Introduction

There is a global epidemic of morbidity and mortality caused by drug overdose, primarily related to opioids. Where data are available, overdose is commonly the leading cause of death among drug users.1 Overdose is a leading cause of death among all youth in some countries, and the leading cause of accidental death among all adults in some regions.2

A growing body of evidence demonstrates that targeted overdose programming can reduce overdose death rates. While the scale at which overdose programming is implemented is still limited, pilot programmes show that barriers to implementation can be overcome.

What is an overdose?

Overdose happens when a person takes more of a drug or combination of drugs than the body can handle. As a consequence, the central nervous system is not able to properly control basic life functions. The person may pass out, stop breathing, have heart failure or experience seizures. Overdose can be fatal, although in a majority of cases it is not. Non-fatal overdose, which can be associated with several health harms, is also a cause for concern.

An overview of overdose epidemiology

Information on overdose mortality is collected through national reporting systems in some high-income countries. These rates are often expressed as the number of deaths per 100,000 in the adult population, thereby allowing comparison over time and between countries. Nevertheless, the different methods of ascertaining death and collecting data make international comparisons difficult. Definitions of overdose also vary, as do the individuals and agencies reporting the data and coding for cause of death or toxicology. Overdoses may not come to medical attention in many countries and it is presumed that data on overdose mortality in general suffer from considerable under-reporting.

Overdose mortality rates are also derived from research where cohorts of people who inject drugs are followed over time. These studies calculate annual death rates and the causes of death. Death rates are often expressed as deaths per 100 or 1,000 life years in order to allow comparison between studies and with death rates in non-drug-using populations. The latter comparison assesses ‘excess mortality’ (i.e. deaths attributed to drug use).

The United Kingdom and Australia have demonstrated epidemiologic coordination and reliable data collection on overdose. In the United States, national data are estimates, although several cities have recently made advances in data collection and selected national agencies are increasingly involved in data analysis efforts. Most other countries have limited national data on overdose, requiring alternative data sources and, frequently, expert opinion to estimate overdose.

This chapter examines the epidemiology of opioid overdose, describes the different elements of overdose prevention programmes and outlines barriers to implementation.

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Overdose data are limited by poor efforts to ascertain causes of death, concern from both witnesses and health care providers about police involvement, limited access to toxicological resources and inadequate collation of data across municipalities and countries. In Russia, overdose death data are available only for registered drug users, who represent approximately 20% of the drug-using population. In some states in Eastern Europe and Central Asia, emergency departments and medical examiner’s offices frequently do not record overdose as the cause of admission or death. This is due to a combination of lack of reimbursement for services, legal implications for patients and families and the social stigma of drug use.

A few surveys have begun to characterise overdose in, for example, Iran, Viet Nam, Thailand and China. While overdose data from African states remains elusive, heroin and other injection drug use appears to have become increasingly prevalent in the region in recent years (see Chapter 2.9).

**Fatal overdose**

Annual mortality rates among people who inject drugs are between thirteen and seventeen times greater than among their non-drug-using peers. The leading cause of death among people who inject drugs in most countries is overdose. Over half of deaths among heroin injectors are attributed to overdose, far exceeding deaths due to HIV/AIDS or other diseases. These trends hold true in the European Union and the United States, where drug overdose exceeds motor vehicle accidents as the primary cause of accidental death in sixteen US states. Overdose remains a leading cause of death among Australian drug users. It is the second leading known cause of death among drug users in Russia, at the highest rate documented in any country, and is a leading cause of death among drug users in most other Eastern European and Central Asian states for which any data are available.

There is evidence to suggest that overdose death has been increasing in many countries over the past decade. For example, drug overdose deaths among adults in the US have risen from 4.0 per 100,000 population in 1999 to 8.8 per 100,000 (26,389 deaths) in 2006.

A review of overdose in several Eastern European and Central Asian states found 17 overdose deaths (among medical examiner cases) in Latvia in 2007; 35 deaths (1.7% of autopsies) in Bucharest, Romania in 2006; 21 deaths (12.7% of ambulance calls for overdose) in Khorog, Tajikistan in 2006; and 57 deaths (9.4% of ambulance calls) in Bishkek, Kyrgyzstan in 2006. Nonetheless, drug overdose is considered by expert opinion to be the leading cause of death among drug users in the last three countries.

