



European Monitoring Centre
for Drugs and Drug Addiction

TECHNICAL REPORT

Drug-related deaths and mortality in Europe

Update from the EMCDDA expert network

May 2021

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About this report

This report provides an update on drug-related deaths in Europe based primarily on presentations and discussions held at the 2019 meeting of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) expert network on drug-related deaths. The meeting brought together experts and representatives from over 40 countries and provided a platform for discussing new trends in and analyses of drug-induced deaths in Europe and beyond and responses to them.

About the EMCDDA

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) is the central source and confirmed authority on drug-related issues in Europe. For over 25 years, it has been collecting, analysing and disseminating scientifically sound information on drugs and drug addiction and their consequences, providing its audiences with an evidence-based picture of the drug phenomenon at European level.

The EMCDDA's publications are a prime source of information for a wide range of audiences including policymakers and their advisors; professionals and researchers working in the drugs field; and, more broadly, the media and general public. Based in Lisbon, the EMCDDA is one of the decentralised agencies of the European Union.



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The invited external experts are Amanda Roxburgh, Christopher Jones, Elina Kotovirta, Kari Grasaasen, Andrew McAuley and Sabrina Molinaro.

Statement regarding the United Kingdom

This report covers a reference period until 2019. The United Kingdom had left the European Union as of 1 February 2020. Unless stated otherwise, for the purpose of this report, the term 'Member States' includes the United Kingdom.

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At a glance: a summary of key points

Overdose deaths: a very high burden of preventable premature deaths

- Over 8 300 deaths involving one or more illicit drugs were reported in 2018 in the European Union. This estimate rises to over 9 200 deaths when Norway and Turkey are included. Men account for three quarters of drug-induced deaths. Most of the deaths were very premature, affecting people in their thirties and forties. Multiple drug toxicity is implicated in most cases.

Opioids: the main driver of fatal overdoses in Europe

- Opioids, often heroin, or opioid substitution treatment medicines, such as methadone and buprenorphine, are involved in 80-90 % of drug-related deaths overall, although differences between countries exist.
- Deaths associated with fentanyl and its analogues might be underestimated in some countries. Fentanyl-related deaths decreased markedly in Estonia and Sweden in 2018.

New psychoactive substances: stimulants and benzodiazepines involved in many deaths

- Most new psychoactive substance-related deaths are reported in the United Kingdom and in Turkey (where synthetic cannabinoids largely dominate). Fake and diverted medicines and new benzodiazepines are involved in an increasing proportion of drug-related deaths.

Highlights and concerns

- When information on post-mortem investigation is available it shows that the proportion of drug-related deaths involving 'other opioids' is increasing in some countries, while the proportion involving heroin is decreasing.
- Cocaine was reported to be involved in an increasing number of deaths in 2018, mainly associated with heroin or other opioids.
- Mortality rates due to overdose are higher in Scotland than in the rest of the United Kingdom or in other European countries or the United States. Most deaths in Scotland are related to heroin, other opioids and benzodiazepines (etizolam in particular was implicated in more than half of the deaths in 2018).

Implications for public health and for monitoring

- There are still major limitations and gaps in the monitoring of drug-related deaths. Special mortality registers are a key source of information, in particular on polydrug use patterns and on prescription opioids and other medicines implicated in deaths.
- Further triangulation of drug-related deaths and other opioid indicators is needed to consolidate estimates of the number of deaths.

Responding to drug-related deaths

- While the coverage and diversity of responses to drug-related deaths vary between and within countries, drug consumption rooms and take-home naloxone programmes expanded across Europe in 2019. The evidence base for their effectiveness is growing. However, more research is needed on the population impact of these and other responses.

Introduction to and aim of this report

This report provides an update on drug-related deaths in Europe (EMCDDA, 2019a, 2019b). It is primarily based on presentations and discussions held at the annual 2-day meeting of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) expert network on drug-related deaths in Lisbon on 21 and 22 October 2019 (EMCDDA, 2019b). The meeting brought together experts and representatives from over 40 countries and provided a platform

for discussing new trends in and analyses of drug-induced deaths in Europe and beyond and responses to them.

Drug-related mortality is a complex phenomenon. The EMCDDA has defined a drug-related death and mortality (DRD) epidemiological indicator, which has two complementary components: (i) national, population-based statistics on deaths directly attributable to the use of drugs (drug-induced deaths, also known as poisonings or overdoses); and (ii) estimations of the overall and cause-specific mortality among high-risk drug users, derived from longitudinal cohort studies among drug users (EMCDDA, 2010, 2015, 2019c, 2019d). This technical report focuses on the first component.

Monitoring drug-induced deaths

The EMCDDA defines drug-induced deaths as those ‘happening shortly after consumption of one or more illicit psychoactive drug, and directly related to this consumption’, and these often occur in the context of the co-use of other substances such as alcohol or psychoactive medicines (EMCDDA, 2010). Deaths indirectly associated with drugs (such as those linked to traffic accidents or HIV infection) are not considered here. Monitoring drug-induced deaths requires the existence of good-quality information sources, in particular general mortality registries and/or special mortality registries.

The EMCDDA protocols define operative criteria for extracting relevant deaths from these registries. Extracting from both sources allows cross-validation of the data, but some countries have data available from only one source. The general registers provide official statistics with a national coverage, and the special registers provide detailed information on the drugs and combinations of drugs identified in the post-mortem investigations of the cases. The findings of toxicological investigations are reported by countries to the EMCDDA through standardised tools (Fonte and annual workbooks). The final decision on the cause of the death is made by the pathologists or coroners, in the light of the toxicological findings and other available information. The interpretation of data related to drugs is complex because, in most cases, multiple drugs are involved: drugs can be reported as ‘mentioned’ or ‘involved’ or as being the ‘cause’ of the death.

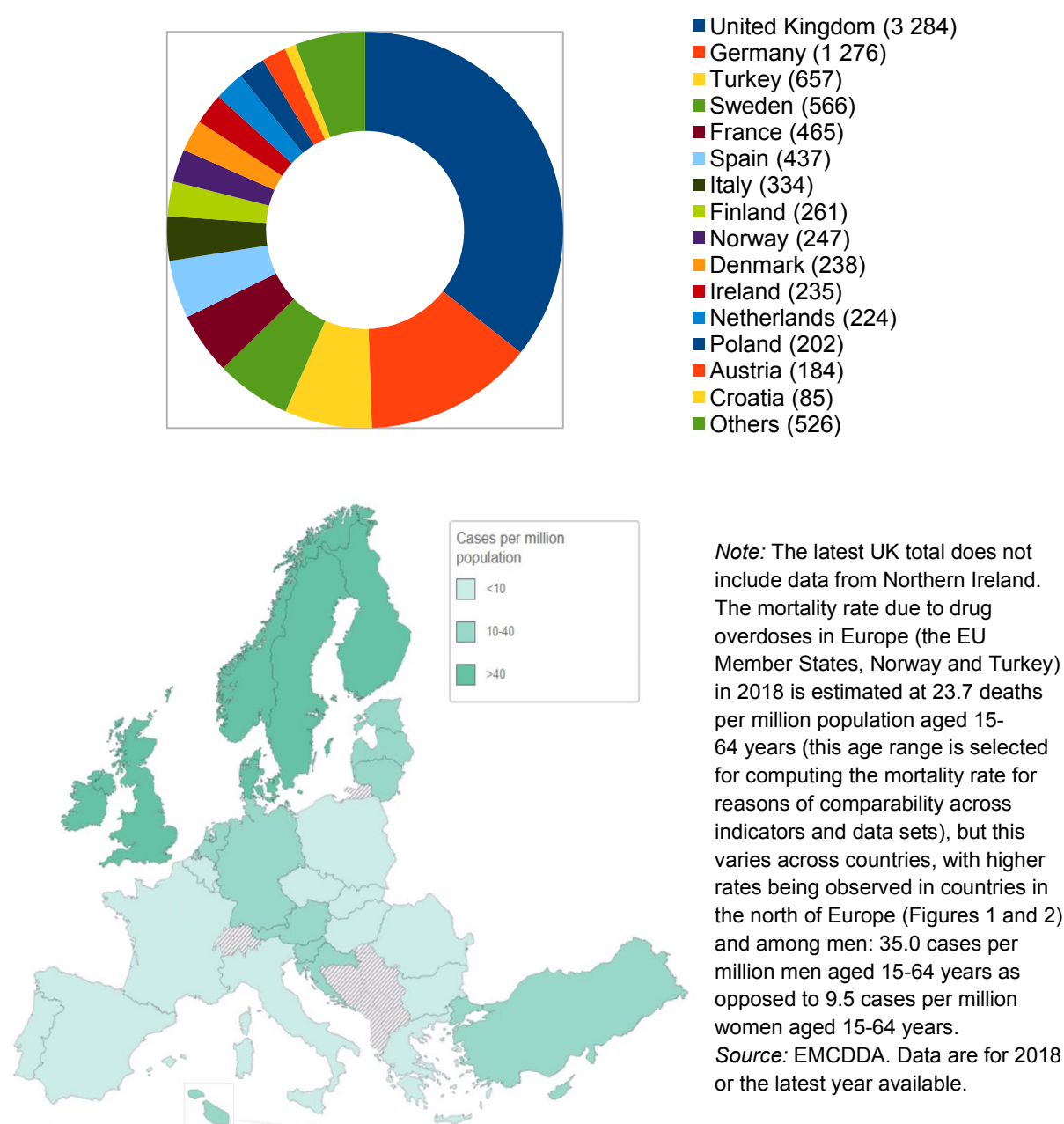
Although most countries are able to fully apply the operative criteria for extracting relevant deaths, there are important limitations in drug-induced deaths data, particularly in cumulative European totals (EMCDDA, 2019e, 2019f). Of importance are differences between (and within) countries with regard to identifying and certifying the cause of death and coding and reporting the number of drug-induced deaths. This relates to the quality and frequency of post-mortem investigations, the availability of this information for determining the cause of death, the coding system used and the quality of coding, and the coverage and quality of the overall reporting system (England, 2017a, 2017b, 2017c; Leifman, 2017). There are also differences in forensic laboratory capacities and different standard procedures for post-mortem toxicological investigation of suspected drug-induced deaths (EMCDDA, 2019g). These factors have an impact on the sensitivity of the analysis and hence on the comparability of the data within and across countries. Caution is thus advised when interpreting and comparing drug-induced deaths data over time and between countries.

More information is available from http://www.emcdda.europa.eu/topics/drug-related-deaths_en.

