OECD Health Policy Studies

Addressing Problematic Opioid Use in OECD Countries

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Foreword

This report was commissioned by Health Canada with the aim of mapping out countries current stance in terms of opioids use, both legal and illegal, and to review evidence about the existent policies to prevent and reduce associated negative consequences. In addition, other member countries expressed their interest in the topic due to past experience or current problematic situations.

This is the first project in the OECD Health Division devoted to the area of drug policy, particularly, including illicit substances. In particular, this report builds on the OECD's long-standing programme of work on the economics of public health, applying this extensive expertise to country-specific challenges.

Health systems across OECD are increasingly under pressure from emerging or re-emerging health challenges, along with growing citizen's demand for strong public health responses. In the area of drug policy, the latter requires a particular focus on multisectoral actions and coordinated efforts. The report presents data on the magnitude of the problem across OECD countries, describes the main drivers of the crisis, and identifies a set of policy actions within health systems, social policy and law enforcement sectors, with strong health information systems and better research as policy levers. It highlights best practice examples that allow learning from shared experiences and the spreading of innovative approaches.

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Executive summary

Over-prescription of pain killers by doctors has contributed to a growing problematic opioid use in parts of the OECD with a surge in overdose deaths in the United States, Canada, Sweden, Norway, Ireland and parts of the United Kingdom pointing to a mounting health and social crisis fuelled by the illicit drugs trade.

The inappropriate use of opioids has hit diverse groups of the population, showing that a broad approach is needed to reach all the people at risk. Better treatment, care and support for people with use disorders to legal and illegal opioids (OUD) and better support for communities blighted by opioid dependence are vital at a time when opioid prescriptions and illicit sales by drug gangs are rising. Better and more closely monitored prescription by doctors and use of alternatives for dealing with chronic pain are also key to address the crisis. Awareness of the risks of the opioid crisis is growing but is relatively low outside countries where the crisis is most pronounced, such as the United States and Canada.

The average availability of prescription analgesic opioids has been steadily growing in the past 15 years across the OECD. There was a boom in the last decade. Between 2002-04 and 2005-07 analgesic opioids availability grew on average by more than 58%. More recently, between 2011-13 and 2014-16, the growth rate dropped to around 5% on average.

Not only has the average availability of both legal and illegal opioids risen across the OECD in the past 15 years but opioid-related deaths (ORD) have also climbed in many countries. Opioid abuse has also put a growing burden on health services through hospitalisation and emergency room visits. High opioid doses can lead to potentially fatal respiratory depression. Interventions such as needle and syringe programmes, supervised drug consumption rooms and opioid awareness in communities could all make a difference. More than half of all fatal overdoses occur in victim's homes and more than half of deaths occur with another person present.

In 25 OECD countries for which data is available, the average of ORD has increased by more than 20% in 2011-2016, with the rise most pronounced in the United States, Canada, Sweden, Norway, Ireland, and England & Wales.

The majority of those who die are men, accounting for 3 out of 4 deaths. Other population groups, such as pregnant women have also been experiencing problematic opioid use. In the United States, having a mental health disorder was also associated with a two-fold greater use of prescription opioids. Prisoners too are vulnerable. The prevalence rate of opioid use disorders in Europe was less than 1% among the general public but 30% in the prison population. Social and economic conditions have also contributed to the crisis with opioid use and unemployment linked in some research.

In the United States, 399 230 people have died from an opioid overdose between 1999 and 2017, while in the years 2015 to 2017 life expectancy has decreased for the first time in more than 60 years, in part because of the opioid crisis. The United States is by no means alone in facing this crisis. In Canada, there were more than 10 000 opioid-related deaths between January 2016 and September 2018. In Australia, more than 1 000 people are dying a year due to opioid abuse with around three-quarters of those deaths linked to prescription opioids.

Opioid overprescribing is considered one of the most important root causes of the crisis. In the United States alone, there were 240 million opioid prescriptions dispensed in 2015, nearly one for every adult in the general population. In North America, hydrocodone, oxycodone, codeine and tramadol are the main prescription opioids used for non-medical purposes, while methadone, buprenorphine and fentanyl are the most misused opioids in Europe. The influence of pharmaceutical manufacturers on pain management has been considered significant, by conducting marketing campaigns targeted mainly at physicians and patients, downplaying the problematic effect of opioids.

However, higher rates of opioids availability are not necessarily correlated with higher overdose death rates, for instance, in Germany, Austria, Belgium, Denmark and the Netherlands. This suggests that appropriate regulation of prescription opioids can be compatible with higher availability of these drugs for medical use. Prescription monitoring and regulation to assure appropriate use of medical opioids is critical.

Opioids are used for the treatment of moderate to severe pain, including after surgery. Some opioids are also used in combination with counselling and behavioural therapies for the treatment of heroin and other drug addictions.

Opioid drugs work by binding to specialised receptors on the surfaces of opiate-sensitive cells, reducing pain messages and feelings of pain. These interactions trigger the same biochemical brain processes associated with feelings of pleasure in activities such as eating and sex. These reward processes can motivate repeated use and can lead to the development of opioid use disorders (OUD).

Illicit opioids constitute a significant product of international illicit trade. Heroin is a semi-synthetic opiate synthesised from morphine and is the most prevalent illicit opioid worldwide. Approximately twice as potent as morphine, heroin has a high potential for problematic use. In recent years, fentanyl and fentanyl analogues have become much more prominent in the illicit drugs scene in many countries.

Prescription opioids are analgesic medications that include natural opiates (e.g. morphine, codeine), semi-synthetic opioids (e.g. oxycodone, hydrocodone, hydromorphone, oxymorphone) and synthetic opioids (e.g. methadone, fentanyl, tramadol).

The opioid crisis is not only a health crisis. It also is a social and law enforcement dimensions.

Opioids have been over-prescribed by health care systems with limited alternatives for chronic pain management. There has also been inadequate access to the right treatments for opioid use disorder (OUD). Research and development on non-addictive treatments for chronic pain has not received the same priority as other areas.

Illicit opioids are increasingly available at low cost and with high purity, including highly toxic substances such as fentanyl and its analogues. A miniscule amount of pure fentanyl (about the size of a pinch of salt) can be fatal. In the United States, Canada and some European countries fentanyl analogues account for a large component of the opioid crisis.

Economic and social conditions, such as unemployment, housing and exclusion are also linked to the opioid crisis.

Countries can consider four key areas for a better approach to dealing with opioid use and harms.

- **Better Prescribing:** Doctors can improve their prescribing practices, for instance, through evidence-based clinical guidelines (e.g. for opioid prescription, for adequate medication-assisted therapy for OUD patients), prescribers training, surveillance of opioid prescriptions, and regulation of marketing and financial relationships with opioid manufacturers. In addition, patients and the general public can also benefit from clear educational materials and awareness interventions to enhance their opioid-related literacy and reduce stigma.
- **Better care:** Including the expansion of coverage for long-term medication-assisted therapy (e.g. methadone, buprenorphine, naltrexone) coupled with specialised services for infectious diseases

management (e.g. HIV, hepatitis) and psychosocial interventions. Some countries have implemented interventions such as the availability of overdose reversal medications for all first responders, needle and syringe programmes, and medically supervised consumption centres. Quality of care must be improved and measured.

- **Better approach**: There can be better coordination across the health, social and criminal justice systems. Governments can consider setting up of coordinated networks among the three sectors aiming to facilitate access to integrated services for people with OUD. In addition to health services, social interventions around housing and employment support, and law enforcement uptake of a public health approach are central.
- **Better knowledge and research**: Including the use of big data and impact evaluations to generate new information from different sources along with the application of advanced analytics. In addition, quality of care measurement should be enhanced in areas such as opioid prescription, OUD health care services, and patient reported indicators (e.g. PROMs, PREMs). Research and development is needed in key areas such as new pain management modalities and OUD treatments.

1 Introduction

Opioids are a type of narcotic medication that have become the basis of therapy for the treatment of moderate to severe pain in many developed countries, for instance, in cases of acute pain management, post-operative pain, and palliative care. In addition, some opioids are used in combination with counselling and behavioural therapies for the treatment of heroin and other opioid dependence. Opioid analgesic prescribing has steadily increased in the past years in OECD countries, and many patients are being treated with opioids for chronic non-malignant pain.

In parallel, opioids have been used as nonmedical drugs, creating illegal global markets where illicit opioids are increasingly commercialised. Both diverted prescription opioids (e.g. oxycodone, hydrocodone, morphine, fentanyl) and illicitly produced opioids (e.g. heroin, fentanyl analogues) are present in dynamic domestic and international trade networks, including on the surface web and darknet. Other illicit drugs (e.g. cocaine) are not part of the scope of the present paper, since the current crisis in some OECD countries involves opioids as the main substance of problematic use. However, it is important to note that polysubstance use is prevalent and that non-opioid drugs are sometimes contaminated with powerful synthetic opioids, such as fentanyl.

Growing use of opioids has rapidly escalated the use of health care services such as emergency consultations and hospitalisations. The number of overdose deaths has mounted to alarming numbers, creating the so-called ‘opioid crisis’, impacting Canada and the United States. Other OECD countries, such as Australia and some European countries are also experiencing a trend of rising opioid consumption and overdose deaths.

The purpose of this paper is to develop a comparative analysis of international strategies to address and prevent problematic opioid use, and their effectiveness in reducing/preventing opioid-related harm. The paper analyses the rates of problematic opioid use that OECD countries are facing and identifies the main drivers underpinning these rates. It also identifies best practices to address problematic opioid use in OECD countries. The paper presents data analysis on selected priority indicators, as well as the results of an extensive literature review and a short questionnaire addressed to countries.

This document is organised into four sections. Section 2provides a brief description of what opioids are and the main characteristics of opioid use. Section 3 explores the magnitude of the opioid crisis in OECD countries and the factors underpinning it. Section 4 presents a policy framework to guide actions to address the opioid crisis, along with existing evidence about their effectiveness and some examples of good practice in OECD countries. Finally, Section 5 highlights preliminary policy lessons for OECD countries.

2 Opioid use in context

2.1. What are opioids and how have they been used?

Opioids can be natural, semi-synthetic or synthetic chemicals. Opiates are the naturally occurring alkaloids of the opium poppy (Papaver somniferum L.), which is a plant that grows in many countries around the world with moderate climates. Opioids, in terminological rigor, are synthetic or semi-synthetic compounds derived from opiates but are not opiates themselves. In this report, the term 'opioids' will be used to refer both to natural and synthetic substances.

Opioids, according to their legal status, can be divided in two groups.

- Prescription opioids are analgesic medications that include natural opiates (e.g. morphine, codeine), semi-synthetic opioids (e.g. oxycodone, hydrocodone, hydromorphone, oxymorphone) and synthetic opioids (e.g. methadone, fentanyl, tramadol). These are given by doctors as painkillers, during anaesthesia, or as treatment of heroin and other opioid dependence. (United Nations Office on Drugs and Crime, 2016[1]). Codeine is also available in low doses without a prescription in some countries.
- Illicit opioids constitute a significant product of international illicit trade. Heroin is a semi-synthetic opiate synthesised from morphine and is the most prevalent illicit opioid worldwide. Approximately twice as potent as morphine, heroin has a high potential for problematic use (United Nations Office on Drugs and Crime, 2016[1]). In recent years, fentanyl and fentanyl analogues have become much more prominent in the illicit drugs scene in many countries (see Box 2.1).

Box 2.1. Fentanyl and new fentanyl analogues

Fentanyls are a family of short-acting and highly potent opioids that have gained relevance in the past years by significantly worsen the crisis. Four fentanyl compounds are approved for medical use in anaesthesia and pain management, but a range of fentanyl analogues are produced clandestinely in chemistry labs, which makes its production and distribution much easier.

Fentanyl is often sold mixed with heroin, cocaine or other drugs (in many cases users are not aware of the content), and can have severe repercussions for users as a result of their high potency or toxicity, which can be as high as 10 000 times stronger than morphine in the case of the analogue called carfentanil. A miniscule amount of pure fentanyl (e.g. about the size of a pinch of salt) can be fatal. In the US, Canada and some European countries fentanyl analogues account for a large component of the opioid crisis (ECDD-WHO, 2017[2]; United Nations Office on Drugs and Crime, 2016[1]). In recent years, fentanyl overdose deaths have been also reported in Australia, Finland, Germany, Greece, and the United Kingdom (UNODC, 2017[3]).

2.2. The thin line between appropriate and inappropriate opioid use

Opioid drugs work by binding to specialised receptors on the surfaces of opiate-sensitive cells, reducing pain messages and feelings of pain. These interactions trigger the same biochemical brain processes associated with feelings of pleasure in life activities (e.g. eating and sex). These reward processes can motivate repeated use and can lead to the development of opioid use disorders (OUD) (Kosten and George, 2002[4]).

Prescription of higher doses of opioids, as it has been used for treating chronic pain, is correlated with 32% to 188% higher risk of unintended overdoses and with opioid related morbidity and mortality (Chou et al., 2015[5]). A systematic review found that the incidence of iatrogenic opioid dependence or problematic use in the United States was 4.7% of those patients prescribed opioids for pain (Higgins, Smith and Matthews, 2018[6]). Another study found that one out of 16 surgery patients who use opioids becomes a chronic opioid user (Brummett et al., 2017[7]).

Inappropriate use of prescribed opioids (e.g. to induce feelings of pleasure, to tackle withdrawal symptoms or to alter the effects of other consumed drugs) is also a relevant component of the crisis. In North America, hydrocodone, oxycodone, codeine and tramadol are the main prescription opioids used for non-medical purposes, while methadone, buprenorphine and fentanyl are the most misused reported in Europe (World Drug Report, 2018[8]). In the United States, four out of five heroin users report that their opioid use began with nonmedical use of prescribed opioids. However, only about 4% of people who inappropriately use prescription opioids initiate heroin within five years after the first prescription (Muhuri, Gfroerer and Davies, 2013[9]). Similarly, a simulation study found that policies aimed at reducing opioid prescription supply and related deaths might have led some dependent prescription users to switch to heroin use, which may increase heroin-related deaths (Pitt, Humphreys and Brandeau, 2018[10]).

Higher opioid doses can result in respiratory depression that can lead to overdose death. An increased risk of inadvertent prescription opioid overdose has been found with 20-50 morphine milligram equivalents a day (comparable to three to seven 5mg oxycodone tablets a day) with fatality more likely with opioid doses above 50 morphine milligram equivalents a day (seven or more 5mg oxycodone tablets a day) (Adewumi et al., 2018[11]).

Polysubstance use is common in people who inappropriately use opioids, consuming them jointly with alcohol and other drugs. This is corroborated by the fact that in many opioid-related overdose deaths there are other drugs involved simultaneously (Frisher et al., 2012[12]). In addition, there is a link between problematic opioid use and ***mental health*** illness (Davis et al., 2017[13]).

Patients with OUD who manage to reduce their opioid use, frequently ***relapse***. Over the long term, mortality rate of people with OUD is about six to 20 times greater than that of the general population. Among those who remain alive, the prevalence of stable abstinence from opioid use is quite low (less than 30% after 10–30 years of observation), and many continue to use alcohol and other drugs after ceasing to use opioids (Hser et al., 2015[14]).

Injection as a route of administration increases the risk of acquiring ***infectious diseases***. The sharing of needles or other injection tools increases the risk of invasive infections from skin bacteria and fungi (e.g. Staphylococcus aureus, Candida sp.) and viral infections (e.g. HIV, hepatitis). A review found that heroin injectors had 2.8 times the risk of HIV seroconversion compared with those not injecting in the past 6 months (Tavitian-Exley et al., 2015[15]).

3 The opioid crisis and the rise of an epidemic in some OECD countries

3.1. What is the magnitude of the opioid crisis in OECD countries?

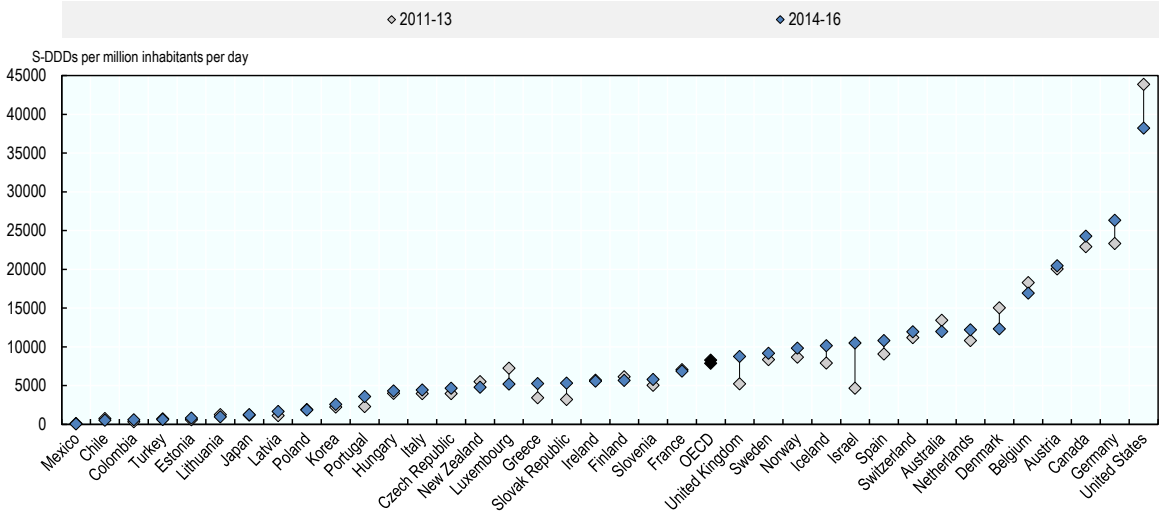
Several different countries have had epidemics associated with the use of opioids. For instance, France, Portugal and Switzerland had a sizeable heroin epidemic in the 1980s and 1990s (EMCDDA, 2000[16]); and the United States had opiate epidemics in the late 19th century, after World War II and in the 1960s (Lawson, 2018[17]). Today's situation is challenging because it involves both prescribed and illicit opioids at the same time. The predominance of use and harms of one versus the other varies across OECD countries, but the threat now also comes from the global diffusion of information and commercial exchanges.

