

PERSPECTIVES ON DRUGS Preventing overdose deaths in Europe

More than 8 000 lives were reported to be lost to drug overdoses in Europe (EU28 plus Turkey and Norway) in the past year and this is an underestimate. Reducing drug-related deaths therefore remains a major challenge for public health policy. This analysis describes some of the factors that increase the risk of fatal and non-fatal overdoses and a number of interventions developed to prevent these events. The heroin epidemics that spread across Europe in the 1980s resulted in increasing numbers of overdose deaths among opioid users, which peaked for the first time around the turn of the millennium (¹), and then again in 2008 with 8 174 cases. A new record number was registered in 2015 with 8 440 (EU28 plus Turkey and Norway) overdose deaths. At country level, the most recent data from a number of EMCDDA reporting countries with relatively robust reporting systems, including Sweden, Lithuania, Ireland and the United Kingdom, show an increase.

Drug overdose continues to be a major cause of death, especially among young people in Europe, with recent data showing that young males are disproportionally affected, with 53.5 death cases per million among those aged 35–39, compared to 14.3 deaths per million in the whole population. European countries have implemented a variety of approaches in their attempt to reduce overdose deaths at the national level using evidence-based interventions drawing on an understanding of individual and environmental risk factors.

Which factors increase the risk of fatal and non-fatal overdose?

The type of substance used, the route of administration and the health of the user all have an impact on the risk of overdose. Most overdose deaths are linked to the use of opioids, primarily the injection of heroin. Heightened levels of risk are also associated with the misuse of certain prescription

(¹) In this analysis, the term 'overdose deaths' refers to deaths that are caused directly by the consumption of one or more illicit drug (http://www.emcdda.europa. eu/activities/drd). Generally, overdose deaths occur shortly after the consumption of the substance(s). These deaths are also known as 'poisonings' or 'drug-induced deaths'.

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drugs (e.g. benzodiazepines), and the non-medical use of prescribed substitution medications and opioid analgesics (Giraudon et al., 2013). Potent synthetic opioids, such as fentanyl and its newer derivatives seem to play an increasing role in drug overdose in Europe. In addition, a substantial number of deaths involve polydrug use, particularly heroin in combination with other central nervous system depressants, such as alcohol or benzodiazepines.

A number of environmental factors increase the risk of drug overdose death including, in the case of opioid users, disruption of treatment provision or discontinuity of treatment and care. In certain situations, for example following detoxification or discharge from drug-free treatment, the tolerance of drug users to opioids is greatly reduced and as a result they are at particularly high risk of overdosing if they resume use. For these same reasons, inadequate throughcare between prison and community has also been identified as an important environmental risk factor (Zlodre and Fazel, 2012). In a cohort study in England, differences in the risk of fatal opioid poisoning were identified, dependent on the type of treatment received: opioid users who received only psychological support appeared to be at greater risk than those who received opioid agonist pharmacotherapy (Pierce et al., 2016).

Finally, the lack of response or inadequate interventions by those witnessing overdoses, whether due to poor first aid knowledge, lack of access to effective medication or fear of legal repercussions, increases the risk of an overdose event having a fatal outcome (Frisher et al., 2012). A study in Bergen, Norway analysed differences in the time emergency services needed to arrive after overdose call-outs to private or public addresses. Ambulance response times were more likely to be longer for private locations; victims at private homes were more likely to be left at the scene after being treated and less likely to be transported to hospitals (Madah-Amiri et al., 2016).

A range of responses: reducing the number of overdoses and preventing deaths

Drawing on the insights gained from risk and protective factors, the prevention of overdose deaths is generally addressed at two levels: the first involves a set of interventions geared towards the complete prevention of overdoses, while the second focuses on reducing fatal outcomes when overdoses do occur (Frisher et al., 2012). At both levels, strategies used include the scaling-up of known protective factors and the reduction of existing risks. Below, we introduce some of the most important strategies used by countries to address these intervention levels.

