

Fatal poisoning in drug addicts in the Nordic countries in 2017

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Declaration of interest: None

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Abstract

This study is the seventh report on fatal poisonings among drug addicts in the Nordic countries. In this report, we analyse data from the five Nordic countries: Denmark, Finland, Iceland, Norway and Sweden. Data on gender, number of deaths, places of deaths, age, main intoxicants and substances detected in blood were recorded to obtain national and comparable Nordic data, and to allow comparison with earlier studies conducted in 1984, 1991, 1997, 2002, 2007 and 2012.

The death rate (number of deaths per 100,000 inhabitants) was highest in Iceland (6.58) followed closely by Sweden (6.46) and then lowest in Denmark (4.29). The death rate increased in Finland (5.84), Iceland and Sweden and decreased in Denmark compared to earlier studies. The death rate in Norway, which has decreased since 2002, has stabilised around 5.7 as of 2017. Women accounted for 7–23% of the fatal poisonings. The percentage was lowest in Iceland and highest in Finland and Norway. The age range was 14 to 70 years. The median age (41 years) was highest in Denmark and Norway. The other countries had a median age between 33 and 35 years.

Opioids were the main cause of death. Methadone remained the main intoxicant in Denmark, while heroin/morphine was still the main intoxicant in Norway, as was buprenorphine in Finland.

However, the picture has changed in Sweden compared to 2012, where heroin/morphine caused most deaths in 2017. Sweden also experienced the highest number of deaths from fentanyl analogues (67 deaths) and buprenorphine (61 deaths). Deaths from fentanyl analogues also occurred in Denmark, Finland and Norway, but to a smaller extent. Over the years, the proportion of opioid deaths has decreased in all countries except Sweden, which has experienced an increase. This decline has been replaced by deaths from CNS stimulants like cocaine, amphetamine and methylenedioxymethamphetamine (MDMA). Cocaine deaths have occurred in all countries but most frequently in Denmark. MDMA deaths have increased in all countries but mostly in Finland.

Poly-drug use was widespread, as seen in the earlier studies. The median number of detected drugs per case varied from 4–6. Heroin/morphine, methadone, buprenorphine, cocaine, amphetamine, methamphetamine, MDMA, tetrahydrocannabinol (THC) and benzodiazepines were frequently detected. Pregabalin and gabapentin were detected in all countries, especially pregabalin, which was detected in 42% of the Finnish cases. New psychoactive substances (NPS) occurred in all countries except Iceland.

Highlights

- Finland had a different drug profile compared to the other countries.
- Opioids were the main cause of death among fatal poisoned drug addicts in all countries.
- Cocaine and MDMA deaths increased in all countries.
- Sweden saw a high number of deaths from fentanyl analogues.
- New psychoactive substances have emerged in all countries except Iceland.

Keywords: Fatal poisoning, Drug addict death, Nordic country, Main intoxicant, Drug abuse, New psychoactive substance

1. Introduction

According to the World Drug Report 2019, the severity and complexity of the world drug situation is increasing [1]. During the last decade, drug overdose deaths have continued to rise in Europe and, even more prominently, in North America. Opioids, often in combination with other substances, are present in the majority of fatal overdoses reported in Europe. Heroin remains the major illicit opioid, but methadone, buprenorphine, fentanyl and new synthetic opioids are increasingly involved [2]. The average mortality rate due to overdoses in Europe in 2017 is estimated at 22.6 deaths per million in the population aged 15–64, but this is likely to be an underestimation [2,3]. In the United States, synthetic opioids, primarily illicit fentanyl, surpassed prescription opioids in 2016 as the most common drugs involved in overdose deaths [4], and the drug overdose mortality rates in the US are now 3.5 times higher than in its peer countries (Denmark, Finland, United Kingdom, Australia etc.) [5].

The Nordic Countries – Denmark, Finland, Iceland, Norway and Sweden – report among the highest drug overdose mortality rates in Europe and some other Northern European countries, with more than 40 deaths per million inhabitants per year. The above average quality of forensic and toxicological investigation in the Nordic Countries at the European level, because of the reliable data produced, provides a better understanding of drug trends and health threats in the area [2,6]. Fugelstad et al. [7] have pointed out that statistics based on forensic toxicology are more complete, provide more detail on abused substances and are usually available earlier than national mortality register-based statistics.

