



DELIVERABLE 2.3.
**Report of Summary data of demographics,
cause(s) of death, substances
detected/implicated in deaths, geographical
location, circumstances of death, trends
over time and detailed analysis.**

Grant Agreement number 806996-JUSTSO



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Acronym:	JUSTSO
Full title:	Analysis, knowledge dissemination, JUstice implementation and Special Testing of novel Synthetic Opioids
Principal Investigator:	Prof. Gaetano Di Chiara, University of Cagliari
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Project duration:	24 months

Beneficiary/Partner:	<ol style="list-style-type: none"> 1) University of Cagliari (UNICA); 2) Università Politecnica delle Marche (UNIVPM); 3) Universitaetsklinikum Essen (UKESSEN); 4) Università G. D'Annunzio Chieti-Pescara (UD'A); 5) Institut Catala De La Salut (ICS); 6) Universidad Nacional de Educación a Distancia (UNED); 7) Istituto Superiore di Sanità (ISS); 8) Latvijas Organiskās Sintēzes Institūts (LIOS); 9) Aristotelio Panepistimio Thessalonikis (AUTH); 10) Consorci Mar Parc De Salut De Barcelona (IMIM)
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Work Package 2:	Collecting and monitoring data of adverse effects/near misses/deaths linked to NSO
Deliverable:	D. 2.3: Summary data of demographics, cause(s) of death, substances detected/implicated in deaths, geographical location, circumstances of death, trend over time and detailed analysis.
Lead Beneficiary:	INSTITUT CATALA DE LA SALUT (ICS)
Deadline:	March 31th 2020



1. Summary

This deliverable summarizes most recent data, period 2018/19, about number of deaths associated to opioids, focusing new synthetic opioids in Europe.

Even though the latest "European Drug Report 2020: Trends and Development" EMCDDA report has not yet been published, we have collected the most recent data available in order to provide an overview of the issue. It is relevant to take in to account that countries do not provide individual data before the publication of the European Drug Report.

In addition, this deliverable has been written during the actual pandemic of coronavirus in all Europe, the majority of countries did not provide the most recent data because this emergency situation.

For the preparation of this deliverable we have relied mainly on the following documents:

- European Drug Report 2019: Trends and Developments
http://www.emcdda.europa.eu/system/files/publications/11364/20191724_TDAT19001ENN_PDF.pdf
- Drug-related deaths and the mortality in Europe
http://www.emcdda.europa.eu/system/files/publications/11485/20193286_TD0319444ENN_PDF.pdf
- Drug-related hospital emergency presentations in Europe: update from the Euro-DEN Plus expert network.
http://www.emcdda.europa.eu/system/files/publications/11485/20193286_TD0319444ENN_PDF.pdf

Also, we have included the most recent data provided, if provided, by the national authorities of the countries participating to our Consortium (Italy, Germany, Spain, Greece, and Latvia).