Overdose deaths in Europe: an overview

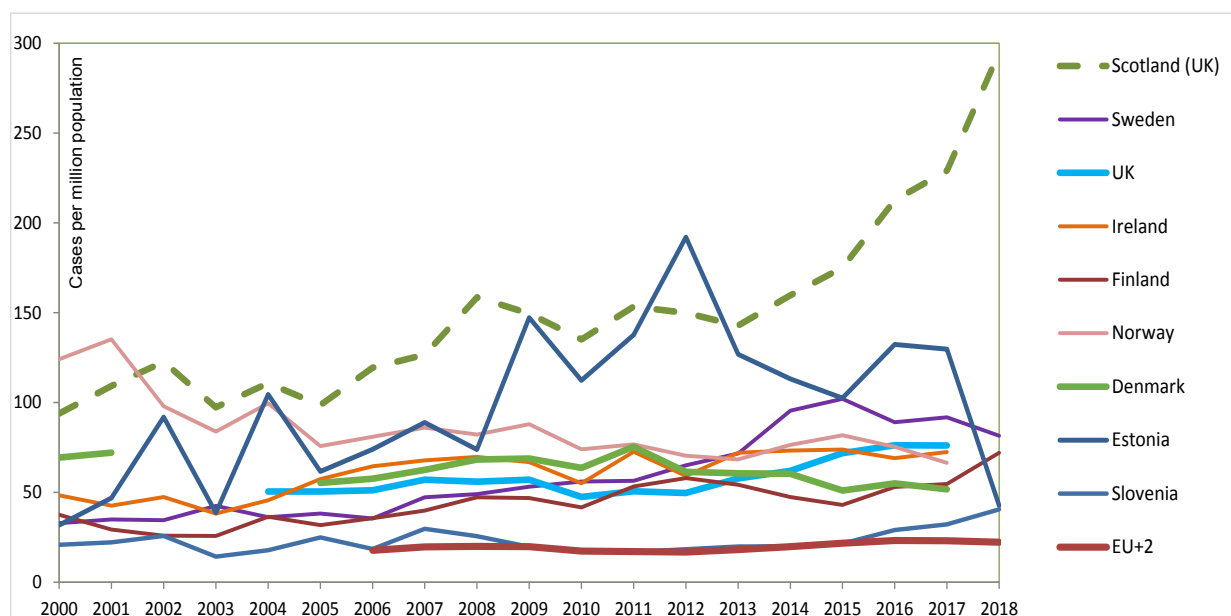
It is estimated that at least 8 300 overdose deaths occurred in the European Union as it was constituted in 2018. This rises to an estimated 9 200 deaths if Norway and Turkey are included, representing a slight decrease compared with the most recent previous estimate of 9 500 deaths in 2017 (EMCDDA, 2020b). This European figure must be understood as a minimum estimation, as there are some countries in which deaths are probably underestimated, which will affect the European cumulative totals (see the box above). As in previous years, the United Kingdom and Germany together account for around half of the total reported deaths in Europe (Figure 1).

Figure 1. Drug-induced deaths in the European Union, Norway and Turkey: total number (top figure) and mortality rates among adults aged 15-64 years, 2018 (bottom map)



While the UK data as a whole show a progressive increase in drug-induced mortality rates, the number of overdose deaths in Scotland has risen rapidly, and the mortality rate is now almost 13 times higher than the average in Europe (and above the mortality rate reported in comparable data from the United States; see box ‘Overdose deaths in the United States and Australia’). The trend in overdose deaths in Estonia is improving (i.e. the numbers are falling), and the mortality rate dropped from 130 deaths per million adults in 2017 to 43 deaths per million population aged 15-64 years in 2018 (see more information later in the report) (Figure 2).

Figure 2. Drug-induced mortality rates among adults (15-64 years) per million: selected trends and most recent data



Note: Caution is advised when interpreting and comparing data on drug-induced deaths over time and between countries.

Source: EMCDDA. Trends in the eight countries (plus Scotland, United Kingdom) reporting the highest rates in 2018 or 2017, and overall European trend. EU+2 refers to EU Member States, Turkey and Norway.

Overdose deaths in the United States and Australia

In 2018, 67 367 drug overdose deaths were reported in the United States, and opioids (in particular pharmaceutical opioids but also heroin) were involved in 46 802 of these deaths (69.5 %). Almost 60 % of the opioid overdoses are attributed to fentanyl and its analogues (CDC, 2020; NIDA, 2019), and a recent study found that a positive test for fentanyl analogues was reported in one fifth (20.6 %) of all opioid-related deaths (O'Donnell et al., 2018). The age-adjusted rate of overdose deaths decreased by 4.6 % from 217 per million in 2017 to 207 per million in 2018 (Hedegaard, 2020).

In 2018 in Australia, 1 740 overdose deaths were reported and opioids were involved in 1 123 of these deaths (65 %) (AIHW, 2020). The age-standardised rate of drug-induced deaths was 70 per million population, following a continuous increase since 2006, when the rate was 30 deaths per million population. Pharmaceutical opioids and heroin are both drivers of the increase. Deaths associated with the former occur in older people being treated for chronic pain, who do not have a history of injecting drugs, and are more likely to occur in the regions or remote parts of the country. In contrast, the deaths associated with heroin are more likely to occur in major cities among younger men with a history of injecting drugs.

Demographic characteristics of drug-related fatalities in Europe

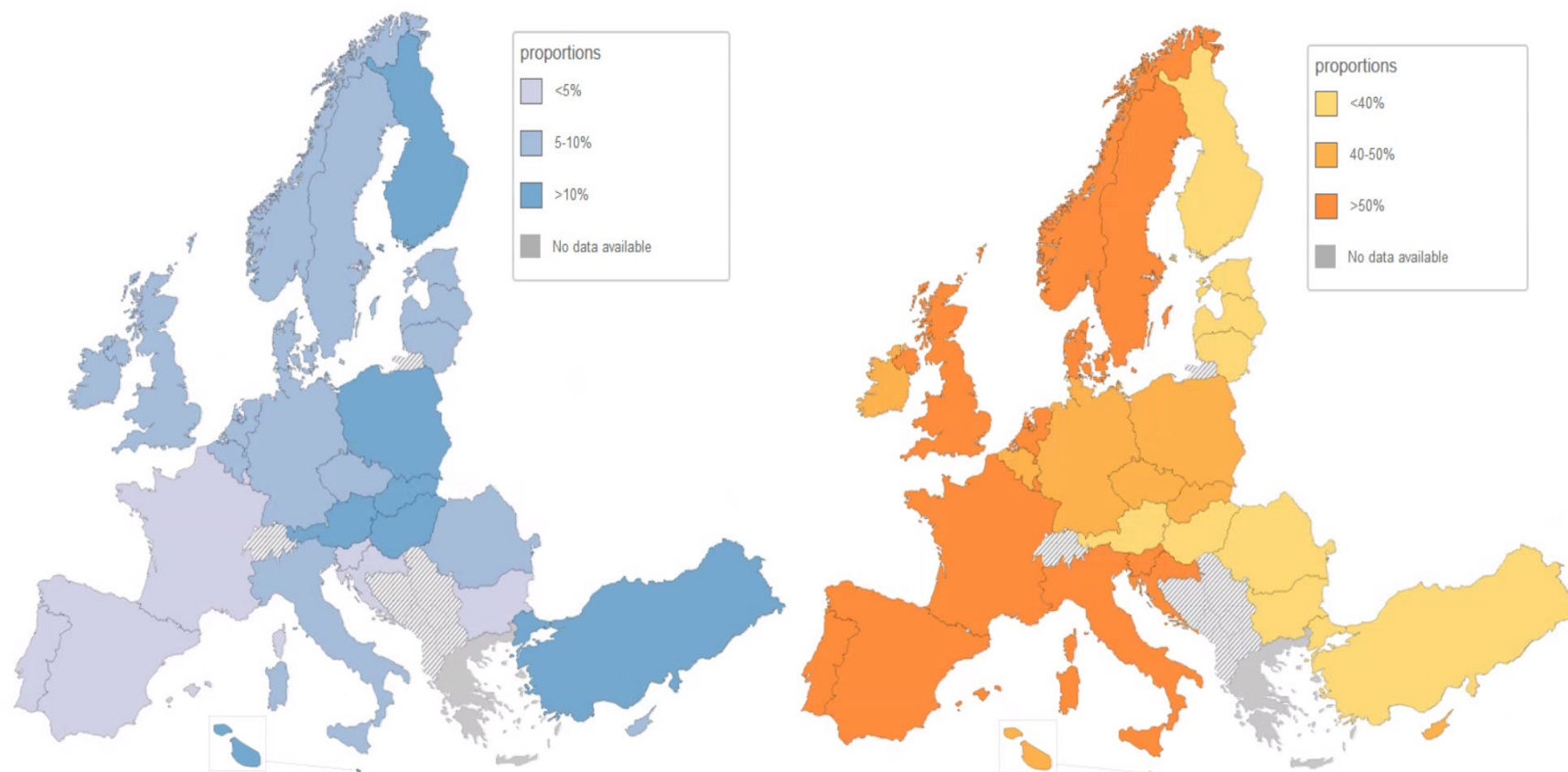
There is an ongoing increase in the reported number of overdose deaths among older age groups in Europe. Those aged over 40 years represent a large proportion of all drug-induced deaths in many western European countries (Figure 3).

In 2018, the overall mean age at death due to a drug overdose was 40 years, compared with 37 years in 2012. Men aged 35-44 years are the worst affected, with a mortality rate of 53.7 deaths per million, more than double the average for men of all ages (23.7 deaths per million men, all ages), and more than three times the highest mortality rate in women (13.9 deaths per million women aged 35-44 years).

Some countries fall outside this general characterisation, and higher levels of drug-related deaths occur among younger people. In Turkey and in Hungary, almost one in four deaths occurs among those aged less than 25 years, and in Finland, Malta, Slovakia and Poland, around one in five deaths occurs among those aged less than 25 years. In comparison, for those European countries ⁽¹⁾ where data are available, only 8.5 % of the deaths occurred among those aged less than 25 years. Overall in Europe, 215 drug-induced deaths among people aged less than 20 years were reported in 2018 or the most recent year for which data are available.

(1) Greece is excluded from this calculation, as no age breakdown of the cases was available.

Figure 3. Proportion of drug-induced deaths in people aged less than 25 years (left) and aged 40 years or more (right), 2018 or latest data available



Note: For Germany, 2017 data are used, as a breakdown by age is not available for 2018. Northern Ireland (United Kingdom) data are missing.

Source: EMCDDA.

Heroin-related deaths in selected European countries

Most drug-induced deaths in Europe are attributed to multiple drug toxicity, and several drugs are commonly identified in post-mortem examinations. Opioids are involved in most of the drug-induced deaths reported in Europe ⁽²⁾.

In 2019, 22 out of 30 countries reported to varying extents information on the substances involved in drug-related deaths. There were 4 149 deaths for which some toxicological information was reported, and 2 853 (68 %) involved an opioid. The most common opioid involved was heroin, which was identified in 1 281 cases (31 % of the cases with toxicological information available or 45 % of the cases with opioids). The second most frequently identified opioid was methadone, identified in 696 cases (17 % of all cases with toxicological information available or 24 % of the cases with opioids). Buprenorphine was the third most common opioid and was identified in 203 cases (5 % of all cases with toxicological information available or 7 % of the cases with opioids). Most deaths involved several drugs.

Extrapolating from the number of deaths for which the toxicology is known to the total number of deaths should be done with caution, given possible selection and information biases. In summary, where information was available, heroin was the most common opioid identified in drug-related deaths reported in 2019 for 2018 or 2017 if no more recent data were available. There were at least 3 154 deaths involving heroin (1 873 in England, Wales and Scotland and 1 281 in the remaining European countries reporting). The section below describes in more detail the situation for heroin-related deaths in selected countries.

