Opioid-related deaths: health and social responses

Introduction

This miniguide is one of a larger set, which together comprise *Health and social responses to drug problems: a European guide 2021*. It provides an overview of the most important aspects to consider when planning or delivering health and social responses to opioid-related deaths, and reviews the availability and effectiveness of the responses. It also considers implications for policy and practice.

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Overview

Key issues

Mortality directly or indirectly related to the use of opioids is a major cause of avoidable premature deaths among adults in Europe, with drug-related mortality rates estimated at around 1–2 % per year among people

who inject opioids. Overall, opioids are detected in more than three quarters of fatal overdoses in Europe. The risk of dying from an opioid overdose increases following periods of abstinence when tolerance is lost, in particular on release from prison or on leaving abstinence-based treatment.

Suicide, accidents and complications from infections also contribute to the excess mortality observed in this group. Studies have also shown that people who use opioids may suffer from higher-than-expected rates of certain non-communicable diseases, including some cancers and cardiovascular problems. An association between opioid-related problems and other substance use issues, such as smoking or high levels of alcohol use, may partly explain this observation.

Evidence and responses

Approaches taken to reduce opioid-related deaths include interventions that focus on preventing the occurrence of overdoses and those that aim to improve the survival chances of people who do overdose.

- **Opioid agonist treatment** ([1]): Enrolling and retaining people who use opioids in effective treatment reduces opioid-related deaths.
- **Naloxone**: The opioid antagonist naloxone can reverse the potentially fatal effect of an opioid overdose. Several interventions seek to ensure the availability of naloxone and promote appropriate use by peers and professionals responding to or intervening in drug overdoses.
- **Extended-release naltrexone implants**: Although their effectiveness in reducing overdose deaths remains uncertain, they may be useful to prevent relapse in opioid-dependent individuals.
- **Continuity of care**: Ensuring continuity in health and drug services during transitions between prison and the community is important as evidence shows that people who use opioids are particularly vulnerable to overdose in the first weeks after release.
- **Overdose risk awareness**: Awareness raising among people who use opioids is particularly important with respect to key risks, including concurrent alcohol or benzodiazepine use.
- **Drug consumption rooms**: Current evidence is insufficient to assess their impact on overdose deaths, but there is an indication that this intervention may support safer injecting behaviour.

In addition, a number of policies and interventions may contribute to reducing people’s vulnerability to overdose. These include, for example, the provision of outreach and low-threshold services that lower access barriers for those seeking help, and integrated overdose prevention policies.

European picture

- It is estimated that one in two people who use opioids in Europe receive opioid agonist treatment, but coverage varies widely between countries. The provision of overdose risk information is available in most European countries although the coverage and approach taken may vary.
- Take-home naloxone programmes exist in more than a third of European countries.
- Just under a third of European countries have one or more drug consumption rooms in operation.

Key issues related to opioid use and mortality

Key questions that need to be addressed when identifying and defining a drug-related problem include who is affected, what types of substances and patterns of use are involved, and where is the problem occurring.

Responses should be tailored to the particular drug problems being experienced, and these may differ between countries and over time. The wide array of factors that have to be considered at this stage in the process are discussed in the *Action framework for developing and implementing health and social responses to drug problems.*

Mortality directly or indirectly related to the use of opioids is a major cause of avoidable premature deaths among European adults. Opioids are implicated in approximately three quarters of fatal drug overdoses. The overall mortality rate for overdose deaths in Europe is close to 15 deaths per million population, although national rates and trends vary considerably. This variation is due to a range of factors, including differences in the numbers at risk of overdose death and variations in the reporting and coding of overdose cases in national mortality databases. In some countries it is likely that opioid deaths are under-reported, making inter-country comparisons more difficult.

All-cause mortality rates among cohorts of people who inject opioids are typically in the range of 1–2 % per year, which is 5 to 10 times that found among peers of the same age and gender in the general population. The primary cause of this increased mortality is drug overdose, but important contributions are made by factors indirectly related to drug use, such as infections, accidents, violence and suicide. Poor physical health is common among people who use opioids and is reflected in high rates of chronic pulmonary and cardiovascular conditions (often tobacco-related) and liver problems from hepatitis C virus (HCV) infections and heavy alcohol use. These conditions account for an increased share of hospitalisations and deaths among this group. There is now an increasingly ageing opioid-using population in many European countries, which may have an impact on both direct and indirect mortality rates. Over the last decade, European data suggest that the number of reported opioid overdose deaths has increased among older age groups and decreased among younger age groups.