In Asia, one study in northern Thailand found a drug overdose death rate of 8.97 per 1,000 person-years among HIV-negative drug users between 1999 and 2002. In Xichang City, China, another study found a heroin overdose death rate of 4.7 per 100 person-years among 379 people who injected drugs from 2002 to 2003.

Little is known about the epidemiology of stimulant overdose, although data are slowly emerging.

Drug overdose death rates are high among people living with HIV/AIDS and account for a substantial proportion of deaths among this population in countries with injection-driven HIV epidemics. Figure 3.6.1 displays non-HIV causes of deaths among all those living with HIV/AIDS in New York City. In 2007 overdose was responsible for 21% of all deaths among people living with HIV/AIDS in Russia and was the second leading cause of death among people living with HIV/AIDS (after tuberculosis).

Figure 3.6.1: Non-HIV causes of death among all people living with HIV/AIDS, New York City 1999–2004

| Table 3.6.1: Overdose mortality in selected countries/regions |
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| **Country/ Region** | **Number of drug overdose deaths** | **Rate per 100,000 person-years** | **Definition** | **Population** |
| Russia | 9,354 | 6.6 | Opioid overdose | Registered drug users (14% to 20% of total drug user pop) / national population | 2006 | Koshkina, Petrozavodsk, Russia, 2008 |
| US | 18,304 | 6.2 | Opioid overdose | National population over the age of 18 | 2004 | MMWR 2007 56: 93–6 |
| EU | 7,557 | 4.4 | Drug-related deaths (60% to 100% are opioid overdose) | National population aged 15 to 39 | 2005 | EMCDDA Statistical Bulletin 2007 |
| Australia | 354 | 3.1 | Opioid overdose | National population aged 15 to 54 | 2004 | Opioid Overdose Deaths in Australia 2004 |
Non-fatal overdose
In addition to the burden of overdose mortality, people who inject drugs experience a high prevalence of non-fatal overdose. Studies found that the proportion of people who inject heroin reporting at least one non-fatal overdose in their lifetime was 59% in sixteen Russian cities, 48% in San Francisco, 41% in Baltimore, 42% in New York City, 68% in Sydney, 38% in London, 30% in Bangkok, and 83% in Bac Ninh, North Viet Nam. Rates of non-fatal overdose within the previous twelve months range from 10% to 20%, with 12% of heroin users in Xichang City, China reporting at least one such overdose. Non-fatal opioid overdose has been associated with numerous negative health outcomes, including pulmonary oedema, pneumonia, cardiac arrhythmia and cognitive impairment in between 5% and 10% of cases.

Risk factors for overdose
Following a relative hiatus in research during the 1980s, overdose has been increasingly studied over the last two decades. Investigations were initially most prominent in Australia in the mid-1990s, with researchers describing drug overdose in ways that have proven fairly consistent with reports from elsewhere. Based on reviews of medical examiner data, ambulance and emergency centre records and drug user surveys, overdose is believed to be primarily due to opioids, mostly injected, with death occurring most often among older users, although younger users may have more frequent non-fatal overdose events.

The most notable risk factors for overdose among drug users are a prior overdose, a recent period of abstinence (e.g. substance abuse treatment, incarceration, self-imposed abstinence) and concomitant use of other drugs including depressants (alcohol, benzodiazepines and barbiturates) as well as stimulants. HIV-positive status is associated with a two or three times increased risk of overdose death. Although the reason for this is unclear, it may be due to the presence of an HIV-related condition such as liver, pulmonary or systemic dysfunction. While drug potency and impurities may contribute to overdose, variations in purity appear to account for only about one-quarter of variations in overdose mortality.

Who can overdose?
There are estimates of what constitutes a ‘lethal dose’ of a particular substance, but these can only really help to determine what might cause overdose for someone using it for the first time and without mixing it with other substances. For most people who use drugs, it can be difficult to predict how much of a certain drug, or combination of drugs, will lead to an overdose. Individual characteristics such as a person’s weight, health, tolerance for a drug at a particular time, drug potency, route of administration and speed of use all play a role in determining how much a person’s body can handle.