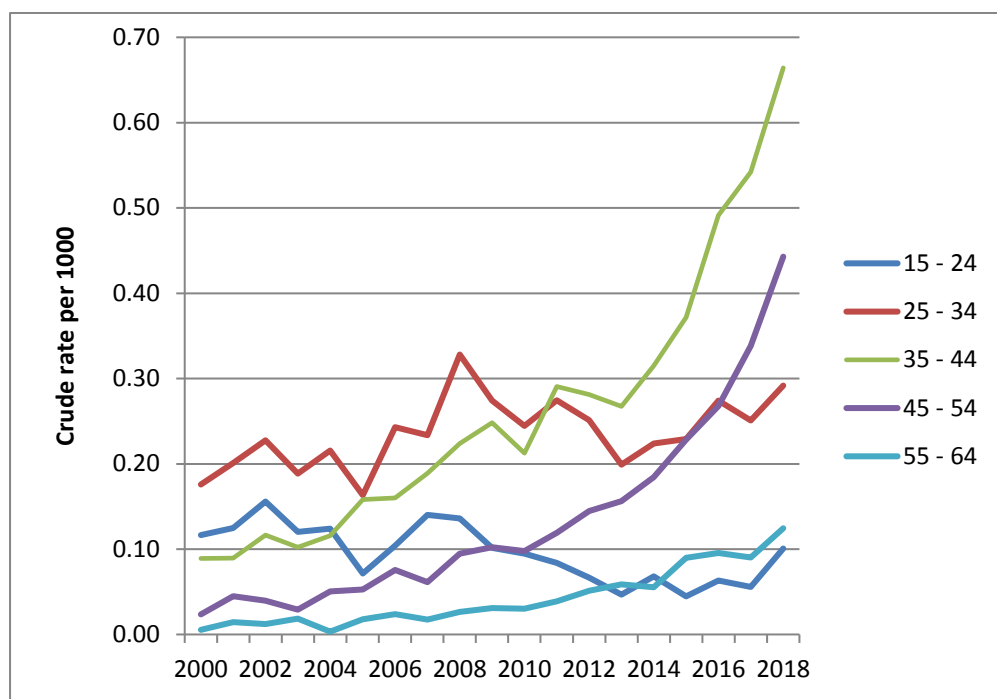
In Germany, heroin/morphine (or its metabolites) is recorded in 405 deaths reported by the police, or 45.5 % of the 890 fatal drug poisonings with known toxicology (out of the 1 276 drug-related deaths in 2018).

Where recent information was reported on the substances involved in drug-related deaths in England and Wales (United Kingdom), heroin/morphine is mentioned in 1 336 deaths, or 46 % of the 2 917 deaths due to drug misuse registered in 2018 (ONS, 2019) ⁽³⁾. This proportion is very likely to be underestimated because of a lack of detailed information on death certificates.

In Scotland (United Kingdom), opioid-related deaths dominate – often linked to polydrug use and benzodiazepine use, the latter being associated with 7 out of 10 deaths. Against this background, heroin was reported as being implicated in, or having potentially contributed to, almost half of all drug-induced deaths in 2018 (537 deaths, 45 %) (National Records of Scotland, 2018). Most of the increase in drug-related deaths reported over the last two decades is accounted for by deaths among those aged between 35 and 44 years (Figure 4).

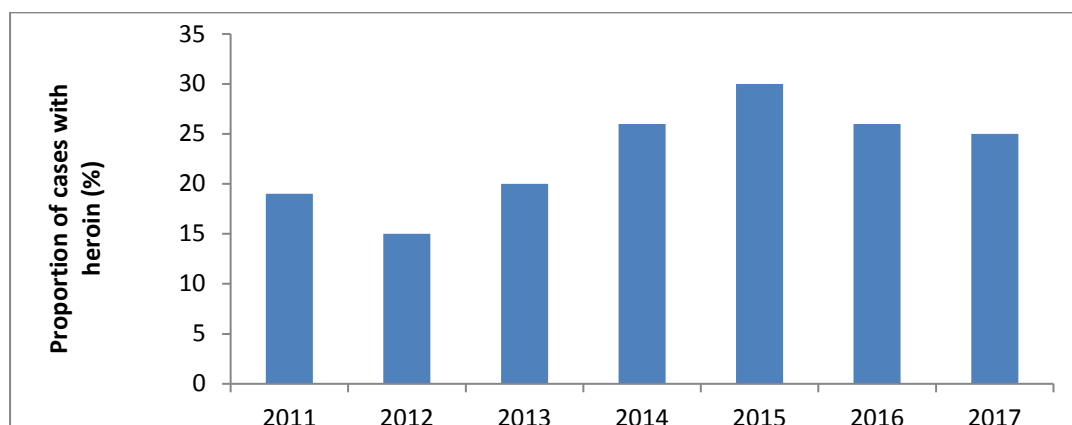
⁽²⁾ See more information on the possible under-reporting of opioid drug-induced deaths the box on the opioid multi-indicator pilot project.

⁽³⁾ The data on registrations of 'drug poisoning' deaths reported by the UK Office for National Statistics for 2018 are more recent than the data on deaths occurring in 2017 reported by the UK focal point. The denominator used here is the 'number of deaths due to drug misuse' for England and Wales, and all heroin-related deaths are registered as 'drug misuse' deaths. The drug misuse definition is closer to the definitions used in other countries (including Scotland) than the 4 359 total 'drug poisonings'. Data reported under the drug misuse definition provide a good proxy for the official consolidated number of drug-related deaths to be reported in the coming months by the United Kingdom to the EMCDDA.

Figure 4. Crude rates of drug-related deaths per 1 000 population by age group, Scotland, 2000-2018

Source: Data from National Records of Scotland (2019), presented by Andrew McAuley at the expert meeting on drug-related deaths, 21-22 October 2019, Lisbon.

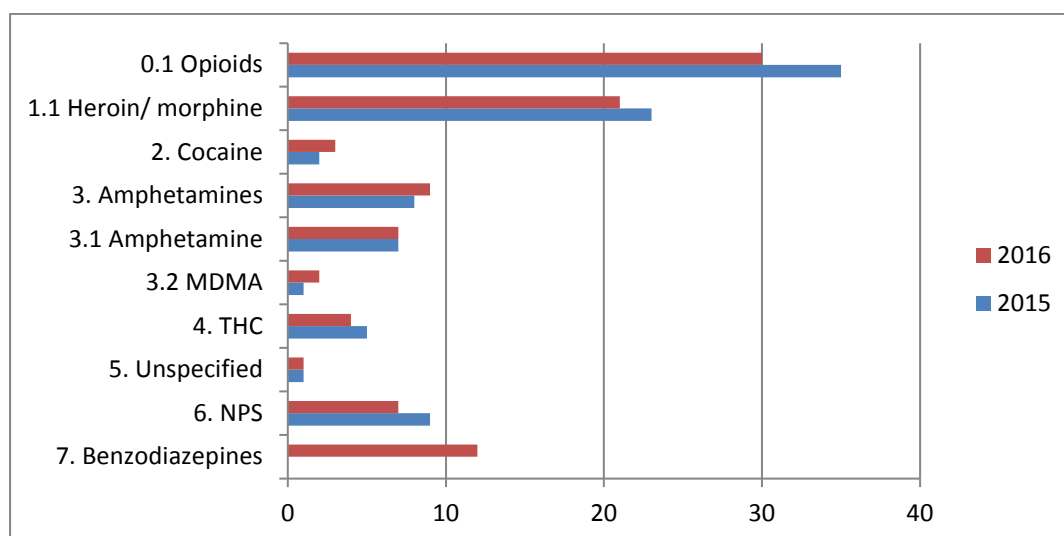
In France, heroin has been involved in around 15-30 % of the drug-related deaths since 2010. According to the special mortality register (Drames network), heroin was reported in 135 cases, (31 %) of the deaths in 2017. The proportion of heroin-related cases peaked in 2015 (30 %), when it was double the proportion in 2012 (15 %) (Figure 5). Similar to previous years, in 2017, heroin was reported less frequently than methadone, which was found in more than one third of the cases (37 %). The deaths involving heroin among those aged 15-49 years appear to be linked to the availability and purity of the drug. The median purity of brown heroin seized in France peaked in 2015 at 11 %, more than double the median purity in 2012 (5 %).

Figure 5. Proportion of drug-related deaths (all ages) involving heroin, France, 2011-2017

Source: Special mortality register Drames. Proportions rather than numbers are shown because the number of participating laboratories has not been constant over the years.

In Poland, most deaths are related to opioids, primarily heroin. According to the general mortality register (Central Statistical Office), there were 202 deaths from overdose reported in 2017 in Poland, and toxicological information was available for five of these cases. Meanwhile, information on the substances involved in drug-related deaths was available from the special register data for the Warsaw region for 2016. According to this source, there were 47 deaths reported in 2016 for the region, mostly related to opioids and in particular heroin, which was identified in 45 % ($n = 21$) of the cases (Figure 6).

Figure 6. Psychoactive substances detected in the post-mortem toxicology examinations following deaths from overdose, Warsaw, 2015-2016 (categories are not mutually exclusive with more than one drug detected in a single case)



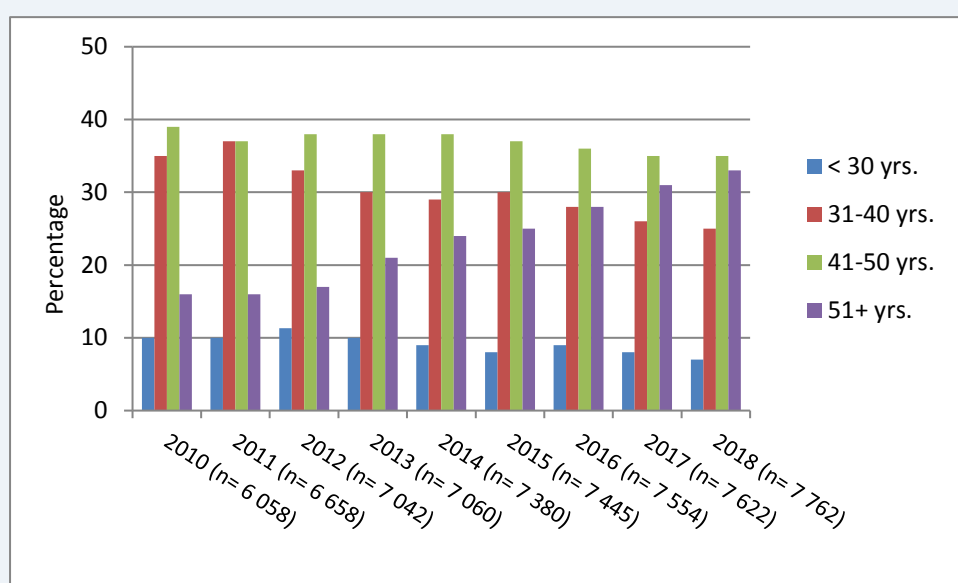
Note: NPS, new psychoactive substances; THC, tetrahydrocannabinol.