The type of substance used, the route of administration and the health of the person using the drug all have an impact on the risk of overdose. Heroin and its metabolites are found in the majority of fatal overdoses in Europe, often in combination with other substances. Other opioids (methadone, buprenorphine and, to a lesser extent, other prescription opioids and fentanils) are detected in a substantial proportion of overdose deaths and predominate in a few countries. The role of illicitly produced synthetic opioids is probably under-reported because their presence is not routinely tested for in many countries.

Typically, multiple substances are implicated in overdose deaths. Benzodiazepines together with alcohol, are frequently found alongside opioids in drug-related deaths in Europe, and they all have respiratory depressant properties. Some benzodiazepines are prescribed medications but, increasingly, new and fake benzodiazepines are being found on the illicit market (see *New psychoactive substances: health and social responses* and *Non-medical use of medicines: health and social responses* and also *Spotlight on… Non-medical use of benzodiazepines*).

Stimulants such as cocaine, MDMA and amphetamines are implicated in a smaller number of overdose deaths in Europe, although their significance varies by country. Outbreaks of deaths associated with new psychoactive substances, such as synthetic cannabinoids, are also a cause of concern in some countries.

A number of situational factors can increase the risk of drug overdose death, including, in the case of people who use opioids, the disruption of treatment provision or discontinuity of treatment and care. In certain situations, for example following detoxification or discharge from drug-free treatment or involuntary abstinence during incarceration, a person’s tolerance to opioids is greatly reduced and as a result there is a particularly

high risk of overdosing if use is resumed. For these reasons, European public health guidance for prison settings recommends ensuring continuity of care between prison and community through referral to suitable community care services and follow-up on release from prison. Finally, the lack of response or inadequate first-aid interventions from those witnessing overdoses, whether due to poor knowledge, lack of access to effective medication or fear of legal repercussions, increases the risk of an overdose event having a fatal outcome.

Evidence and responses to opioid-related deaths

Choosing appropriate responses that are likely to be effective in dealing with a particular drug-related problem requires a clear understanding of the primary objectives for the intervention or combination of interventions. Ideally, interventions should be supported by the strongest available evidence; however, when evidence is very limited or unavailable, expert consensus may be the best option until more conclusive data is obtained. The *Action framework for developing and implementing health and social responses to drug problems* discusses in more detail what to bear in mind when selecting the most appropriate response options.

Responses aimed at reducing opioid-related deaths include interventions geared towards preventing overdoses happening in the first place and those that focus on preventing death when overdoses do occur. In addition, broader public health approaches may be utilised, such as the provision of outreach and low-threshold services that reduce access barriers for people seeking help and may contribute to reducing vulnerability to overdose.

Reducing vulnerability to overdose

Reducing overdose morbidity and mortality is a major public health challenge in Europe. A broader public health response in this area aims to reduce vulnerability among people who use drugs by lowering barriers to, and encouraging engagement with, drug treatment services and other support services, and by providing easily accessible harm reduction services.

As with any other area of healthcare, ensuring quality of care and implementing evidence-based responses are important. In this context the development of national and local overdose prevention strategies can play a major role, particularly if embedded in an integrated approach that holistically addresses the various health and support needs of people who use opioids and encourages engagement between the different stakeholders providing services in this area. Integrated approaches may include, for example, coordination with housing and employment programmes and interventions to combat stigma. The adequate resourcing of services and policy support for their implementation are also crucial factors.

In some European countries, the increasing number of new uncontrolled opioids and other new psychoactive substances being reported to the EU Early Warning System adds to concerns in this area (see *New psychoactive substances: health and social responses*, *Spotlight on… Fentanils and other new opioids* and *Spotlight on… Synthetic cannabinoids*). Given the potential of these drugs to cause harm, it is important that Europe continues to be vigilant and is prepared to respond quickly and effectively to any increase in the threats observed from such substances. This requires investment in surveillance capabilities, including better toxicological information on drug-related deaths. It also signals the need to identify the sources of the substances involved in these deaths in order to formulate appropriate responses (see *Non-medical use of medicines: health and social responses*).

The forensic analysis of drugs has an increasingly important role to play in this area, particularly in identifying

the presence of fentanils, benzodiazepines and other substances on the illicit market that may pose a risk of causing severe harm to users' health, or even death. This may include the analysis of substances provided by people who are using drugs, residues in syringes handed back to needle exchanges, and drugs placed in amnesty bins or obtained from seizures. This information can be used to inform the design of targeted overdose prevention programmes and also constitutes essential and timely input to public health alerts that try to reduce the risk of overdose.