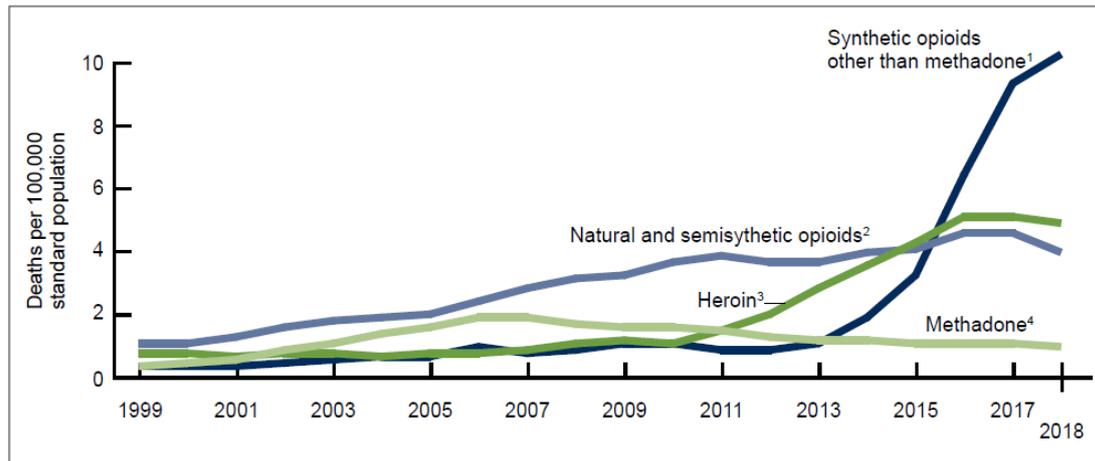
2. Introduction

New psychoactive substances (NPS) are a large and growing group of substances of abuse that are not controlled by international drug laws (Rivera et al., 2017; United Nations Office on Drugs and Crime (UNODC), 2017). The EMCDDA and UNODC define NPS 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”. They present a chemical composition similar to those substances that are controlled by the law, and they emulate their effects (United Nations Office on Drugs and Crime (UNODC), 2017). So, the NPS emerge in the illicit market as a substitute of these substances. Main group of NPS are stimulants, but there is an increase of new synthetic opiates (NSO) that are offered on the illicit market especially in last two years (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2018).

Respond to new synthetic opioids (NSO) is a current challenge since it has become a global health problem. United States (US) reported an increase of overdose deaths with synthetic opioids involved rising from 3007 deaths involving NSO in 2010 to 19,413 in 2016 and they represent early the 50% of opioids overdose (Jones et al., 2018). Of the 70,237 drug overdose deaths in the United States in 2017, approximately two thirds (47,600) involved an opioid substance. In recent years, increases in opioid-involved overdose deaths have been driven primarily by deaths involving synthetic opioids other than methadone (hereafter referred to as synthetic opioids). During 2018, a total of 67,367 drug overdose deaths occurred in the US, a 4.1% reduction from 2017; 46,802 (69.5%) involved an opioid (2). From 2017 to 2018, deaths involving all opioids, prescription opioids, and heroin decreased 2%, 13.5%, and 4.1%, respectively. However, deaths involving synthetic opioids increased 10%, likely driven by illicitly manufactured fentanyl (IMF), including fentanyl analogues (Wilson et al., 2020).

Figure 1. Death rates by type of opioid (US, 1999-2018).

Figure 3. Age-adjusted drug overdose death rates involving opioids, by type of opioid: United States, 1999–2018