Source: Data from the Forensic Science Department of the Medical University of Warsaw, presented by Małgorzata Dalmata (Polish focal point) at the expert meeting on drug-related deaths, 21-22 October 2019, Lisbon.

Understanding opioid-related deaths in Norway

In Norway the overall number of overdoses has been stable for 10 years at between 240 and 280 cases per year. However, there is a decreasing trend in the number of deaths involving heroin and an increasing trend in the numbers of deaths involving other opioids such as methadone, oxycodone, fentanyl, morphine and codeine. Methadone is prominent and was identified in 23 % of the overdose-related deaths in Norway in 2017. This occurs against a background of an ageing cohort of patients receiving opioid substitution treatment. One third (33 %) of the patients receiving opioid substitution treatment in 2017 in Norway were over 50 years old, compared with 16 % in 2010 (see figure below).

Age distribution of patients receiving opioid substitution treatment, Norway, 2010-2018



Source: Data from the Norwegian Institute of Public Health for 2019, presented by Thomas Clausen at the expert meeting on drug-related deaths, 21-22 October 2019, Lisbon.

Tramadol-related deaths

Tramadol is an opioid associated with deaths in Europe, although data are reported and available in a limited number of countries. In the United Kingdom, where tramadol became a controlled drug in June 2014, tramadol was mentioned in 220 deaths (7.4 % of all drug-related deaths) in England and Wales in 2018, an increase from 185 deaths registered in 2017 (ONS, 2019). Tramadol was involved in 75 deaths in Norway in 2018, an increase compared with the average number recorded over the previous 10 years. In France (2017), 49 deaths were reported through surveillance of deaths related to analgesia poisoning, and 11 additional deaths were reported through the special mortality register Drame. Tramadol was also involved in 31 deaths reported in Northern Ireland in 2017. In Slovakia, the number of tramadol-related deaths was stable between 2017 (11 deaths) and 2018 (13 deaths).

The medicine is often used in combination with other drugs, and it is therefore difficult to assess its contribution to deaths where it is recorded. However, the presence of tramadol (and other substances) might be underestimated, as it might not be systematically looked

for, or not reported when found. Several countries, including France, the United Kingdom and Norway, have reported an increase in the prescription of tramadol and other opioids in recent years. In January 2020, France announced the launch of enhanced surveillance of tramadol prescriptions. Meanwhile, since 15 April 2020, the maximum duration of a prescription was reduced from 12 to 3 months (ANSM, 2020).

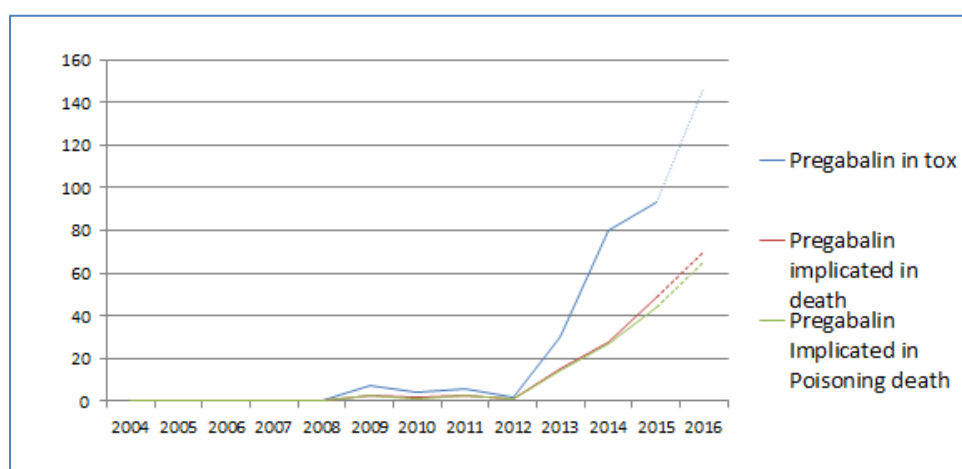
Pregabalin causing concern in some countries

Pregabalin (a gabapentinoid drug) is causing concern in several countries. It is commonly sold under the brand name Lyrica and it is indicated in the treatment of epilepsy, neuropathic pain and generalised anxiety disorder. A known side effect of the drug is central nervous system depression. There is evidence of misuse, particularly in those with a history of opioid and alcohol misuse. Pregabalin and gabapentin are said to be used to 'boost' the effects of opioids and alcohol (Baird, 2014).

In Ireland, pregabalin has emerged since 2012, and the medicine was involved in one out of five (18 %, or 65) drug-related deaths in 2016 (Figure 7). In all cases, other drugs and medicine were implicated with pregabalin. The majority of the deaths (60 %) involved people who had a history of mental health issues, and over half were among people who used opiates and had had no recent contact with drug services. According to the primary care reimbursement service in Ireland, there was an increase of 26 % in prescription rates of pregabalin from 2013 to 2016. There was also an increase in the number of deaths (all causes) in which pregabalin was implicated and in the number of positive forensic toxicology findings for pregabalin (Figure 7).

In England and Wales (United Kingdom), mirroring the trend in Ireland, the number of deaths involving pregabalin was very low until 2012 (four cases), increased to 90 cases in 2015 and doubled to 187 cases in 2018. Pregabalin-related deaths have also been reported in Finland (42 % of fatal poisonings) and in Sweden (30 % of fatal poisonings) according to a recent review of fatal poisoning deaths in the Nordic countries (Simonsen, 2020). Pregabalin-related deaths may occur in other countries but are either undetected or under-reported.

Figure 7. Number of deaths involving pregabalin in toxicology and implicated in poisoning deaths, Ireland, 2004-2016



Source: National Drug-Related Deaths Index, presented by Suzi Lyons at the expert meeting on drug-related deaths, 21-22 October 2019, Lisbon.

Pilot project: Opioid multi-indicator analysis/validation to identify and estimate possible under-reporting of (opioid) drug-induced deaths

The usefulness of the drug-related deaths indicator for policymaking is sometimes questioned because of concerns that data quality issues may result in under-reporting in some countries. Indeed, some countries declare a likely under-reporting of their drug-related deaths in their annual reporting to the EMCDDA. In France, under-reporting was assessed through a capture-recapture analysis (Janssen, 2011), while in other cases it was identified by comparing different sources (e.g. special and general mortality registries, results of mortality cohort studies – in which many deaths were codified as of ‘undetermined cause’) or on the basis of expert opinion. Until now, there has been no common method of assessing the underestimation of drug-related deaths.

At the 2018 expert meeting, the EMCDDA presented a model of opioid multi-indicator cross-validation that helped to assess under-reporting of drug-related deaths on the basis of other opioid indicators (see figure below). The model consists, roughly, of taking the estimated population of high-risk opioid users in the country and applying to that population the overdose mortality rate observed among high-risk opioid users in cohort studies. If there is no cohort study in the country, the overdose mortality rates observed in pooled studies are used. The mortality rates applied are also fine-tuned depending on the proportion of injectors among high-risk opioid users, the proportion of those people receiving opioid substitution treatment and the type of such treatment prescribed in the country (methadone or buprenorphine). More details are available in recent publications (EMCDDA, 2019a, 2019f) and in the expert presentations at the meeting on drug-related deaths (EMCDDA, 2019b) ⁽¹⁾.

In preparation for the 2019 expert meeting on drug-related deaths, the EMCDDA drafted an ‘opioid multi-indicator country profile’ for 11 countries (Czechia, Finland, France, Ireland, Italy, Netherlands, Norway, Poland, Portugal, Romania and Sweden), following the common methodology proposed in a Reitox document. This preparatory work led to more focused discussions on discrepancies between ‘expected’ and ‘reported’ numbers of drug-related deaths and on the need for national work.

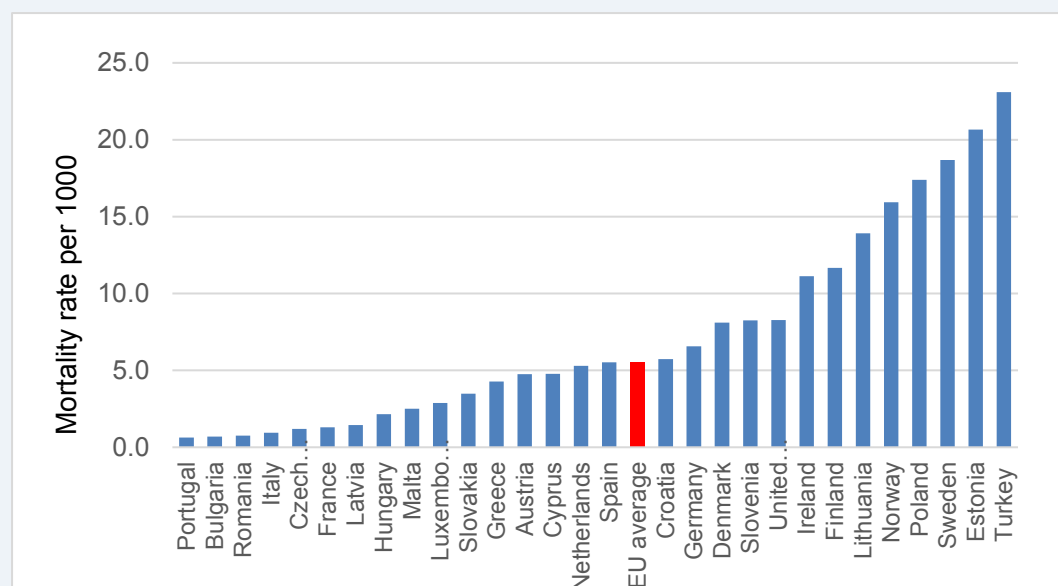
During the meeting, experts from Czechia, France, Italy, Norway and Poland discussed and further elaborated the results of their national profiles or presented additional analysis. In Czechia, the initial marked discrepancy between the ‘expected’ and the reported number of drug-related deaths could be explained by the nature of the opioid problem in the country, which is mostly related to buprenorphine misuse. The relatively low risk of deaths for people using buprenorphine compared to methadone is illustrated by existing studies (Sordo et al., 2017) that show a low overdose mortality in buprenorphine clients not receiving treatment (4.6/1 000 per year, compared to 12.7/1 000 per year out of methadone treatment). This illustrates the need to have good information on the characteristics of the national opioid situation (substance use and patterns of use, including injection and polydrug use) and of national mortality data.

The model estimated drug-related deaths lower than reported deaths in some instances, which could be explained by low estimated values for the inputs into the model (number of high-risk opioid users, mortality rate) for these countries. Poland presented an unusual situation: the ‘expected’ number of drug-related deaths was lower than the reported number, whereas there is thought to be some under-reporting of drug-related deaths in the country (EMCDDA, 2018b). Similarly, in Norway, the reported number of opioid-related deaths was much higher than the ‘expected’ number, possibly because the inputs were estimated values. The Norwegian national expert on drug-related deaths discussed the possible existence of differentiated sub-populations of opioid users with different patterns of use and

mortality risks (people who inject drugs not in treatment, people receiving opioid substitution treatment and people using prescription opioids, both legal and illegal) (Clausen, 2008).

