epidemic were reported and discussed by the participants. These include regulations of prescription opioids, intensified border control, opioid substitution treatment (OST), emergency medical technician (EMT) ambulances to respond to overdoses, street-based care interventions, drug checking, overdose prevention sites, and naloxone distribution. Particularly the adequate coverage of good quality OST was highlighted as an effective measure in reducing the use of illegal opioids. Strength and weaknesses of the interventions from the viewpoint of the interviewees, challenges towards implementing these services, and lessons that Europe can learn from the experience of the US and Canada are discussed in detail.

In conclusion, the US and Canada were unprepared for the emerge of SOs. Despite ongoing efforts, both countries are still struggling to adequately respond to protect people who use opioids. The North American experts interviewed in this study believe that, over time, an increase in the availability of SO in Europe is unavoidable. Results of the present study may help European policy makers to take timely and evidence-based actions to respond to the harms caused by SOs. Effective responses require well-prepared and coordinated actions on the side of the government. Services will need to be available, accessible and accepted by those who are in need of them. A coordinated effort of varying stakeholders and services will be necessary to mitigate the burden of SOs in Europe and prevent a potential crisis in this region.

1. Introduction

Synthetic Opioids (SOs) are among the leading causes of death attributable to drug use, and one of the most important challenges towards drug policy in today's world [1-3]. Synthetic opioids are one of the NPS subgroups with a chemical structure similar to natural opioids. Synthetic opioids, however, are more potent than natural opioids. For example, as one of the best-known SOs, fentanyl is around 100 folds more potent than heroin [4]. Due to their potency, fentanyl and its analogues are responsible for a large number of overdoses and overdose deaths among people who use drugs in the world [5].

Evidence leaves no doubt that over the past two decades North America has been influenced by the consequences of SOs more than any other region in the world [6]. The Center for Disease Control and Prevention (CDC) has estimated that between 1999 and 2019 almost half a million people lost their lives due to overdoses involving opioids, including SOs, in the US [7]. Similarly, from 2004 to 2011 emergency department visits for non-medical use of prescription opioids doubled and reached 488,000 in 2011 [8]. According to the CDC, from the beginning of the epidemic the US has faced three waves of opioid-related mortality. The first wave of overdose mortality involving prescription opioids began in 1990s; the second wave began in 2010, where most overdose deaths was attributable to heroin; and the third wave started in 2013 with a rapid increase in overdose mortality involving synthetic opioids, specifically illicitly-manufactured fentanyl [7].

Similarly, Canada has been facing a high rate of opioid-related overdoses and overdose deaths in recent years. These are mostly attributable to counterfeit opioid tablets, heroin laced with fentanyl, illicit fentanyl patches, and stimulants [9]. In 2016, almost 3000 "apparent opioid-related deaths" occurred in Canada, corresponding to eight deaths per day [10]. From July to September 2020, overdose mortality involving opioids in Canada showed a 120% increase compared to the same period in 2019, where most deaths occurred among men and people aged between 20 and 49 years [11]. Similar to the US, the opioid crisis in Canada began with an increase in prescription opioid use. Since the early 1980s, there has been a 3000% increase in the volume of opioids sold to pharmacies and hospitals for prescription in Canada [12]. Currently, non-medical fentanyl and its analogues are the main drivers of the opioid crisis in Canada, where over 80% of total deaths involving opioids in 2020 were attributable to fentanyl [11].

The COVID-19 pandemic has worsened the North American opioid epidemic where both the US and Canada have witnessed a spike or increase in fatal overdose and other harms of opioids. In the US, between February and May 2020 monthly overdose deaths increased by 50% and reached 9000, while monthly deaths in 2019 never exceeded 6,300 [12]. In Ontario, Canada, between March and December 2020 a total of 2,050 people died of an opioid overdoses; this is a 75% increase in overdose deaths compared to the same time period in 2019 [13]. Increased volume of toxic drugs and interruption of the existing harm-reduction

and social services are among the main reasons for the increased overdose mortality during the COVID-19 pandemic in North America.

2. Methods

With a qualitative design, the present study was carried out to collect data on the development of the opioid epidemic in North America and experience of the US and Canada to control the opioid crisis. Data was collected through semi-structured interviews from six health experts in the field of drug use. The process of data collection had multiple stages. First, an interview guide was developed and finalized with the comments and contributions from all SO-PREP partners. After reviewing the literature and consulting with the SO-PREP partners, six experts (three from the US and three from Canada) were selected and invited to participate in the in-depth interviews. The interviewees were selected based on their professional backgrounds, as reflected in their publications, and based on recommendations from SO-PREP partners.