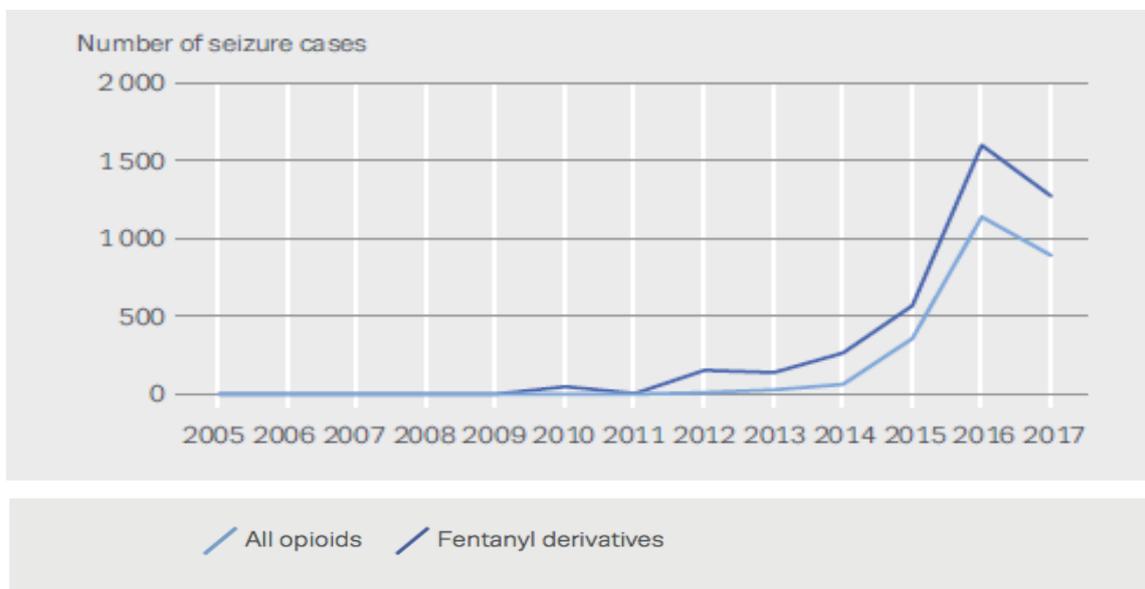


¹Significant increasing trend from 1999 through 2006 and 2013 through 2018, with different rates of change over time, $p < 0.05$.
²Significant increasing trend from 1999 through 2018, with different rates of change over time, $p < 0.05$.
³Significant increasing trend from 2005 through 2015, with different rates of change over time, $p < 0.05$.
⁴Significant increasing trend from 1999 through 2006, then significant decreasing trend from 2006 through 2018, with different rates of change over time, $p < 0.05$.
 NOTES: Deaths are classified using the *International Classification of Diseases, 10th Revision*. Drug-poisoning (overdose) deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Drug overdose deaths involving selected drug categories are identified by specific multiple-cause-of-death codes: heroin, T40.1; natural and semisynthetic opioids, T40.2; methadone, T40.3; and synthetic opioids other than methadone, T40.4. Deaths involving more than one opioid category (e.g., a death involving both methadone and a natural or semisynthetic opioid) are counted in both categories. Deaths may involve multiple drugs. The percentage of drug overdose deaths that identified the specific drugs involved varied by year, with ranges of 75%–79% from 1999 through 2013 and 81%–92% from 2014 through 2018. Access data table for Figure 3 at: https://www.cdc.gov/nchs/data/databriefs/db356_tables-508.pdf#3.
 SOURCE: NCHS, National Vital Statistics System, Mortality.

This warning in the US along with over 250 fentanyl related overdoses reported by the EMCDDA (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2018) makes Europe to target NSO as a public health challenge. Although intoxications are reported it is probably that are underestimated mainly due to NSO overdose are not enough studied and given the difficulty identifying these compounds (Pichini et al., 2017). Witch concern to Europe, heroin still remain the most commonly used illicit opioid and, in most European countries, with some exceptions, is involved in 9 of 10 drug-induced deaths (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2019a). Nevertheless there are some available data that suggest the increasing use of NSO. First, is their presence in the European drug market. Since 2009, 49 new synthetic opioids have been detected, including 11 reported for the first time in 2018. This represents a significant increase (as shown in Figure 1).

In the number of different substances available that belongs to the group of new synthetic opiates. Although currently playing a small role in Europe’s drug market, many new opioids (particularly those of the fentanyl family) are highly potent substances that pose a serious threat to individual and public health.

Figure 2: Number of seizures of synthetic opioids reported to the EU Early Warning System:



Secondly, there are some available data about intoxications/overdose in the direction of an increasing use of NSO. Some countries have reported: deaths related to opioids drugs as oxycodone and tramadol, found in post-mortem analysis opioids used in substitution treatments and deaths associated with fentanyl and their analogues.

Overdoses and opioids

Opioids, mainly heroin or its metabolites, often in combination with other substances, are present in the majority of fatal overdoses reported in Europe. In most drug-related deaths, more than one substance is detected, indicating poly-drug use.

Overall, opioids are involved in 85% of fatal overdoses, with large differences across countries (see more country-level data in the Statistical Bulletin 2019 from the EMCDDA: <http://www.emcdda.europa.eu/data>).