A working group of investigators representing the Nordic forensic authorities has been closely following the trends of fatal drug poisonings in the Nordic Countries over the course of 35 years. A remarkable series of previously published Nordic studies is available, covering the years 1984,

1991, 1997, 2002, 2007 and 2012, and all use the same definition for the term drug addict [8-13]. Interestingly, in 1984, drug addicts accounted for 62% of all fatal intoxications in the Danish data, while the corresponding figures were 33% in the Norwegian, 16% in the Swedish and 5% in the Finnish data, and no deaths of drug addicts were found in Iceland [8]. Over the years, the death rates of drug addicts among the Nordic Countries have become more homogeneous. Nevertheless, significant differences in the principal toxic drugs have remained, with various opioids being the predominant agents [13].

In the present follow-up study, we investigate the fatal intoxications in Nordic drug addicts in 2017 and compare the results with those of the previous studies using the established tables and figures. As earlier, the special forensic toxicology register-based information comprises poisoning mortality statistics, age distribution and a detailed account of the drugs of abuse that were involved.

2. Materials and methods

This study analysed data on fatal poisonings in drug addicts that were submitted for medico-legal autopsy and toxicological analysis in the five Nordic countries in 2017. A few medical autopsies were also included. These data were compared with similar findings reported in 1991, 1997, 2002, 2007 and 2012. A drug addict was defined as “a person who, according to information from the police and/or autopsy report, is known to have abused drugs intravenously and/or abused the drugs listed in the Single Convention on Narcotic Drugs 1961, schedule I, and/or the International Convention on Psychotropic Substances 1971, schedules I and II”.

In almost all cases, except for a few in which suitable material was not obtained at autopsy, screening was performed for opiates, methadone, other opioids, amphetamines, cocaine, THC and

benzodiazepines. Additional drugs detected by the screening procedure or at the special request of the police were recorded, and the blood alcohol concentrations (BAC) were routinely determined.

The cause of death according to the autopsy report was systematically recorded, along with toxicological findings, police information about the deceased and the circumstances surrounding the death. Drugs and poisons were divided into four groups:

Group I: Drugs listed in the Single Convention on Narcotic Drugs 1961, schedule I (cocaine, fentanyl, heroin/morphine, methadone, oxycodone etc.) and schedule II (codeine, etc.). Tramadol, mitragynine and terpentadol were included because of their classification as opioids. Fentanyl analogues were also included in this group.

Group II: Drugs listed in the International Convention on Psychotropic Substances 1971, schedules I and II (amphetamine, methamphetamine, MDMA, GHB, methylphenidate, THC etc.). NPS (3-MeO-PCP, 5-APB, synthetic cannabinoids etc.) were also included in this group. Ketamine was included in this group.

Group III: Drugs listed in the International Convention on Psychotropic Substances 1971, schedules III and IV (benzodiazepines, buprenorphine, barbiturates, zolpidem etc.). Zopiclone was included because of its classification as a substance related to benzodiazepines.

Group IV: All other drugs and poisons, including ethanol.

Buprenorphine is an opioid and is therefore included in the comparison of opioid deaths. The number of opioid deaths is calculated per 100,000 inhabitants in the age group 15-64 in each Nordic country for the sake of comparison between the countries in figure 3.

Deaths caused by poisoning were recorded according to the drug that a forensic pathologist judged to be the main intoxicant. In cases involving multiple drugs in which the cause of death could not be

ascribed to a single substance, the drug with the lowest group number (see above) was considered the main intoxicant. Cases involving two or more drugs in the same group were recorded according to the drug judged to be the main contributor to death.

Heroin is rapidly metabolised to 6-monoacetylmorphine and further to morphine. Consequently, if 6-monoacetylmorphine was not detected, it was impossible to determine on the basis of the analysis whether heroin or morphine was used. However, heroin intake was often indicated in police reports. In the present study, fatal intoxication by heroin/morphine was verified by the presence of morphine in the blood and, in many cases, also by the presence of 6-monoacetylmorphine in a biological specimen (usually blood or urine).

All laboratories participate in more than one international proficiency testing scheme relevant for the forensic analysis.