About two-thirds of people who inject drugs will experience an overdose at some time. Based on experience and estimates from developed countries, approximately one-half of overdoses will receive medical attention, while the other half will be managed by bystanders, with roughly 4% resulting in death. If medical attention is received within a couple of hours of the overdose, most people will survive. However, drug users may be reluctant to call for help due to fear of police attendance or perceived mistreatment by medical personnel. People who overdose and bystanders have in rare cases faced legal consequences. If reported by the media these cases can perpetuate fear and deter people from seeking assistance for overdose.

Regional variations
While the characteristics of overdose epidemiology are fairly well researched in many high-income countries, information is confined to anecdotal reports or small-scale surveys in much of the rest of the world. Factors that may influence overdose epidemiology in different settings include the types of drugs used and patterns of use, social support networks of drug users and the availability and accessibility of health care for people who use drugs. Further understanding of these factors and their influence on overdose risk in different settings would help to inform the planning and evaluation of overdose prevention programmes in community contexts.

In Eastern Europe and Central Asia, for example, there is wide variation in the availability of heroin versus other injectable opioids. Ukraine has a largely seasonal market for shirka, an injectable opioid produced from locally grown poppy, which may contribute to overdose as users’ cycle in and out of opioid use. Drug users in this and other regions also frequently live at home and have close family relationships and so may benefit from overdose prevention programmes targeted at educating and distributing naloxone to family members. Opium remains the dominant cause of overdose in Tehran, Iran and is a major drug of choice in China although overdose rates are unknown. The predominance of cocaine in Latin America and of amphetamine-type stimulants in much of Asia and parts of Eastern Europe is likely to have a significant effect on overdose incidence and mortality. It is also likely that limited availability of ambulances, delayed arrival of medical services and lack of availability of naloxone for use by medical personnel in many countries affects the morbidity and mortality of overdose.

An overview of overdose prevention programming
Overdose was not traditionally considered preventable. Over the past fifteen to twenty years, however, researchers and service providers have developed several strategies to reduce overdose incidence and mortality. Driven by experience and research findings, overdose prevention programmes generally include education and awareness building, efforts to create supportive public policy environments, first responder training and increasing the availability of naloxone, both as take-home doses for opioid users and for medical personnel in severely under-resourced settings.

Although not designed as overdose prevention programmes per se, opioid substitution (methadone and buprenorphine) maintenance services are strongly associated with reduced overdose. For example, there was a 79% reduction in opioid overdose over the four years following introduction of buprenorphine maintenance in France in 1995. Similarly, safer injection facilities in eight countries have overseen millions of injections and experienced no overdose deaths. As overdose risk is higher among those who inject, efforts to encourage transition to other routes of administration might prove useful in reducing overdose.
Since the late 1990s there has been an increase in overdose prevention programmes in many countries, particularly programmes targeting heroin and other opioid users. The majority of these programmes are run by non-governmental organisations, although government public health agencies have become increasingly involved in several EU countries. Current overdose prevention education aims to alter individual behaviours that increase risk of fatal overdose and to increase the likelihood that people who inject drugs recognise and properly respond to witnessed overdoses.58

What is an overdose prevention programme?
An overdose prevention programme is any cooperative effort designed to give people who use drugs the skills and materials necessary to prevent overdose from occurring and to respond effectively to those that do occur. A programme may involve harm reduction, medical, criminal justice or any other professionals engaging with drug users, and necessarily involves people who use drugs as leaders. Programmes are usually, but not always, integrated with an array of other drug or HIV services. They operate on any scale and in any setting where there is an opportunity for reducing the experience of overdose or its impact.

Major elements of an overdose prevention programme may include:

Community needs assessment: Most programmes develop a needs assessment to understand the unique characteristics of overdose in that locality. This often involves surveys and focus groups with people who use drugs and a review of relevant scientific literature. Some programmes seek partnerships with political leaders, law enforcement personnel and/or emergency medical providers to create greater buy-in, improve the care that drug users receive and reduce the involvement of police when emergency assistance is requested.