In terms of ***prescription analgesic opioids***, at the global level there is a lack of access to pain relief and palliative care, including a staggering lack of access to opioids in low income countries (Knaul et al., 2018[18]). In OECD countries, the reality is quite different. The average availability, defined as the amounts that each country's competent national authority estimates are used annually (including reporting of medicine destroyed, losses during manufacturing, etc.), has been steadily growing in the past 15 years (see Figure 3.1). The sharpest increases happened in the 2000s, where between 2002-04 and 2005-07 analgesic opioids availability grew on average by 58.6%. More recently, between 2011-13 and 2014-16, the growth rate dropped to 5.4% on average. It is important to highlight that this data does not directly reflects the consumption of analgesic opioids in countries, but the general availability for different purposes, which the largest component is for medical use.

In the triennium 2014-16, among the countries above the OECD average in availability of analgesic opioids, only the United States (-12.9%), Belgium (-7.3%), Denmark (-18.2%) and Australia (-10.9%) have reduced use. The countries who experienced an increase of over 50% between 2011-13 and 2014-16 are Israel (125%), the United Kingdom (67.8%), Slovakia (64.9%), Greece (53.9%), Portugal (56.3%) and Colombia (76.6%), but the latter four countries remain below the OECD average.

The increasing availability of analgesic opioids in OECD seems to be associated with increasing medical prescription of opioids in health systems. Other than the United States and Canada, different studies have shown increasing trends of medical opioid prescription in the past 10 to 15 years in countries such as France (Chenaf et al., 2019[19]); Germany (Schubert, Ihle and Sabatowski, 2013[20]); Italy (Musazzi et al., 2018[21]); Netherlands (Wagemaakers et al., 2017[22]); Poland (Dzierżanowski and Ciałkowska-Rysz, 2017[23]); Spain (AEMPS, 2019[24]); United Kingdom (Zin, Chen and Knaggs, 2014[25]); Australia (AIHW, 2018[26]); Denmark, Norway and Sweden (Muller et al., 2019[27]). It is relevant to note that although prescriptions may be rising, in some countries this might not necessarily equate to a rise in dosages as they can be for lower doses and/or quantities of opioids.

Figure 3.1. Mean availability of analgesic opioids in OECD countries 2011-13 and 2014-16. S-DDDs per million inhabitants per day



Note: Analgesic opioids include codeine, dextropropoxyphene, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, morphine, ketobemidone, oxycodone, pethidine, tilidine and trimeperidine. It does NOT include illicit opioids.
S-DDD: Defined daily doses for statistical purposes.
Source: (INCB, 2018[28]).

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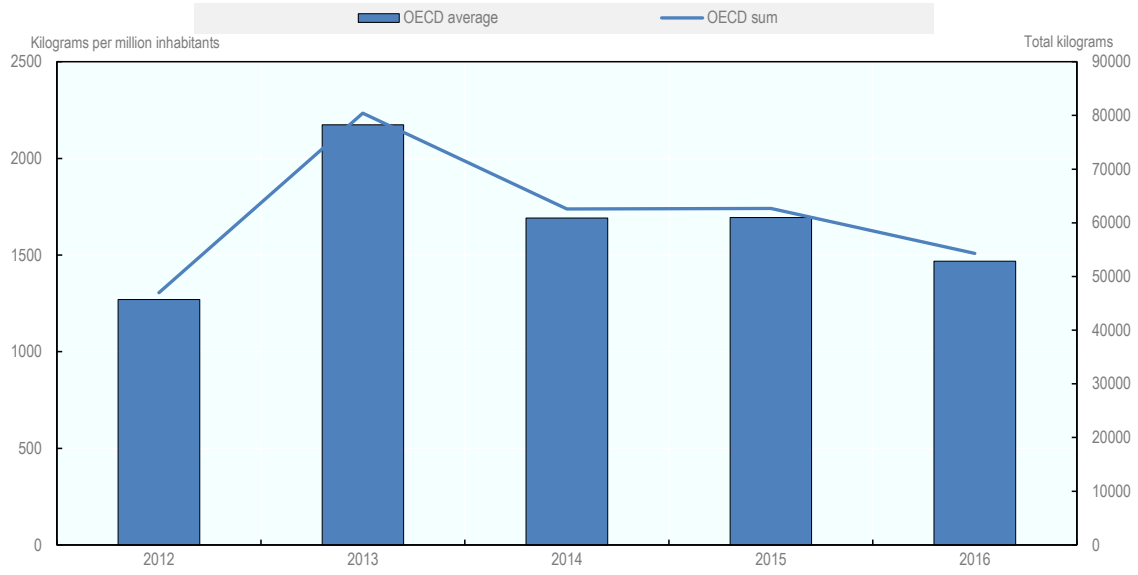
Capturing the size of the ***illicit opioids market*** is very difficult. Seizures of drugs are one way of approaching it, but important limitations should be noted when interpreting this data. For instance, seizures depend on law enforcement, customs regulations and capacity across countries. Countries can be producers or transit countries, not necessarily consumers of the seized opioids. Between 2012 and 2016, opioids seizures have been relatively stable in OECD countries – particularly in the last three years (see Figure 3.2) – with 2013 as the year with the highest record of over 80 000 kilograms seized in total and 2012 with the lowest level, with almost 47 000 kilograms.

Figure 3.2. Trend in kilograms of opioids seized in OECD countries 2012-16



Note: The blue line refers to the right vertical axis and the bars to the left vertical axis.
Source: (UNODC, 2018[29]).

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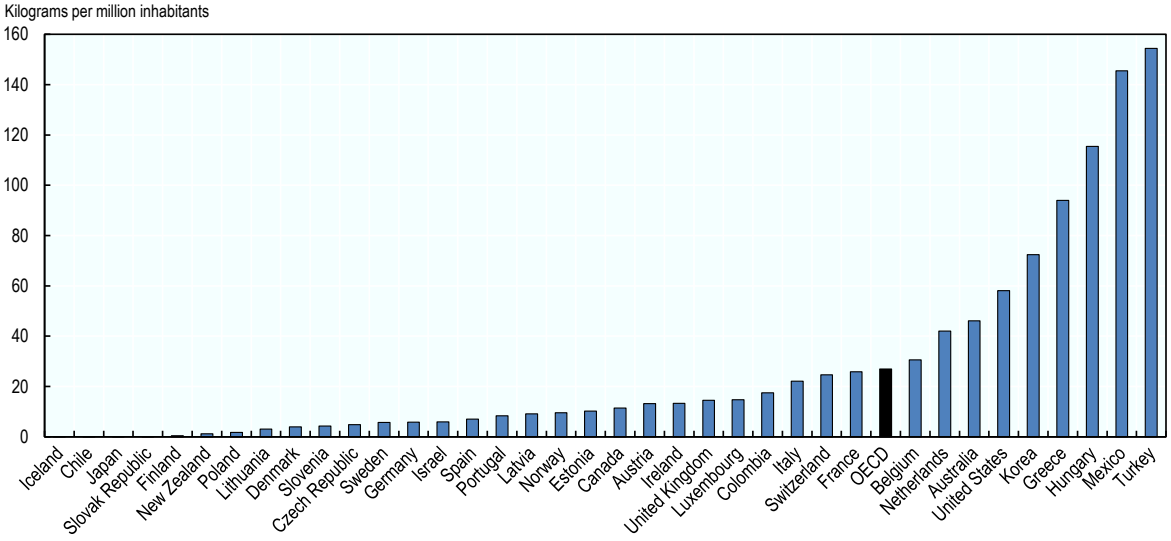
Taking the average of seizures per million inhabitants between 2012 and 2016 (see Figure 3.3), Turkey, Mexico, Hungary, Greece, Korea, United States, Australia, Netherlands and Belgium are above the OECD average. Comparing the periods of 2013-14 and 2015-16, Mexico, Korea, France, Luxembourg, Colombia, Austria and Canada have increased their opioids seizures, according to this indicator, and Turkey, Hungary, Greece, United States, Australia, Netherlands and Belgium have decreased.

Figure 3.3. Average annual kilograms of opioids seized per million inhabitants in OECD countries 2012-16



Source: (INCB, 2018[28]).

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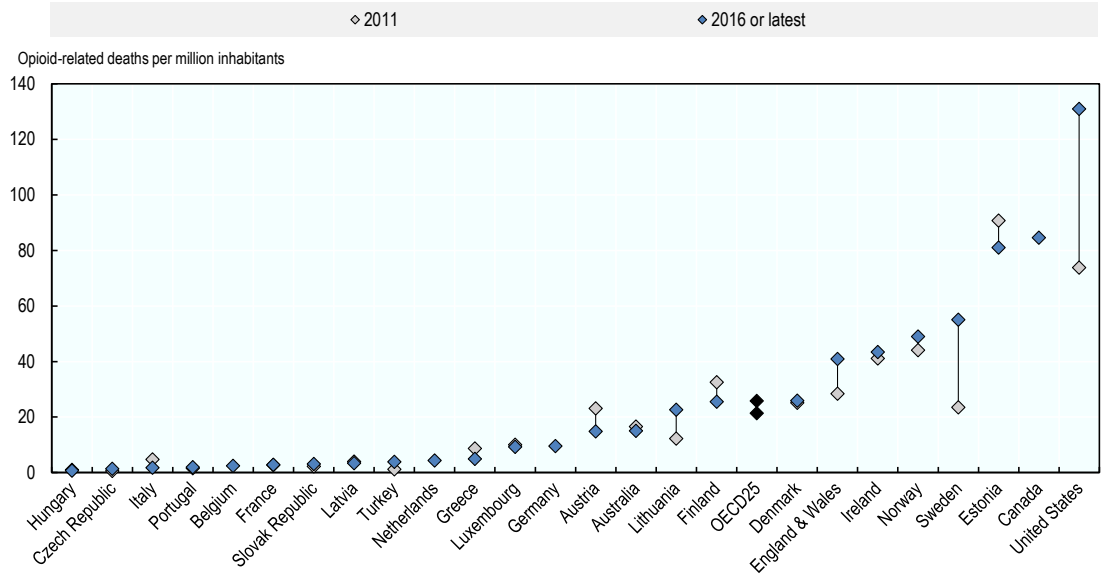
Opioid-related deaths (ORD) is a key indicator that reflects the impact of problematic use on population health and, at the same time, how health systems and other related government services are performing in this area. In 25 OECD countries for which data is available, the average of ORD has increased by 20% in recent years (see Figure 3.4). Among the countries above the average, the United States, Canada, Sweden, Norway, Ireland, and England & Wales have seen increasing trends.

Figure 3.4. Opioid-related deaths per million inhabitants, 25 OECD countries, 2011-16



Note: Countries ranked by latest year with available information.
Source: EMCDDA for European countries and country responses to ORD data questionnaire.

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Men represent the largest share of ORD in Europe, accounting for three out of four deaths in the last five years for which information is available (see Table 3.1).

Table 3.1. Gender distribution of opioid-related deaths in European countries with data, 2012-16

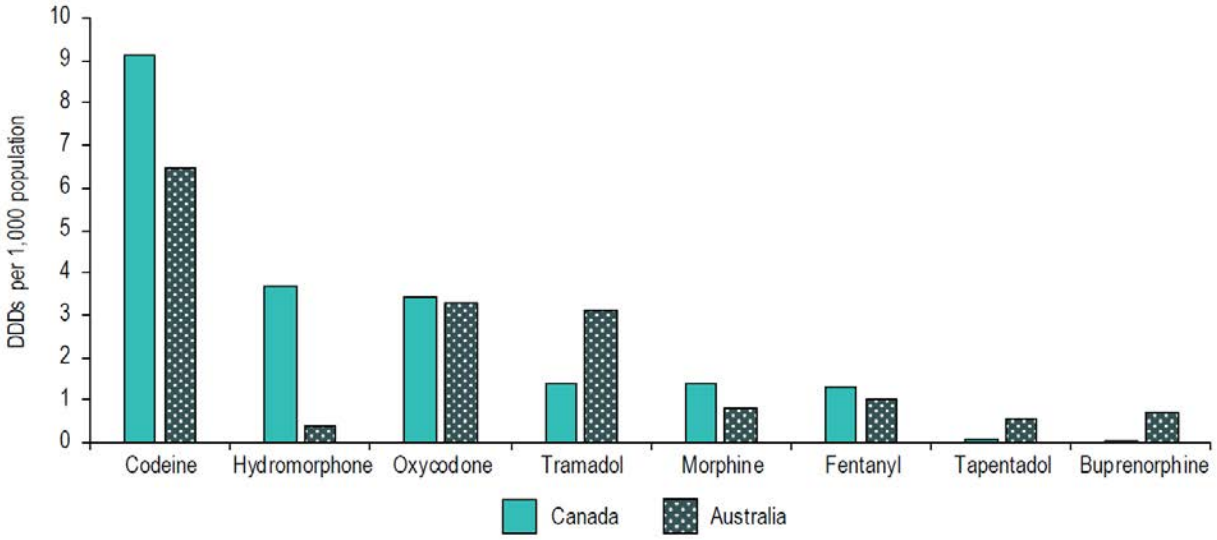
	2012	2013	2014	2015	2016
Number of countries	18	18	19	18	14
Male deaths	1 494	3 095	3 445	3 612	1 219
Female deaths	412	1 022	1 117	1 218	297
Total deaths	1 906	4 117	4 562	4 830	1 516
M/F ratio	3.63	3.03	3.08	2.97	4.10
% males	78.38%	75.18%	75.52%	74.78%	80.41%

Note: 2012 and 2016 does not include the UK, which represents 36-40% of total deaths in the other years.
Source: EMCDDA.

The opioid crisis has unfolded in different magnitudes across OECD countries. For instance, in Australia there were 1 119 opioid-induced deaths. More than 900 of these included mention of prescription opioids. After adjusting for age, there was a 62% rise between 2007 and 2016 (from 2.9 to 4.7 deaths per 100 000 people) but it is still lower than the peak in 1999. The rate in men was also 2.1 times as high as for women (AIHW, 2018[26]). The majority of these deaths (76%) were attributable to prescription opioids. Figure 3.5

compares the data on prescription opioids between Australia and Canada in 2017, showing that codeine ranks first in both countries, hydromorphone plays a larger role in Canada, and that tramadol and buprenorphine are more common in Australia (CIHI, 2018[30]).

Figure 3.5. Number of defined daily doses dispensed of prescription opioids Australia and Canada, 2017

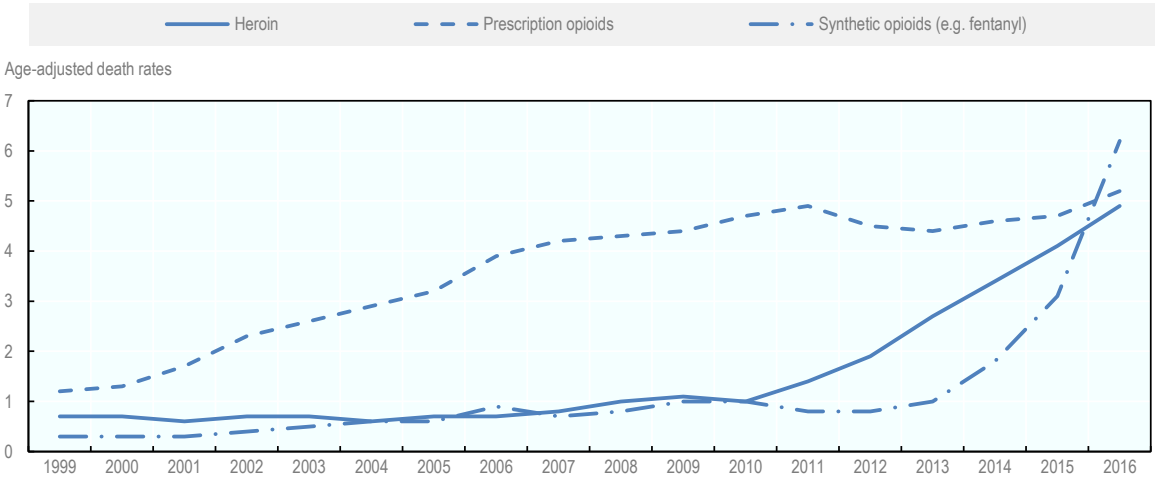


Note: DDD – daily defined dose.
Source: (CIHI, 2018[30]).

In Canada, there were 10 337 ORD between January 2016 and September 2018, with death rates increasing from 8.4 per 100 000 population in 2016 to 11.1 in 2017 and 11.8 in 2018. Canada registered 4 034 apparent opioid-related deaths in 2017, 3 017 in 2016 and 3.286 between January and September 2018. Among these deaths, around 73-74% involved fentanyl or its analogues, and the great majority were accidental deaths (Special Advisory Committee on the Epidemic of Opioid Overdoses, 2019[31]). In relation with years-of-life-lost, life expectancy at birth was analysed in British Columbia, showing that life expectancy decreased by 0.38 years from 2014 to 2016, and fatal drug overdoses (the majority involving opioids) accounted for 32% of the decrease (Ye et al., 2018[32]).

In the United States, 399 230 people have died from an opioid overdose between 1999 and 2017, while in 2015-17 life expectancy fell for the first time in more than 60 years largely as a result of the opioid crisis. Moreover, prescription rates appear to be higher where labour force participation is lower, showing that the dislocation of opportunities is also associated with the opioid crisis (OECD, 2018[33]). The cost of the opioid drug epidemic in 2015 was USD 504 billion or 2.8% of GDP that year, showing the great economic impact of the crisis (Council of Economic Advisers, 2017[34]).

Figure 3.6. Overdose deaths involving opioids, by type of opioid, United States, 1999-2016



Source: (CDC-NCHS, 2018[35]).