It is important to bear in mind that most drug-induced deaths are attributed to multiple drug toxicity. Opioids, mostly heroin, are involved in most of the drug-induced deaths reported in Europe. Heroin, in particular, claims a high toll of deaths in a number of countries. In England

and Wales (UK), heroin/morphine is mentioned in 1164 deaths, or 47 % of the cases, registered in 2017 (ONS, 2018). In France, it is mentioned in 131 deaths recorded in the special mortality register, or 40 % of the cases with information available. In Germany, heroin is recorded in 409 deaths reported by the police, or 32 % of cases, and in Norway it is mentioned in 49 deaths reported in the general mortality register in 2017, or 20 % of the cases.

In England, Public Health England's inquiry into increases in drug-induced deaths highlighted changes in heroin purity and an ageing of the drug-using population with multiple co-morbidities as the principal factors behind the increases in the number of heroin-related deaths over the previous years. Mortality cohort studies in England and in Scotland have also highlighted higher methadone-specific death rates in older methadone clients (Gao et al., 2016; Pierce et al., 2018), and a narrowing of risk between men and women with age (Pierce et al., 2016).

Overdoses and non-heroin opioids

Some countries now report that opioids other than heroin are associated with a high number and sometimes an increasing share of drug-induced deaths. In France, according to the latest available data (2016) from the special mortality register, opioids were present in 80 % of all drug-induced deaths. Methadone was associated with four out of 10 opioid-related cases, a slightly higher proportion than heroin. This continues a pattern observed for several years.

In Norway, a shift has been observed in the relative importance of different opioids, with heroin now identified as the main intoxicant involved in a fifth (20 %) of the overdose deaths in 2017, compared with around half of the deaths (49 %) in 2006 (Figure 5). Methadone (22 %) and the category 'synthetic opioids including fentanyl and buprenorphine (17 %) are commonly identified as a main intoxicant in post-mortem examinations. These changes are concurrent with significant shifts in the dispensing of prescribed opioids in Norway over the last decade (Muller et al., 2019). There has been a scaling-up of buprenorphine prescription for the management of opioid dependence, and an increasing trend in the prescription of other opioids (namely tramadol and oxycodone) in the general population over the last 10 years. For example, oxycodone was prescribed to 5 200 males in 2006, compared with 19 700 in 2016 (a 279 % increase), and tramadol was prescribed to 29 600 males in 2006,

compared with 94 200 in 2016 (a 218 % increase). Tramadol is an opioid associated with a significant number of deaths in Europe. At least 300 drug-induced deaths were reported in 2017 in which tramadol was either present or implicated: most notably 185 in England and Wales (10 % of all opioid-related deaths where the opioid was known), 40 in Spain, 37 in France and 20 in Finland. In Sweden, concerns have been raised regarding its use among young people. Tramadol is often used in combination with other drugs, and it is therefore difficult to assess its contribution to deaths where it is recorded. In addition, 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, report an increase in the prescription of this and of other opioids.

Fentanyl analogues

More than 30 fentanyl analogues have been detected and reported to the EMCDDA since 2012. Available from the surface web, from the darknet and at street level, they are used to make fake medicines or sold as 'legal' replacements to illicit opioids. They are also found in, or sold as, heroin, other illicit opioids and cocaine. Novel dosage forms such as nasal sprays and e-liquids have emerged in recent years. Fentanyl and its analogues can cause rapid onset of life-threatening respiratory depression, and their appearance on the drug market has been associated with increases in poisonings. Cyclopropylfentanyl, carfentanil and acryloylfentanyl, in particular, have been associated with large numbers of deaths: 78, 61 and 47 deaths, respectively, at the time of their risk assessments (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2019b). While illicit fentanyl and its analogues have been associated with deaths in Europe, there is some evidence of diversion of medicinal fentanyl (e.g. patches) to illicit markets, and this might also be associated with deaths but to a much lesser extent.