All findings, after primary screening by immunological analysis, gas chromatography (GC), GCMS, liquid chromatography (LC), UPLC–TOF-MS, and (UP)LC/MS, were confirmed and quantified by specific (UP)LC- and GC-chromatography methods.

All age groups (14–70 years) were included in the study. The death rate in each country was calculated as the number of deaths per 100,000 inhabitants in the 15–64 year age group, as the addicts were, with few exceptions, younger than 65 years old. Poisson distribution with 95% CI is used in Fig. 1.

Due to its low number of deaths, Iceland was sometimes considered and discussed separately, and comparisons were performed mainly for the other four countries.

2.1. Ethical issues

The Danish part of the study was approved by The Danish Data Protection Agency. The National Committee on Health Research Ethics in Denmark was informed about the Danish part of the study and determined that the survey did not need to be reported to the Committee. Only anonymised data is presented.

According to the Finnish legislation, no separate ethical approval is needed for studies that utilise de-identified register-based data (Personal Data Act 523/1999). Permission to use data was obtained from the maintainer of the register (Finnish Institute for Health and Welfare).

The Icelandic part of the study was approved by the Icelandic National Bioethics Committee (VSN-18-194), by the Icelandic Data Protection Authority and by the Directorate of Health, including the National Death Registry.

The Norwegian part of the study was approved by the Regional Committees for Medical and Health Research Ethics, Norway, 2017/2474/REK sør-øst C and by the Public Prosecutor at the Office of the Director of Public Prosecutions, 2017/01269-005 BIS/ggr 639.2. Only anonymised data is presented.

The Swedish part of the study was approved by the Regional Ethics Review Board in Linköping Sweden, before start (Dnr 2016/489-31).

3. Results

3.1. Death rates

Figure 1 shows the death rate per 100,000 inhabitants for all the Nordic countries from 1991 to 2017. The death rate increased in Finland, Iceland and Sweden in 2017 compared to 2012, and decreased in Denmark and Norway. The death rate has been relatively stable in Denmark, with

variations from 6.54 in 1997 to 5.19 in 2012. In 2017, the death rate (4.29) in Denmark was at its lowest level compared to the earlier years and also to the other countries. In Finland, the death rate has increased since 1991, from 1.16 to 5.84 during these years. A similar increase was seen in Iceland, where the death rate was 0.64 in 1991 and 6.58 in 2017. In 2017, Iceland and Sweden had the highest death rates among the Nordic countries for the first time during the observed period. In Norway, the number has decreased since 2002, and 2017 was the first year in 20 years where Norway did not have the highest death rate of the Nordic countries. The death rate in Sweden increased, similarly to Finland and Iceland, from 1.53 in 1991 to 6.46 in 2017.

3.2. Places of death

The percentage of fatal poisonings among drug addicts in the capital and suburbs were similar in Denmark (29 %), Finland (26 %), Norway (30 %) and Sweden (29 %) and comparable to earlier years. The percentage of each country's population that live in this region is relatively similar as well. In Iceland, however, where a larger proportion of the population lives in the capital area, 87 % of the deaths occurred in the capital and suburbs. For all countries, more than 83 % of the deaths occurred indoors.

3.3. Distribution of deaths by gender and age

Fatal poisonings in the Nordic countries in 2017 mainly occurred in men; the percentages of women were 15 % (Denmark), 23 % (Finland and Norway), 17 % (Sweden) and 7 % (Iceland). These percentages were similar to those registered in 2012, with some differences for Finland, Denmark and Iceland [13].

The age ranges of the fatally poisoned drug addicts were 16–70 years (Denmark), 17–65 years (Finland), 14–68 years (Norway), 17–68 years (Sweden) and 20–41 years (Iceland). The mean and median ages were similar within each country. The median age in 2017 was 41 years for Denmark,

35 years for Finland, 41 years for Norway, 33 years for Sweden and 34 years for Iceland. In comparison to earlier years, the difference in median age between the Nordic countries is getting smaller [13]. The median age of the fatally poisoned drug addicts has increased in Finland and Norway and was almost unchanged in the other countries. Figure 2 shows that the highest death rate for Denmark and Finland was in the group aged 35–39 years, whereas in Norway, it was highest in the group aged 30–34 years and almost as high in the group aged 55–59 years. In Sweden, the highest death rate was observed in the group aged 25–29 years, although it was almost as high in the group aged 30–34 years.