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A particularly relevant group of the population are pregnant women and new-borns. Opioid use among pregnant women is associated with the neonatal abstinence syndrome (NAS), which refers to a postnatal opioid withdrawal syndrome that can occur in 55 to 94% of new-borns (McQueen and Murphy-Oikonen, 2016[36]). In the United States, the use of opioids among pregnant women has been rising, affecting more women who are non-Hispanic White, with less educational and income level, and who have health insurance coverage. In addition, pregnant opioid-polydrug users are likely to report past-year anxiety/depression and are also most likely to report past alcohol/drug use treatment, reflecting the important role played by mental health in the crisis (Metz et al., 2018[37]).

3.2. Factors underpinning the development of the opioid crisis

The current opioid crisis has been caused by the co-occurrence of several factors over the years, both from the supply and demand sides. The main determinants of the crisis can be summarised into four factors, as follows.

3.2.1. Increased opioids prescription and over-prescription in health systems

The use of opioids is useful for pain management, particularly for acute pain, which can be derived from many sources including poor or unstable material conditions of life and mental health issues, not just physical symptoms. Pain was a neglected issue before the 1990s, with health care professionals focussing more on whether they can cure or treat the underlying problem, rather than manage symptoms that affect the well-being of the person involved. The factors that caused this neglect have, however, changed over time.

Uncorroborated claims about the safety and risks of prescription opioids

In 1980, a letter published in a prestigious journal (Porter and Jick, 1980[38]) concluded that “despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction”. A bibliometric analysis (Leung et al., 2017[39]) revealed that it was ‘heavily and

uncritically cited as evidence that addiction was rare with long-term opioid therapy'. A second study (Portenoy and Foley, 1986[40]), which analysed a sample of only 38 patients, described opioid maintenance therapy as a safer and 'more humane' alternative for patients with intractable non-terminal pain and no history of problematic drug use. Despite these reports, which were widely accepted by the medical community, high-quality evidence of opioids' safety in terms of addictive effects did not exist at the time (Christie et al., 2017[41]). Given the lack of evidence about adverse effects, in the 1990s pain was called the 'fifth vital sign' encouraging health care professionals to assess pain more widely and urged more aggressive use of opioids for chronic non-cancer pain. This contributed to create a culture that was more prone to the use of opioids (Kolodny et al., 2015[42]).

Opioid manufacturers and advocacy groups have influenced pain management

Opioid manufacturers have played a significant role in escalating opioid prescription. In the United States, manufacturers have funded pain advocacy organisations, medical societies, clinical practice guideline development efforts, and medical education (US Senate, 2017[43]). They have also developed marketing campaigns spreading the message that opioids were low-risk medications and effective at managing a wide range of chronic pain conditions (Van Zee, 2009[44]). Subsequently, advocacy groups have petitioned for the prescription of opioids in several ways, including issuing guidelines recommending the use of opioids for pain management and opposing efforts to monitor and regulate opioid over prescription (Whyte, Mulvihill and Wieder, 2016[45]) (see Box 3.1).

Box 3.1. Influence of prescription opioid manufacturers in the United States

The influence of pharmaceutical manufacturers on pain management advocacy groups and prescribers has been considerable. During the late 1990s and the 2000s, opioids manufacturers conducted marketing campaigns, targeted mainly at physicians and patients, downplaying the problematic effect of opioids arguing that concerns over dependence and other dangers from the drugs were overstated (Van Zee, 2009[44]).

Opioid manufacturers have directed considerable amounts of financial resources to different actors involved in the market of prescription drugs. A report from the United States Senate Committee on Homeland Security and Governmental Affairs found that opioid manufacturers contributed USD 9 million to 14 third-party advocacy organisations between 2012 and 2017, and have destined USD 1.6 million in payment to physicians affiliated with these advocacy groups (McCaskill, 2018[46]). The report signals that initiatives from the advocacy groups often echoed and amplified messages favourable to increased opioid use. Another study found that physicians who received any opioid-related payments from industry had 9.3% more opioid claims compared to physicians who received no such payments, and that each additional industry-sponsored meal received was associated with an increase of 0.7% in opioid claims (Hadland et al., 2018[47]). Along this line, a study reported that between 1 August, 2013, and 31 December, 2015, there were USD 39.7 million in non-research-based opioid marketing distributed to 67 507 physicians across 2 208 US counties and found that increased county-level opioid marketing was associated with elevated overdose mortality one year later, an association mediated by opioid prescribing rates (Hadland et al., 2018[47]).

Recently, there has been a widespread negative reaction to the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain. One study (Lin et al., 2017[48]) shed light on the correlation between the opposition to the guideline and the financial relationships with opioid manufacturers, concluding that 'opposition to the guideline was significantly more common among organisations with funding from opioid manufacturers than those without funding from the life sciences industry'.

In 2007, one of the main opioid manufacturers pled guilty in federal court to overstating the benefits and understating the dependence risk of an extended release formulation of oxycodone. The settlement of USD 600 million is one of the largest in history with a drug company (US Western District Court of Virginia, 2007[49]). Similarly, in March 2019 the same manufacturer reached a USD 270 million settlement with the state of Oklahoma to avoid going to a state court trial over the company's role in the opioid crisis. Despite the several government and class action settlements against opioid companies in the past 15 years, opioid litigation has not come near the USD 13 billion-a-year opioid industry (Haffajee and Mello, 2017[50]).

Poor opioid prescribing practices and insufficient education in pain management

Opioids overprescribing is considered one of the most important root causes of the crisis. In the United States alone, there were 240 million opioid prescriptions dispensed in 2015, nearly one for every adult in the general population (Makary, Overton and Wang, 2017[51]). Among overprescribers, three group of doctors can be identified: physicians who appear to have a doctor–patient relationship with people who deceive them into treating them as patients in pain (e.g. "doctor shopping strategies"); physicians who treat patients in pain but with high doses of opioids; and doctors who abuse their privileges and knowingly arrange for opioids to be taken by people who don't necessarily need them (e.g. 'pill mills') (Reidenberg and Willis, 2007[52]). In addition, health care purchasers have generally failed to influence or regulate the prescription and use of opioids. In the United States, for example, a recent study found that many insurers failed to apply "utilisation management" rules (e.g. prior authorisation, quantity limits, and cost sharing) to discourage opioid overuse and encourage safer and more effective alternatives (Lin et al., 2018[53]). Another study highlighted the policy adopted by some payers (including Medicaid) that encouraged doctors to prescribe methadone due to its low cost as a risk factor for overprescribing (Webster et al., 2011[54]).

Medical education in pain management, opioid prescribing and screening for substance use disorders has been inadequate in institutions and medical schools (Chiu et al., 2018[55]; Webster et al., 2017[56]). While high-quality evidence on the direct relationship between insufficient physician education and the opioid crisis is still lacking, inadequate education has been hypothesised to influence opioid overprescribing (Christie et al., 2017[41]).

Limited alternatives for chronic pain management and lack of insurance coverage

Alternative treatments for pain management, such as non-steroidal anti-inflammatory drugs (NSAIDs), gabapentoids, antidepressants and muscle relaxants, are not always effective. Opioid analgesics are often used when these other treatments have not worked (Kroenke and Cheville, 2017[57]). Unfortunately, research & development on non-addictive treatments for chronic pain has not received the same priority as other areas (Charumilind et al., 2018[58]). In addition, non-pharmacological interventions such as exercise, multidisciplinary rehabilitation, acupuncture, cognitive behavioural therapy, and mind-body practices have been associated with durable slight to moderate improvements in function and pain for specific chronic pain conditions, but these are less utilised or lacking insurance coverage (Skelly et al., 2018[59])

Defective approach to mental health and opioid use

Mental health conditions and their treatments can interact with opioid use, but these interrelations are not always appropriately addressed. For instance, in the United States, 18.7% of all patients with mental health conditions receive 51.4% of the total opioid prescriptions distributed each year, meaning that having a mental health disorder was associated with a two-fold greater use of prescription opioids (Davis et al., 2017[13]). Risk for opioid overdose is higher for individuals with depression and prescribed opioids, while longer duration of benzodiazepine use is associated with drug overdose. Notably, antidepressant use for

more than 90 days is associated with reduced odds of overdose for persons with depression (Bair and Bohnert, 2015[60]).

3.2.2. A dynamic illicit drugs market has fuelled the crisis

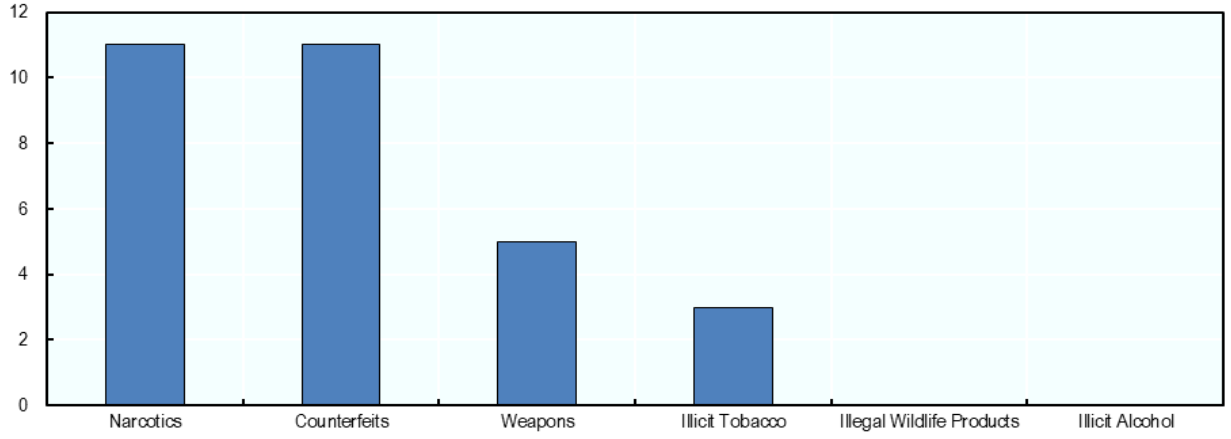
The illicit trade in drugs has been growing globally, boosting supply. Opioids, including the clandestine development of synthetic chemicals, like fentanyl and its analogues, are a significant driver of this growth.

High purity and increasing availability of illicit opioids at a low cost

The current opioid crisis has also been linked with the increased availability and purity of opiates (e.g. heroin) at lower prices. Total global opium production in 2017 was the highest estimate recorded by UNODC since it started estimating global opium production. Opium prices fell in Afghanistan (the largest producer in the world) by 47% from December 2016 to December 2017 and the price of high-quality Afghan heroin decreased by 7% over the same period (World Drug Report, 2018[8]). In the United States, heroin purity has increased by almost 40% from the 1980s to 2000, while its price has decreased, going from over USD 3 200 per gram in 1981, to just over USD 600 per gram in 2012 (US Drug Enforcement Administration, 2017[61]). Clandestinely produced fentanyl and fentanyl analogues are newcomers in the opioids landscape, where, for instance, carfentanil seizures had a tenfold increase and fentanyl a fourfold increase in 2016 (World Drug Report, 2018[8]).

Small shipments constitute a relatively new source for trafficking drugs, where online sales and shipment via the postal service or express consignment appear to be driving to some extent the increases (OECD, 2018[62]). Figure 3.7 shows that narcotics top the list of the most frequent type of seizures among 15 OECD countries.

Figure 3.7. Most frequent types of seizures of small shipments



Note: The figures on the left scale correspond to the number of countries that mentioned the most frequent types of seized illicit goods.
Source: Based on fifteen country responses to OECD Survey (OECD, 2018[62]).

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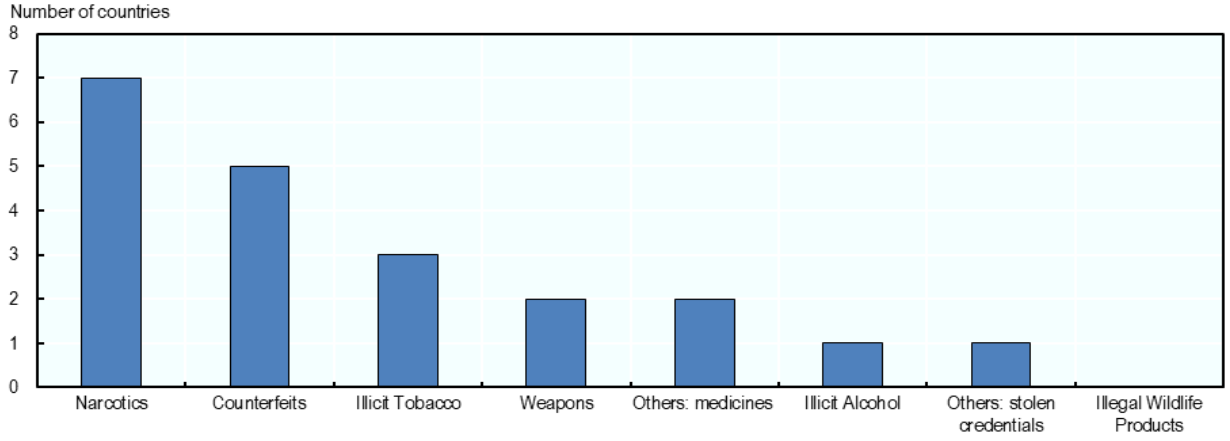
The darknet is as a relatively new market for accessing opioids and drugs (Box 3.2). According to a recent survey to 15 OECD countries, the most commonly seized products via the darknet were narcotics, confirming the use of small shipments to spread risk across a wider range of shipments and to avoid large-scale seizures of illicit narcotics (Figure 3.8).

Figure 3.8. Most common forms of illicit trade via "darknet"



Note: The left scale corresponds to the number of countries that mentioned the types of illicit goods most commonly seized involving the "darknet".
Source: Based on fifteen country responses to OECD Survey (OECD, 2018[62]).

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Box 3.2. The "darknet" as a small but growing source for illicit drugs, including opioids

Darknet is a term associated with the use of online platforms that anonymise the identities of users and vendors. It shares many characteristics with legal online marketplaces, including the provision of digital open markets in which geographically dissimilar vendors advertise goods and customers provide scores to rank sellers´ product quality and service. Untraceable crypto-currencies are often used to avoid financial scrutiny, which is why they are also called "cryptomarkets" (Finklea, 2017[63]).

A darknet study conducted by European agencies (EMCDDA and Europol, 2017[64]) found that more than 60% of all listings on five major darknet markets worldwide up to August 2017 were related to the illicit sale of drugs. They also estimated that world drug sales on the darknet from November 2011 to February 2015 amounted to roughly EUR 44 million per year. However, in early 2016 drug sales were between EUR 150 million and EUR 270 million per year (Kruithof et al., 2016[65]). Regarding the darknet market for opioids, US-based vendors comprise 36% of global opioid transactions, followed by the UK (16%), France (14%), Germany (12%), the Netherlands (9%) and Australia (9%) (Martin et al., 2018[66]).

However, the sale of online drugs remains comparatively small. The global darknet drug market is estimated to account for no more than 0.1–0.2% of the combined annual drug retail markets of the US and the EU (World Drug Report, 2018[8]). The online Global Drug Survey, based on a non-representative convenience sample of around 100 000 self-selected people in over 50 countries, found that the proportion of Internet users who purchased their drugs via the darknet rose from 4.7% in 2014 to 9.3% in 2018. The highest proportions of Internet users reporting the purchase of drugs via the darknet were found in North America, Oceania and Europe (Winstock et al., 2018[67]).

Polysubstance use and problematic use

Polysubstance use combining different types of opioids with benzodiazepines, alcohol (e.g. binge drinking), psychoactive prescriptions (perhaps due to mental health issues), and "top up" opiate in addition to

prescriptions are associated with fatal overdoses (Frisher et al., 2012[12]). Early polysubstance use (e.g. youth) often sets the stage for a later transition from medical to problematic use of opioids prescribed for pain. However, polysubstance use is a problem across the lifespan. For example, in 2010, the percentage of emergency department visits in the U.S. that involved prescription opioids and alcohol was highest among persons aged 30-44 years (20.6%) and 45–54 years (20.0%). Among deaths due to prescription opioids, persons aged 40–49 years (25.2%) and 50–59 years (25.3%) had the highest percentage of alcohol involvement (Jones, Paulozzi and Mack, 2014[68]).

Prison and jail post-release period

Prisons and jails are a common factor in opioid related deaths and overdoses. In fact, prisons present a striking concentration of people with OUD. While the prevalence rate of OUD in Europe is less than 1% among the general public, the rate reaches 30% in the prison population. Given that heroin-related fatal overdoses occur mainly after a period of abstinence, opioid users are particularly at risk during the post-release period. The highest risk of fatal overdose episodes is registered during the first two weeks after release, where the risk of overdose death increases more than sevenfold (Strang et al., 2016[69]).

3.2.3. Poor treatment and actions to minimise the negative consequences for OUD patients

Several interventions have proven to be effective to treat OUD. However, there are barriers to their use, both in health systems and in other sectors (e.g. criminal justice). This lack of access to treatment has contributed to the crisis.

Barriers to access medication assisted therapy

There is strong evidence showing that medication assisted therapy (MAT) significantly reduces the risk of mortality. Compared with patients receiving MAT, untreated patients have 2.2 to 3.2 times higher risk of all-cause mortality and 4.8 to 8.1 times higher risk of overdose mortality. Retention in MAT of over 1-year is associated with lower mortality rate than that with retention of less than one year, meaning that long-term care is beneficial for patients (Ma et al., 2018[70]; Sordo et al., 2017[71]). Barriers for MAT access can be classified into financial/economic aspects and governmental support (e.g. insufficient funding, lack of non-economic governmental support, economic crisis); formularies (e.g. reimbursement issues, insufficient service provision, shortage of palliative care experts, inadequate integration of MAT into primary care); education and training (e.g. insufficient under-, post-graduate and continuing education); and societal attitudes (e.g. fear, lack of awareness, inadequate information, stigma) (Larjow et al., 2016[72]; Kolodny and Frieden, 2017[73]; Maksabedian Hernandez, 2017[74]).