The interview guide had three main sections including:

1. Lessons from development of the opioid epidemic in NA
2. Lessons from responding to the opioid epidemic in NA, and
3. Additional recommendations

The first section contained questions on the development of the epidemic, including for example the influence of the pharmaceutical industry and the role of the dark web and online markets. The next section was on the response to the opioid epidemic, including questions on services and policies in both countries as well as strengths and weaknesses of the existing interventions. In the third section participants were asked about other lessons that European countries can learn from their experience, both on systemic and service levels. The interview guide is presented in **Appendix 1**.

The interviews were conducted by Babak Moazen, Heino Stöver and John-Peter Kools from October 20th to November 2nd, 2020. The interviews lasted between 40 and 125 minutes. Prior to starting the interviews the participants were informed about the aims and objectives of the SO-PREP project as a whole and of this activity in particular. Informed consent was granted by the participant after being assured that their personal data (e.g. name and contact details) would remain confidential. Participants were allowed to skip questions or leave the interviews at any time. The records were transcribed and analyzed using content analysis method.

3. Results

3.1. Development of the epidemic in North America

The discussions around development of the opioid epidemic in the US were in line with the above-mentioned information published by the CDC. The participants did agree that the opioid epidemic in the US began with a rise in prescription of opioids e.g. Oxycodone (a sustained-release medication known as OxyContin® in the market) in 1990s. Before 1990s American physicians were reluctant to prescribe strong opioids to manage pain due to the risk of dependence and misuse. However, increasing pressure from the movements and campaigns against pain, as well as non-scientific claim of the US Food and Drug Administration (FDA) on lower abuse potential for slow-release formulation led to a sudden increase in prescription of opioids at that time.

In Canada, however, development of the opioid epidemic was different from that in the US. In some areas such as Ontario rise in opioid prescription was the starting point of the crisis. However, some other areas e.g. British Columbia had a huge influx of high purity drugs for decades, and previous epidemics of heroin-related overdose even before synthetic opioids arrive the country. Evidence shows that between 2015 and 2017 only 2% of total overdose mortality was associated with prescribed opioids while most lethal overdoses at the same time involved other forms of opioids. One of the current challenges faced by the healthcare system of Canada is that although people who use drugs are aware of the risks of synthetic opioids they purposively seek them because of their strong effects. One of the participants highlighted this issue as follows:

> *"I think a really challenging dynamic now is people have habituated to fentanyl. They're used to the strength and the effect, and actually seek it. So there is a lot of effort made to dissuade people through education, from using fentanyl, but people are actually seeking and wanting to use it, partly because heroin is so poor. So, you know, now we have this challenging situation where fentanyl and other synthetic opioids have kind of become the new normal for people"*
> *(Interviewee 4, Canada)*

According to the participants, a number of factors were involved in developing and directing the opioid epidemic in the US. Role of the pharmaceutical companies in developing the epidemic was one of the topics discussed in the interviews. Evidence suggests that pharmaceutical companies played a role in development of the epidemic by initiating and supporting the campaigns against the existing pain management norms at that time. One of the participants believed that pharmaceutical companies spent a large amount of money for marketing their products:

> *"They lied. We know that they lied about inductive properties. We know that they were spending ten/twenty million dollars a year for marketing it to physicians. We know that they got physicians to change the indicators of care for it…"* (Interviewee 3, the US)

Although the interviewees did not deny the role of pharmaceutical companies in developing and directing the current opioid epidemic in North America, they believe that the blame should not be put only on pharmaceutical companies. In other words, pharmaceutical companies alone were not responsible to shape the current situation in this region. The

interviewees mentioned numerous other parameters involved in the opioid epidemic, among them lack of proper pharmaceutical regulations was mentioned as one of the main factors:

> "*Did they [pharmaceutical companies] act in the way it was terrible? Of course! But most of the terrible things they did were perfectly legal. We have pharmaceutical regulations that tolerate terrible behavior. It's like we live under capitalism and we allow our medications to be on a competitive market. What do you expect? "*
> (Interviewee 1, the US)

Lack of scientific evidence, poor drug education, and lack of knowledge dissemination among prescribers, patients, and people who used drugs were mentioned as the other contributing factors in all stages of the opioid epidemic in the US. At the starting point, more liberal use of opioids for patients with chronic pain was supported by two non-generalizable studies that misinformed both policy makers and anti-pain activists about the consequences of opioid-based medications. In addition, years after beginning the opioid epidemic not all people who used drugs were aware of the existing harm-reduction services implemented by the government that indicates a lack of proper information, education and risk communication in the field of drug use. This issue was pointed out by one of the participants as follows:

> *"I think there is a lot of blame to put on our sheer lack of drug education and drug awareness. Even at late 2016 I met individuals who were using prescription opioids recreationally or self-treatment. And I asked them if they're even interested in a program like buprenorphine or methadone, and they were like: "but that's for people who use opioids"".*
> (Interviewee 1, the US)

From the participants' point of view, most probably the dark web and online markets have contributed in the current epidemic in North America; however, their role in developing and directing the epidemic has not been significant. It should be considered that not all people who use drugs have access to the online markets and darkweb. In addition, there are multiple other ways in which people can access drugs, as in the last years a large amount of illegally-produced synthetic opioids were sent to the US and Canada via post. In this regard, one of the participants stated that:

> *"I think drugs always find their ways into cities from other countries. Has the internet made it easier? Probably, but I don't know if that's like a mass level or individual ordering or something. When I think of online markets at least for an individual drug user, with the community we work with, most even don't have access to computer or internet."*
> (Interviewee 6, Canada)

3.2. Responding to the opioid epidemic

Multiple interventions were implemented by the governments of the US and Canada to mitigate the use and harms of synthetic opioids during the pandemic. The participants discussed a number of main interventions as well as the strengths and weaknesses of these interventions implemented by the US and Canada to respond to the epidemic.

In terms of supply-side interventions, most efforts were focused on monitoring opioids prescribed by physicians, intensifying border control, as well as revising/developing pain management guidelines to restrict opioid prescription in order to reduce the use and harms of synthetic opioids in North America. Development of the guidelines on using nonpharmacologic and non-opioid pharmacologic therapies for patients with chronic pains advanced by the CDC was one of the aforementioned activities.

In parallel with the supply-side interventions, numerous harm-reduction services were implemented by the US and Canada to mitigate the burden of opioids in these countries. The successful interventions discussed by the participants include:

- Different forms of opioid substitution therapy (OST),
- drug checking
- emergency medical technician (EMT) ambulances to respond to overdose,
- street-based interventions e.g. wound care,
- initiating buprenorphine treatment in the hospitals,
- warm handoff (bringing drug users to the treatment centers),
- naloxone program, and
- overdose prevention sites

Although the above-mentioned interventions were at least partially successful to reduce the risks and harms of non-medical use of opioids, according to the interviewees there are still a large number of shortcomings that need to be addressed. Despite the recent improvements in availability, coverage and quality of the services, lack of treatment centers in the US is one the above-mentioned shortcomings, since a large number of drug users in high demand cannot find a free slot to start treatment. Another issue is that many drug users may have no health insurance that hinders them from seeking treatment due to the high costs of opioid substitution therapy. These issues were pointed out by one of the participants:

> *"We're moving on the right direction, but it is still easier to get prescription opioid and oxycodone from your doctor than to get buprenorphine, and methadone is very restricted. If you have high treatment demand it [the situation] is better than it was few years ago but still not perfect. We still have not made it easier for people to walk in and get buprenorphine. Not everyone has health insurance, that's another problem."*
> (Interviewee 2, the US)

General stigma around drug use is another barrier towards implementation of harmreduction interventions for people who use opioids in the US and Canada. One of the participants pointed out their efforts undertaken to implement needle and syringe program in a rural area in the US. Short after beginning, the program was stopped as soon as the authorities realized that in addition to needles some other equipment e.g. cookers, cotton swaps and alcohol pads are distributed among clients as well. The decision was based on the misconception of policy

makers that distributing cookers would encourage injection. In this regard, role of the campaigns and movements to fight drug-related stigma and to facilitate access to treatment for people who use drugs should not be overlooked:

> *"I think another thing that influenced everything is a large campaign and a large movement within Canada to destigmatize addiction and people who use drugs. There has been a big move by my organization to influence substance use and addiction as a stigma campaign to describe addiction as a health issue, and to trying to reduce barriers to basic healthcare services."*
> (Interviewee 5, Canada)

Naloxone is known as one of the most effective medicines that rapidly reverse overdose caused by opioids and prevent mortality. In Canada, naloxone kits are available free of charge in most provinces. Yet, access to naloxone is limited in many states of the US and some provinces in Canada. In some states, access to naloxone is dependent on the personal judgement of the pharmacist on whether or not the client needs naloxone. In some other states, only those who carry naloxone are allowed to purchase that from pharmacies. Together with the other harm-reduction services, naloxone must be available, accessible, and affordable for all people in need. One of the participants highlighted this issue as follows:

> *"Now they [people who use drugs] purchase naloxone in most states I think, without a prescription at a pharmacy, if they carry it and if the pharmacist agrees to give it to them. Even though we had great success at giving naloxone, we probably need to increase it exponentially to deal with the fentanyl challenges.* (Interviewee 3, the US)

3.3. Additional recommendations

In addition to the above-mentioned points, the North American interviewees suggested a number of strategies that can assist Europe in order to mitigate the burden of synthetic opioids and to prevent a pandemic in this region, both on a systemic and on a service level.