The EMCDDA will encourage national work, including promoting national meetings of the different stakeholders (national focal points, national experts on drug-related deaths and high-risk drug use, experts in the WHO International Classification of Disease (ICD) coding, forensic services, and experts on mortality studies).

Reported opioid overdose-related deaths per estimated 1 000 high-risk opioid users in 2017



Notes: The estimated number of high-risk opioid users is based on the figures available in the 2018 *EMCDDA Statistical Bulletin*, except for some countries where different or older data was used: Bulgaria (2016), Denmark (2009), Estonia (2009), Slovakia (2008) and Sweden (2007).

The number of opioid overdoses for 2017 (or the closest year for which data are available) is based on the 2018 *EMCDDA Statistical Bulletin*.

Source: Data for drug-related deaths and high-risk opioid users from the 2018 *EMCDDA Statistical Bulletin*.

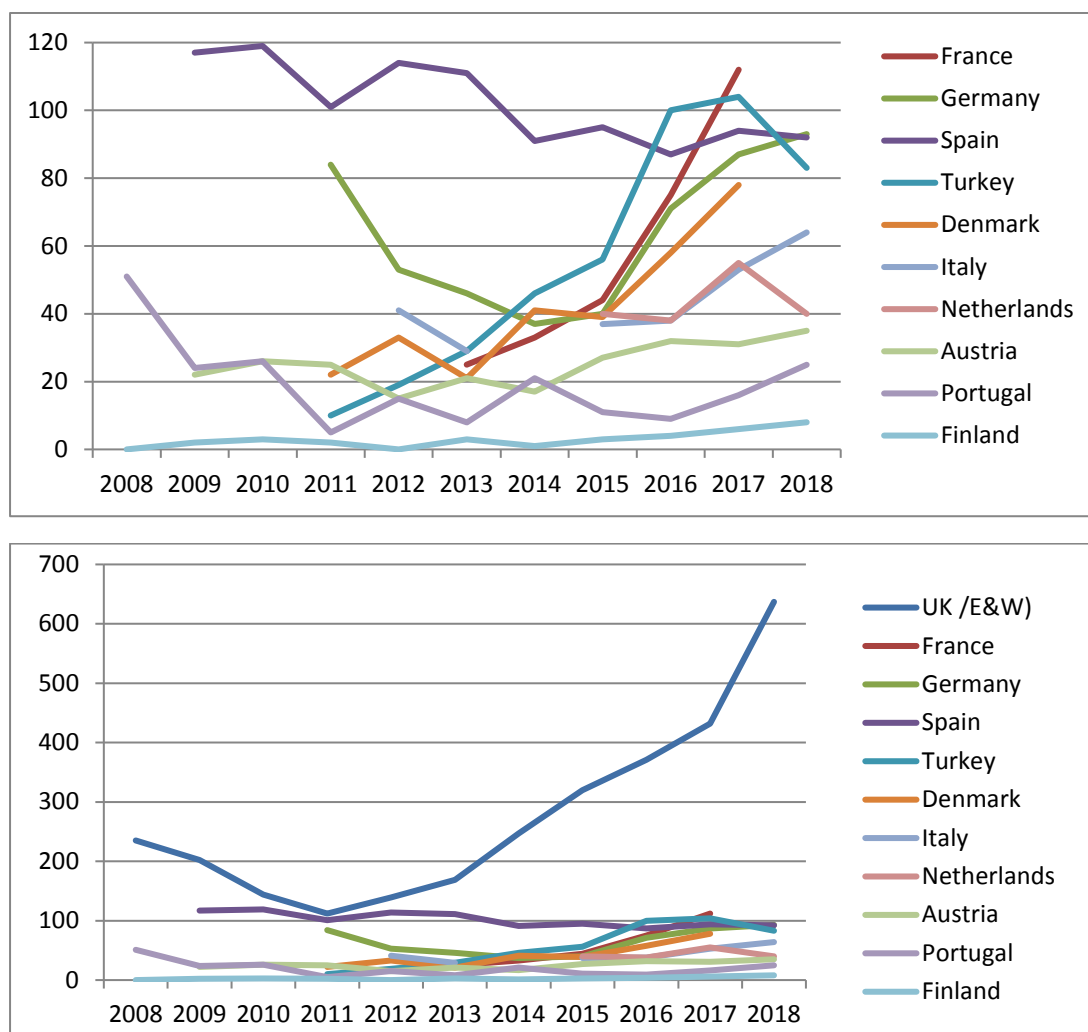
(1) See details of the EMCDDA expert meeting on the epidemiological indicator drug-related deaths (DRD), Lisbon 21-22 October 2019 (<http://www.emcdda.europa.eu/meetings/2019/drd>). Some presentations are available on the web restricted area for the drug-related deaths experts and focal points.

Cocaine-related deaths in selected European countries

In recent years, the European drug market has been experiencing an increase in both the availability and the purity of cocaine. A rise in powder injection and in the use and injection of crack cocaine has also been noted in some countries. These developments have resulted in significant public health impacts, with more cocaine-related hospital emergencies and deaths and HIV outbreaks linked to cocaine use reported over the past few years (EMCDDA, 2018a).

Where information is available, the number of deaths involving cocaine increased in most countries in 2018 compared with previous years (Figure 8). Although limited information is available on the detailed toxicity of polydrug use, the majority of the deaths related to cocaine also involved other drugs, typically opioids.

Figure 8. Number of deaths reported with presence or mention of cocaine, selected countries, 2008-2018 (top) and same countries plus England and Wales (United Kingdom) (bottom)



Source: EMCDDA analysis of data reported by the Reitox network of national focal points through the annual standard tables and workbooks. The data for Spain come from six cities. The data for England and Wales come from the UK Office for National Statistics.

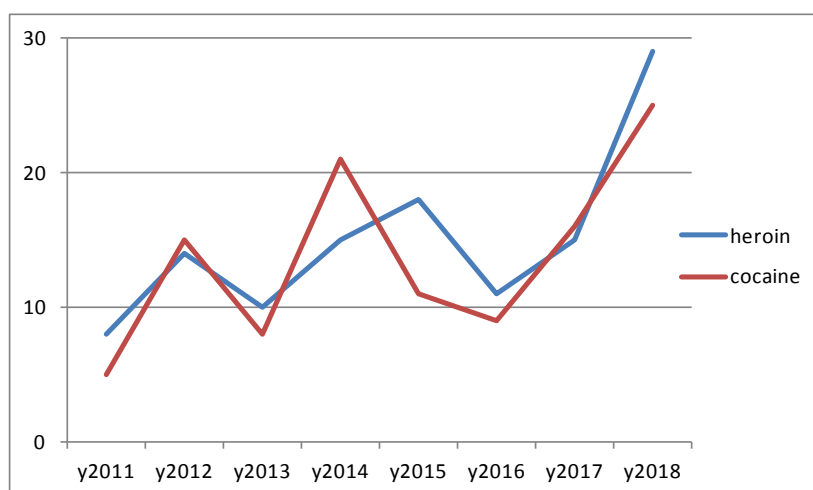
In England and Wales (United Kingdom), the number of deaths involving cocaine almost doubled over 3 years, from 320 in 2015 to 637 in 2018 (representing 22 % of the total drug misuse-related deaths in 2018) (ONS, 2019). Meanwhile the number of deaths involving any opiate increased, but to a lesser extent, from 1 989 in 2015 to 2 208 in 2018.

In France, cocaine was present in over one quarter (26 %) of the deaths reported in 2017 through the Drame special register, doubling the proportion compared with 2015 (13 %). In Ireland there was an increase in the number of deaths in which cocaine was implicated, rising from 42 deaths in 2016 to 53 in 2017. Most of the cocaine-related deaths in 2017 were deaths involving polydrug use (83 %) and one third (17/53, 32 %) involved heroin.

In Spain in 2017, half of the deaths (94/189) reported in six large cities ⁽⁴⁾ involved cocaine. One third of these cocaine-related deaths (36) involved other drugs, including opioids, and another third (33) involved other drugs without opioids. Only six cases involved cocaine alone, 10 involved cocaine and alcohol alone and nine involved cocaine and opioids alone. More than half (52/94) involved alcohol (independently of other drugs). The number of deaths involving cocaine was stable in 2018 (92 cases).

In Portugal, the recent increase in the number of deaths involving cocaine was mirrored by an increase in the number of deaths involving heroin (Figure 9). In many cases, both drugs were identified in post-mortem analysis. There were 25 deaths involving cocaine in 2018, and most (19) also involved an opioid (alone in eight cases or with another drug in 11 cases). Alcohol was found in seven cases (independently of the presence of any other substance). Part of the increase could be due to an improvement in the quality of the data, made possible by the automated coding of the cause of deaths in Portugal.

Figure 9. Number of mentions of cocaine and of heroin in post-mortem analysis of drug-related deaths, Portugal, 2011-2018



Source: Instituto Nacional de Medicina Legal (INML), Portugal, presented by Mario Dias at the expert meeting on drug-related deaths, 21-22 October 2019, Lisbon.

⁽⁴⁾ Barcelona, Bilbao, Madrid, Seville, Valencia and Zaragosa.

Mapping forensic toxicology services in Europe – preliminary findings

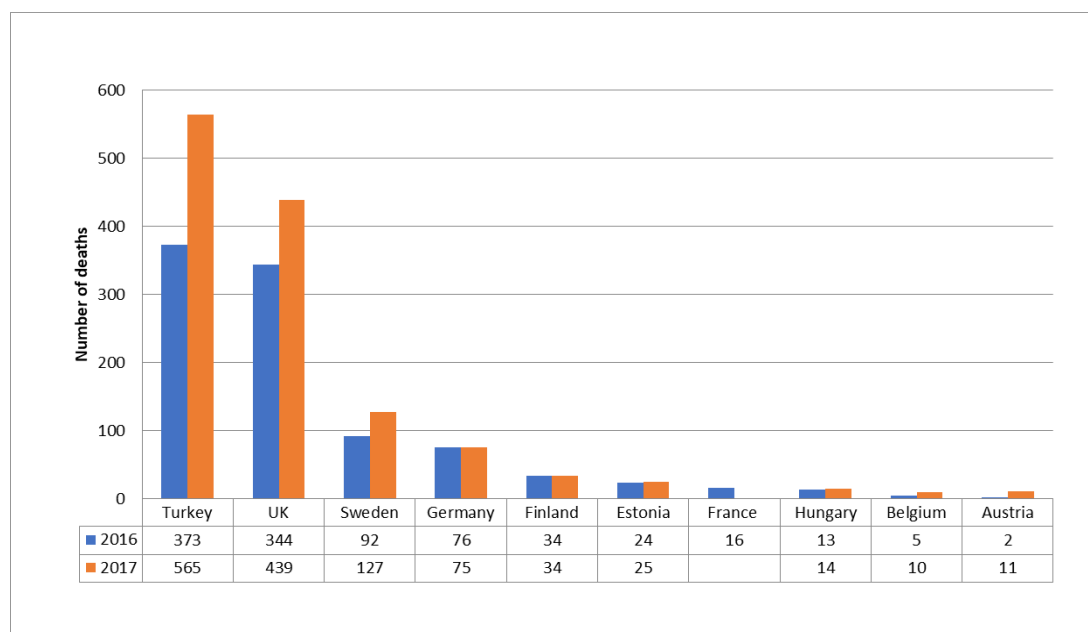
Following on from recently published work (EMCDDA, 2019g), a review was conducted in 2019-20 to map and understand the organisation of the forensic services in charge of toxicology investigations in drug-related deaths in Europe. Toxicologists from 25 countries provided the information requested. In 10 countries – Cyprus, Estonia, Finland, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta and Sweden – there is a centralised system whereby one institution is in charge of investigating cases of suspected drug-related deaths. In Portugal, the national institution, Instituto Nacional de Medicina Legal, coordinates all the analyses carried out for the country at three sites: Lisbon, Coimbra and Porto. In other countries, from two to around 30 laboratories are involved in the post-mortem toxicological investigation of suspected drug-related deaths. Some of the laboratories handle more than 1 000 post-mortem cases each year, whereas others handle fewer than 10 cases per year.