Predominance of abstinence-only rehabilitation therapies

In the United States and Canada, rehabilitation programmes are still mainly abstinence based (Annan et al., 2017[75]). More specifically, in the United States only 8-9% of all substance treatment facilities between 2006 and 2016 had MAT programmes certified by SAMHSA. The proportion of all clients receiving methadone ranged from 23-30% and between 1-5% for buprenorphine in the same period (Substance Abuse and Mental Health Services Administration, 2017[76]). This happens despite evidence showing that opioid users who are treated only with psychological support are at twice greater overdose death risk than those who receive opioid agonist pharmacotherapy (Pierce et al., 2016[77]).

Inadequate access to evidence-based harm minimisation interventions

Harm minimisation interventions such as needle and syringe programmes (Abdul-Quader et al., 2013[78]) and naloxone availability for overdose management (Chimbar and Moleta, 2018[79]) have substantive

evidence supporting their effectiveness. Similar is the situation for supervised drug consumption rooms (EMCDDA, 2018[80]) , where some countries have also implemented them. Despite this, access to these interventions has been lacking or could be improved in many countries. For instance, inadequate responses by people who witness overdose episodes and lack of access to naloxone has contributed to the increase in opioid related deaths. This aspect is critical, since more than half of all fatal overdoses occur in the victim's home and more than half of deaths occur with another person present. It is estimated that one in four fatalities could have been prevented if the witness had acted differently (Frisher et al., 2012[12]; Strang et al., 2016[69]).

3.2.4. Social and economic conditions contributing to the crisis

The environment in which people live is linked to drug use, including the consumption of opioids. Social and economic conditions, particularly of vulnerable groups of the population, have contributed to the crisis.

Unemployment appears to be linked to the opioids issue

A recent study in the United States found that as county unemployment rates increase by one percentage point, the opioid death rate per 100 000 rises by 3.6% and the opioid overdose emergency department visit rate per 100 000 increases by 7% (Hollingsworth, Ruhm and Simon, 2017[81]). The relationship between problematic opioid use and unemployment, however, is very complex and some studies suggest a reverse causality, claiming that it is problematic use that leads to an increase in unemployment. For instance, Krueger (2017[82]) indicates that the increase in opioid prescriptions between 1999 and 2015 could have accounted for 20% of the decline in the prime-age male and 25% of the prime-age female labour force participation rate over those years. Another study (Gitis and Soto, 2018[83]) came to similar conclusion linking a decline in labour force participation in the United States due to OUD.

Economic recession has also been correlated with an increase in teenage illicit drug use (Arkes, 2007[84]) and in self-reported substance-use disorders related to analgesics (including opioid and non-opioid forms) (Carpenter, McClellan and Rees, 2017[85]). Economic recessions and unemployment influence illegal drug use through three mechanisms (Nagelhout et al., 2017[86]). First, people may use drugs to cope with the psychological distress caused by unemployment; second, drug use could be motivated by the increase in time available; and third, drug use could be motivated by the social exclusion incurred as a consequence of the loss of social status caused by unemployment.

Lack of housing affecting the most vulnerable population

The evidence on the relationship between drug use and housing condition has explored primarily the influence of the former on the latter, identifying drug use as one of the causes of homelessness and unstable housing (Zerger, 2012[87]). Nonetheless, the literature available on the impact of housing conditions on drug use highlights that the opposite causal relationship also holds true, with an unstable housing situation increasing problematic use of opioids and other drugs. Unstable housing prevents people who use drugs from accessing treatment, both by discouraging people to engage with health services (Burkey, A. Kim and Breakey, 2011[88]) and by posing practical obstacles, such as lack of medical insurance. Drug and alcohol use is sometimes a necessary social ritual to be accepted among the homeless community (Zerger, 2012[87]). Unstable housing negatively affects treatment retention rates and effectiveness. Finally, it also exacerbates psychiatric symptoms, which are often a co-occurring condition affecting many drug users (Fox et al., 2016[89]).

Social stigma as a relevant barrier for prevention and recovery

The role of stigma towards people who use drugs is considered as a barrier to individual care/treatment, as well as a barrier to societal support for broader policy shifts. Research indicates that stigma contributes

to individuals poor mental and physical health, non-completion of substance use treatment, delayed recovery and reintegration processes, and increased involvement in risky behaviour (e.g. needle sharing) (Livingston et al., 2012[90]). Stigma themes include individual perceptions of opioid dependence, community perceptions of opioid dependence, blame as a stigmatising factor, language surrounding opioid use, and treatment experience (Cooper and Nielsen, 2017[91]).

Box 3.3. Exploring the factors associated with opioid-related deaths in OECD countries

There have been few studies exploring the magnitude of the opioid crisis at the international level, and much less revising the potential factors related to its impact on population health across countries. In this context, an assessment of whether a relationship exists between a range of societal factors and opioid-related deaths (ORD) rates in 25 OECD countries was conducted.

Methods included using national level data for variables such as household income and savings rates, unemployment, poverty, GDP per capita, divorce rate, health and social spending, incarceration rates and country governance indicators. A series of econometric techniques were applied in order to fit the best models that could identify the factors associated to ORD. Finally, fixed regression analysis was performed with the most suitable variables identified through econometric criteria and literature review.

The findings were not sufficiently robust to draw meaningful scientific conclusions nor policy considerations. In particular, the differences of ORD data collection across countries limits the analysis, so relevant efforts should be placed on improving the information infrastructure to better capture drug-related deaths and other harms data, including incidence of problematic opioid users, health services utilisation, recovery rates, etc.

4 Policies to address the opioid crisis and prevent opioid-related harms

This section outlines the main policy areas that countries can consider for addressing the opioid crisis. As explained in previous sections, problematic use of opioids is a complex phenomenon, influenced by the combined effects of multiple interconnected factors. For this reason, the policy response is likely to require interventions cutting across sectors and policy fields. In order to assist countries in addressing opioid use, and identify a clear set of effective policy actions, a preliminary policy framework has been created (see Table 4.1).

The policy framework was developed following the range of actions and policies identified in reports by the Government of Canada (Government of Canada, 2018[92]), EMCDDA (EMCDDA, 2017[93]), the US Presidential Commission about the opioid crisis (Christie et al., 2017[41]), and both the literature review and interviews with experts. It will be further enriched with comments from OECD country delegates, so the current framework should be considered a preliminary version. The framework draws attention to sectors beyond health systems, such as social and law enforcement sectors. It thus emphasises the necessity of combined policy action. Finally, further good practices from OECD countries will be identified to complement the current version of the paper.

Table 4.1. Policy framework to address opioids use and harms

	PRESCRIPTION OPIOIDS	ILLICIT OPIOIDS
1. HEALTH SYSTEM		
Prevention	Patient and family literacy, general population awareness and stigma reduction	
	Prescription support and surveillance	
	Regulation of opioids marketing and financial relationships	
Opioid use disorder treatment and harm minimisation	Medication assisted therapy within long-term care programmes	
	Coordination for early detection and linkage with specialised services	
	Needle and syringe programmes	
		Medically supervised consumption centres
2. SOCIAL POLICY		
Housing	Housing services	
Employment	Employment support services	
Recovery services	Social services/Residential rehabilitation	
3. REGULATION AND ENFORCEMENT		
Law enforcement practice		Customs interventions
		Internet-darknet illicit trade of opioids
	Prevention of medication diversion	

	PRESCRIPTION OPIOIDS	ILLICIT OPIOIDS
Criminal justice system	Law enforcement officials interventions	
	Drug treatment interventions	
	Laws around personal use and possession of drugs	

This framework is organised into three dimensions, which apply to both prescription and illicit opioids. Within each dimension, there are policy areas that can relate to both subgroups of opioids or to just one. The dimensions are the following:

- Health system interventions: including prevention, treatment, harm minimisation and health financing issues that are designed and implemented mainly in the health sector.
- Social policy: covering housing, employment and recovery support services for people with OUDs and their families.
- Legal system and law enforcement: interventions around international cooperation, customs, and the criminal justice system, including police and investigation.

In addition, the area of information and knowledge generation was identified as a key policy lever. These are cross-cutting issues covering data, information and research that could contribute to better decision making at different levels of the health system, social affairs and law enforcement institutions.

In order to gain a more comprehensive understanding of countries' response to problematic opioid use, a survey was administered to OECD countries. The 20 countries that responded show a mixed picture with respect to the development of policies and actions. Table 4.2 provides an overview of the main policy initiatives identified through the questionnaire in the dimensions of health system and social policies. The remainder of this section discusses these initiatives in more detail, complementing it with an extensive review of academic articles, grey literature and national reports.

Table 4.2. Health system and social policies for opioid control identified from the survey responses – 20 OECD countries

	AUS	CAN	CHE	COL	CZE	DEN	DEU	EST	FRA	IRL	ITA	JPN	KOR	LTU	LUX	LVA	NOR	SWE	SVN	USA
HEALTH SYSTEM DIMENSION																				
Clinical guidelines	●	●			●	●	●		●	●	●	●		●		●	●	●	●	○
Stewardship programmes	●	○		●		●	○			●		●				●	●	○	●	○
Medical treatment	●	○	●	●	●	●	●	●	●	●	●			●	●	●	●	●	●	○
Disciplinary actions for physicians overprescribing	○	○	○			●	●	●		●	●				●	●	●	●		○
Self-help and mutual aid groups	●	○	○	●		●	●	●	●	●	○		●		●	●	●	●	●	○
Needle/syringe programmes	●	○	○	○	●	○	○	●	●	●				●	●	●	●	○	●	○
Drug consumption rooms	○	○	○			○	○		●						○		○			
SOCIAL POLICY DIMENSION																				
Residential rehabilitation	●	○	○	●	●	●	●	●	●	●	●		●	●	●	●	●	●	●	○
Social reintegration support	●	○	○	●	●	●	●	●	‣	●	●	●	●	●	●		○	●	●	○

Level of implementation:
● = Nation wide
○ = Sub-national
‣= Single / group of providers
* Stewardship programmes aims at promoting judicious use of opioids and at avoiding over-prescription. They generally include one or more of the following activities: i) creation of multidisciplinary teams composed by experts in pain management, clinical pharmacists, etc.; ii) training of prescribers; iii) review of prescribing practices and feedback; iv) use of prescribing tools as formulary with restricted prescribing of opioids or clinical computer systems.
** Support programmes, which may include behavioural and psychosocial interventions, education, and access to medicines (medication assisted therapy) such as naloxone (including take-home), naltrexone, methadone or buprenorphine, for instance, in emergency rooms (e.g. acute overdoses treatment), ambulatory care, etc.
*** Residential rehabilitation involves living in a treatment facility and following a structured care programme.
Source: OECD 2018 survey on opioids control.

4.1. Health system policies and interventions to address the needs of opioid use disorder patients and the population

Health system interventions include three main aspects: prevention initiatives -- targeted at the general population, high-risk people and families, prescribers, and industry; treatment, targeted at patients who suffer from an OUD; and interventions aimed at reducing the harm and negative consequences associated with opioid use or inappropriate use.

4.1.1. Prevention: changing behaviours of patients, providers, and industry practices

Patient and family opioid-related literacy, general population awareness and reduction of stigma

Primary prevention actions directed at patients and their families aim to improve opioid-related literacy, as patients commonly report not receiving sufficient information on the problematic potential of opioid analgesics and the consequences of abusing opioids (Hadden, Prince and Barnes, 2016[94]). At the same time, awareness initiatives serve to combat the stigma around opioid use, which represents a significant limitation to treatment access and social integration of people with OUDs (Olsen and Sharfstein, 2014[95]). A recent randomised controlled trial evaluated the effectiveness of an educational intervention (a one-page information sheet about hydrocodone-acetaminophen) and concluded that this strategy improved by 25% several, although not all, aspects of patient knowledge (McCarthy et al., 2015[96]).

Canada has emphasised on patient opioid literacy and awareness campaigns. Canada's initiatives include making warning stickers and patient information handouts mandatory with all opioids dispensed to Canadians at pharmacies or in doctors' offices (Health Canada, 2018[97]). Furthermore, the Canadian Government has supported summer festivals and post-secondary school orientation activities, as well as producing online interactive resources to help promote awareness on preventing opioid overdoses (Government of Canada, 2018[98]). In the UK, the initiative Opioids Aware (The Royal College of Anaesthetists and Public Health England, 2018[99]) is a web-based awareness resource, funded by Public Health England and hosted by the Royal College of Anaesthetists. The initiative includes a section targeted at patients, aimed to help them make an informed decision about starting opioid therapy, as well as to provide them with information on the opioid undesirable consequences.

In relation to stigma, one review (Livingston et al., 2012[90]) found evidence for interventions at three levels: self-, social and structural stigma. Self- stigma can be reduced through therapeutic interventions such as group- based acceptance and commitment therapy. Effective strategies for addressing social stigma include motivational interviewing and communicating positive stories of people with substance use disorders. For changing stigma at a structural level, contact- based training and education programs targeting medical students and professionals (e.g. police, counsellors) have shown to be effective.

Drug take-back actions constitute a viable strategy to reduce the harm associated with problematic use of prescription opioids, since often pills dispensed exceed the quantity prescribed (Maughan et al., 2016[100]; Kennedy-Hendricks et al., 2016[101]). Drug take-back programmes provide a way of facilitating the proper disposal of controlled substance medications, including opioids (Gray and Hagemeier, 2012[102]). Studies have shown positive impacts on patient awareness (Yanovitzky, 2016[103]) and have proven that such programmes collect a significant quantity of medications (Stewart et al., 2015[104]), but there is no evidence about the effects on inappropriate use or harms associated with opioid use.

Opioid prescription support and surveillance to improve provider practices

The development and use of *clinical practice guidelines* (CPG) to steer the appropriate use of prescription opioids, for instance for chronic pain, has been expanding. CPG mostly agree on several opioid risk mitigation strategies, including upper dosing thresholds; cautions with certain medications; attention to drug–drug and drug–disease interactions; and use of risk assessment tools, treatment agreements, and urine drug testing (Nuckols et al., 2014[105]). Reviews have shown positive results of CPG implementation, with smaller percentages of patients managed with high dose opioids; higher percentages of providersavoiding long-acting opioids for acute pain or in combination with benzodiazepines; and physicians more likely to use tools like drug screens in patients with substance use disorder. Similar findings occurred in emergency department and hospital CPG, showing declines in number and rate of opioid prescribing, lower average daily doses, and decreases in emergency department visits and deaths. However, the design of the studies were weak and these findings must be interpreted carefully (Haegerich et al., 2014[106]). More recently, the release of the Guideline for Prescribing Opioids for Chronic Pain of the Centers for Disease Control and Prevention in the United States was associated with a greater decline on the overall opioid prescribing rate when compared with the pre-guideline period from 23.48 to 56.74 average prescriptions per month (Bohnert, Guy and Losby, 2018[107]).

Across OECD, 15 countries have clinical opioid guidelines in place. Except for the United States, where opioid prescribing guidelines are developed at the national level and are implemented at a sub-national level, opioid CPG are generally implemented at a national level. In most cases, clinical guidelines focus specifically on the use of opioid medications for chronic pain. For example, the Canadian guidelines address opioids for chronic non-cancer pain and do not look at opioid use for acute pain, nor for patients with pain due to cancer or in palliative care, or those under treatment for opioid use disorder (Busse et al., 2017[108]). Similarly, the guidelines released in Germany by the German Pain Society (Häuser et al., 2015[109])address long-term opioid therapy for chronic non-cancer pain. Germany's guidelines represent a good example of evidence-based recommendations and included the participation of 26 scientific societies and two patient self-help organisations in their development.

Initiatives aimed at *training opioid prescribers* through specific evidence-based guidelines combined with educational initiatives, positively impact prescribing behaviours and lower inadequate treatment of pain (Stanek, Renslow and Kalliainen, 2015[110]). Accordingly, an opioid prescriber education programme among 2 850 clinicians licensed to prescribe opioid analgesics found an increase in correct responses to knowledge questions both immediately after the programme (60% to 84%) and two months later (60% to 69%). Among clinicians, 67% reported increased confidence in applying safe opioid prescribing care and 86% reported implementing practice changes (Alford et al., 2015[111]). Academic detailing, a structured educational strategy of visits to health care providers by trained professionals who can provide tailored training and technical assistance, has shown promising results in reducing opioid dosage and in opioid treatment discontinuation (Zolekar et al., 2018[112]). Furthermore, some OECD countries have recognised addiction medicine as a full medical specialty. For example, over the last years, specialisation programmes in addiction medicine were created in Norway (Welle-Strand, 2015[113]), Australia (Haber and Murnion, 2011[114]) and the Netherlands (De Jong, Luycks and Delicat, 2011[115]).

Twelve OECD countries have implemented stewardship programmes, either at a national (8) or sub-national (4) level. Stewardship programmes aim at promoting judicious use of opioids and generally include training of prescribers and review of prescribing practices and feedback. In the province of Ontario, Canada an opioid stewardship programme for primary care providers has been available since 2014. The programme, funded by the Ministry of Health and Long Term Care, involves weekly training sessions, which include both a didactic lecture and a de-identified patient case presentation, with the aim of promoting safe and effective chronic pain management, as well as treatment follow-up (University Health Network, 2018[116]). In Australia, the Chief Medical Officer wrote to general practitioners who were identified in the top 20% of opioid prescribers for their region asking them to reflect on their prescribing practices.

There is a website available to support GPs containing information and links to external resources regarding the use and safety of opioids in clinical practice (Department of Health, 2019[117]).

Box 4.1. Choosing Wisely® recommendations to promote rational use of opioid medications

Choosing Wisely® is an international health educational campaign aimed at improving doctor-patient relationships and reducing unnecessary health care by pulling evidence-based medicine into the public domain (ABIM Foundation, 2018[118]).