3.4. Cause of death/main intoxicant

The main intoxicants in the included drug addict deaths for all five Nordic countries are shown in Table 1; the three previous investigations 2002, 2007 and 2012 are included for comparison.

Group I drugs dominated as the main intoxicants in Denmark (90%), Norway (76%) and Sweden (72%) in 2017. Conversely, the proportion of fatal poisonings due to Group I drugs (35%) was almost at the same level as fatal poisonings due to Group III drugs (36%) in Finland, which is due to the high amount of buprenorphine intoxications.

Opioids including buprenorphine (Group III) were the most prevalent cause of death; these are illustrated in Figure 3. Overall, compared to earlier investigations, fatal poisonings due to opioids decreased in Denmark and Norway, but opioids were still the main intoxicants, with 3.5 cases and 4.5 cases per 100,000 inhabitants, respectively, in 2017. Finland and Sweden saw an increase in opioid intoxications, with 3.3 cases and 5.4 cases per 100,000 inhabitants observed, respectively, in 2017. On the contrary, when looking at the proportion of opioid deaths among all fatally poisoned drug addicts, Finland saw a decrease from 62% in 2012 to 55 % in 2017, and the decreasing trend continued in the proportion of opioid deaths observed since 1997 in Denmark (82%) and Norway

(77%). Furthermore, the trend toward an increase in opioid deaths observed since 2002 continued in Sweden (84%) in 2017. Regarding deaths caused by specific opioids, heroin/morphine has shown a decreasing trend in Denmark and Norway over the years, while the numbers have fluctuated over time in Sweden. Heroin/morphine was the most common main intoxicant in both Sweden and Norway in 2017. Intoxications by heroin/morphine almost disappeared in Finland in 2007 and have been continuously low in the follow-up studies.

Fatal poisonings with methadone have decreased since 2012, but it was still the most common main intoxicant in Denmark in 2017 (Table 1). In Finland, however, a small increase was observed in intoxications due to methadone.

Oxycodone deaths showed a threefold rise compared to 2012 in Finland and was the second most common intoxicant in 2017. Deaths due to oxycodone increased in all the Nordic countries.

Intoxications due to tramadol were still high in Finland and Sweden. Fentanyl deaths decreased in Finland and Sweden but increased in the other Nordic countries. Deaths by codeine have declined in all countries except in Norway.

Included in the Group I drugs were also a considerable number of deaths due to fentanyl analogues, e.g. 52 fatal intoxications of cyclopropylfentanyl in Sweden alone. Deaths by fentanyl analogues were also seen in Denmark, Finland and Norway. Carfentanil deaths occurred in Finland, Norway and Sweden. Three deaths from the opioid U-47700 occurred in Finland and Sweden (Table 1).

This increase in deaths due to other opioids can also be seen in Figure 3, for all the Nordic countries, when related to the number of inhabitants. This graph includes other opioids, mainly oxycodone and tramadol, besides the fentanyl analogues.

A little more than half of the fatal intoxications in Iceland were due to opioids, mostly fentanyl and oxycodone.

Since 2012 there was also a notable increase of cocaine intoxications in all the Nordic countries, especially in Denmark.

Group II drug intoxications have increased over the years in all countries except Sweden, Table 1. Amphetamine intoxications were most frequently seen in Finland, while a notable increase occurred overall in deaths due to MDMA. Methamphetamine poisonings were seen in all countries except Denmark but most frequently in Finland and Norway. Six deaths occurred due to NPS in group II; these were seen in Finland, Norway and Sweden. GHB as cause of death was only seen in Finland and Norway, while there was one single fatal intoxication with methylphenidate in Iceland.

Group III drugs as main intoxicants were significant in Finland, but an increase of deaths due to group III drugs was seen overall. In accordance with our previous publications, buprenorphine was the single most frequent cause of death in Finland in 2017. The number of buprenorphine intoxications has increased in all the Nordic countries, and especially in Sweden; where it was the second main intoxicant after heroin/morphine.

Fatal intoxications with benzodiazepines were seen in all countries except Iceland; these included non-prescription benzodiazepines in Denmark (flubromazolam) and Sweden (norfludiazepam).