Facts and figures

1.3 million high-risk opioid users in Europe, including Norway

8 440 overdose deaths in 2015 (EU28 plus Turkey and Norway) — Highest number of overdose deaths ever reported

54 deaths per million male population aged 35–39 due to overdose

667 000 cclients in opioid substitution treatment in 2015

10 countries with take-home naloxone programmes

8 European countries, including Switzerland, with drug consumption rooms

Increasing awareness of and information about overdose risks

As many drug users either are unaware of or seriously underestimate overdose risks, effective communication with users can act as a catalyst for reducing harm. Ideally, overdose prevention, education and counselling interventions would be provided by trained professionals as a matter of routine in the relevant health and primary care settings. Screening for overdose risk by those treating heroin users may contribute to reductions in overall mortality (Darke et al., 2011), while the use of overdose risk assessment interventions can assist the early identification of high-risk individuals. Twenty-eight EMCDDA reporting countries now report the distribution of overdose risk information, which is sometimes also available in different languages in order to be accessible to migrant drug users. There is increasing use of the internet and new channels of communication in this field, for example an e-health overdose risk assessment tool and overdose awareness videos, which may be projected in the waiting rooms of drugs facilities (e.g. http://vimeo.com/ album/1655129). Acknowledging the similarity of trends in mortality related to prescription opioids in Europe to those witnessed in the United States, countries now have an opportunity to adapt and scale up their prevention measures, reinforce surveillance and introduce improved regulatory measures to prevent deaths reaching epidemic proportions (Giraudon et al., 2013).

Provision of effective drug treatment and retention in treatment

There is convincing evidence that opioid substitution treatment (OST) substantially reduces the risk of mortality, as long as doses are sufficient and continuity of treatment is maintained (e.g. Degenhardt et al., 2011, Pierce, 2016). A prospective observational cohort study conducted in Edinburgh confirmed that survival is increased by cumulative exposure to treatment (Kimber et al., 2010). As retention in drug treatment is a protective factor against overdose deaths, many European countries have given priority to increasing access to and coverage of treatment services.

With OST provision high, medical staff and service planners face the challenge of minimising the diversion of substitution medications to those without prescriptions while continuing to ensure that access to treatment is not impeded, for example by supervising consumption. Another widely used approach to reducing the risk of overdose is the implementation of good treatment practice, which involves the use of clinical guidelines and training doctors in prescribing practices (including benzodiazepine prescribing).

Improving throughcare between prison and community

Several interventions are recommended to help reduce the high number of overdose deaths among former prisoners in the period shortly after leaving prison (Merrall et al., 2010; Binswanger et al., 2013). These include pre-release education on overdose risks and prevention, continuation and initiation of substitution treatment (Degenhardt et al., 2014) and improved referral to aftercare and community treatment services (WHO Regional Office for Europe, 2010). In England, an individually randomised trial (NALoxone InVEstigation: N-ALIVE) aimed to test the hypothesis that giving naloxone on release to prisoners with a history of heroin injecting would reduce heroin overdose deaths in this population during the first 12 weeks after release, when there is an increased risk of drug-related death (Strang et al., 2013) (see further information in section 'Improved bystander response' and section 4: 'Take-home naloxone' below). Results from the third year of the Scottish National Naloxone Programme were released around the time of an interim analysis of the N-ALIVE trial in 2014. The results indicated a significantly lower proportion of opioid-related deaths had occurred within four weeks of prison release and it was decided to stop the N-ALIVE trial and to recommend naloxone be offered to all remaining prisoners upon release (Bird et al., 2016; Information Services Division, 2016; Parmar et al., 2016).

Prevention of deaths in overdose situations

A second set of responses focuses on the prevention of fatalities when overdoses occur. These include a range of targeted interventions, the purpose of which is to enhance safety and ensure a rapid and effective response in emergency situations.



Supervised drug consumption rooms

A total of 78 facilities for supervised drug consumption operate across six EU Member States (Denmark, France, Germany, the Netherlands, Luxembourg, Spain) and Norway, serving specific subgroups of highly marginalised and homeless drug users. Supervised drug consumption facilities aim to reach marginalised high-risk drug users and connect them to the wider network of care, to reduce the acute risks of diseases and overdose death associated with injecting or inhalative drug use, and to reduce public drug use (EMCDDA, 2015a). Consumption rooms are highly targeted services, usually integrated within facilities that offer a broad range of other health and social services. They provide a safer drug use environment, advice on safer injecting and medical supervision, and are equipped to manage drug overdoses and reduce related morbidity and mortality. Millions of injections have been supervised and no overdose fatalities have occurred in the facilities. Evidence from robust studies documents increased access to health and social services among clients of supervised drug consumption facilities, and decreased public drug use and associated nuisance. A reduction in overdose mortality at the population level was documented in the city of Vancouver, in the local area where a supervised injecting facility operates (Marshall et al., 2011). See also Drug consumption rooms (EMCDDA, 2015b).