The campaign was launched in 2012 and it is currently implemented in eleven OECD countries (Levinson et al., 2015[119]). Some countries have put in place educational campaigns specifically targeted at reducing problematic opioid use and over-prescription.

- In the United States, the City of Philadelphia launched a campaign involving 1 300 physicians who were visited by Department representatives for brief discussions to gauge their awareness of opioid guidelines, understand their situations and re-enforce safe prescribing with a packet of resources (ABIM Foundation, 2018[120]).

In March 2018, Canada launched the Opioid Wisely campaign (Choosing Wisely Canada, 2018[121]). The campaign aims to reduce harms associated with opioid overprescribing through two main strategies: 1) providing information resources to help patients have informed conversations with their physicians about safe options for managing pain; 2) providing clinicians with recommendations for when the use of opioids should not be first line therapy. So far, a set of 15 specialty-specific recommendations are available.

Prescription monitoring programmes (PMP) consist of an electronic database that tracks controlled medicines prescriptions providing health authorities with timely information about prescribing and patient behaviours. Evaluations suggest that they have a positive impact in controlling problematic use by influencing both the health care and law enforcement systems. It has been shown that the use of data collected through PMP reduces the time spent by law enforcement authorities in investigating irregularities (GAO, 2002[122]). A review summarised that PMP effectively reduce "doctor shopping" strategies, and prescription substances problematic use while improving physicians' prescribing behaviour (Worley, 2012[123]). More recent studies in the United States have shown that problematic opioid use increased more slowly in states with PMPs than in states without it (Reifler et al., 2012[124]; Rutkow et al., 2015[125]; Patrick et al., 2016[126]) and that states with more robust PMP have fewer prescription opioid overdose deaths (Pardo, 2017[127]). Moreover, the comprehensive legislative mandates to use PMP implemented during 2011-15 were associated with a 6–9% reduction in opioid prescriptions with high risk for inappropriate use and overdose (Bao et al., 2018[128]). In Australia, the real time prescription monitoring assists doctors and pharmacists in identifying which patients are at risk of harm due to dependency or problematic use of controlled medicines. The national system is designed to provide information relating to prescription dispensing events from all states and territories to prevent cross-border drug shopping abuses. Another recent initiative is the Turkish Coloured Prescription System (*Renkli Reçete Sistemi*), which started in 2017 and has helped to control counterfeit, lost and/stolen printed prescriptions and non-standard medicine use. At the same time, the system ensures proper doses and amounts of controlled medicines with the prescription, including opioids (TMMDA, 2019[129]).

In order to regulate opioid prescription, regulators or insurers have experimented with *'utilization management' schemes* that place quantity limits, stepwise therapy rules, and/or prior authorisation requirements on opioid prescriptions (Lin et al., 2018[53]). Unfortunately, evidence evaluating the effectiveness of these schemes is relatively scarce. In this context, a programme in Oregon Medicaid in the United States developed a prior authorization policy for opioid prescriptions finding that it reduced the number of opioid-naive patients initiating extended-release/long-acting opioid use by more than half, but

may also have increased short-acting opioid prescriptions by 7% (Keast et al., 2018[130]). Likewise, the programme reduced high dosage opioid prescriptions and multiple pharmacy use but saw no changes in opioid overdose (Hartung et al., 2017[131]).

In addition to the implementation of stewardship programmes, 13 OECD countries have put in place disciplinary actions for physicians overprescribing opioid medications. For instance, the German narcotic drug law explicitly states that narcotic drugs can only be prescribed if there is no other therapeutic option. Physicians who do not comply with this indication can face up to five years of imprisonment or a fine (Bundesamt für Justiz, 2018[132]). In some countries, opioid prescription monitoring schemes are part of wider monitoring actions. For example, in the United States prescription drug monitoring programs (PDMPs) are administered by single states, which collect and distribute data on the prescription of federally controlled substances, such as opioids and other potentially problematic prescription drugs (Finklea, Sacco and Bagalman, 2014[133]).

Regulatory actions can also support health systems' work. In the case of prescription opioids, this entails regulating approved opioid medications, for instance, scheduling modifications, limiting access to high-dosage-unit versions and requiring abuse-deterrent formulations. For instance, on February 2018, the Australian Therapeutic Goods Administration rescheduled all over-the-counter medicines containing codeine as prescription only medicines. A Nationally Coordinated Codeine Implementation Working Group has been established to assist with implementing a communication and engagement strategy to help inform the community of the changes to the availability of low-dose codeine containing medicines (TGA, 2019[134]).

While strategies to reduce opioid over-prescribing are important, patients' need for pain treatment should always be taken into consideration. Coverage of *non-opioid evidence-based pain treatments* can be fostered by incentives and actions from payers. Particularly for non-chronic pain, these strategies can be applied with success (Ballantyne, Kalso and Stannard, 2016[135]). Pharmacy policies are rarely aligned with corresponding medical policies for pain treatment, in part owing to separation in the design and administration of these two types of benefits. In a study among United States insurers exploring the coverage policies for pharmacologic treatments for low back pain, only one plan out of 50 had fully integrated non-pharmacological therapies into its step therapy requirements for opioid initiation (Lin et al., 2018[53]).

Regulation of industry: marketing of prescription opioids and financial payments to providers

In some OECD countries, there has been widespread marketing and financial incentives directed towards opioid prescribers and patients. These practices have raised concerns about potential conflict of interest, which can drive opioid overuse going over the strictly medically appropriate use that benefits patients. OECD countries have relied significantly on self-regulation of prescribing practices by prescribers and industry. Lately, governments have expanded regulations, particularly through enhancing transparency of marketing and financial relationships, but there is a remarkable lack of impact evaluations.

Although no evidence specifically on opioids is available, the general trend is to increase transparency. In 2013, the United States instituted a disclosure law wherein firms were required to publicly declare the payments that they made to physicians. A recent study found that through a 29-month period between 2013 and 2015, the monthly pharmaceutical companies' payments to physicians declined by 2% on average. However, there was considerable heterogeneity in the effects with 14% of the drug-physician pairs showing a significant increase in their monthly payment. Moreover, the decline in payment was smaller among drugs with larger marketing expenditure, and among physicians who were paid more heavily pre-disclosure and who prescribed more heavily (Guo, Sriram and Manchanda, 2017[136]). In Europe, a Disclosure Code by the European Federation of Pharmaceutical Industries and Associations (EFPIA), the trade association of the research-based pharmaceutical industry, was mandated to implement disclosure programmes in 33 countries. A study found that in many cases, individuals can still opt out and

reporting is incomplete, with common influential gifts such as food and drink excluded. In addition, in several countries data are only available as separate PDFs from companies, thus making the payment reports difficult to access and analyse (Fabbri et al., 2018[137]). Canada is in the process of restricting most forms of marketing and advertising of prescription opioids. Until new regulations are in place, Health Canada is calling on opioid manufacturers and distributors to immediately cease marketing activities associated with opioids in Canada, on a voluntary basis (Health Canada, 2018[138]).

4.1.2. Effective treatment and actions to minimise opioid use negative consequences are key for patient management

Medication assisted therapy can be part of long-term programmes benefits patients

Policies focusing on increasing the availability of medication assisted therapy (MAT) increase the quantity of opioid agonists/antagonists provided and widen the range of medications used, in order to maximise the chances of effectively treating patients who do not respond to methadone, buprenorphine and other common first-line opioid substitutes (Sordo et al., 2017[71]). Ideally, MAT should be part of a long-term comprehensive treatment and rehabilitation programme. MAT for OUD is provided by all OECD countries, except for Japan and Korea. In France, for example, MAT was implemented in 1996 and it is currently administered to around 180 000 patients who suffer from a substance use disorder (Fédération Française d'Addictologie, 2004[139]). The Canadian province of British Columbia offers MAT as a long-term treatment and explicitly recommends prescribing it without a pre-determined end-date (British Columbia Ministry of Health, 2017[140]). Once stabilization is achieved, and if patient and prescriber agree that de-intensification of treatment is appropriate, the province supports voluntary, long, gradual stepped-tapering schedules where dose reductions are scheduled to occur monthly or bimonthly, over a period of many months, as suggested by the available evidence (Bruneau et al., 2018[141]). Similarly, Australia recognises psychosocial support as an inherent component of MAT and recommends tailoring the duration of MAT to the unique needs and processes of every patient (Gowing, Ali and Dunlop, 2014[142]).

An extensive body of evidence supports the effectiveness of MAT for the treatment of OUDs. A systematic review found that methadone maintenance treatment was more effective than non-pharmacological approaches in retaining patients in treatment (3 RCTs, RR=3.05) and in the suppression of heroin use (3 RCTs, RR=0.32) (Mattick et al., 2009[143]). A second systematic review conducted by the same authors on buprenorphine found similar results (Mattick et al., 2014[144]). Addressing OUD as a chronic illness, and thus not restricting MAT to a short period of time is particularly important, since premature termination of treatment increases the likelihood of overdose-related deaths (Degenhardt et al., 2009[145]; Strang et al., 2016[69]). In the case of prescription opioid dependence, a systematic review found that methadone and buprenorphine work well to keep people in treatment, and to reduce opioid use with similar side effects. The review also showed that buprenorphine is associated with a 19.5% increase in treatment retention compared with methadone treatment and that buprenorphine may reduce use of opioids (Nielsen et al., 2016[146]). Extended-release injectable naltrexone is another alternative of MAT, for which a recent review found that it might decrease opioid use but there are few experimental demonstrations of this effect (Jarvis et al., 2018[147]).

Integration and coordination with specialised services contributes to early detection and managing co-occurring diseases

The needs of people with OUD seem to be better addressed when integration with other parts of the health system occurs. The aim is early detection and treatment of any substance use disorder and other health conditions, such as infectious diseases (hepatitis B and C, HIV, tuberculosis) and mental health illness. In addition, psychosocial interventions can complement the treatment to obtain better results for patients.

In relation to *co-occurring infectious diseases*, a review studied the impact of behavioural interventions, substance-use treatment, syringe access, syringe disinfection, and multicomponent interventions, finding that multiple combined strategies reduced risk of HIV seroconversion by 75%, significantly better than single-method interventions (Hagan, Pouget and Des Jarlais, 2011[148]). More specifically, the main evidence-based programmes for HIV and HCV prevention interventions which should be covered in order to halt the HIV and HCV epidemics for persons who inject drugs were identified, including: MAT, HIV counselling and testing, HIV antiretroviral therapy, and condom distribution (Larney et al., 2017[149]). Models to organise the integration or co-location of OUD, HIV and hepatitis services have been implemented in different settings such as primary care, HIV specialty care, opioid treatment programs, transitional clinics, and community-based harm minimisation programs (Rich et al., 2018[150]).

Psychosocial interventions can represent an important resource to promote a people-centred medicine, address co-occurring mental health illnesses, and provide a complement to MAT. Psychosocial interventions can be delivered in different treatment modalities (e.g. inpatient, outpatient) and in a variety of formats (e.g. social skills training, individual, group and couples counselling, cognitive-behavioural therapy, contingency management, 12-step facilitation therapy, motivational interviewing, family therapy and others (Dugosh et al., 2016[151]). A systematic review found that the addition of a psychosocial intervention to medication detoxification treatment improved the number of people who completed treatment, reduced the use of opiates, increased abstinence from opiates at follow up and halved the number of absences (Amato et al., 2011[152]). However, a systematic review found that combining psychosocial interventions and MAT may not change the effectiveness of retention and opiate use during treatment (Amato et al., 2011[153]). Among adolescents, a qualitative review found that most of them have positive experiences with self-help groups and stress the importance of the group component of the therapy and the learning experiences they have when participating, which highlights that network support appears to be an important facilitator for recovery (Hannes et al., 2017[154]). Psychosocial interventions play a central role in the administration of MAT in Ireland, where MAT is conceived within an integrated perspective that emphasises the importance of psychosocial needs (HSE Primary Care Division, 2014[155]). Accordingly, MAT is administered in Ireland along with a wide spectrum of other interventions, including complementary and alternative therapies, individual and couple cognitive behaviour therapy, coping skills, motivational interviewing, relapse prevention, dialectical behaviour therapy, contingency management, counselling and psychotherapy, community reinforcement approach, as well as family interventions and family therapy.

Both in the case of prescribed and illicit opioids, strategies can be developed to identify people who are at risk of developing an OUD and effectively engage people who need specialised treatment. For illicit opioids, a review found that *screening, brief intervention and referral to treatment (SBIRT)* schemes were an effective method to address adolescent substance use (Beaton, Shubkin and Chapman, 2016[156]), which can be provided in primary care by paediatricians or embedded behavioural health care practitioners obtaining good results (Sterling et al., 2015[157]). A 2015 study on the Florida BRITE (BRief Intervention and Treatment of Elders) Project showed that thirty days after the initial screening, the average use of illegal drugs among older adults decreased from 36.2% to 11.8% (Schonfeld et al., 2015[158]). Likewise, emergency departments have implemented SBIRT-like schemes for illicit substances showing good results in improving abstinence, reducing consumption, controlling overdose risk behaviours and non-medical opioid use (Hawk and D'Onofrio, 2018[159]). For prescription opioids, a review found insufficient evidence to assert the effectiveness of SBIRT schemes for reducing inappropriate use of psychoactive substances (Young et al., 2014[160]).

Australia's National Drug Strategy 2017-26 includes primary assessments and brief interventions to be performed by general practitioners, nurses, allied health professionals, in both health care facilities and other relevant settings, including criminal justice (Australian Department of Health, 2018[161]). Similarly, SBIRT schemes have been implemented in the United States, where since 2003 the Centre for Substance

Abuse Treatment (CSAT) has awarded 32 SBIRT grants to enhance services for persons with, or at risk for, substance use disorders (Bray et al., 2017[162]).

Naloxone is an effective harm minimisation intervention

The efficacy of opioid antagonists such as naloxone to treat the acute phase of an opioid overdose and save lives has been documented by a robust international literature (Chimbar and Moleta, 2018[79]). Additionally, providing overdose medications to first-aid responders and other people who may witness unintended overdoses (such as opioid users' relatives, friends or partners) has proven effective in different contexts. For instance, widening the availability of overdose programmes in New York City in the United States was associated with a 27% decrease in the unintentional heroin poisoning mortality rate (WHO and UNDOC, 2014[163]). Similar results were obtained in Massachusetts, where non-governmental organizations are allowed to distribute naloxone without the presence of a physician (Walley et al., 2013[164]). In fact, evidence shows that overdose reversal medications can be successfully administered by non-medical professionals (Green, Heimer and Grau, 2008[165]).

Take-home Naloxone (THN) programmes have been implemented in Australia, Canada, Estonia, France, Germany, Ireland, Italy, Lithuania and the United States. In Australia, the Government has made rapid progress in removing regulatory barriers to naloxone in recent years, and THN programmes currently operate in five Australian jurisdictions. Moreover, a multi-faceted approach to drug dependence has been adopted in Australia, where alcohol and other drug-related health agencies have recognised the opportunity for THN provision through interactions with their clients (Dwyer et al., 2018[166]). Additionally, a number of OECD countries are considering (or in the process of) implementing THN programmes (Strang, 2016[167]). For instance, France has made naloxone "ready-to-use" ("take-home naloxone") available at an early stage via a temporary authorization of use in 2016, then by granting a marketing authorization in 2017. This is a nasal form that can be used outside a health care facility and in the absence of a health professional, and can be dispensed without a prescription (optional medical prescription) by providers related to substance use disorders, in emergency services, and in a penitentiary environment (ANSM, 2018[168]).

Increasing naloxone distribution is likely to be a cost-effective intervention. A cost-effectiveness analysis modelling the societal impact of the distribution of naloxone to users of illicit opioids (Coffin and Sullivan, 2013[169])found the intervention cost-effective, with 6% of overdose deaths prevented with naloxone distribution and one death prevented for every 227 naloxone kits. Similarly, a more recent cost-effectiveness analysis of take-home naloxone for heroin users in the United Kingdom (Langham et al., 2018[170]) found that the distribution of take-home naloxone decreased overdose deaths by around 6.6% and was deemed cost-effective with an incremental cost per QALY gained well below a GBP 20 000 willingness-to-pay threshold set by UK decision-makers.

Needle and syringe programmes help to reduce blood borne diseases

Needle and syringe programmes (NSP) aim to prevent acquisition of blood borne diseases such as hepatitis C virus (HCV) and HIV in people who inject drugs, as well as invasive bacterial and fungal infections caused by pathogens present on skin at the site of injection. A systematic review of the evidence on NSP (Abdul-Quader et al., 2013[78]) found that such programmes are associated with a significant reduction in the prevalence of HIV and HCV and decreases in the incidence of HIV, among people who inject drugs. More recently, another review found that high NSP coverage in Europe was associated with a 76% reduction in HCV infection. Moreover, the impact of combined high coverage of NSP and MAT may result in a 74% reduction in the risk of HCV acquisition (Platt et al., 2017[171]). Needle and syringe programmes are available in 32 OECD countries that have at least one operational programme (Stone and Shirley-Beavan, 2018[172]). Among the 20 countries that responded to the OECD questionnaire, eight have programmes implemented at a national and six at sub-national level. These programmes are not currently

available in Japan and Korea, while in Italy are implemented by social and health care workers in mobile units, not yet uniformly distributed throughout the country.

Furthermore, NSP are a cost-effective policy action. For instance, the needle and syringe programme implemented in New York City has been shown to reduce HIV treatment costs by USD 325 000 per case of HIV averted, and to have averted 4–7 HIV infections per 1 000 clients, producing a net cost savings (Belani and Muennig, 2008[173]). It has been predicted that increasing investment in needle and syringe exchange programs would entail a high rate of financial return on investment (USD 7.58–6.38 for each USD invested), and both main and sensitivity analyses strongly suggested that it would be cost-saving for the United States to invest in syringe exchange expansion (Nguyen et al., 2014[174]).