Education: Most programmes provide face-to-face education and informational materials with the aim of reducing overdose frequency by educating people who use drugs about the risk factors for overdose in their region. Modifiable risk factors include advice about how to use drugs after a recent period of abstinence, such as incarceration, hospitalisation, detoxification or self-imposed abstinence, as well as problems with the concomitant use of other drugs with opioids, such as cocaine, benzodiazepines or alcohol.1 Other major risk factors include previous overdose, older age and health status. Using alone, while not known as a risk factor for overdose, almost certainly increases the risk of fatal overdose in the case of overdose and is a major issue for drug users who are socially isolated.59 Educating people who use drugs on the risks of injecting versus other routes of administration such as smoking may also be useful in overdose prevention programmes.60

Training: Training people who may be present during an overdose (e.g. family or friends of drug users, or people working in places where overdose might occur) to identify and respond correctly to overdose is the most common approach employed in prevention programmes. Training is offered in a variety of settings and sessions may range in length from five minutes to three hours depending on the circumstances. Most programmes offer training for people who use drugs (as well as non-using friends or family) in identifying overdose based on breathing and response to stimuli, and teach participants how to respond to overdose with rescue breathing, a simple intervention that addresses the primary cause of opioid overdose death – respiratory depression. Cardiopulmonary resuscitation (CPR) training can be important to managing stimulant or polydrug overdoses. Research has demonstrated that people who use drugs can learn first response and rescue breathing techniques and can remember what to do when asked at a later date,61 62 63 and that bystander-administered CPR improves outcomes for heroin overdose victims.64 If a programme distributes naloxone, training on its proper use must also be provided. It is also important to dispel incorrect beliefs and myths around overdose prevention and to identify what does not work.

Naloxone distribution: Naloxone distribution is the centrepiece of many programmes, mainly because of its capacity to overcome barriers to seeking medical care for overdose (fear of arrest, inadequate or disrespectful care etc.). Existing programmes have adopted a very wide range of distribution schemes, in part due to local regulations or other policies. However, the basic goal is to maximise the probability that naloxone will be in the hands of a trained responder who is present at the time of an overdose.

Policy advocacy: Advocacy goals often include legislative reform, improved collaboration with police and emergency medical providers and greater overdose awareness among professional and research bodies. Laws covering ‘good Samaritan’-type actions can be enacted that protect witnesses from prosecution when calling for help with an overdose and that protect individuals from liability for administering naloxone to others in the case of a suspected overdose. For example, police orders have been issued in Australia and elsewhere to restrict the role of police accompanying paramedics to an overdose incident and avoid arrests.40 Advocacy has also been undertaken to encourage government agencies to take responsibility for oversight of national policy on overdose.

Monitoring and evaluation: While small or under-resourced programmes may avoid creating more work through data collection, most programmes routinely document basic demographic and overdose history data from their participants, as well as information on training, naloxone distribution and reports of overdose response from participants. As data on overdose is generally lacking, prevention programmes are often an important source of basic information that can inform research on viable intervention strategies and other aspects of overdose.

A recently launched website – www.take-homenaloxone.com – provides information on existing naloxone programmes worldwide.
While overdose education is not new to harm reduction, the major innovation of recent programmes has been to put naloxone in the hands of opioid users and their friends and family in order to maximise the potential that the medication is available immediately at the scene of an overdose. Naloxone is uniquely effective at reversing opioid overdose, with response times of one to three minutes, no contraindications except for allergy and no well-established side effects distinct from the medical consequences of overdose itself. The effects of naloxone last for between thirty minutes and one hour, long enough for adequate metabolism of most short-acting opioids (including heroin) so that significant respiratory depression is unlikely to reoccur.

Naloxone can be administered intravenously, intramuscularly or subcutaneously with similar response times (due in part to the time required to find a vein). Intranasal administration, through the use of atomisers, has emerged as a novel approach that avoids the distribution and use of needles and, according to several studies, is between 80% and 100% as effective as injected naloxone.

**What is naloxone?**

Naloxone, also known as Narcan and other brand names, is a medication used to reverse the effects of opioids, most importantly the respiratory depression that causes death from overdose. Naloxone is a pure opioid antagonist, meaning it ‘kicks out’ opioids from receptors in the body. It is safe, with no significant side effects and no potential for misuse. Naloxone is usually effective one to three minutes after intravenous, subcutaneous, intramuscular or intranasal administration. It is mainly available in a 0.4 mg/ml liquid formulation, with 1–2 ml considered a standard effective dose when injected, or slightly higher when administered intranasally.