In England, in the spring of 2017, intelligence from post-mortem results and drug seizures suggested that fentanyl and its analogues had been introduced into the heroin supply in the north of the country. Public Health England issued an alert at the end of April 2017 advising:

1. On the availability of, and harms from, heroin that had been mixed with fentanyl or carfentanil.
2. That warnings be cascaded and, of the naloxone dosing regime in the event of an overdose.



Around the same time, police and the National Crime Agency disrupted a laboratory that could have been the site for processing and mixing fentanyl and other analogues, and they sought to raise awareness. Official data from the Office for National Statistics, analysed by Public Health England, indicate that around 26 deaths registered in 2017 appeared to fit the pattern of the incident, these are only those on which the inquests have currently concluded; there will be more that are yet to be registered and will appear in the data for 2018 when these are released by the Office for National Statistics (even though all the deaths occurred in 2017).

In Sweden, data from forensic analyses show that there has been a major decrease in the reported number of deaths related to fentanyl analogues, with 11 reported in 2018 compared with 101 in the previous year. In 2017, there were 30 cases related to fentanyl and 107 related to heroin. The drop in 2018 may be related to the number of fentanyl analogues that were classified as narcotic drugs or 'goods dangerous to health' over the previous year. That classification resulted in new possibilities of prosecuting those who sell not-yet-classified new psychoactive substances (NPS), which influenced supply. Recent evidence suggests that the classified fentanyl analogues disappeared from the open web shops in Sweden.

3. Activity

This deliverable summarizes the most recent available data about the number of deaths produced by opioids, including new synthetic opioid derivatives, in Europe. These data are those communicated by the agencies of each country to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). In addition, we have included the most recent data provided by the national authorities of the countries participating to our Consortium (Italy, Germany, Spain, Greece, and Latvia).

The EMCDDA drug-related deaths (DRD) indicator focuses on deaths directly caused by illegal drugs (drug-induced deaths) and mortality among drug users across the European Union (EU) Member States, Norway and Turkey. The EMCDDA monitors national statistics on DRD and reports the results in the data and statistics section (Statistical Bulletin) of the European Drug Report (EDR). Because in some countries cases are not defined with the same code between countries, these differences in the national practices of coding the causes of deaths implies that direct comparisons between countries in the numbers or rates of DRDs should be made with caution. However, the trends observed can give valuable insight if methods are consistent within a country, especially when interpreted together with other drug indicators (a more detailed description can be found in: <http://www.emcdda.europa.eu/data/stats2019/methods/drd>).

In the case of the EMCDDA databases, we utilized the data from every country reported in each country web page: <http://www.emcdda.europa.eu/countries>

As mentioned above, the data on poisoning and mortality for the period 2018/2019 provided by the EMCDDA are not yet available. That is why we provide data from the previous period, 2016/2017.

In addition, we collected the more recent data, if available, from the countries involved in this action (Italy, Germany, Spain, Greece, and Latvia).



4. Results

Global results

It is estimated that at least 8 238 overdose deaths occurred in the European Union in 2017. This rises to an estimated 9461 deaths if Norway and Turkey are included, representing a stable figure (an increase of 0.7 %) compared with the revised 2016 figure of 9 397. These overall numbers must be understood as underestimations, as there are limitations to drug-induced deaths data, particularly to European cumulative totals (see the box 'Monitoring drug-induced deaths', page 6). As in previous years, the United Kingdom (34 %) and Germany (13 %) together account for around half of the EU total. This relates partly to the size of the at-risk populations in these countries, but also to the under-reporting in some other countries.