Special focus: a European overview of deaths related to new psychoactive substances

New psychoactive substances (NPS) include a wide range of substances of different pharmacological groups (see box 'New psychoactive substances') that have emerged since 2005 on to the European drug market and have been causing considerable concern. The EMCDDA, together with Europol, has a key role in identifying, monitoring and assessing these substances. By the end of 2018, 730 NPS had been identified and monitored by the European Union Early Warning System (EU EWS) on new psychoactive substances since its implementation in 1997. Just over half of these (390 out of 730) NPS were found at least once in biological or other samples in Europe in 2018 (EMCDDA, 2019c).

In 2019 the EMCDDA conducted the first epidemiological overview of NPS-related deaths in Europe, covering the period 2016-2017. The main source of data for this review was the structured annual national reporting to the EMCDDA from the 28 EU countries, Norway and Turkey (2017 and 2018 Workbooks on harms and harm reduction), the *EMCDDA Statistical Bulletins* for 2018 and 2019 (EMCDDA, 2019f) and the results of formal 'risk assessments' on NPS conducted in 2017 and 2018 (EMCDDA, 2020c). In some cases the information was complemented with data reported through the EU EWS (EMCDDA, 2020a), which, although providing complementary information, has different purposes and is not directly comparable. Most countries (27 in 2016 and 24 in 2017) provided information on drug-related deaths in their workbooks and were included in the analysis.

Between 2016 and 2017 just over half of the countries (16) reported at least one death in which an NPS was involved, 14 countries in 2016 (997 cases) and 12 countries in 2017 (1 310 cases). The increase between 2016 and 2017 was mainly related to the increase of 188 cases in Turkey (synthetic cannabinoids) and, to a lesser extent, to increases in the number of cases involving new benzodiazepines (an increase of 57) and new opioids (an increase of 45) in the United Kingdom (Figure 10).

Figure 10. Number of NPS-related deaths in countries that reported 10 or more deaths with at least one NPS involved, 2016-2017

Source: EMCDDA, presented by Hugo Lopez, Spain, at the expert meeting on drug-related deaths, 21-22 October 2019, Lisbon.

Combining the information from 2016 and 2017, an NPS was involved in 14.0 % (2 307) of all drug-related deaths with known toxicology (16 491 for 2016 and 2017). One of the main findings of the review was that most of the NPS-related deaths in 2016/2017 (74.8 %) were concentrated in two countries and in most cases related to two types of substances: Turkey (synthetic cannabinoids) and the United Kingdom, in particular Scotland (new benzodiazepines, primarily etizolam). As an illustration, if in 2017 novel benzodiazepines from the United Kingdom (340) and synthetic cannabinoids from Turkey (564) were excluded, only 406 out of 7 385 deaths (with known toxicology) in which NPS were present (5.5. %) remained in Europe. In 2016, the proportion was 3.7 % (337 out of 9 106 with known toxicology). There were no indications that NPS reporting in these two countries was particularly different from any others.

New psychoactive substances

What is a new psychoactive substance (NPS)?

An NPS is defined as ‘a new narcotic or psychotropic drug, in pure form or in preparation, that is not controlled by the United Nations drug conventions, but which may pose a public health threat comparable to that posed by substances listed in these conventions’ (Council of the European Union, 2017; EMCDDA, 2020a). This definition is legal (controlled or not) and not medical or pharmacological. NPS are notified through the EU EWS on new psychoactive substances, which is operated by the EMCDDA and Europol (EMCDDA, 2020a). In principle, once an NPS is controlled, it should no longer be considered an NPS. However, in this report, and in particular in this overview, all substances that have been notified through the EU EWS are included, regardless of their current legal status.

What is an NPS-related death?

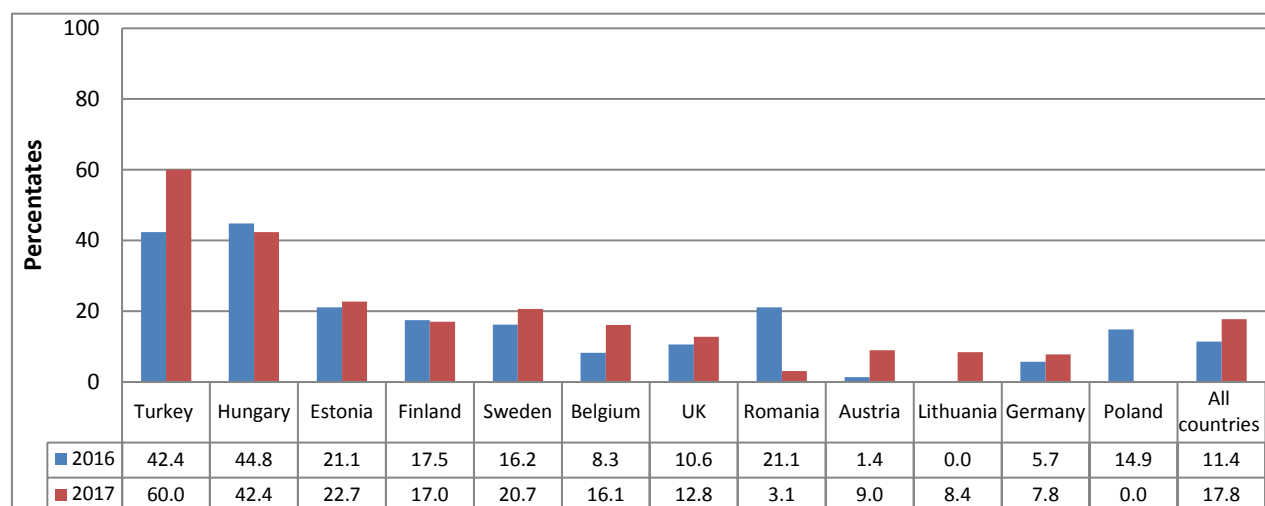
It is a death in which exposure to an NPS is confirmed from biological (post-mortem) samples. The presence of a drug (including NPS) in post-mortem toxicological analysis does not imply that the substance can be considered the main cause of death or even a contributory factor. The causality is established by the experts who conduct the post-mortem investigations on the basis of all the information available. As an example, in Scotland, in most cases in 2017 in which the NPS etizolam was found, opioids were also present, and in only seven cases was etizolam the only substance implicated. However, without the contribution of etizolam (and often alcohol) a number of opioid-related deaths may not have occurred. EMCDDA ‘risk assessments’ determine whether a substance can be considered the cause of a death or likely to have contributed to a death using an expert rating system called the ‘toxicological significance score’ (TSS) (Elliott et al., 2018).

Limitations and strengths of monitoring NPS-related deaths

Some under-detection of NPS-related deaths is likely, as many of the 730 NPS monitored are not routinely screened for in laboratories. However, many European countries are able to identify NPS-related deaths and report these cases to the EU EWS and through routine annual reporting.

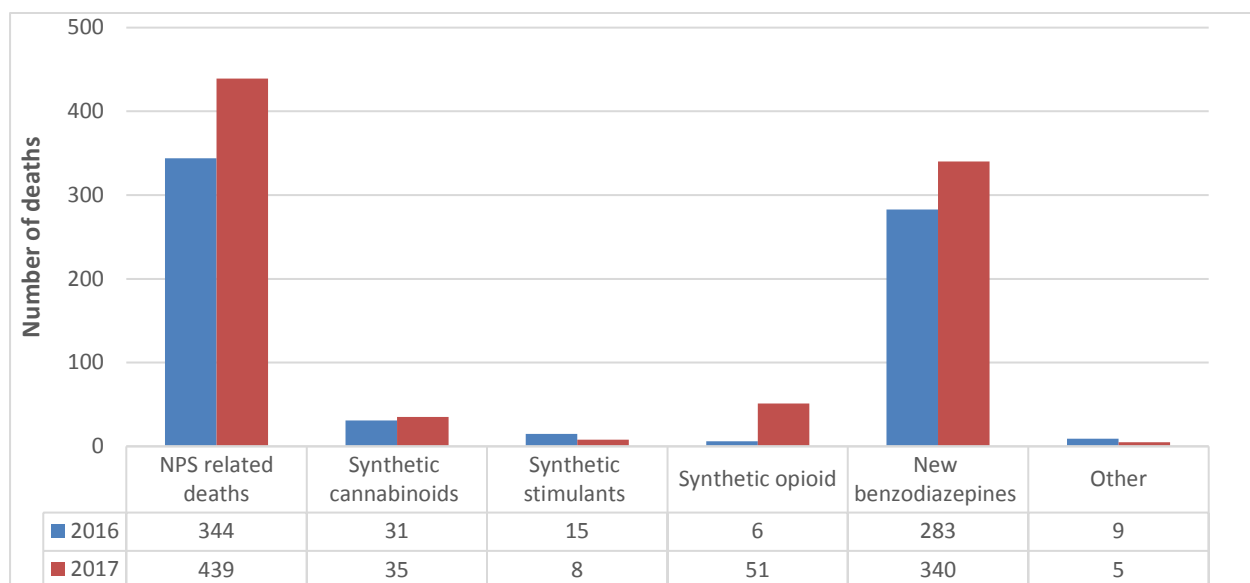
There were substantial differences in the proportion of drug-related deaths involving NPS across countries, as reported in the EMCDDA workbooks. According to this source, in 2017 in Turkey, NPS were present in 60 % of the drug-related deaths (565/941) and in Hungary – although the numbers are much smaller – in 42 % of the deaths (14/33). In four more countries, 10-25 % of the deaths involved an NPS (Estonia, Finland, Belgium and the United Kingdom). Romania and Poland (Warsaw) reported that an NPS was involved in over 15 % of all drug-related deaths in 2016, although in Romania the proportion was substantially lower in 2017, and in Poland there was no information available for that year (Figure 11).

Figure 11. Proportion of the drug-related deaths with an NPS involved: countries reporting the presence of an NPS (causal or contributory role) in 5 % or more of all drug-related deaths with known toxicology, 2016-2017



Note: For Poland, 2016 data were available only for Warsaw and an NPS was present in 7 out of 47 cases. There was no information available for 2017.