On the supply side, most recommendations were around strengthening the existing SO monitoring system in Europe. According to the participants, to reach this goal Europe needs to intensify its border control and increase control on SO prescription and distribution. In addition, one of the participants highlighted the need for establishment of an international alliance of inspectors to help China improve its monitoring system in order to fight black market manufacturers:

> *"What the US really I hope does in the next administration is to integrate a plan with China, in cooperation with the European Union, UNODC, etc. and build an alliance coming together to China."*
> (Interviewee 2, the US)

In terms of demand and harm-reduction, all services must be available, accessible and affordable to people who use drugs. Using innovative methods could facilitate access to services and encourage people who use drugs to use the existing services. The dispensing devices for Narcan, paraphernalia and hygiene products in Canada are good examples of such innovative methods that may decrease personal contact and encourage people to seek

naloxone. Implementing innovative treatment modalities was another recommendation by the interviewees in order to increase effectiveness of the program. In this regard, one of the participants suggested that a deregulation in methadone treatment would help people under treatment to deal with withdrawal easier and improve their quality of life:

> *"Instead of giving 80 mg or 100mg of methadone once a day, what if we give them (people under treatment) like 30mg three times a day? They are all these things that would be helpful to patients, and would help them have better lives, and we're not even thinking about them."*
> (Interviewee 3, the US)

Importance of equal attention to demand and supply reduction at the same time was one of the main recommendations of the participants that will help European countries to deal with the use and harms of SOs. 'Prescription drug monitoring programs (PDMP)' are a set of interventions rolled out in the US in order to crack down irresponsible prescribing and control people who receive prescription opioids. Evidence shows that these programs not only did not decrease lethal overdoses, but also persuaded people who used prescription opioids to switch to the street drugs e.g. illegal fentanyl that can be even more harmful. In this regard, one of the participants underlined the need for an equal attention to demand and supply reduction and suggested how to deal with that as follows:

> *"As you reduce supply, you're gonna have your demand to go up. You can make sure that there is treatment space for anybody who wants treatment. In Canada we're turning to look at a kind of safer supply model for some segments, because among that segment of people who don't want treatment there is some people who may be open to different kinds of treatments. And at the same time for those people who are just not interested at all, you can make sure that they are safe."* (Interviewee 5, Canada)

A strong early warning system for communication between different sectors e.g. police, forensic labs, and healthcare system, and with people who use drugs is a crucial requirement to mitigate overdose mortality involving synthetic opioids via monitoring drugs and informing people who use drugs about any toxic component in the drugs they use. To strengthen the existing NPS early warning system in Europe was one of the main recommendations of the interviewees of this study. Special attention needs to be paid to create a rapid communicating system with people who use drugs who are hard-to-access due to stigma. One of the participants pointed out an existing messaging system in Vancouver that has been implemented to communicate with people who use drugs in case of detecting any threats:

> *"In Vancouver and British Columbia they have a text message-based service, so if there is like some sort of contaminated drug you get a text message like 'oh, this drug being sold as Crack contains carfentanyl' in this city. That's not perfect because obviously people don't know where that came from, but it's at least getting a word out there. "*
> (Interviewee 6, Canada)

Challenges caused by the COVID-19 pandemic were the other topics discussed by the participants. Evidence shows a considerable increase in overdose and lethal overdose

involving opioids in the time of COVID-19 pandemic in North America. This issue was not only because of the supply of a large amount of contaminated drugs but also sudden and unprepared reduction of access to the harm-reduction services and social support. Prior to the COVID-19 pandemic, one of the strategies of the healthcare system of Canada was to encourage people who use drugs not to be alone while using/injecting drugs. It is not surprising that this strategy was interrupted by the pandemic restrictions. Besides, the lockdown led to temporary closure of the existing harm-reduction services e.g. safe drug consumption rooms. European countries need to make sure about continuity of services and social support for people who use drugs during the present pandemic and similar potential crises in the future.