The mortality rate due to drug overdoses in Europe in 2017 is estimated at 22.6 deaths per million population aged 15-64, but this varies across countries, with higher rates being observed in countries in the north of Europe (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2019b). Nevertheless, drug overdose continues to be a major cause of premature death among people who use drugs in Europe, predominantly affecting males: 35.8 cases per million males aged 15-64 years, which is almost four times that among females (9.3 cases per million females aged 15-64 years). Furthermore, it was estimated that drug overdoses accounted for 4 % of all deaths among 15- to 39-year-olds in Europe.

Individual results for each country

As mentioned above, the data on poisoning and mortality for the period 2018/2019 provided by the EMCDDA are not yet available. That is why we attach the table with the detail of the data for each country for the previous time period, 2016/2017.

The following section provides an approximation of the subject with the preliminary data received by each of the participants of the grant agreement.

Table 1: Individual data for European countries (adding Norway and Turkey) of drug-related emergencies, drug-induced deaths (DID) and opioid-induced deaths provided by the European Drug Report 2019: Trends and Developments” (available at http://www.emcdda.europa.eu/publications/edr/trends-developments/2019_en).

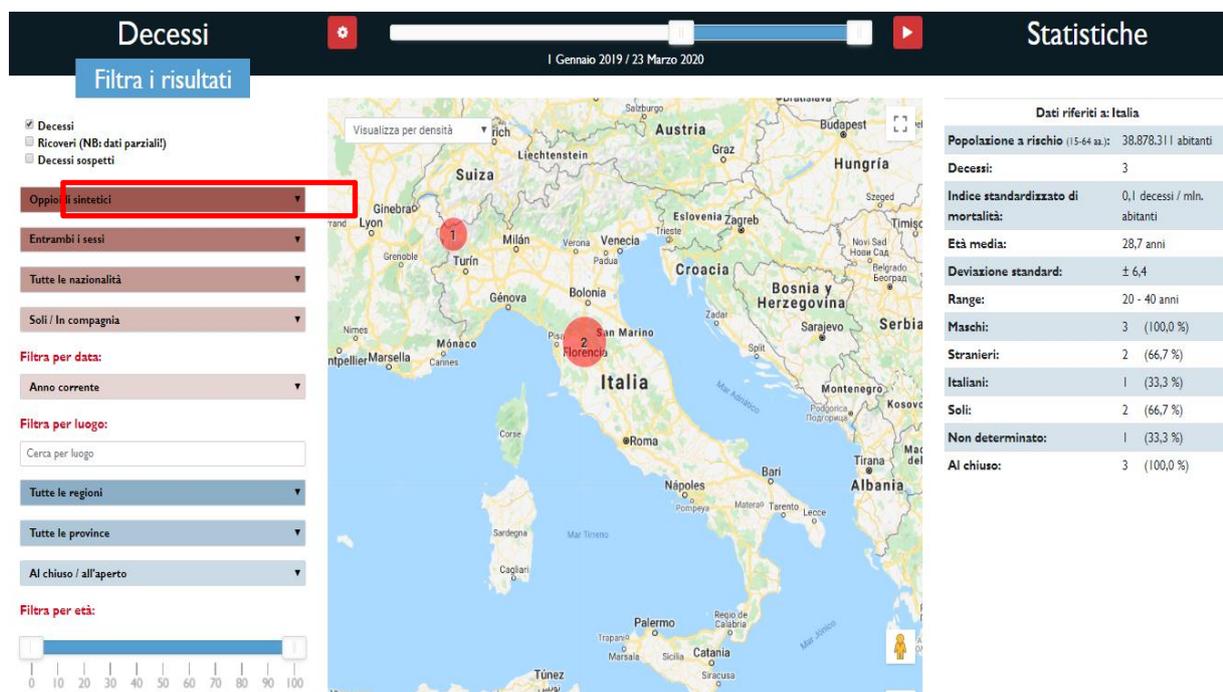
Country	Year	Drug related-emergencies	Drug induced-death DID	DID-opioids	DID-type opioids	DID new synthetic opioids
Austria	2017		154	Majority	ND	ND
Belgium	2017	1750	62	50%	heroin	fentanyl: 6, U-47700: 5
Bulgaria	2017	595	18			
Croatia	2017		65			
Cyprus	2017		16	Opioids: 11		
Czechia	2017	1101	42	Majority	fentanyl, morphine and codeine	
Denmark	2017	2 523	237	80%: methadone, heroin and morphine		
Estonia	2017	1396	110	Majority synthetic opioids	Majority synthetic opioids	fentanyl: 28; carfentanyl: 15
Finland	2017	6000	200	Majority	buprenorphine	U-47700: 10
France	2015	11500	373	25%		
Germany	2017	23500	1272	33%		24
	2016					4
Greece	2017	213	62	33%		fentanyl: 2
	2018					fentanyl: 1
Hungary	2017		33	33%		
Ireland	2017	4233	224			
Italy	2017		294	Majority	heroin	2 U-47700: 1 no data
	2018					no since october
Latvia	2017	3800	22/27	33%	tramadol, morphine, methadone	
Lithuania	2017	400	83	90%	heroin, methadone	fentanyl; carfentanyl
Luxemburg	2017	2200	8	Majority	heroin, methadone	
Malta	2017	28	5	60%		
Netherlands	2017	5117	262			
Norway	2017		282	Majority	heroin, morphine, oxycodone (36%)	
Poland	2017	4 324	204			
Portugal	2017		30	66%	heroin and methadone	
Romania	2017	3000	32	Principal	heroin and methadone	
Slovakia	2017	177	19	78%		
Slovenia	2017	143	47	heroin 18	heroin, tramadol	
Spain	2016/2017	4565	483	most common		ciclopropyl fentanyl: 1
Sweden	2017		626	Vast majority		
Turkey	2017		941	25%	heroin	
United Kingdom	2017	8500	3256	90%	heroin, methadone	fentanyl: 75; fentanyl-derivatives: 31