The first large-scale effort at naloxone distribution began in 1997 through the Chicago Recovery Alliance, with similar programmes established around the same time in Berlin. Programmes were later set up in a number of other US cities and in the UK, Canada, Russia, Ukraine, Tajikistan, Afghanistan and elsewhere. Most recently, programmes have been launched in Georgia and Kazakhstan. More sporadic or semi-underground naloxone distribution has occurred in Cambodia, China, Thailand and other countries. Naloxone has been available over the counter at pharmacies in Italy since the 1980s. In Chicago, which is still home to one of the largest programmes, by May 2009 the programme had distributed over 11,000 naloxone kits and received reports from participants of more than 1,000 successful overdose reversals. Newer and smaller programmes are also finding ways to scale up. In Russia, five pilot overdose prevention programmes trained more than 1,500 people who inject drugs in overdose prevention and response and distributed more than 6,000 doses of naloxone in 2009.

Overdose prevention programming has been taken up in a much wider range of settings, including primary care medical clinics, HIV and homeless services, opioid substitution therapy programmes and prisons and jails. In the US, evidence to suggest that prescription opioid overdose death rates have risen to similar levels as heroin overdose prompted the launch of programmes, including Project Lazarus in North Carolina and at least one arm of the US military, to develop education protocols to provide naloxone to patients receiving opioid prescriptions.

Though growing, the overall level of funding for overdose prevention programmes remains small. Early programmes were often initiated with private contributions. Today, funding for programmes is largely from government public health agencies in higher income countries, and from private and multilateral donor agencies in lower income countries. The Global Fund to Fight AIDS, Tuberculosis and Malaria, the largest single donor agency for HIV/AIDS programmes, has indirectly supported overdose prevention programming (including naloxone purchase) in Russia and Ukraine, where overdose is a significant health issue for people living with HIV/AIDS.

Interest in the evaluation of overdose prevention programmes has increased with the number of programmes, but research is still in the early stages. Although several qualitative studies and small pilot evaluations suggest the effectiveness of naloxone distribution, there are no definitive studies demonstrating effectiveness and no formal cost-benefit analyses. Importantly, no study has shown a statistically significant association between overdose prevention programmes (including naloxone distribution) and population-level reductions in overdose mortality.

Obstacles include weak or inconsistent data collection, which means that there are often no reliable baseline data and that officially reported data on overdose may not be comparable from one location to another or over time. Research funding has been scarce, such that most studies have been relatively small-scale collaborations between overdose programmes and researchers, or limited to documenting basic overdose history data and self-reported overdose reversals by programme participants. Moreover, experimental study designs with control groups not receiving naloxone raise substantial ethical questions. Finally, overdose death is a ‘statistically rare event’ that varies over time for reasons that are not yet clear. Therefore, large studies are required to investigate an impact on mortality rates. Case-control studies may prove more feasible.

Nonetheless, existing data are promising. Ample data demonstrate the acceptability of naloxone distribution for service providers and drug users. Programmes in the US and the UK have been shown to be effective at teaching people who use drugs how to prevent and manage overdose. Ecological data suggest a reduced level of overdose fatality in some locations during a period of naloxone distribution.

Programmes in the US and UK, which routinely record the number of naloxone kits distributed and the number of clients reporting use of naloxone to save a life, generally report that between 10% and 20% of kits result in a ‘save’, almost all of which were considered appropriate uses by programme staff. New research efforts include the N-ALIVE study in the UK, which is evaluating naloxone dispensing to prisoners.

In the absence of more compelling evidence of effectiveness, many people, including some within the harm reduction movement, remain sceptical and caution against the wider roll-out of overdose prevention programmes, particularly with regard to resource issues related to the expense of naloxone. Others feel that better data are not necessary to support naloxone
distribution programmes. Many providers and advocates have lost clients and friends to overdose and believe – much as syringe exchange advocates did in the 1980s – that research may lag behind service.