Reducing the risk of overdose

RETENTION IN TREATMENT

The risk of opioid-related overdose is reduced while people who use opioids remain in opioid agonist treatment. A meta-analysis of observational studies has shown that opioid agonist treatment, using either methadone or buprenorphine, reduces the incidence of overdose and all other causes of death in people dependent on opioids. The mortality rate of clients in methadone treatment is less than a third of that found among people who use opioids and are not in treatment.

Analyses of overdose deaths at different stages in opioid agonist treatment suggest that preventive interventions need to be focused on the first four weeks of treatment (particularly for those taking methadone) and the first four weeks after leaving treatment. These are two periods when the risk of overdose is especially elevated. As clients' exit from treatment may be unplanned, this implies the need to also incorporate overdose awareness-raising activities into the ongoing care plans of those receiving help for opioid-related problems. It should also be noted that people who frequently enter and leave treatment are particularly vulnerable to overdosing. People who use opioids immediately after leaving prison have also been shown to have an elevated risk of overdose. During the first four weeks after release from prison, offenders with a history of heroin use have a markedly elevated risk of death, with relapse and opioid overdose being more common during this period. To prevent post-release deaths, proactive and planned referral to community opioid agonist treatment or other appropriate treatment options ('throughcare' or 'continuity of care') are important steps. Services also need to ensure that clients are aware of the risks of overdose and how to reduce them. Training prison staff and engaging prisoners who use opioids with local health services in the weeks following their release also helps to prevent overdose deaths in this population.

In some countries, naltrexone is used to prevent relapse in opioid-dependent individuals. Extended-release naltrexone is a sustained-release injectable formulation of the full mu-opioid receptor antagonist taken monthly. There is some evidence to suggest that extended-release naltrexone may be associated with lower mortality rates than opioid agonists during treatment; however, some uncertainty remains around its effectiveness and more research on this topic is warranted.

PREVENTION OF THE DIVERSION OF OPIOID AGONIST MEDICATIONS

While needing to ensure easy access to and adequate provision of opioid agonist treatment, medical staff and service planners will also need to ensure that prescribing regimes are in place and appropriate controls are abided by to prevent the diversion of agonist medications to those without prescriptions. This will include making clinical guidelines and training available to doctors with respect to appropriate prescribing practices (see *Non-medical use of medicines: health and social responses*). For those with take-home prescriptions, addressing storage and child safeguarding issues is also important to reduce any risk of unintentional overdose by minors.

OVERDOSE AWARENESS TRAINING, SCREENING AND RISK ASSESSMENT

Effective communication can act as a catalyst for reducing harm, as many people who use drugs underestimate or are unaware of their overdose risk. Ideally, overdose prevention, education and counselling interventions should be routinely provided by trained professionals in health and primary care settings, including harm reduction services, such as needle and syringe programmes. Screening people who use opioids for overdose risk may also potentially reduce overall mortality through identifying and offering support to high-risk individuals.

DRUG CHECKING

Although drug-checking services have usually focused on the testing of stimulant drugs, often in recreational settings, in recent years some drug-checking services have been testing for opioids, and in a small number of countries these facilities may be located in harm reduction and low-threshold services.

Drug-checking services enable people who use drugs to have their drugs chemically analysed, providing information on the content of the samples as well as advice, and, when feasible, counselling or brief interventions. Service priorities vary, ranging from information collection to harm reduction by informing and warning people who use drugs about the substances on the market. An important aspect of drug-checking services is how the results are communicated to individuals and whether this is accompanied by harm reduction advice and brief interventions.

Reducing fatal overdoses

Most overdoses occur when others are present, and most people who inject drugs have witnessed or experienced overdoses. Therefore, people who use drugs, and their friends and family, are likely to be both bystanders and potential first responders in emergency overdose situations. These human networks, with appropriate training and awareness raising, may potentially be utilised to prevent overdose deaths. Interventions that aim to improve bystander responses involve training drug users' peers and family members in overdose prevention, recognition and response. Other interventions that seek to reduce fatal overdoses include the distribution of naloxone to reverse overdose effects and the provision in some countries of spaces where people may use illicit drugs under the supervision of trained staff (see *Spotlight on… Drug consumption rooms*).

NALOXONE TO REVERSE OVERDOSE

Naloxone is an opioid antagonist that can reverse the effect of opioid overdoses. In 2014, the World Health Organization (WHO) recommended that naloxone should be made available to anyone likely to witness an opioid overdose. Ensuring that it is available to, and used appropriately by, first responders, such as the police or ambulance staff, and in emergency rooms, is therefore essential.