Individual data provided by national bodies in countries of the grant action

The following section includes a commentary on the results provided by the individual data provided by the national bodies included in the grant actions which are: Italy, Germany, Spain, Greece, and Latvia. We included additional data from United Kingdom.

Italy

Data from the Geoverdose website (<https://www.geoverdose.it>), a total of 3 cases of death related with new synthetic opioids were reported in 2019 and no new cases for the current year 2020.



Germany

In addition to the data reported to the EMCDA (see Table 1), data provided by the Drogen und Suchtbericht der Bundesdrogenbeauftragten, 2019 (Governmental Report on Drugs and Addictions in Germany, 2019) are presented in the following Table 2.

Reasons	2018
Monovalent intoxications by opioids/opiates	260
Heroin/morphine	175
Opioids from maintenance group	50
Methadone (including levo-methadone)	44
Buprenorphine	4
Others	2
Analgesic opioids	30
Fentanyl	25
Synthetic opioids (fentanyl derivatives)	5
Polyvalent intoxications by opioids/opiates	369
Heroin/morphine in combination with other substances	230
Opiate maintenance drugs in combination with other substances	155
Methadone in combination with other substances	133
Buprenorphine in combination with other substances	7
In combination with other substances	17
Analgesic opioids in combination with other substances	54
Fentanyl	28
Synthetic opioids in combination with other substances	1

Spain

No supplementary information was obtained, official data were that reported to the EMCDDA (see Table 1).

Greece

No supplementary information was obtained, official data were that reported to the EMCDDA (see Table 1).

Latvia

No supplementary information was obtained, official data were that reported to the EMCDDA (see Table 1)

United Kingdom

Most recent delivery from the Advisory Council on the Misuse of Drugs (ACMD) entitled "Misuse of fentanyl and fentanyl analogues, January 2020", showed an increase along the years of the intoxication by NSO, but the number are more less than heroin and morphine. The data are showed in this table.