Medically supervised consumption centres and alternative medical approach to opioids are used in some OECD countries

Medically supervised consumption centres (MSCCs) are legally sanctioned facilities where users can consume pre-obtained drugs under medical supervision (May, Bennett and Holloway, 2018[175]). A wide body of internationally-sourced evidence has documented the effectiveness of MSCCs in reducing the harm associated with drug injection. A systematic review of the evidence on MSCCs found that all studies converged to find that MSICs were efficacious in attracting and staying in contact with highly marginalised target populations, meaning safer injection conditions, enhanced access to primary health care and reductions in overdose frequency. MSCCs were not found to increase drug injecting, drug trafficking or crime in the surrounding environments, and were found to be associated with reduced levels of public drug injections and dropped syringes. For instance, the opening of Sydney's first MSIC saw a 12% reduction in public injection and a 21% reduction in dropped syringes (Potier et al., 2014[176]). A recent EMCDDA report concluded that "these services facilitate rather than delay treatment entry and do not result in higher rates of local drug-related crime" (EMCDDA, 2018[80]). MSCCs are currently available with at least one facility in Australia, Belgium, Canada, Denmark, France, Germany, Luxembourg, Netherlands, Spain and Switzerland (Stone and Shirley-Beavan, 2018[172]).

Concerning illicit opioids, *drug checking* has been developed as a relatively new harm minimisation strategy. Drug checking (also referred to as pill testing or adulterant screening) is a service that chemically tests drug samples, which are voluntarily submitted by drug users, in order to help them identify the content and purity of substances they intend on consuming. Thus, this strategy aims to prevent the main harms associated with the consumption of unknown substances (Brunt, 2017[177]). Drug checking services are being implemented in an increasing number of OECD countries, and the evidence on their effectiveness appears promising, although not yet sufficiently robust. In fact, the impact of drug checking on drug consumption and substance use behaviour has not yet been analysed through a clinical trial (Kerr and Tupper, 2017[178]) and the available evidence on drug checking's effectiveness is based on drug users' self-reported intentions to avoid dangerous drugs and adopt a safer behaviour (see, for example, (Sherman and Green, 2018[179]; Tupper et al., 2018[180]). A recent study (Karamouzian et al., 2018[181])evaluating a fentanyl drug checking service in Vancouver (Canada) shed light on the relevance of drug checking services for fentanyl contamination. The study found that 80% of the drugs checked were contaminated with fentanyl. Following such results, more than one third (36.3%) of participants reported planning to reduce their drug dose, while only 11.4% planned to fully dispose of their drug. In light of these findings, further research is needed to corroborate the effectiveness of drug checking services on substance use behaviour.

Prescription-grade heroin (diacetylmorphine) is an alternative that has been used for selected patients refractory to standard treatment. Reviews (Ferri, Davoli and Perucci, 2011[182]; Strang et al., 2015[183]) have found that heroin prescribed alongside flexible doses of methadone in a maintenance programme might help these patients remain in treatment, limit the use of street drugs, reduce involvement in criminal activity and incarceration, and possibly reduce mortality. Moreover, heroin assisted therapy shows a cost-saving

benefit, attributable mainly to the reduction in the cost of criminal procedures and imprisonment. Furthermore, heroin maintenance appeared to be more cost-effective than methadone maintenance when costs of crime are included (EMCDDA, 2012[184]). Among OECD countries, heroin assisted treatment is currently implemented in Canada, Denmark, Germany, Luxembourg, Netherlands, Switzerland and the UK.

4.2. Social policies to address the economic and societal factors of the opioid crisis

Social policies play a crucial role in addressing the multi-faceted phenomenon of opioids problematic use, since individuals with problematic opioids use may be vulnerable people at risk of social exclusion, and because recovery and re-integration of those people into society may require policies beyond the health sector. Social policies can support people's (re)integration into society, particularly in areas such as employment, housing and recovery support (Hollingsworth, Ruhm and Simon, 2017[81]; Krueger, 2017[82]).

Social reintegration support initiatives, such as employment services, housing and education, are in place in 19 out of the 20 countries analysed. Ireland's National Drug Strategy strongly emphasises that the provision of accommodation and vocational rehabilitation are integral elements of drug treatment, fostering close collaboration between the Homeless Preventative Strategy and all agencies working on behalf of drug users (Keane, 2007[185]).

Although often neglected, housing policies constitute a crucial component of the strategy to address problematic opioid use. In fact, research shows that problematic drug and alcohol use is associated with a higher likelihood of experiencing homelessness (Fitzpatrick, Johnsen and White, 2011[186]). More specifically, substance use is one of the determinants of *chronic homelessness,* rather than *transitional homelessness*, which is shorter in length and associated with factors such as loss of employment and relationship breakdown (OECD, 2015[187]). Stable housing is cited by people with drug use disorders as one of the main elements leading to successful abstinence from drug use (Davis and O'Neill, 2005[188]). Such perceptions have been confirmed by studies showing that drug treatment has better results when associated with housing interventions. A subgroup analysis within a systematic review found that full abstinence was achieved by 50% of individuals in the recovery housing and treatment group, compared with 37% for recovery housing alone and 13% for usual care. At three months, participants in both of the recovery house conditions were significantly more likely to be earning money from employment than those in usual care (Chambers et al., 2018[189]). Stable housing is also an important tool in the prevention and reduction of harms associated with HIV and Hepatitis C (CORNEIL et al., 2006[190]). Nonetheless, the integration between housing policy and the other social and health services involved in the response to the opioid crisis is often insufficient. For example, a recent report (Bowen Matthew, 2018[191]) showed that in the United States, as a consequence of the insufficient integration between social services, the consumption of illicit opioids is often sanctioned with eviction from public housing.

Box 4.2. Housing First: a viable strategy to address OUD-related homelessness

Initially developed in New York in the early 1990s by the nongovernmental organisation Pathways to Housing, the Housing First model has been adopted by seven OECD countries (Canada, Denmark, Finland, France, Ireland, Norway and the United States), and is currently being explored by an increasing number of OECD countries, including Australia, Germany, Italy, the Netherlands, New Zealand, Portugal, Sweden and the United Kingdom (OECD, 2015[187]). The key principles of the Housing First approach are:

- Stable housing as the first priority. As opposed to many housing services, that aim to make homeless people with high support needs 'housing ready' before they are rehoused, the Housing First approach emphasises the need to provide stable housing before providing any other support service (Housing First Europe Hub, 2018[192]).
- Choice for service users: Housing First is a recovery-oriented model, which actively encourages service users to minimise drug and alcohol related harms, as well as to seek medical treatment. Unlike other housing models, however, such behaviours are not required (ibid.).
- Housing as a human right: The Housing First model explicitly emphasises the need to treat homeless people with compassion and respect, and it recognises access to suitable and stable housing as a human right (Tsemberis, 2010[193]).

A large body of evidence has shown that, as concerns ending chronic homelessness for people with high support needs, the Housing First model appears very effective (Tsemberis, 2010[193]; Latimer et al., 2014[194]).

The effectiveness of Housing First appears to hold true also with specific respect to substance dependence. With respect to opioid use, a randomised trial performed in Toronto, Canada (Kirst et al., 2015[195]), found that opioid use among participants in the Housing First intervention group was 50% less (6% vs. 12%) than the control group, which had received no specialised services. Further research is needed to corroborate these results, as the majority of studies on Housing First focus on housing stability and use of publicly funded services, rather than on its effects on substance use (Collins et al., 2012[196]).

Providing people recovering from OUD with employment opportunities is an action to favour their social reinsertion. Not many studies have been performed about employment support and OUD, but there are more studies about drug use. Vocational training, simulated employment and contingency management interventions show good results, albeit more evidence is needed (Sumnall and Brotherhood, 2012[197]). A more recent review found that employment support initiatives might be effective as relapse prevention measure, and to reduce substance use and homelessness rates (Walton and Hall, 2016[198]).

Residential rehabilitation programmes, compared to outpatient treatment, provide patients with safe housing conditions, peer support for recovery and self-control skills to resist the pressure to relapse. A review of the evidence on residential programs for people with severe mental illness and co- occurring substance use disorders found that nine out of the ten studies examined suggested advantages for integrated residential programmes (Brunette, Mueser and Drake, 2004[199]). A more recent review evaluating recovery housing programmes found that they might have positive substance use outcomes and improvements in functioning, including employment and criminal activity (Reif et al., 2014[200]). Furthermore, in implementing social policies and recovery support initiatives, particular attention should be paid to the cultural specificities of ethnic minorities and indigenous communities affected by OUD (Catto and Thomson, 2008[201]).

With the exception of Japan, all of the 2018 survey respondents offer residential rehabilitation programmes. The majority have implemented residential rehabilitation programmes at a national-level, while a small

percentage of countries (20%) have implemented residential rehabilitation programmes at a sub-national level. In the US, the Centers for Medicare & Medicaid Services (CMS) has announced a new policy that enhances access to residential rehabilitation programmes by increasing the flexibility for States to apply for new expenditure authority (CMS, 2017[202]). States will be able to pay for a fuller continuum of care to treat OUD, including critical treatment in residential treatment facilities that Medicaid is unable to pay for without a waiver.

4.3. Regulation and enforcement to address illegal opioids use

Regulation and law enforcement related actions aim to reduce the supply of illegal opioids by preventing illegal manufacturing, trafficking, and the diversion of substances from medical use and scientific research into the illegal market. In addition, law enforcement actors can be a first point of contact between opioid users and the institutions that could provide support and help. This dimension of the policy framework mainly focus on the links of the law enforcements sector with public health issues and the coordination between the health, social and judicial systems.

4.3.1. Law enforcement practice

Customs services, as part of their duty of enforcing regulation and documenting the flow of goods in and out of countries, are a key actor that can contribute to reduce the supply of illegal opioids, particularly since narcotics are one of the central illicit shipment concerns for OECD countries (OECD, 2018[203]). Recent actions have been proposed aiming to more accurately identify high-risk shipments, including the registration of import of pill presses, encapsulators and certain chemical precursors (Suzuki and El-Haddad, 2017[204]; INCB, 2018[205]); pre-load or pre-arrival air security, focusing on requirements for the provision of advance data, in electronic form, before the loading of goods onto airplanes; and allowing customs to open low-weight mail if suspected of containing unauthorised controlled substances (McCaskill, 2018[46]). For instance, Canada now allows border officials to open mail weighing 30g or less if there is reasonable grounds to suspect it is not in conformity to laws/regulations (Health Canada, 2017[206]).

Prevention of *medication diversion* can be augmented by increasing inspection and education activities to regulated parties, for instance, about the proper storage of controlled substances. Law enforcement authorities can also leverage on prescription monitoring programmes to identify and investigate individuals who may be engaging in diversion, leading to raids of clinics that prescribe significantly more than is medically justifiable (“pill mills”) (Compton, Boyle and Wargo, 2015[207]). For example, France monitors unusual sales of medicines; in December 2018, the National Medicines Agency (ANSM) and the National Council of the Association of Pharmacists signed an agreement to strengthen the control of unusual drug sales, thanks to a specific monitoring and reporting system. A pilot phase started including wholesaler-distributors, farmers and regional health agencies to monitor three opioid medicines.

Law enforcement officials (LEO) are commonly the first point of contact with opioid users, which makes them a central actor in the public health perspective needed to address the crisis. LEO can be trained as first responders to assist OUD patients going through an overdose episode, ensuring that LEO will have support to avoid disrupting their usual activities. Training LEOs in naloxone administration can increase knowledge and confidence in managing opioid overdose emergencies and may have positive effects for overdose victims (Wagner et al., 2016[208]). Likewise, LEO can create synergic partnership to work cooperatively with some of the newest harm minimisation strategies, such as supervised consumption centres, in order to hold greater and more sustainable public health and law enforcement value. In a qualitative study covering Australia, Canada, Denmark, France, Germany, Netherlands and Spain, the main contributors for cooperative actions between LEO and supervised consumption centres were early engagement and dialogues; supportive police chiefs; dedicated police liaisons; negotiated boundary agreements; and regular face-to-face contact (Watson et al., 2018[209]). Box 4.3 presents the example of a programme in the United States that goes in line with these collaborative approaches.

Box 4.3. 'Law Enforcement Assisted Diversion' programme as an experience of coordination between law enforcement and public health sectors

Law Enforcement Assisted Diversion (LEAD) is a pre-booking diversion pilot programme developed with the community to address low-level drug and prostitution crimes in Seattle, Washington in the United States (LEAD, 2018[210]). The program allows law enforcement officers to redirect low-level offenders engaged in drug or prostitution activity to community-based services, instead of jail and prosecution. The LEAD pilot program was established in 2011 and comprises three primary components: 1) an initial program entry process, which includes diversion from the criminal justice and legal systems; 2) harm-reduction case management (i.e., low-barrier counselling and connection to social and clinical services that is offered with neither requirement of nor pressure towards substance-use treatment or abstinence); and 3) higher-level coordination of legal system involvement.

Compared to the usual arrest, incarceration and prosecution scheme, LEAD participants had 60% lower odds of arrest during the six months subsequent to evaluation entry; and both a 58% lower odds of arrest and 39% lower odds of being charged with a felony over the longer term (Collins, Lonczak and Clifasefi, 2017[211]). In terms of costs, a study found that the LEAD program averaged USD 899 per person per month, including programme start-up, but then decreased to USD 532 per month towards the end of the evaluation. Across nearly all outcomes, there was a significant reductions for the LEAD group compared to the control group on average yearly criminal justice and legal system utilization and associated costs. Notably, from pre- to post-evaluation, entry LEAD participants showed substantial cost reductions (USD -2 100), whereas control participants showed cost increases (USD +5 961) (Collins, Lonczak and Clifasefi, 2015[212]).

Finally, investigation entities in countries could strengthen capacity to control the illicit trade of opioids through the internet, particularly the darknet, given its growing use in drug trafficking (Quintana et al., 2017[213]). For instance, advanced machine learning techniques have been used to monitor and detect marketing and sale of opioids by illicit online sellers via Twitter, which can proactively alert regulators and law enforcement agencies of illegal opioid sales. (Mackey et al., 2018[214])

4.3.2. Criminal justice system approaches to people who use drugs

Different legal protection arrangements for people using drugs, including opioids, have been established in some countries in recognition of the fact that this is a chronic health issue requiring multiple strategies. Among the relevant possible interventions, we focused on discussing drug treatment courts, 'good Samaritan laws', and the legal status of personal use of drugs, since these have been more widely implemented and explored.

Drug treatment courts are specialised court process to allow defendants charged with drug possession or other eligible offences to enroll in court-directed treatment and rehabilitation, rather than having their case handled through the traditional process and sanctions such as imprisonment. Drug treatment courts have been established in Australia, Austria, Belgium, Canada, Chile, Ireland, Mexico, New Zealand, Norway, United Kingdom and the United States. The evidence about the effects of drug treatment courts is mixed, with some studies showing lower re-arrest rates for any offence and drug-related offences (GAO, 2011[215]; Mitchell et al., 2012[216]), while other studies find that these courts "cherry-pick" by targeting drug users who do not need treatment in order to obtain better results (Csete and Tomasini-Joshi, 2016[217]), and "punish" individuals for failing treatment giving them longer prison sentences (Sevigny, Fuleihan and Ferdik, 2013[218]). Evidence from Canada shows that drug treatment courts can be a catalyst for increased participant engagement with community health and social supports, which can help in the recovery process (Rezansoff et al., 2015[219]).

"Good Samaritan" laws usually provide a level of immunity from prosecution for drug possession to anyone who seeks emergency assistance in the event of a drug overdose; these have been implemented in both the United States and Canada. For the latter, the federal "Good Samaritan Drug Overdose Act" provides some legal protection for those who seek emergency medical or law enforcement assistance for themselves or another person following an overdose on a controlled substance. The implementation of these laws has shown mixed results. A study covering 35 states in the United States did not find an association of these laws with significant changes in opioid-related deaths or nonmedical use of prescription painkillers (Rees et al., 2017[220]). A similar study covering 30 states found that Good Samaritan laws were associated with 15% lower incidence of opioid-overdose mortality and no increases in non-medical opioid use (McClellan et al., 2018[221]). Since lack of awareness about the law has been identified as a barrier, a study found that the odds of a trained bystander calling emergency number were over three times greater than when the witness had incorrect knowledge (Jakubowski et al., 2018[222]).

Box 4.4. Drug decriminalisation and public health approach in Portugal

In 2001, Portugal decriminalised the possession and consumption of all narcotics and psychotropic substances for personal use, intended as the quantity required for an average individual consumption during a period of ten days. Exceeding this quantity, criminal procedures apply. Portugal's decriminalisation reform has been particularly influential, since by introducing a *de jure* decriminalisation (changes in the law instead of changes in the daily practice), it has been a pioneer of the explicit decriminalisation of all drugs. Some of the main benefits of decriminalisation mentioned by Portuguese authorities can be summarised as follows:

- Changes in the mind-set of the general population, contributing to consider drug use disorders as a medical condition rather than a criminal offence.
- Creation of supplementary entrance doors to the public health system, particularly, through the Commissions for the Dissuasion of Drug Dependence.
- Coherence enhancement between the health and judicial systems, markedly, to provide and expand access to public health interventions.

Portugal has a National Plan for the Reduction of Dependence Behaviours and Dependency 2013-20 and takes a strong intersectoral approach integrating actions from 13 government sectors, with the leadership of the General Directorate for Intervention on Dependence Behaviours and Dependencies (SICAD). The Commissions for the Dissuasion of Drug Dependence provides an opportunity for an early, specific and integrated interface with drug users. Through these commissions, the decriminalisation policy was connected with universal access to public health services through the National Health Service, including MAT (e.g. methadone), psychosocial services, medical specialty services (e.g. psychiatry, infectious diseases), social services (e.g. aid on job seeking, vocational training), school programmes for alcohol and drug use prevention, needles exchange, and outreach activities on recreational settings. Notably, many of the prevention and harm minimisation activities taking place in the community are implemented by non-profit NGOs, which are mainly funded and supervised by the Ministry of Health through the five Regional Health Authorities.