The United Kingdom information is of particular interest because of the high overall number of drug-related deaths (3 429 in 2017) and the identification of NPS from several pharmacological groups in a diversified drug market. In 2017, 12.8 % (439) of the deaths involved at least one NPS. Out of the 439 deaths reporting the presence of an NPS, the majority (77.4 %, 340 cases) involved new benzodiazepines, in particular etizolam (68.3 %, 300 cases), and all of them occurred in Scotland and in most cases also involved opioids (Figure 12 and Table 1).

Figure 12. Overall number of deaths in which NPS were present at post-mortem investigation, and number of deaths for selected NPS, United Kingdom, 2016-2017

Note: Cases from Northern Ireland not included (breakdown by NPS group not available). Totals: 7 cases (2016) and 12 cases (2017). Cases involving gamma-hydroxybutyrate (GHB) (23 in 2016 and 17 in 2017) were excluded.

Source: EMCDDA, presented by Hugo Lopez at the expert meeting on drug-related deaths, 21-22 October 2019, Lisbon.

Table 1. Drug-related deaths involving NPS in the United Kingdom, totals and by country, 2017

Country	Total NPS	Stimulants	New benzodiazepines	Opioids	Synthetic cannabinoids	Other or unknown drug
England and Wales	104	8	6	51 ⁽¹⁾	35	4
Scotland	335	0	334 ⁽²⁾	0	0	1
Northern Ireland ⁽³⁾	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Total United Kingdom	439	8	340	51	35	5

⁽¹⁾ Most (in 2017 especially) were fentanyl analogues, but there have been other opioid NPS-related deaths.

⁽²⁾ Including 300 involving etizolam.

⁽³⁾ Northern Ireland not included (12 cases), as no breakdown by substance was possible. Cases involving gamma-hydroxybutyrate (GHB) (17) were excluded.

Source: Personal communication from Martin White (UK focal point).

Turkey reported a high number of deaths in which NPS (almost exclusively synthetic cannabinoids) were present at post-mortem investigation. In 2016, synthetic cannabinoids were present in 98.9 % (373) of the 377 deaths with presence of NPS and in 2017 in 99.8 % (564) of 565 deaths with presence of NPS. Severe and fatal acute toxicity of synthetic cannabinoids has been described in several systematic reviews, and major complications include cardiovascular events (myocardial infarction, ischaemic stroke and emboli), acute kidney injury, seizures and psychiatric presentations (including first-episode psychosis,

paranoia, self-harm/suicide ideation). In 2016, FUB-AMB and 5F-ADB were the two synthetic cannabinoids most frequently found in the toxicological analysis of overdose deaths in Turkey. There is limited information on the Turkish drug situation, which may explain these unusual figures, but different sources, including hospital emergency data, support their plausibility (Çoban, 2014; Aksel et al., 2015; Anonymous, 2017; Caliskan et al., 2018).

In Germany, 75 deaths with NPS present at post-mortem investigation were reported (5.8 % of all drug-related deaths) in 2017 and 25 deaths in 2018 (1.9 %)

Fentanyl and fentanyl analogues

This group of substances deserves particular attention because of their high potency, leading to a high risk of fatal overdose. In Europe, fentanyl and fentanyl analogues are usually found in the same countries and in some cases they are found together in post-mortem investigations. Since 2017, the EU EWS has responded to seven new fentanyl derivatives posing health concerns at the EU level, and all seven are now under international control.

On the basis of the review of data on NPS received by the EMCDDA, in 2016 and 2017 there were, respectively, 326 and 333 deaths involving fentanyl, and 141 and 242 deaths involving fentanyl analogues reported. Thirteen countries reported cases, and Estonia, Germany, Sweden, the United Kingdom and – with lower numbers – Finland accounted for most of the cases reported, for both fentanyl and fentanyl analogues.

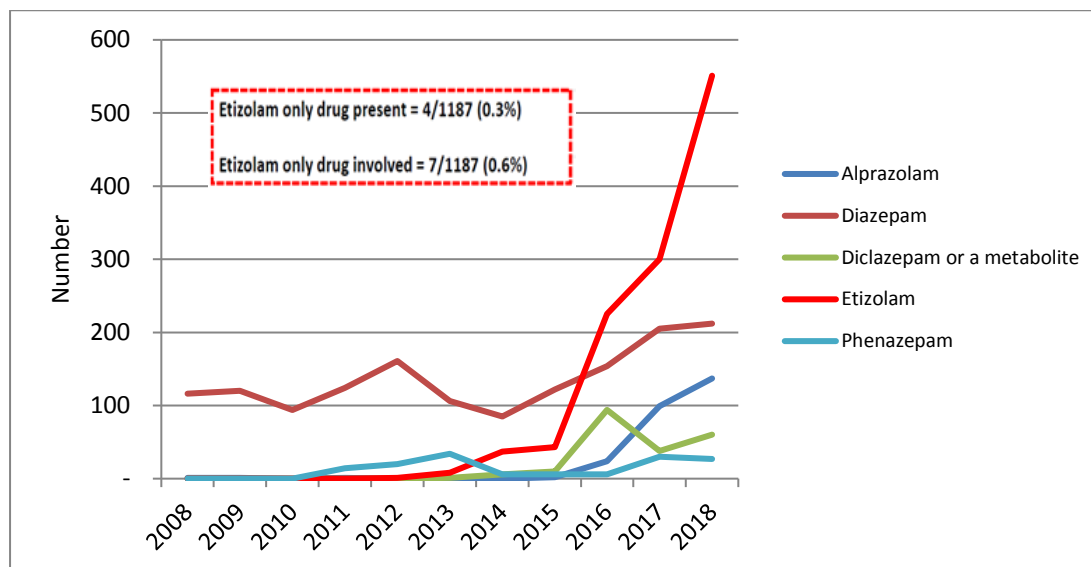
Between 2017 and 2018 Sweden, Estonia and Germany reported marked decreases in the numbers of deaths related to fentanyl and fentanyl analogues, whereas in Finland an increase in fentanyl-related deaths was reported, although the numbers were small (from 4 to 11 cases). Fentanyl and its derivatives are usually detected in extremely low concentrations, which may make their detection difficult in some laboratories. In addition to under-detection, under-reporting of cases related to fentanyl and fentanyl analogues is possible in some countries.

Etizolam: concern around new benzodiazepines in Scotland

Benzodiazepines are a family of psychoactive medicines commonly prescribed for anxiety disorders, insomnia, muscle spasms and seizures. They are a risk factor for fatal drug overdose because of their strong depressant effect on the central nervous system, which can potentiate the respiratory depression caused by heroin and other opioids. In addition to prescription benzodiazepines, NPS belonging to the benzodiazepine class, which are not controlled under international drug control laws, are available on the European drug market.

The rate of high-risk drug use is higher in Scotland than anywhere else in Europe, and most of the increase is accounted for by opioid-related deaths involving etizolam and to a lesser extent deaths involving diazepam and alprazolam (Figure 13). Etizolam belongs to the group of benzodiazepines. It was until 2020 classified as a new psychoactive substance (see box 'Etizolam'). Etizolam is readily available online and at street level.

Figure 13. Number of mentions of benzodiazepine, by substance, in drug-related deaths in the period 2007-2018 and proportion of cases involving etizolam among the 1 187 cases in 2018, Scotland



Source: Data from the National Records of Scotland (2019), presented by Andrew McAuley at the expert meeting on drug-related deaths, 21-22 October 2019, Lisbon.

Social determinants such as living in deprived areas, unemployment and poverty are also linked to drug overdose, and research indicates that age-standardised rates for drug-related deaths among young adults rose during the 1990s in Scotland due to an increased risk of drug-related deaths in the cohort born between 1960 and 1980, especially for men living in the most deprived areas (Parkinson et al., 2018). The study concluded that this cohort effect is consistent with the hypothesis that exposure to the changing social, economic and political contexts of the 1980s created a delayed negative health impact. As described for other countries where data are available, polydrug use is the norm among high-risk drug users in Scotland, where only 15 % (178/1187) of drug-related deaths in 2018 involved a single substance. Heroin, benzodiazepines and alcohol were a typical combination.

A number of benzodiazepines are sold as 'street Valium' and, while they may have a similar appearance to Valium tablets, some were found to contain diclazepam, other new benzodiazepines, a mixture of etizolam and the synthetic opioid U-47,700, or U-47,700 on its own – increasing the risk of accidental overdose.

Etizolam

Etizolam is a thienodiazepine derivative, which is a benzodiazepine analogue. Commercialised as medicine in a few countries (Japan, India and Italy), its clinical effect is similar to that of benzodiazepines – as a benzodiazepine receptor agonist (amnesic, anxiolytic, anticonvulsant, hypnotic, sedative and skeletal muscle relaxant). The usual dosage is one tenth of that of diazepam (0.5 mg compared with 5 mg) and etizolam is clinically 10 times more active for the same weight. However, the median lethal dose (LD₅₀) of etizolam is 4 300 mg/kg (orally) and diazepam is more lethal on its own (WHO, 2019a). The deaths related to etizolam have to be considered in the context of polydrug use and the substance contributing to fatal outcomes in combination with other central nervous system depressants such as opioids and (often) alcohol and the risk increasing with the amount ingested (number of pills). Until now the substance has not been controlled under the United Nations drug conventions, and therefore it has been considered a new psychoactive substance. In November 2019, the WHO recommended that etizolam be placed in Schedule IV of the 1971 Convention on Psychotropic Substances (WHO, 2019b). This was confirmed at a meeting of the Commission on Narcotic Drugs in March 2020.

In summary, although NPS are found in a significant minority of drug-related deaths in Europe (14 % in 2016/2017), most of them are disproportionately concentrated in only two countries and related to only two substance groups. These deaths are concentrated in specific populations: chronic opioid users in the United Kingdom, in particular in Scotland, and a poorly understood population of synthetic cannabinoid users, mainly young men, in Turkey. Leaving aside these two groups of deaths, only 4-5 % of drug-related deaths in Europe in 2016-2017 were related to NPS, although possibly there is some underestimation due to analytical challenges. The number of deaths with fentanyl and fentanyl analogues present at post-mortem investigation is relatively low in Europe as a whole, but they are concentrated in a limited number of countries, and in some of them they account for a relevant proportion of drug-related deaths. Despite a substantial decrease in fentanyl-related deaths in Estonia, Germany and Sweden in 2018 compared with 2017, the phenomenon presents a significant risk of harm and should be followed closely.

Responding to drug-related deaths

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 high-risk drug users, especially by removing barriers and making services accessible and by empowering them to take fewer risks (EMCDDA, 2013). In recent years, some European countries (e.g. Norway and Sweden) have developed national overdose prevention strategies, and specific inquiries into drug overdose have been conducted in the United Kingdom (ONS, 2018).

An overview of other responses to drug-related deaths, including retention in opioid substitution treatment, which has a strong protective effect, is available at the EMCDDA's online Best practice portal and in the European guide *Health and Social Responses to Drug Problems* (EMCDDA, 2017). Updates on two key intervention types, drug consumption rooms and take-home naloxone, are presented below.