Improved bystander response

Most overdoses occur when others are present and most injecting drug users have witnessed or experienced overdoses. Therefore, drug users themselves, or their friends and family, are likely to be both bystanders and potential first responders in emergency overdose situations (Strang et al., 2008). These human networks, with appropriate training and awareness raising, can be utilised to prevent overdose deaths. Interventions that aim to improve bystander responses consist of training peers and family members of drug users in

overdose prevention, recognition and response. A contextual analysis of ambulance call-outs to emergencies at private addresses (Madah-Amiri et al., 2016, see section on risk factors above) also indicates potential opportunities for peer overdose prevention interventions. In their new guidelines on community management of opioid overdose, the Word Health Organization (WHO) recommends that people likely to witness an opioid overdose should have access to naloxone — an effective antidote that can reverse opioid intoxication — and should be instructed in its administration (WHO, 2014). Evidence shows that educational and training interventions for peers and family members, complemented by take-home naloxone, help decrease overdose-related mortality. With evidence on its effectiveness growing, take-home naloxone provision has gained more attention in recent years. In January 2016, the EMCDDA launched a publication that brings together evidence as well as experiences from take-home naloxone projects in Europe and elsewhere (EMCDDA, 2016).

Conclusions

Drug overdose deaths are preventable, and there is good evidence to show that specific interventions can both reduce the occurrence of overdose events and prevent fatal outcomes in overdose situations. The accumulated knowledge about risk and protective factors associated with overdoses, and about the successful management of overdose situations, has grown. Access to OST, which constitutes an important protective factor, has been substantially scaled up across the region. In addition, some countries have introduced new and targeted approaches, searching for innovative ways to identify those at risk of overdose, to raise risk awareness and to enable those who witness overdoses to intervene and prevent fatal outcomes.

Interactive element: videos



Video: example of an overdose awareness video projected in waiting rooms of drugs facilities available on the EMCDDA website: emcdda.europa.eu/topics/pods/ preventing-overdose-deaths



Video:Take-home naloxone programmes in Europe — overdose prevention available on the EMCDDA website: emcdda.europa.eu/topics/pods/preventing-overdose-deaths

Peer naloxone distribution

Naloxone is an opioid antagonist medication used worldwide in emergency medicine to reverse respiratory depression caused by opioid overdose. Naloxone is listed by the World Health Organization as an essential medicine and is available in injectable form (intramuscular and intravenous) and in some countries as an intranasal spray, e.g. a nasal formulation has been approved by the U.S. Food and Drug Administration and is in use since 2015. The number of community-based opioid overdose prevention programmes that train potential bystanders, such as opioid users and their peers and family, on how to administer naloxone in order to reverse the effects of opioid overdose are increasing as overdose prevention response in the United States and Europe (CDC, 2012, Clark et al., 2014; Williams et al., 2014; Madah-Amiri et al., 2017).

In its 2015 systematic review of 21 studies on take-home naloxone, the EMCDDA found evidence that educational and training interventions complemented by take-home naloxone decrease overdose-related mortality and that opioid-dependent patients and their peers involved in such programmes effectively improved their knowledge on the correct use of naloxone and the management of witnessed overdoses (EMCDDA, 2015). A meta-analysis of pooled data from four studies on bystander naloxone administration and from five studies on overdose education programmes (Giglio, Li and Di Maggio, 2015) confirmed these findings, finding an association of such programmes with increased odds of recovery and improved knowledge of overdose recognition and management in non-clinical settings. Currently, ten European countries (Denmark, Estonia, France, Germany, Italy, Ireland, Lithuania, Norway, Spain and the United Kingdom) report the existence of take-home naloxone programmes or local projects, some of which are small and time-limited. Scotland and Wales run nationwide programmes of naloxone distribution to high-risk users in the community and provide the medication to inmates released from prison. A comparison of the proportion of opioid-related deaths that occurred within four weeks of release from prison before (2006–10) and after (2011–13) the introduction of a national naloxone programme in Scotland showed a significant reduction from 9.8 % to 6.3 % of all opioid related deaths (Bird et al., 2016).

As increased access to the opioid antagonist naloxone can reduce opioid-related morbidity and mortality, many US states have changed policies and legislation to increase layperson access to naloxone. For example, 44 states permit naloxone to be prescribed for administration to a person with whom the prescriber does not have a prescriber-patient relationship. Furthermore, pharmacy naloxone dispensing is encouraged (Davis and Carr, 2016).