Table 3. Drug related deaths from 2008 - 2018, including selected opioids; (a) England and Wales [ONS, 2019] (b) Scotland [NRS, 2019] and (c) Northern Ireland [NISRA, 2019]

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
(a) England and Wales											
Total drug-misuse related deaths	2004	1976	1903	1737	1636	1957	2248	2479	2596	2503	2917
Heroin and morphine	897	880	791	596	579	765	952	1201	1209	1164	1336
Fentanyl	6	9	10	31	22	22	40	34	58	75	74
Fentanyl analogues	1	0	0	0	2	0	0	1	1	31	31
(b) Scotland											
Total drug-related deaths	574	545	485	584	581	527	614	706	868	934	1187
Heroin	261	270	193	147	135	143	219	238	326	314	375
Fentanyl	1	1	1	4	7	4	4	3	7	15	12
Acetylfentanyl	0	0	0	0	0	0	1	0	0	0	0
Alfentanil	0	0	0	0	0	0	0	0	0	1	0
(c) Northern Ireland											
Total drug-misuse related deaths	53	57	63	59	75	79	88	114	112	110	-
Heroin and morphine	6	9	16	17	24	25	11	27	25	24	-
Fentanyl	0	1	6	3	7	4	1	15	13	13	-
Fentanyl analogues	0	0	1	0	0	0	0	1	0	1	-

Notes:

Figures quoted for Northern Ireland, England and Wales are drug misuse-related deaths where the underlying cause is either drug abuse, drug dependence or drug poisoning and any of the substances controlled under the Misuse of Drugs Act 1971 are involved. Figures are for deaths registered, rather than deaths occurring in each calendar year.

For Scotland, numbers represent selected drugs or substances which were implicated in, or potentially contributed to, the cause of death [NRS 2019]

Data for 2018 is not available for Northern Ireland.

(Advisory Council on the Misuse of Drugs (ACMD), 2020)



5. Conclusions

Thousands of drug-induced deaths are reported in Europe every year. These deaths are preventable and premature. Opioids, mainly heroin, continue to take the highest toll, but there are worrying trends highlighted by forensic toxicology evidence in some parts of Europe. These are related to changes in the drug market and the availability of new opioids (including fentanyl analogues), prescription opioids, other medicines such as new benzodiazepines, and cocaine in both powder and crack form. There are also challenges arising from the changing populations at risk, in particular the continued ageing of opioid users in west European countries.

The updates presented in this report shed light on important public health challenges faced by European policymakers and stakeholders, with regard to prevention, risk assessment, harm reduction and drug treatment. Overdose is a multifaceted problem requiring a combination of responses tailored to the particular circumstances of at-risk populations. Beyond overdose, other causes of morbidity and mortality disproportionately affect people using drugs. Reducing drug-related mortality associated with somatic causes, such as HIV/AIDS, hepatitis and liver failure, and also alcohol-related problems, suicide and violence, will demand additional responses. Cohort studies contribute to a better understanding of drug-related mortality in Europe, including the impact of particular responses. The implementation of cohort and linkage studies in EU Member States that have not yet done so requires relatively little investment and may be as simple as linking treatment data with mortality registers.

There is a need to improve the epidemiology of drug-related deaths in order to get more accurate and informative figures. Doing so includes strengthening the completeness and comparability of information available from forensic toxicology sources, if the exact drivers and triggers of deaths and outbreaks are to be understood and tackled. Investing in enhanced monitoring, preparedness and responses in Europe is crucial, particularly against the backdrop of the drug overdose crises currently experienced by the United States and Canada.

As a summary, the most recent data available in 2019 and first trimester of 2020, they show an increase in the number of opioid-related deaths in some European countries. The most



common opioids are mainly heroin and methadone and buprenorphine, and in some countries tramadol. New opioid derivatives are less common, and the number of intoxication and deaths-associated to these substances seem stable in the last two years in most countries. The main NSO involved are fentanyl and fentanyl derivatives.

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