4. Conclusions and recommendations

The aim of the present qualitative study was to learn from the experience of the US and Canada on how to prevent an opioid epidemic in Europe. Based on interviews with experts from the US and Canada, a set of lessons were identified and reported together with a bundle of recommendations that are crucial to prevent a SO epidemic in Europe:

4.1. Supply-side lessons and recommendations

- Initiation of the opioid epidemic in North America was mostly supply-driven, in the way that availability of SOs persuaded people who use drugs to use SOs.
- Intensified border control is required to prevent entering SOs through parcels or passengers, especially from China and South America.
- Policies need to be in place to avoid health care professionals to be 'bought' by pharmaceutical companies and to elude corruption.
- To address and reduce overprescription of synthetic opioid medications is a crucial intervention to prevent an opioid crisis in Europe.

4.2. Demand-side lessons and recommendations

- Education of the general population with regard to the dangers and addiction potential of prescription opioids, as well as the dangers of new SOs is required.

- As one of the main demand reduction interventions, OST should be provided with adequate coverage and good quality.
- Services should be tailored to the needs of people who use SOs, e.g. fentanyl patches to serve the needs of people who use potent SOs.
- It is necessary to establish trust between the services and PWUD, to ensure that PWUD actually use the services. To involve Peers/ peer-led initiatives for building trust is an example.
- All demand reduction interventions need to be available, accessible and acceptable to people who use drugs, and implemented with sufficient quality.

4.3. Lessons and recommendations on Early Warning Systems

- National drug situation including pattern of drug use and supply chain needs to be carefully monitored in European countries.
- To establish and continuously improve rapid Early Warning Systems on national and transnational levels is necessary to track drugs in the market, detect potential toxic substances and notify all beneficiaries including PWUD as soon as possible.
- There is a need for continuous national consultation/monitoring meetings with a range of relevant stakeholders including civil society, harm-reduction services, communities, and government.

4.4. Lessons and recommendations on harm-reduction interventions

- Naloxone program is a key intervention to reverse opioid overdose and prevent overdose deaths. Easy access and wide availability of naloxone are recommended.
- Needle and syringe programs and safe drug consumption rooms have proven to reduce the harms of SOs and mitigate opioid-related mortalities.
- All harm-reduction interventions need to be available, accessible and acceptable to people who use drugs, and implemented with sufficient quality.

Over time, increase in availability of SO in Europe seems to be unavoidable. It should be considered that effective responses require sense of urgency and well-prepared and coordinated actions on the side of the government. European countries should benefit from their experiences in building supportive health/social systems for their citizens. According to the above-mentioned lessons and recommendations, concrete and urgent actions are required to address SO use and harms and prevent an opioid epidemic in Europe.

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6. Appendix: Interview guide

The main aim of this interview is to identify 'lessons learned' from the US and Canada on how to prevent and/or deal with a potential opioid crisis in Europe.

We will first talk about how the opioid epidemic developed and what factors contributed to it. Then we'll talk about how services and policies developed in response to the opioid crisis and what has been successful or not. Finally we can conclude with some lessons learned.

Development of the opioid epidemic

We would like to talk to you about how the opioid epidemic developed in the United States/ Canada.

- Can you tell us about the different stages of the epidemic? (i.e. from prescription opioids to fentanyl).

- Can you tell us about the influence of the pharmaceutical industry and what impact certain policies had on the development of the opioid epidemic?

- To what extent was the epidemic supply-driven versus demand-driven? (by doctors/pharmaceutical companies and dealers/suppliers)

- Did the dark web/ online markets play a role?

- What other important factors contributed to the development of the epidemic?

Tackling the opioid epidemic

Next we would like to talk to you about how the opioid epidemic is being tackled in the US/Canada.

<u>Services:</u>

- Were drug and health care services in your country prepared for the challenge caused by synthetic opioids? Please elaborate on it.

- What development in drug services for synthetic opioids have there been in recent years (e.g. special services, information leaflets, support groups, treatment, harm-reduction services)?

- What other services might be needed/ beneficial in keeping synthetic opioid users safe and/or preventing use of SO?

<u>Policies:</u>

- What policies and regulations were developed to tackle the opioid epidemic in the US/ Canada?

- What policies would still need to be developed to better tackle the opioid epidemic in the US/ Canada?

Other:

- What other strategies (policies, services, or other) are needed to reduce the use of synthetic opioids in the US/ Canada?

Other lessons learned

- What can other countries learn from your experiences? Both on a systemic level (e.g. policies) and on a service level.

Additional points

- Is there anything else you would like to say about the opioid epidemic in the US/ Canada and what other countries can learn from your experience?

Thank you for accepting our invitation and participating in this interview.