In European countries as well, legislative reform may be needed to allow the low-threshold provision of naloxone, a measure regarded as a low-cost approach that can empower healthcare workers and people who use drugs to save lives (WHO, 2014, p. 9).

References

- Bird, S. M., Mcauley, A., Perry, S. and Hunter, C. (2016), 'Effectiveness of Scotland's National Naloxone Programme for reducing opioid-related deaths: A before (2006–10) versus after (2011–13) comparison', *Addiction*, 111(5), pp. 883–891. http://doi. org/10.1111/add.13265
- Binswanger, I. A., Blatchford, P. J., Mueller, S. R. and Stern, M. F. (2013), 'Mortality after prison release: opioid overdose and other causes of death, risk factors, and time trends from 1999 to 2009', *Annals of Internal Medicine* 159(9), pp. 592–600. doi:10.7326/0003-4819-159-9-201311050-00005
- Centers for Disease Control and Prevention (CDC) (2012), 'Community-based opioid overdose prevention programs providing naloxone United States, 2010', *Morbidity and Mortality Weekly Report* 61, pp. 101–104. Online at: http://www.cdc.gov/mmwr/ preview/mmwrhtml/mm6106a1.htm
- Darke, S., Mills, K. L., Ross, J. and Teesson, M. (2011), 'Rates and correlates of mortality amongst heroin users: findings from the Australian Treatment Outcome Study (ATOS), 2001–2009', *Drug and Alcohol Dependence* 115, pp. 190–195. doi:10.1016/j. drugalcdep.2010.10.021
- Davis, C. and Carr, D. (2016), 'State legal innovations to encourage naloxone dispensing', *Journal of the American Pharmacists Association*, https://doi.org/http://dx.doi.org/10.1016/j.japh.2016.11.007
- Degenhardt, L., Bucello, C., Mathers, B., Briegleb, C., Ali, H., Hickman, M. and McLaren, J. (2011), 'Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies', *Addiction* 106, pp. 32–51. doi:10.1111/j.1360-0443.2010.03140.x
- Degenhardt, L., Larney, S., Kimber, J., Gisev, N., Farrell, M. et al. (2014), 'The impact of opioid substitution therapy on mortality post-release from prison: Retrospective data linkage study 1', *Addiction*. doi: 10.1111/add.12536
- European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (2016), *Preventing opioid overdose deaths with take-home naloxone*, EMCDDA Insights, Publications Office of the European Union, Luxembourg.
- EMCDDA (2015), *Preventing fatal overdoses: a systematic review of the effectiveness of take-home naloxone*, EMCDDA Papers, Publications Office of the European Union, Luxembourg. Online at:
 - www.emcdda.europa.eu/publications/emcdda-papers/naloxone-effectiveness
- EMCDDA (2010), *The Drug related deaths (DRD) standard protocol, version 3.2*, Lisbon (available at: http://www.emcdda.europa.eu/themes/key-indicators/drd).
- Eurostat (2013), *Causes of death statistics*, online at: http://ec.europa.eu/eurostat/ web/health/causes-death
- Frisher, M., Baldacchino, A., Crome, I. and Bloor, R. (2012), *Preventing opioid overdose in Europe: a critical assessment of known risk factors and preventative measures*, EMCDDA Technical paper, EMCDDA, Lisbon.
- Giglio, R. E., Li, G. and DiMaggio, C. J. (2015), 'Effectiveness of bystander naloxone administration and overdose education programs: a meta-analysis', *Injury Epidemiology*, 2(1), p. 10. https://doi.org/10.1186/s40621-015-0041-8
- Giraudon, I., Lowitz, K., Dargan, P. I., Wood, D. M. and Dart, R. C. (2013), 'Prescription opioid abuse in the UK.', *British Journal of Clinical Pharmacology* 76(5), pp. 823–4. doi:10.1111/bcp.12133