Naloxone can be administered through injection (with naloxone provided in glass ampoules or pre-filled syringes) or nasal spray. Studies of the pre-hospital management of opioid overdose have now demonstrated that intranasal naloxone is as effective as injectable naloxone. While more often requiring an additional 'rescue' dose, nasal sprays may become the preferred alternative to injectable naloxone in take-home programmes for laypeople, as they are easier to handle and can facilitate the use of the antidote by a wider range of people.

A priority has been to develop interventions that aim to make naloxone more readily available in places where overdoses might occur, such as take-home naloxone and peer-to-peer naloxone distribution. Take-home naloxone programmes combine training on overdose risk and management with the distribution of naloxone kits to those likely to witness an opioid overdose, such as people who use drugs and their peers, friends and family

members. Take-home naloxone programmes can also target other potential first responders to an overdose, such as frontline service workers who interact with people who use drugs, including healthcare providers, staff in homeless shelters and prison officers. As part of these programmes, trainees learn how to recognise and respond to an overdose, including the administration of naloxone, before the arrival of emergency medical help.

Peer-to-peer naloxone distribution programmes engage people who use drugs as (voluntary or hired) peer workers to extend the reach of naloxone distribution and training. They may operate in similar ways to professionally-run take-home naloxone programmes but tap into the privileged access and trust that people who use drugs have with their peers and others likely to witness an overdose. This initiative aims to extend the provision of naloxone to those who tend not to access treatment services.

Recently released prisoners may particularly benefit from access to naloxone. An evaluation of a Scottish programme to distribute naloxone to prisoners on release found that it was associated with significantly fewer opioid-related deaths within a month of the inmates leaving prison.

While an increasing number of studies suggest that educational and training interventions for peers and family members, complemented by take-home naloxone, help decrease overdose-related mortality, more evidence is needed to assess the impact of these interventions.

DRUG CONSUMPTION ROOMS

In some countries drug consumption rooms are available, offering a fixed or mobile space where people who use drugs are provided with sterile injection equipment and can use illicit drugs under the supervision of trained staff. These rooms aim to reduce the risks of unhygienic injecting, prevent overdoses and link people who use drugs with treatment, health and social services (see *Spotlight on… Drug consumption rooms*). They are also designed to reach people who use drugs but do not engage with other health services, especially marginalised people who inject opioids on the streets, in risky and unhygienic conditions.

Drug consumption rooms provide a number of services that may contribute to a reduction in overdose deaths among people who use opioids, including directly intervening in overdoses that occur on-site and promoting engagement in opioid agonist treatment. Some services provide overdose prevention awareness raising and training, including in the use of naloxone.

While evidence for the effectiveness of drug consumption rooms remains scarce, there are consistent data from observational studies that drug consumption rooms may increase the use of safer injecting practices among those who use them. Reductions in the number of overdose deaths have been documented at the local level following the establishment of such facilities; however, the available evidence is insufficient to assess the impact of drug consumption rooms on mortality.

E-HEALTH APPLICATIONS

New e-health applications are now emerging which aim to help reduce the risk of overdose deaths, especially when people are injecting opioids alone. For example, a mobile application was recently developed that allows people who use drugs to log in before they take a dose. Once the app is activated, it requires a confirmation of safety from the user at regular intervals. If the user fails to respond, the app will sound an alarm and alert emergency services.

Statement	Evidence	
	Effect	Quality
Opioid agonist treatment reduces overdose deaths.	Beneficial	Moderate
Naloxone can reverse the potentially fatal effects of an opioid overdose.	Beneficial	High
Long-lasting naltrexone may be associated with lower mortality than opioid agonist treatment during treatment.	Beneficial	Low
Drug consumption rooms may play a role in reducing injecting risk behaviours.	Unclear	Very low
Drug consumptions rooms – there is insufficient evidence to assess their impact on mortality.	Unclear	Very low
There is insufficient evidence to confirm the impact of **take-home naloxone** and **peer-to-peer naloxone programmes** on mortality.	Unclear	Very low

Evidence effect key:
Beneficial: Evidence of benefit in the intended direction. **Unclear:** It is not clear whether the intervention produces the intended benefit. **Potential harm:** Evidence of potential harm, or evidence that the intervention has the opposite effect to that intended (e.g. increasing rather than decreasing drug use).