**Barriers to overdose prevention services**

Several important policy and logistical barriers have slowed the wider adoption of overdose prevention programmes around the world. Major barriers include poor commitment from public health agencies to reduce overdose-related mortality, lack of investment in systematic data collection on overdose mortality, poor health care systems and, in particular, emergency health care provision, poor availability of naloxone, the prioritisation of law enforcement over public health and more broadly a lack of public support for drug user health initiatives.

**Government commitment:** Few governments have established drug overdose to be within the remit of a specific agency. As a result, overdose prevention programming is often overlooked. In low- and middle-income countries, where available, programmes form small components of HIV programmes and are often funded by international donors.

**Data collection:** Overdose data are inadequate in most countries and almost non-existent in many others. Greater investment in the systematic collection of data on overdose mortality and the characteristics of overdose is necessary to provide a clearer picture of its impact on people who use drugs, particularly in low- and middle-income countries. This information is also important to inform overdose prevention programmes that are tailored to the particular communities they serve.

**Emergency health care services:** While emergency health care and hospital-based overdose care are available in many countries, several factors can impede access for people who use drugs, including distance, inadequate number of ambulances and limited access to naloxone for medical providers.1 Naloxone may not be carried in ambulances, or may be restricted to specialised ambulances, in major city centres. Medical services are often state-funded, although in some countries patients give ‘tips’ for service or have to pay for fuel costs. While police may or may not be involved in emergency medical services, fear of police involvement is a major deterrent to calling for emergency assistance in all countries that have been studied. Some countries, such as Kyrgyzstan and Romania, require witnesses to drug use to contact police.1

**Naloxone availability:** Although naloxone is on the World Health Organization Model List of Essential Medicines, in some countries it is not registered as a medication at all or is available in extremely limited fashion. Even in countries where naloxone is available, some emergency medical services do not carry the drug. Overdose programming in Tajikistan has included providing naloxone to emergency health care and hospital staff, leading to an impressive reduction in mortality among those overdoses attended to by medical professionals in Khorog.1

In some locations, several issues have combined to increase the cost of naloxone. In the US, for example, Hospira became the only manufacturer of the naloxone solution in 2007 and naloxone prices for harm reduction agencies roughly doubled over the following year. Hospira, as well as most European manufacturers, also relies on a single source, a German corporation called Mallinckrodt, for naloxone powder base. Quotas on the availability of noroxymorphone, naloxone’s opioid precursor, may also keep prices unnecessarily high. Elsewhere, there is also local naloxone production, notably in countries with indigenous legal opium manufacture (e.g. India and Ukraine). While the US Food and Drug Administration approved injectable formulations of naloxone in 1971, no device has been approved for intranasal administration in the country, which limits insurance reimbursement opportunities.

**Law and policy:** Overdose is rarely addressed in policy documents and prevention of overdose is frequently not a priority for policy makers. Laws and policies related to overdose often appear contradictory in that overdose bystanders or medical providers may be legally obligated to report overdose to police, while people who use drugs are simultaneously promised access to medical services. Naloxone distribution for use by non-medical people is probably legal in the US,74 has been legal in the UK since 2005 and is either legal or likely to be tolerated in many other countries. Nonetheless, health care providers not accustomed to harm reduction approaches may desire formal support for overdose prevention practices.75 Several US states, including California, Connecticut, New York, New Mexico, Massachusetts and Washington, are at the forefront of developing and harmonising laws and policy to support overdose prevention. This includes laws that protect witnesses who call emergency services, laws that explicitly authorise use by non-medical people of naloxone for opioid overdose and laws and policies establishing funding streams for overdose prevention research and programming.84

**Conclusion**

Drug overdose is a major and longstanding source of morbidity and mortality throughout much of the world. The situation has worsened in many countries over the past twenty years. Although governments have long ignored the subject, service providers and researchers have determined overdose to be largely preventable and have identified several approaches to achieve reductions in medical complications and death. Community-based programmes have emerged to reduce overdose and are often incorporated into other low-threshold drug services and primarily based on the distribution of naloxone. An increasing number of studies are attempting to evaluate the effectiveness of these interventions. Policy changes to improve overdose management and access to emergency medical care have proved possible in several locations and should be a priority in many others. Although current investment in overdose prevention and management remains grossly inadequate to address the number of lives being lost, a vibrant field of intervention and research has emerged that promises to reduce the losses suffered worldwide by people who use drugs and their friends and families.