The decriminalisation of drugs is controversial in nature. However, empirical evidence shows that following decriminalization, Portugal has not witnessed major increases in drug use, but has experienced reductions in problematic use, drug-related harms (e.g. HIV-AIDS, hepatitis, overdose deaths) and criminal justice overcrowding (EMCDDA, 2018[223]; Hughes and Stevens, 2010[224]; Greenwald, 2009[225]). In addition, decriminalisation seems to have caused no harm through lower illicit drugs prices, which would lead to higher drug usage and dependence (Félix and Portugal, 2017[226]).

In the past decade, there has been heated discussions around the *legal status of drug use and possession for personal consumption* and several countries have moved forward with modifying a restrictive approach that previously prevailed, mainly around cannabis legislation. As matter of reference, Table 4.3 presents the legal status about decriminalisation and depenalisation of opioids in OECD countries

Table 4.3. Illicit opioids for personal use: decriminalisation and depenalisation in selected OECD countries

	Decriminalisation	Depenalisation
Australia	○	
Austria	●	
Belgium	-	-
Canada	-	-
Chile	-	-
Colombia	●	
Czech Republic	●	
Denmark	-	-
Estonia	●	
Finland	-	-
France	●	-
Germany	●	-
Greece	-	-
Hungary	-	●
Iceland	-	-
Ireland	-	-
Israel	-	-
Italy	●	
Japan	-	-
Korea	-	-
Latvia		●
Lithuania	-	-
Luxembourg	-	-
Mexico	●	
Netherlands	●	
New Zealand	-	-
Norway	-	-
Poland	-	-
Portugal	●	
Slovak Republic	-	-
Slovenia	●	
Spain	●	
Sweden	-	-
Switzerland	●	
Turkey	-	-
United Kingdom	-	-
United States	-	-

Notes: The 'personal use' threshold is considered as defined by each country. Such quantity may thus vary significantly across OECD countries. Level of implementation: ●= Nation-wide; ○ = Sub-national; - = Illegal where criminal penalties apply. Definitions (EMCDDA, 2016[227]) (p.2): - Decriminalisation refers to the removal of criminal status from a certain behaviour or action. This does not mean that the behaviour is legal, as non-criminal penalties may still be applied. - Depenalisation refers to introducing the possibility or policy of closing a criminal case without proceeding towards punishment, for example as the case is considered 'minor' or prosecution is 'not in the public interest'.
Source: (Hughes et al., 2016[228]; EMCDDA, 2018[229]) and responses from countries.

4.4. Information and knowledge generation as relevant levers for policy development and implementation

All policies should be closely monitored and evaluated. Three main components are considered here: data availability and information generation; research and development in key areas to provide new tools to address and prevent the crisis; and the need for rigorous evaluation of policies.

4.4.1. Better data and analytics for improved decision making

Data collection and information analysis should be improved. First, there is a need for improving collection and harmonisation of data from vital statistics and the services used by opioid users, which is particularly challenging in countries with numerous jurisdictional levels. The need for involving actors that are commonly within non-health sectors such as coroners, forensic institutions, police, criminal justice and social policy sectors also complicates collection. At the same time, data collection relating to population-level opioid use patterns and consequences, especially nonmedical use of prescription opioids and use of illicit opioids, should be upgraded (Bonnie, Ford and Phillips, 2017[230]).

Advanced analytics have the potential to help identify at-risk individuals and provide insights into risk factors, helping to prioritise scarce resources, optimise interventions, compare the efficacy of different approaches and improve the efficacy of each intervention (Charumilind et al., 2018[58]). Linking data from the different sources would provide new and relevant inputs to improve decision making for all sectors involved. An interesting example of formal institutional development is the French Observatory of Analgesic Medicines (OFMA, Observatoire Français des médicaments antalgiques) created in 2017. OFMA aims to synthesize the various available pharmacovigilance and substance use data on these drugs from the literature and national health authorities, promoting observational, pharmaco-epidemiological and clinical studies intended to characterise the use, misuse and complications related to analgesics. The observatory plays a role in informing health professionals and users about the proper use of analgesics and their associated risks. It also plays a role of proactive vigilance that informs the health authorities in case of identification of emerging signals. The observatory, and the members of its team, endeavor not to enter into conflicts of interest related to their expertise on analgesics (OFMA, 2019[231]).

A specific focus should be placed on measuring quality of health care services, at least at three levels.

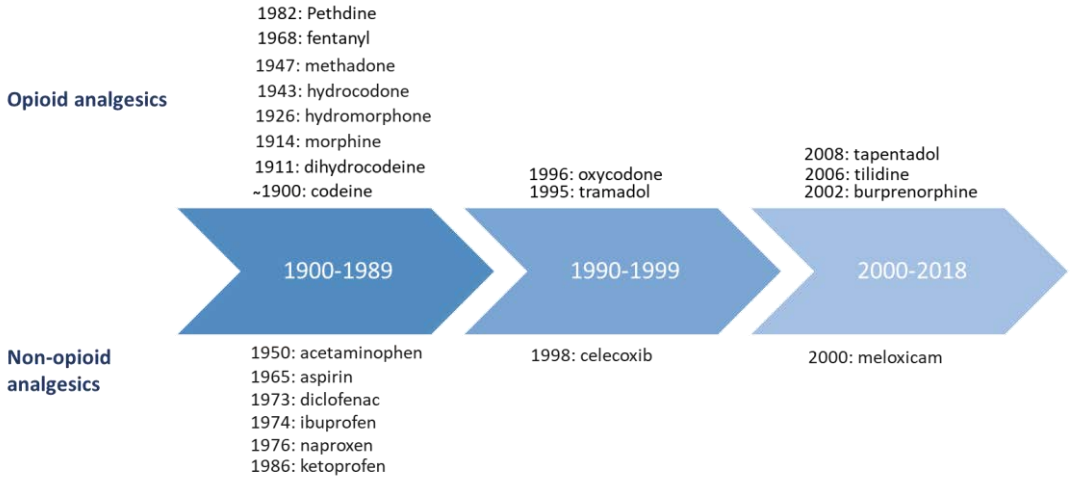
- In the area of prescription opioids, where measurement and monitoring of appropriate prescribing practices is highly needed for high dosages, multiple providers and pharmacies, duration of use, and concurrent use of opioids and benzodiazepines (Cochran et al., 2018[232]).
- Through the opioid use disorder (OUD) health care process where a ‘cascade of care model’ has been proposed comprising the following steps to measure: 1) identification of those with OUD (diagnosis); 2) their engagement in care (access); 3) initiation of medication-assisted treatment (MAT); 4) retention in MAT for at least six months; and 5) remission from dependence (lasting recovery) (Williams, Nunes and Olfson, 2017[233]).
- Innovations on outcome measures relevant for and reported by patients should be developed and implemented within health care services. Measures could draw from developments around Patient Reported Outcome Measures (PROMs) tools such as the brief treatment outcome measure (BTOM) (Lawrinson, Copeland and Indig, 2005[234]) and the substance use recovery evaluator (SURE) (Neale et al., 2016[235]).

The role of national and international medicines regulatory agencies is also relevant to improve monitoring and risk management for opioid medicines. For instance, risk minimisation plans, drug utilisation studies as well as periodic safety update reports for both pain and medication-assisted therapy products can be further strengthened. International collaboration, for instance, to collect data about pharmacovigilance, can be of great use to guide decision making at national levels.

4.4.2. Encouraging research and development for new pain and OUD-related treatments

Research and development (R&D) in the fields of pain management and OUD-related treatment seem to receive relatively little attention. In the United States, only USD 1 billion was invested for opioid-related R&D compared to USD 6 and 7.7 billion for HIV/AIDS and cancer in 2017, and only 27 industry-sponsored clinical trials for OUD-related treatment were registered as of July 2018, compared to 1 400 for HIV/ADIS and 12 720 for cancer (Charumilind et al., 2018[58]). Such underdevelopment of R&D in the field of pain management is reflected in the relatively small number of analgesic drugs approved in the last three decades, where only seven new analgesic drugs have been approved since 1986, two of which are non-opioid analgesics (see Figure 4.1).

Figure 4.1. Pain relief medications – Research & Development timeline



Note: The timeline includes the main Mu opioid agonists, Acetaminophen, Nonsteroidal anti-inflammatory drugs (NSAIDs) approved by the F.D.A. (first approval date) and still marketed.
For analgesics that are not marketed in the US, but are in use in other OECD countries, the date of first patent approval was considered.
The timeline does NOT include adjuvant analgesics or co-analgesics (e.g. anticonvulsants and tricyclic antidepressants) and local or topical anaesthetics.
Source: Authors' elaboration on FDA data (Food and Drug Administration, 2018[236]) and NCBI data (PubChem, 2018[237]).

Given the significant and increasing public health burden of pain and OUD worldwide, some of the areas that have been identified as priorities (Bonnie, Ford and Phillips, 2017[230]; Volkow and Collins, 2017[238]) are the following:

- Refining understanding of the neurobiology of pain by which new pain treatment modalities, especially for chronic pain, can be developed including non-addictive analgesics and non-pharmacologic approaches.
- Improving understanding of the intersection between pain and OUD, including the relationships between use and inappropriate use of opioids, pain, emotional distress, and the brain reward pathway; vulnerability to and assessment of risk for OUD; and how to properly manage pain in individuals with and at risk for OUD.
- Developing new and better OUD-related treatments, including overdose-reversal and prevention interventions to reduce mortality, saving lives for future treatment and recovery; and finding new, innovative medications and technologies to treat OUD.

The National Health Institutes of the United States launched the Helping to End Addiction Long-term (HEAL) Initiative in April 2018 with the aim of speeding scientific solutions to stem the opioid public health crisis. The initiative builds on the established NIH research, including basic science of the complex neurological pathways involved in pain and addiction, implementation science to develop and test treatment models, and research to integrate behavioural interventions with MAT for opioid use disorder OUD (NIH, 2019[239]).

4.4.3. Better evaluation of opioid-related policies and interventions

The evaluation stage of the public policy cycle is often left behind. From the literature review, there are many areas or interventions where scientific evidence is either lacking or of quality insufficient to assert strong conclusions. This is the case for studies using observational data alone, common in the opioid epidemic field, where certainty on the findings is difficult to establish (Binswanger and Gordon, 2016[240]). Therefore, well-designed and rigorous evaluation should accompany the most relevant and innovative actions and policies implemented in relation with the crisis. Responses to the 2018 OECD survey on opioid control suggest that 15 out of the 16 OECD countries analysed have performed evaluations on at least one relevant outcome of their opioid policy.

5 Findings and conclusions

The availability of analgesic opioids in OECD countries has been steadily growing in the past couple of decades, becoming an important public health concern in a few of them, with the United States and Canada experiencing a higher degree of opioid-related harms. Other countries, including Israel, Slovakia, Greece and Portugal, have experienced a growth in the availability of analgesic opioids in recent years but have so far not shown major signs of opioid-related harms.

In the 25 OECD countries where data is available, opioid-related deaths (ORD) have slightly increased in the present decade. The United States, Canada, Sweden, Norway, Ireland and England & Wales have rates above the OECD average, and have also seen increasing trends. Canada and the United States are confronted with a significant crisis, with substantial impact on population health (both overdose deaths and opioid-use disorder patients), health services (hospitalisations and emergency room visits), as well as on societal structures (e.g. families, communities) and the economy (e.g. social costs, unemployment). In both countries, the roots of the crisis are found in prescription and illicit opioids, though in recent years, illicit opioids have caused more deaths. Australia has also experienced increasing rates of overdose deaths, caused in this case by prescription opioids. In a different group, in Estonia, Sweden and Norway illicit opioids consumption are the main cause of overdose deaths, although with different patterns of what is the main illicit opioid substance.

Concerning prescription opioids, higher rates of opioids availability are not necessarily correlated with higher overdose death rates, for instance, in Germany, Austria, Belgium, Denmark and the Netherlands. This suggests that an appropriate use and regulatory environment for prescription opioids can be compatible with having a higher availability of these drugs for medical use. However, countries should take active actions to reach and maintain an appropriate balance to cover the real needs for pain control without exposing patients to the threat of dependence development, especially in light of data showing increasing trends of medical opioid prescription and opioid-related deaths in some European countries. Prescription monitoring and regulation to assure an appropriate use of medical opioids should therefore always be considered.

Some illicit opioid users begin their consumption with prescription opioids. This is important particularly for countries that are experiencing growing trends in prescription opioids use. Furthermore, an increasingly dynamic market of illicit drugs -- that can travel more easily than ever around the world – also means that users of such drugs can more easily have access to them regardless of where they live.

The findings from a review of policies point to the need to consider OUDs as a chronic health condition, which should be addressed primarily as a public health issue. This should guide the design of health policy responses, but also social policy and law enforcement strategies. For example, medication-assisted therapy complemented with psychosocial support is an evidence-based treatment for OUD patients that could be supported not only by the health sector but also by law enforcement strategies, facilitating and promoting the connection of low-level offenders with health care. Likewise, health care networks can offer more recovery and reinsertion opportunities to OUD patients by having fluid channels of communication with employment or housing support services, which is particularly relevant for the most vulnerable population.

Taking a people-centred and public health perspective, countries can consider the following policy considerations to improve their preparation and approach to control opioid-related issues:

- **Better Prescribing:** Doctors can improve their prescribing practices, for instance, through evidence-based clinical guidelines (e.g. for opioid prescription, for adequate medication-assisted therapy for OUD patients), prescribers training, surveillance of opioid prescriptions, and regulation of marketing and financial relationships with opioid manufacturers. In addition, patients and the general public can also benefit from clear educational materials and awareness interventions to enhance their opioid-related literacy and reduce stigma.
- **Better care:** Including the expansion of coverage for long-term medication-assisted therapy (e.g. methadone, buprenorphine, naltrexone) coupled with specialised services for infectious diseases management (e.g. HIV, hepatitis) and psychosocial interventions. Some countries have implemented interventions such as the availability of overdose reversal medications for all first responders, needle and syringe programmes, and medically supervised consumption centres. Quality of care must be improved and measured.
- **Better approach**: There can be better coordination across the health, social and criminal justice systems. Governments can consider setting up of coordinated networks among the three sectors aiming to facilitate access to integrated services for people with OUD. In addition to health services, social interventions around housing and employment support, and law enforcement uptake of a public health approach are central.
- **Better knowledge and research**: Including the use of big data and impact evaluations to generate new information from different sources along with the application of advanced analytics. In addition, quality of care measurement should be enhanced in areas such as opioid prescription, OUD health care services, and patient reported indicators (e.g. PROMs, PREMs). Research and development is needed in key areas such as new pain management modalities and OUD treatments.

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Annex A. Description of the opioid crisis in Australia, Canada and the United States

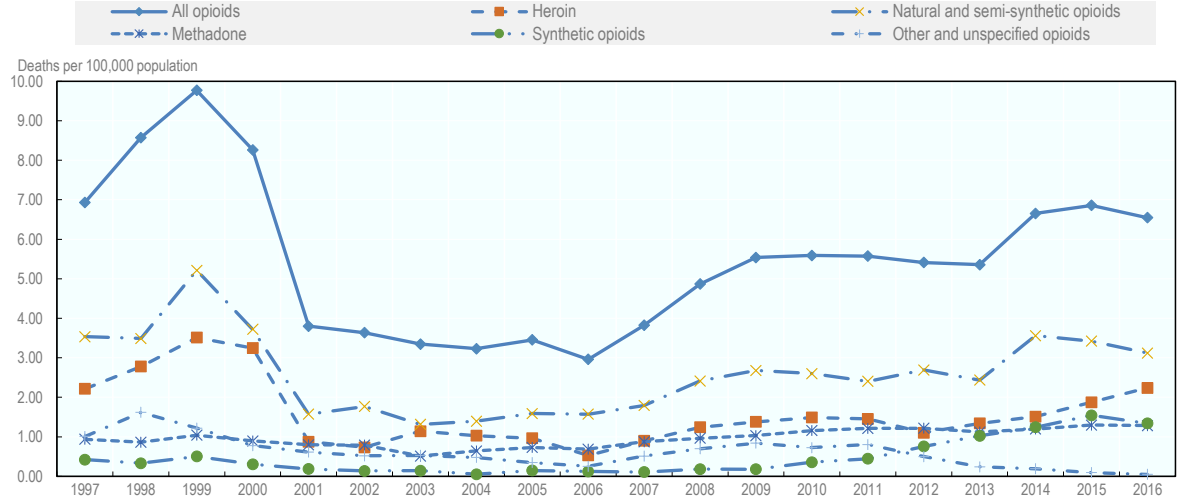
Description of the opioid crisis in Australia, Canada and the United States

Australia's epidemic is situated mainly around prescription opioids

Australia has been experiencing growing rates of opioids consumption that are affecting population health. In 2016, there were 1 119 opioid related deaths (ORD), which represents an increase of 62% compared with 2007, or an increase from 2.9 to 4.7 deaths per 100 000 population. This growth has been driven by an increase in both accidental and pharmaceutical opioid deaths. Males have experienced higher ORD rates than females while lower socioeconomic groups have the highest ORD rates among socioeconomic groups (AIHW, 2018[26]).

The highest rates of opioid-induced death in 2016 were for natural and semisynthetic opioids (e.g., morphine, oxycodone, codeine), with 3.1 deaths per 100 000 people (498 deaths). The rate of deaths attributed to heroin has been increasing with 2.2 deaths per 100 000 people in 2016 (357 deaths) compared to 0.9 in 2007. The rate of deaths attributed to synthetic opioids (e.g. tramadol and fentanyl) has also increased, passing from 0.11 per 100 000 in 2007 to 1.3 deaths per 100 000 people (214 deaths) in 2016 (see Figure A.1). The rate of opioid-induced deaths was higher among males, and among those aged 35-44 years, with low rates recorded among the 15-24 age group, which has been a consistent trend. Most of the opioid-induced deaths were considered accidental (85%), with 12% recorded as intentional (Roxburgh et al., 2018[241]).