Evidence quality key:
High: We can have a high level of confidence in the evidence available. **Moderate:** We have reasonable confidence in the evidence available. **Low:** We have limited confidence in the evidence available. **Very low:** The evidence available is currently insufficient and therefore considerable uncertainty exists as to whether the intervention will produce the intended outcome.

European picture: availability of interventions to reduce opioid-related deaths

While around half of European countries report addressing overdose prevention in their national drug strategy or action plan, only a limited number have a specific drug overdose prevention strategy or plan.

All EU Member States and Norway report the distribution of overdose risk information, which is sometimes also available in different languages to make it accessible to migrant and ethnic minority populations. Information on overdose risk and prevention is increasingly being made available through new channels of communication.

All countries in the European Union provide opioid agonist treatment. As retention in opioid agonist treatment is a protective factor against overdose deaths, many European countries have given priority to increasing access to and coverage of such services. It is estimated that one in two people who use opioids in Europe receives some form of opioid agonist treatment, although coverage varies widely by country.

Over a third of European countries offer some form of naloxone training and distribution programme. As new legal pathways have been identified at the national level, Europe has seen an increase in the community-level

distribution of naloxone to people who use opioids, their partners, peers and families, along with training in recognising and responding to overdoses. Take-home naloxone and peer-to-peer naloxone programmes have also been made available to staff of services that regularly come into contact with people who use drugs. New naloxone products, including pre-filled syringes and nasal sprays, have come on the market. The over-the-counter sale of naloxone products is permitted in some countries, while in others, naloxone access is facilitated by programmes run by drug services. Peer-to-peer naloxone programmes have been piloted in a small number of European countries.

Around a third of the EU Member States and Norway have one or more drug consumption rooms in service, with more than 80 drug consumption rooms operating in total. In addition, other European countries are currently considering the implementation of such facilities, although in a number of countries drug consumption rooms have closed. Some were suspended due to legal challenges, others closed because of declining need (along with cost considerations).

Implications for policy and practice

Basics

Core interventions in this area include:

- Sufficient provision of opioid agonist treatment, with adequate dosage, retention in treatment, case management and additional support.
- Naloxone being made available to and used by first responders, such as ambulance staff, paramedics and others who attend overdose incidents.
- Overdose awareness training to promote less risky practice among people who use opioids.
- Prevention of diversion of opioid agonist medications.

Opportunities

- Establish naloxone peer training and distribution programmes to make naloxone widely available to people at high risk of opioid overdose and to their peers, partners and families, to enable them to intervene and save lives.
- Improve continuity of care between prison and the community to prevent drug-related deaths in the first weeks after prison release, when the risk of overdose is particularly high.
- Where they exist, encourage evaluations of the impact of take-home and peer naloxone interventions and drug consumption rooms.

Gaps

- Identify and review barriers to the establishment of drug consumption rooms in areas with high numbers of people injecting drugs in public places.
- Provide enhanced support to those who leave abstinence-based treatment, as their loss of opioid tolerance increases the risk of fatal overdose.

Data and graphics

In this section, we present some data visualisations relevant to health and social responses to opioid-related deaths in the **EU-27, Norway and Turkey**. To view an interactive version of the infographics below, as well as to access source data, click on the infographic.

Infographic. Availability of take-home naloxone programmes in Europe

Infographic. Location and number of drug consumption facilities throughout Europe

Further resources

EMCDDA

- Drug-related deaths and mortality.
- Frequently asked questions (FAQ): drug overdose deaths in Europe, Topic overview, 2021.
- Prevention of drug-related deaths, Topic overview, 2019.
- Take-home naloxone, Topic overview, 2019.
- Drug-related deaths and mortality in Europe: update from the EMCDDA expert network, Technical report, 2021.
- Drug-related hospital emergency presentations in Europe: update from the Euro-DEN Plus expert network, Technical report, 2020
- Best practice portal.

- Drug consumption rooms: an overview of provision and evidence, Perspectives on drugs, 2018.
- Preventing opioid overdose deaths with take-home naloxone, Insights, 2016.
- Preventing fatal overdoses: a systematic review of the effectiveness of take-home naloxone, EMCDDA Papers, 2015.

Other sources

- UNODC, Opioid overdose: preventing and reducing opioid overdose mortality, 2013.

About this miniguide

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([1]) The term *opioid agonist treatment* is used here as preferred language to cover a range of treatments that involve the prescription of opioid agonists to treat opioid dependence. The reader should be aware this term includes *opioid substitution treatment (OST),* which may still be used in some of our data collection tools and historical documents.