- Hedrich, D., Kerr, T. and Dubois-Arber, F. (2010), 'Drug consumption facilities in Europe and beyond', in Rhodes, T. and Hedrich, D. (eds), *Harm reduction: evidence, impacts and challenges*, EMCDDA Monograph, Publications Office of the European Union, Luxembourg, pp. 305–331. doi:10.2810/29497
- Information Services Division Scotland (2016), *National Naloxone Programme Scotland Monitoring Report 2015/16* (http://www.isdscotland.org/Health-Topics/Drugs-and-Alcohol-Misuse/Publications/2016-10-25/2016-10-25-Naloxone-Report.pdf).
- Kerr, D., Kelly, A. -M., Dietze, P., Jolley, D. and Barger, B. (2009), 'Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose', *Addiction* 104, pp. 2067–2074. doi:10.1111/j.1360-0443.2009.02724.x
- Kimber, J., Copeland, L., Hickman, M., Macleod, J., McKenzie, J., De Angelis, D. and Robertson, J. R. (2010), 'Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution treatment', *British Medical Journal* (Clinical research ed.) 341, p. c3172.doi: 10.1136/bmj.c3172. Online at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2895695/
- Madah-Amiri, D., Clausen, T., Myrmel, L., Brattebø, G. and Lobmaier, P. (2016), 'Circumstances surrounding non-fatal opioid overdoses attended by ambulance services', *Drug and Alcohol Review*, May, 36(3), pp. 288–294, https://doi.org/10.1111/ dar.12451)
- Madah-Amiri, D., Clausen, T. and Lobmaier, P. (2017), 'Rapid widespread distribution of intranasal naloxone for overdose prevention', *Drug and Alcohol Dependence*, 173, pp. 17–23. http://doi.org/10.1016/j.drugalcdep.2016.12.013
- Marshall, B. D. L., Milloy, M.-J., Wood, E., Montaner, J. S. G. and Kerr, T. (2011), 'Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study', *Lancet* 377, pp. 1429–1437. doi:10.1016/S0140-6736(10)62353-7
- Merrall, E. L. C., Kariminia, A., Binswanger, I. A., Hobbs, M. S., Farrell, M., Marsden, J. et al. (2010), 'Meta-analysis of drug-related deaths soon after release from prison', *Addiction* 105, pp. 1545–1554. doi:10.1111/j.1360-0443.2010.02990.x.
- Parmar, M. K. B., Strang, J., Choo, L., Meade, A. M. and Bird, S. M. (2016), 'Randomized controlled pilot trial of naloxone-on-release to prevent post-prison opioid overdose deaths', *Addiction*, https://doi.org/10.1111/add.13668
- Pierce, M., Bird, S. M., Hickman, M., Marsden, J., Dunn, G., Jones, A. and Millar, T. (2016), 'Impact of treatment for opioid dependence on fatal drug-related poisoning: A national cohort study in England' Addiction, Feb, 111(2), pp. 298–308.
- Poschadel, S., Höger, R., Schnitzler, J. and Schreckenberg, D. (2003), *Evaluation der Arbeit der Drogenkonsumräume in der Bundesrepublik Deutschland*, Schriftenreihe des Bundesministeriums für Gesundheit und Soziale Sicherheit. Bd. 149, Nomos, Baden-Baden.
- Strang, J., Manning, V., Mayet, S., Best, D., Titherington, E., Santana, L. et al. (2008), 'Overdose training and take-home naloxone for opiate users: prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses.', *Addiction* 103, pp. 1648–57. doi:10.1111/j.1360-0443.2008.02314.x
- Strang, J., Bird, S. M. and Parmar, M. K. B. (2013), 'Take-home emergency naloxone to prevent heroin overdose deaths after prison release: rationale and practicalities for the N-ALIVE randomized trial.', *Journal of Urban Health: Bulletin of the New York Academy* of Medicine 90(5), pp. 983–96. doi:10.1007/s11524-013-9803-1

- Williams, A. V, Marsden, J. and Strang, J. (2014), 'Training family members to manage heroin overdose and administer naloxone: randomized trial of effects on knowledge and attitudes', *Addiction* (Abingdon, England) 109(2), pp. 250–9. doi:10.1111/add.12360
- WHO (2014), *Community management of opioid overdose*, World Health Organization, Geneva. Online at: http://www.who.int/substance_abuse/publications/management_ opioid_overdose/en/
- WHO (2010), *Prevention of acute drug-related mortality in prison populations during the immediate post-release period*, World Health Organization, Regional Office for Europe, Copenhagen.
- Zlodre, J. and Fazel, S. (2012), 'All-cause and external mortality in released prisoners: systematic review and meta-analysis', *American Journal of Public Health* 102, pp. e67–75. doi:10.2105/AJPH.2012.300764