Figure A.1. Rate of opioid-induced deaths per 100 000 inhabitants, by type of opioid, Australia 1997-2016



Source: (Roxburgh et al., 2018[241]). Adapted and reproduced with permission from the authors.

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In relation to prescriptions, between 2012-13 and 2016-17, rates of prescriptions in Australia increased, in particular for strong opioids such as oxycodone. However, after adjusting to rate of Oral Morphine Equivalent doses to account for the different dosage strengths and potency of each opioid, there was no change over the period indicating prescriptions were on average for lower doses and/or quantities per prescription (AIHW, 2018[26]). Studies have found a considerable geographic variation in opioid utilisation, with higher rates of use in less populated rural areas that had more men and older people, proportionally more low-income earning households and greater proportions in jobs requiring physical labour (Degenhardt et al., 2016[242]).

In the area of inappropriate use and illicit use of opioids, among the population aged 14 and over in 2016, 3.6% had recently used prescription opioids for non-medical purposes, and of those reporting use, over-the-counter codeine products were the most common (2.5%), followed by prescription codeine products (1.4%). Less common was oxycodone (0.6%), tramadol (0.3%), morphine (0.1%) and fentanyl (<0.1%). Only a small proportion (1.3%) reported ever using heroin in their life, and 0.2% reported using it in the last 12 months, situating heroin behind cannabis, methamphetamine, pharmaceutical drugs and psychoactive substances. However, frequency of use is much higher than other drugs with 49% of recent users reported using heroin once a week or more. In addition, heroin is the preferred drug among people who inject drugs in Australia (Australian Institute of Health and Welfare, 2018[243]).

The Australian Burden of Disease Study (AIHW, 2016[244]) estimated that in 2011 opioid use was responsible for 0.9% of the total burden of disease and injuries. Most of the burden due to opioid use was due to accidental poisoning (63%), followed by opioid dependence (30%) and suicide and self-inflicted injuries (7.8%). Opioid use was responsible for just over half (51%) of all accidental poisoning burden, all opioid dependence burden and 3% of suicide and self-inflicted injuries burden.

In terms of health services demand, from 2007–08 to 2016–17, the rate of hospitalisations per 100 000 population with a principal diagnosis of opioid poisoning increased by 25%, from 14.1 to 17.6 hospitalisations, while the rate of hospitalisations with any diagnosis (all reasons for hospitalisation) of opioid poisoning increased by 38%, from 29.0 to 40.1 per 100 000 population. The increase in hospitalisations was mostly driven by increases in the numbers of hospitalisations for poisoning by pharmaceutical opioids. Likewise, there were 4 232 emergency department presentations (17.5 presentations per 100 000 population) with a principal diagnosis of opioid poisoning—12 per day. The rate of ED presentations was 1.3 times as high for males as for females (19.7 and 15.3 per 100 000 population, respectively) (AIHW, 2018[26]).

In terms of treatment, in 2016–17, 8.2% of all alcohol and other drug treatment services had opioids listed as the principal drug of concern—a total of 16 428 closed treatment episodes. In 2016–17, heroin was the fourth most common principal drug of concern and accounted for 5% of all closed treatment episodes (AIHW, 2018[245]).

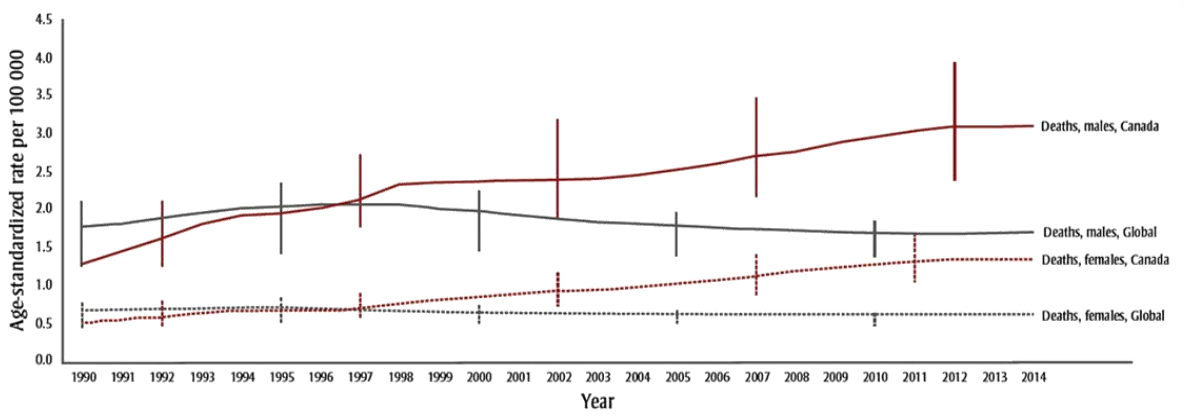
Canada's recent unfold of an opioid crisis

Canada is currently facing an opioid crisis that has affected every part of the country. According to data reported as of March 2019, there were more than 10 300 opioid-related deaths between January 2016 and September 2018. Most deaths were accidental apparent opioid-related deaths (92-94%), happened mainly among males (76-78%) and in individuals between the ages of 30 and 39 (27-28%). In this scenario, the death rate increased from 8.4 per 100 000 population in 2016 to 11.1 in 2017 and 11.8 in 2018 (Jan-Sept). In the latter period, the Provinces of British Columbia and Alberta had the highest death rates with 30.9 and 19 per 100 000 population, respectively (Special Advisory Committee on the Epidemic of Opioid Overdoses, 2019[31]).

From 1990 to 2014, the age-standardized years-of-life-lost rate due to opioid-related mortality in Canada increased by 142.2%. Likewise, the age-standardised opioid-related disability-adjusted life years rate in the

country was 355.5 per 100 000 population in 2014, which was higher than the global rate of 193.2, but lower than the rate of 767.9 in the United States (see Figure 3.5) (Orpana et al., 2018[246]). Life expectancy at birth was analysed in British Columbia, showing that it decreased by 0.38 years from 2014 to 2016 with fatal drug overdoses (the majority involving opioids) accounting for 32% of the decrease (Ye et al., 2018[32]).

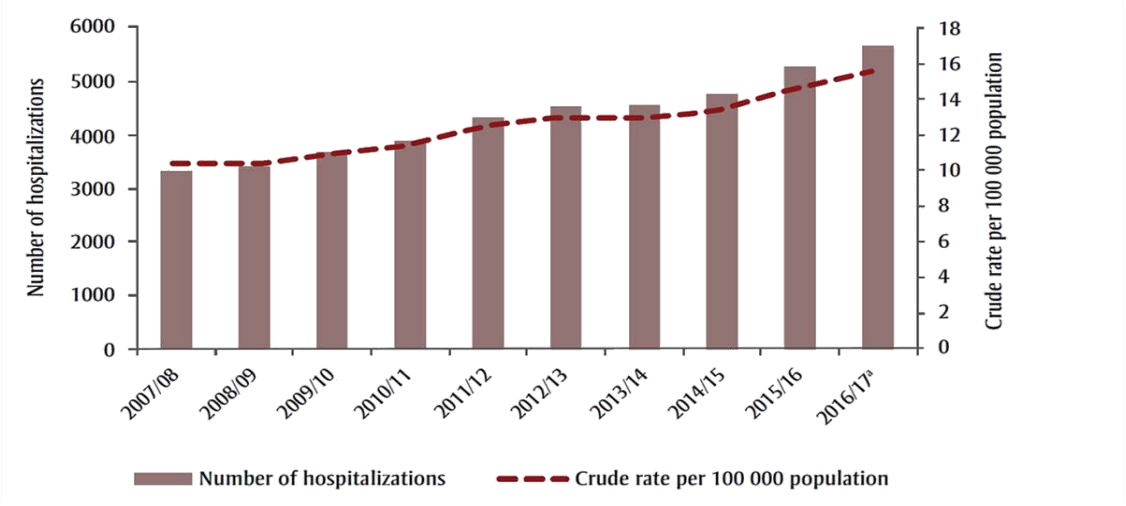
Figure A.2. Age-standardized opioid-related mortality rates per 100 000 population, males and females, 1990-2014, global and Canada



Source: (Orpana et al., 2018[246]); Statistics Canada: Vital Statistics.

The Canadian health system has also experienced increased demand related to opioid harm. In 2016/17, opioid poisonings resulted in an average of 16 hospitalisations a day in Canada, with an increase of 53% in the rate of hospitalizations over the past ten years (see Figure 3.6). In 2016/17, there were an average of 11 emergency department visits in Alberta and 13 in Ontario each day. Over the past five years, the age-adjusted rate of emergency department visits due to opioid poisoning has more than doubled in Alberta and has increased by 47% in Ontario. Both for hospitalisations and emergency department visits, most of the increases have occurred over the last three years (O'Connor, Grywacheski and Louie, 2018[247]).

Figure A.3. Opioid poisoning hospitalisations, Canada, 2007/08 to 2016/17



Source: (O'Connor, Grywacheski and Louie, 2018[247]); Canadian Institute for Health Information: Hospital Morbidity Database.

Between 2012 and 2017, both the number of prescriptions and the amount of opioids prescribed decreased. Compared to 2016, there was a 10.1% of reduction in the quantity of opioids prescribed in 2017 passing from 6 269 to 5 633 DDDs per 1 000 population. In 2017, 21.3 million prescriptions for opioids were dispensed, compared with 21.7 million in 2016. This is still higher than the number of prescriptions in 2012 but the first decline in overall prescription between 2012 and 2017 (CIHI, 2018[248]).

Awareness about the opioid crisis vary across provinces, with 38% of the population in British Columbia declaring being very aware but only 18% in Québec. Remarkably, 71% of the population declares being very aware that drugs illegally obtained have the potential to contain fentanyl. In addition, three-in-ten Canadians aged 18 and over reported using some form of opioids in the past five years. Of those, more than one-in-four have leftover opioids being stored in the home (Statistics Canada, 2018[249]).

Opioid crisis in the United States: a tale of three cumulative waves over more than 20 years

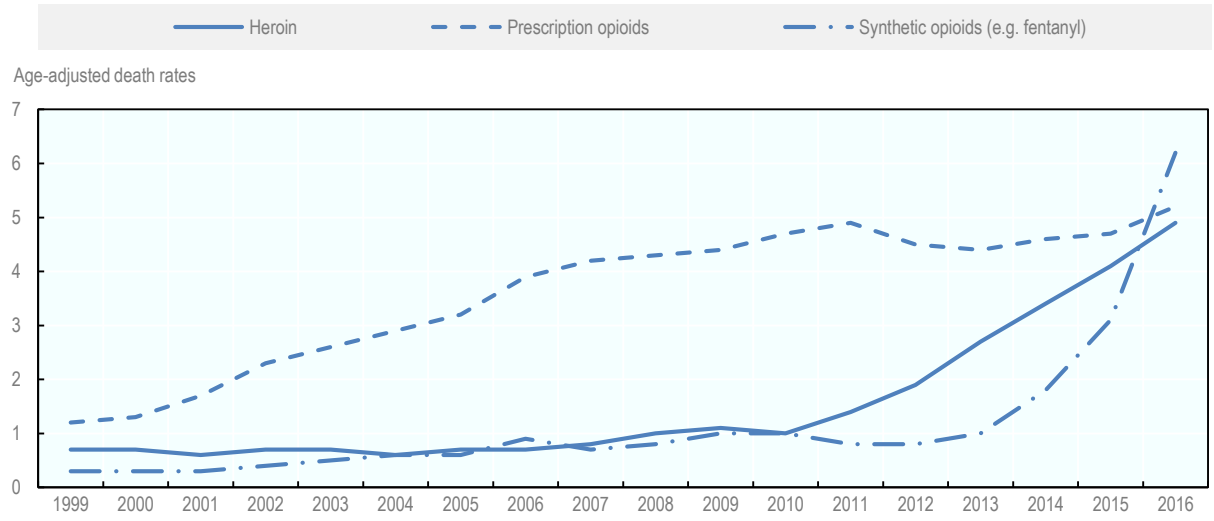
The United States is facing one the worst drug crisis in its history, mainly driven by problematic use of opioids. From 1999 to 2017, 399 230 people died from an overdose involving an opioid, representing 56.8% of all drug overdoses deaths. Opioids were involved in 42 249 deaths in 2016 and in 47 600 overdose deaths in 2017 (67.8% of all drug overdose deaths). From 2013 to 2017, drug overdose death rates increased in 35 of 50 states and DC, and significant increases in death rates involving synthetic opioids occurred in 15 of 20 states, likely driven by illicitly manufactured fentanyl (Scholl et al., 2018[250]).

In 2016, nearly 92 million people reported use of a prescription opioid, while 11.5 million reported inappropriate use, and 2.1 million met the criteria for an OUD (Substance Abuse and Mental Health Services Administration, n.d.[251]). The latter occurred along with an upsurge in injection-related infections, including increments in hepatitis C, endocarditis and osteomyelitis, and HIV diagnoses among persons who inject drugs (Johnson et al., 2018[252]).

This rise in opioid overdose deaths can be outlined in three distinct waves (see Figure 3.7) (CDC Injury Center, 2018[253]; Jones, Einstein and Compton, 2018[254]).

- The first wave began with increased prescribing of opioids in mid-1990s, with overdose deaths involving prescription opioids increasing since at least 1999. In 2016, they were involved in 40% of opioids overdose deaths.
- The second wave began in 2010, with rapid increases in overdose deaths involving heroin. In 2016, they were involved in 36.6% of opioid overdose deaths.
- The third wave began in 2013, with significant increases in overdose deaths involving synthetic opioids – particularly those involving illicitly manufactured fentanyl. In 2016, they were involved in 46% of opioid overdose deaths, which increased to 60% in 2017.

Figure A.4. Overdose deaths involving opioids, by type of opioids, United States, 1999-2016



Source: (CDC-NCHS, 2018[35]).

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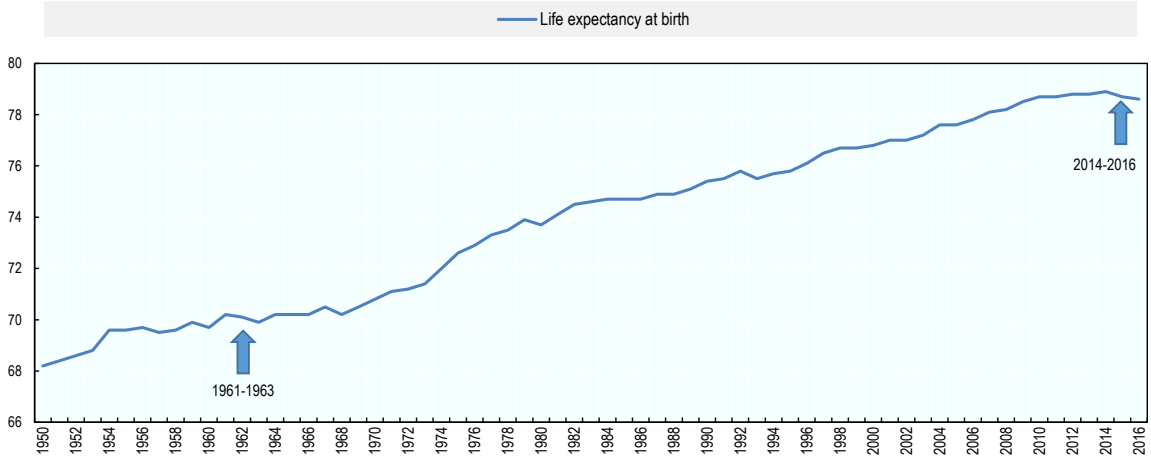
Life expectancy in the United States has fallen in 2015 and 2016, a two-year run that happened for the first time since 1962 and 1963 (see Figure 3.8). These declines in life expectancy are due largely to increases in mortality in younger age groups, especially ages 15-34 and increases in mortality due to unintentional injuries, especially drug overdoses; along with a slowdown in the improvements in mortality. Heart disease mortality in particular is declining at a much slower rate, reportedly driven by the worsening opioid crisis. Recent data for 2017 showed a new slight decline in life expectancy, passing from 78.7 in 2016 to 78.6 years (Murphy et al., 2017[255]).

Figure A.5. Two-year declines in life expectancy at birth: United States, 1950-2016



Source: (CDC-NCHS, 2018[35]).

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Regarding the economic consequences of the opioid crisis, a recent study found that between 1999 and 2015 the decline in labour force participation caused by opioid use in the United States cumulatively cost

the economy 12.1 billion work hours, and the reduction in work hours slowed the real annual economic growth rate by 0.2 percentage points, cumulatively costing USD 702.1 billion in real output (Gitis and Soto, 2018[83]). Likewise, the Council of Economic Advisers in the United States White House estimated the cost of the opioid drug epidemic in 2015 at USD 504 billion or 2.8% of GDP that year, stating that previous data was underestimating the real economic impact of the crisis (Council of Economic Advisers, 2017[34]).

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OECD Health Policy Studies

Addressing Problematic Opioid Use in OECD Countries

Over the past few years, Canada and the United States have been experiencing an opioid crisis as a result of problematic opioid use fueled by the emergence of synthetic opioids such as fentanyl and carfentanil. Problematic opioid use is also spreading in other OECD countries, due to the upward trend of prescription opioid use and the complexities of the illegal drug supply. This report presents evidence on the magnitude of problematic opioid use across OECD countries, describes the main drivers, and identifies a set of policy actions to address them. The report highlights the opioid crisis as a complex public health issue that requires a comprehensive approach across all sectors, including health, social services, and law enforcement. Strong health information systems are also needed, particularly data and research. Preventing problematic opioid use requires a combination of policies that ensure more information is provided to patients and health care practitioners, while providing access to appropriate pain management treatment for patients. A public health approach to problematic opioid use must incorporate socio-economic considerations (e.g. employment and housing), which also need to be addressed to prevent problematic substance use in general.

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