Drug consumption rooms

Drug consumption facilities, where illicit drugs can be used under the supervision of trained staff, have been operating in Europe for 35 years. These facilities primarily aim to reduce the acute risks of disease transmission through unhygienic injecting practices, prevent deaths from drug-related overdoses and connect high-risk drug users with addiction treatment and other health and social services. Eight EU countries (Belgium, Denmark, Germany, Spain, France, Luxembourg, Netherlands and Portugal) Norway, Switzerland and Ukraine ⁽⁵⁾, as well as Canada, Australia and Mexico, have established such facilities as part of an integrated response to specific local problems.

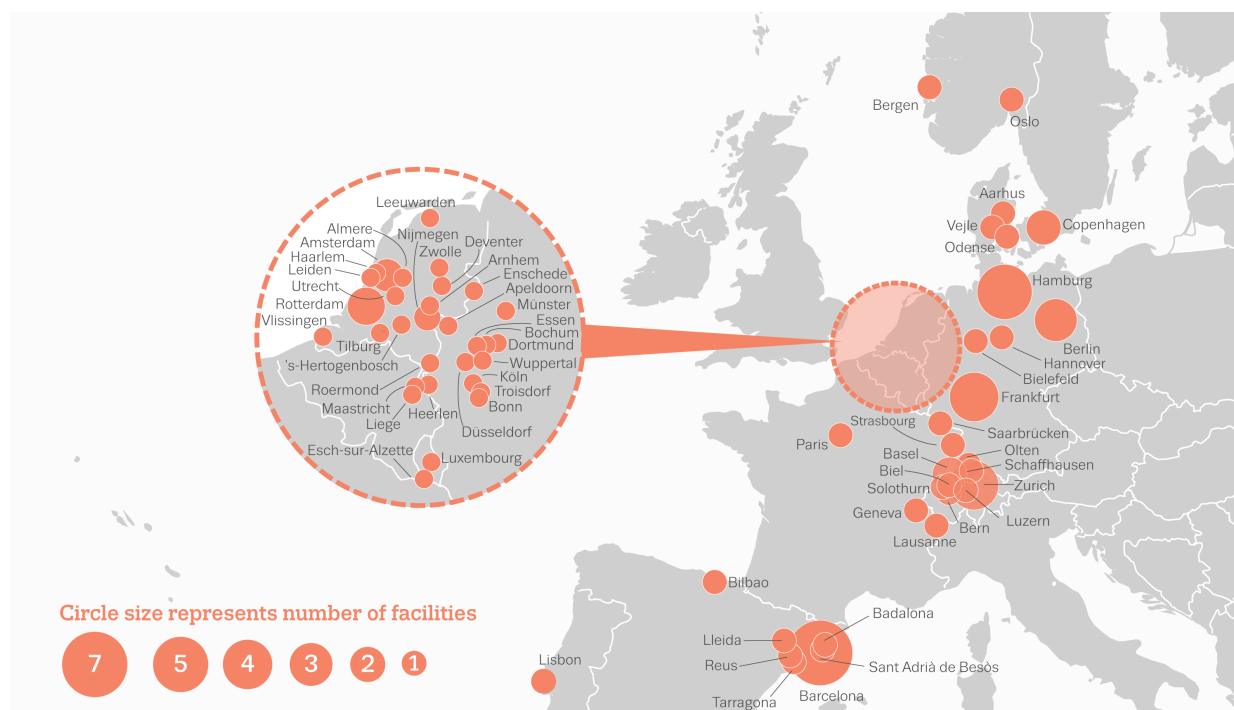
Research shows that, through supervised drug consumption rooms, contact with hard-to-reach populations of people who use drugs, especially marginalised groups and those who use drugs on the streets or in other risky settings, with a high burden of premature mortality can successfully be established. The analysis of two prospective cohort studies in Vancouver, involving at baseline 811 people who inject drugs and tracking their development over more than 10 years, showed that frequent use of such facilities was associated with a lower risk of death, independent of relevant confounders (Kennedy et al., 2019).

Furthermore, these facilities reduce injecting-related infections by providing a hygienic environment, enhance safer injecting practices, especially among their regular users, and promote access to social and health care and drug treatment. In response to their goal to improve public amenity in areas surrounding urban drug markets, clear reductions in drug use in public places and in drug-related litter have been documented (Kennedy et al., 2017; Belackova et al., 2019). At the same time, the operation of supervised consumption facilities has been shown to have a neutral effect on drug-related crime (Wood et al., 2006), and there appears to be little basis for concern about other adverse effects (Caulkins et al., 2019).

In 2019, 78 drug consumption rooms were in operation in the EU and a total of 17 facilities function in nine Swiss and two Norwegian cities (see Figure 14). This number does not include the facility in Sumy in the Ukraine and it is not shown in Figure 14.

⁽⁵⁾ Information on Switzerland from [Infodrog](#); information on Ukraine from [Alliance for Public Health](#).

Figure 14. Geographical distribution of supervised consumption facilities in the EU, Norway and Switzerland

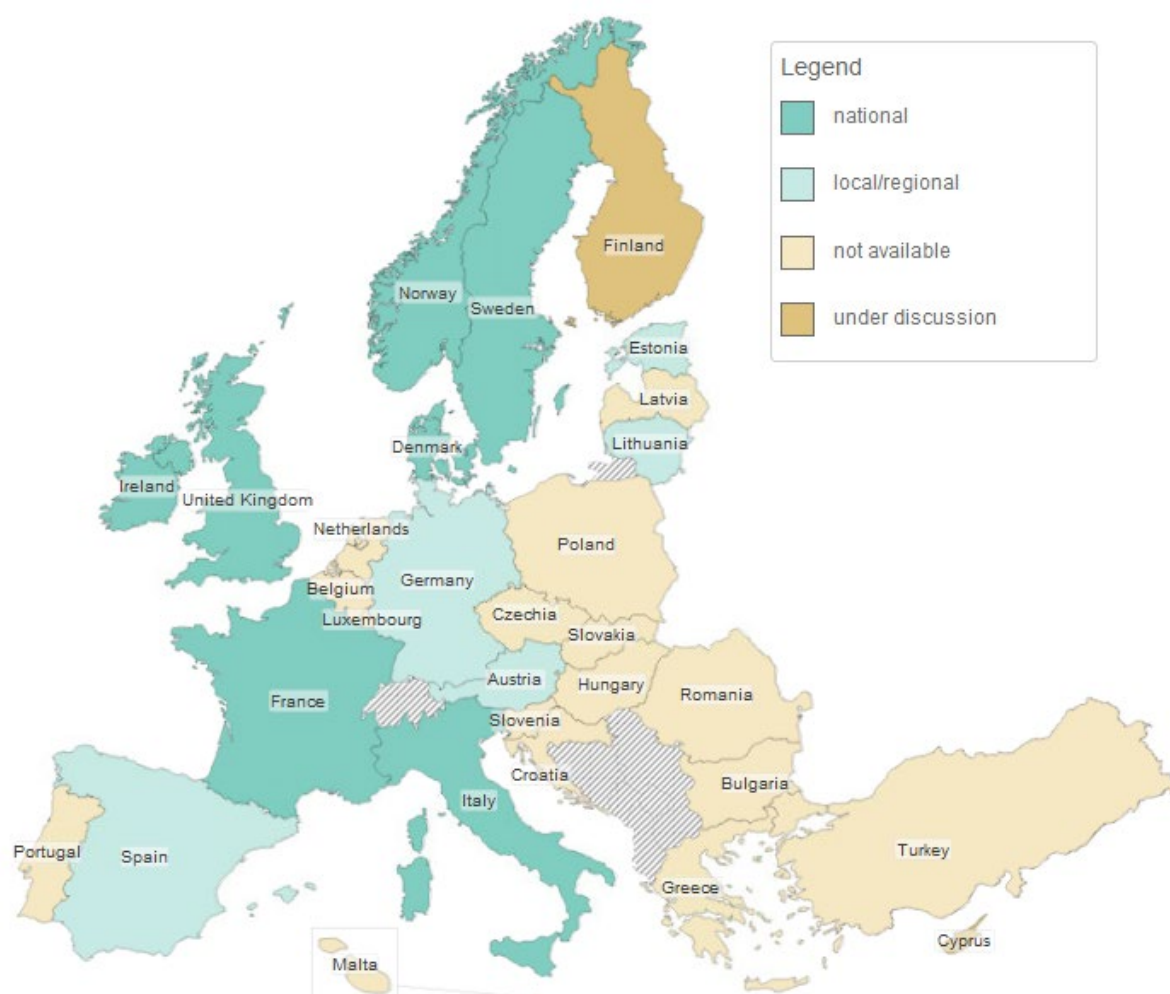


Sources: Data for the EU from EMCDDA national focal points. Data for Switzerland from Infodrog.

Take-home naloxone programmes

Naloxone is an opioid antagonist medication used worldwide in emergency medicine to reverse respiratory depression caused by opioid overdose. Take-home naloxone programmes aim to prevent opioid overdose deaths by providing the medication to potential bystanders (e.g. opioid users, their peers and families) and training them to recognise an overdose and to intervene using naloxone. The medication is available as an injectable solution in ampoules or pre-filled syringes and, since recently, as an intranasal spray.

In 2019, naloxone distribution initiatives were reported to exist in 12 countries: Austria, Denmark, Estonia, France, Germany, Ireland, Italy, Lithuania, Norway, Spain (Catalonia), Sweden and the United Kingdom (Figure 15). In 2018, the legal framework for establishing such programmes was created in Cyprus and preparatory steps for introducing naloxone were taken in Finland (EMCDDA, 2013, 2017, 2020d).

Figure 15. Take-home naloxone programmes in Europe, 2019

Source: EMCDDA Reitox reporting 2018/2019.

A new EMCDDA initiative to support countries in their response to preventing drug-related deaths, in particular from opioid overdose, is under way. The main objectives of the initiative are to improve the monitoring of the situation and responses 'landscape' and to develop new tools and materials to inform practice and policy about how to improve the prevention of drug-related deaths. In this context, barriers and facilitators to take-home naloxone programmes have been analysed (Breidahl, 2019). Barriers or facilitators were grouped as follows: system-level barriers, including regulatory and legal obstacles, lack of advocacy, community stigmatisation of drug users and lack of funding; provider-level barriers to providing take-home naloxone, including high staff turnover and workload; and barriers at the level of first responders (deliverers), including lack of awareness/education about naloxone, and issues limiting practical access to the medication and its use. Identifying and tackling regulatory and legal barriers to take-home naloxone programmes, misconceptions and knowledge gaps, as well as the impact of drug-related stigma among the general population, providers and first responders are important steps to improving the availability of take-home naloxone. Removing some barriers requires changes in national regulatory systems, while others can be solved by increasing staff and clients' knowledge and implementing simple changes in practice. Materials and tools accompanying this initiative will be described in the second edition of the EMCDDA's European guide *Health and Social Responses to Drug Problems* (EMCDDA, 2017), which currently is under preparation.

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