Other causes of death were pregabalin and gabapentin in Finland, Sweden and Norway.

Group IV drugs still constituted 7 to 8% of the fatal intoxications in Finland and Sweden, similar to what was seen in 2012, while group IV drugs decreased to 2% in Denmark but increased to 3% in Norway. This group consists of different pharmaceutical drugs, poisons and alcohols. Norway saw one death from lighter gas. Intoxications due to ethanol were decreasing in all countries in 2017 compared to previous years.

3.5. Toxicological findings

The frequency of all positive findings of medicinal and illicit drugs and alcohol in each country in 2017 in comparison with 2002, 2007 and 2012 are presented in Table 2. That table clearly shows that poly-drug use was widespread in all countries. The median number of drugs (excluding ethanol) per case in each country varied between 4 and 6 (with the highest in Sweden and Finland and lowest in Norway). The abuse, as in the earlier years, was characterised by traditional illicit drugs (heroin/morphine, cocaine, amphetamine, MDMA and THC), medicinal drugs (buprenorphine, methadone, tramadol, oxycodone and benzodiazepines) and alcohol. However, a wide variety of NPS, and especially the fentanyl analogues, were detected in all countries except Iceland. Ethanol was detected in all countries, with 7–47% of the cases being positive for ethanol. The percentage was highest in Finland and lowest in Iceland. The ethanol concentration was above 0.5 mg/g in most these cases.

3.5.1. Illicit and medicinal drugs

Opioids were frequently detected in all countries (Table 2). Heroin/morphine was most often detected in cases in Norway and Sweden, while methadone was the most frequent drug in Denmark. Buprenorphine was the most frequent opioid in Finland, as was the case in earlier studies. The decrease in heroin/morphine-positive cases, which was replaced by a corresponding increase in methadone in Denmark, Norway and Sweden since 1997, has stopped. Denmark and Sweden saw a slight increase in heroin/morphine positive cases, but these cases continued to decrease in Norway. The frequency of methadone-positive cases decreased in all countries except Finland, which experienced an increase. Nevertheless, as in the earlier years, only a few cases were positive for heroin/morphine and methadone in Finland. Norway had a large increase in buprenorphine-positive cases, from 7% in 2012 to 21% 2017, and is now at the same level as Sweden (23%). The frequency of buprenorphine-positive cases was high and unchanged in Finland (54%). By contrast, only few

cases were positive for buprenorphine in Denmark. Heroin/morphine, methadone and buprenorphine were detected in a few cases in Iceland.

Tramadol and oxycodone were observed in all countries but most frequently in Finland. The frequency of oxycodone increased in all countries except Denmark, which had the lowest frequency. Few cases were positive for tramadol and oxycodone in Iceland. Newer designer fentanyl analogues were detected in all countries except Iceland. Many different fentanyl analogues (acryoylfentanyl, methoxyacetylfentanyl, furanylfentanyl etc.) were found primarily in Sweden (Table 2 footnotes). U-47700 a NPS with opioid effect was detected in a few cases in Finland and Sweden.

The finding of amphetamine increased compared to 2012 in all countries except Denmark. The number nearly doubled in Norway and Sweden. Iceland showed the largest increase, and amphetamine was the most frequent drug detected in Iceland. Amphetamine was more frequently detected in Iceland compared to the other countries, followed by Finland. The frequency of methamphetamine increased in Finland from 9% to 20% and in Iceland from 0% to 27% while it decreased in Norway. Only a few methamphetamine-positive cases were seen in Sweden and Denmark. In turn, Denmark saw a large increase in cocaine-positive cases compared to 2012, as cocaine was found in nearly half (44%) of all cases in Denmark. Cocaine was detected in all countries.

MDMA abuse increased in all countries and was most frequent in Finland and Iceland. Many different central stimulating NPS (Alpha-PVP, Alpha-PHP, 2-CB, 5CI-AB-PINACA etc.) were detected almost exclusively in Finland and Sweden. A single case of 5-APB was detected in Norway. GHB was detected to a lesser extent (1.5–5%) in Norway and Finland. Methylphenidate

was found in all countries and 2–8% of the cases were positive for methylphenidate. Four cases (27%) were positive for methylphenidate in Iceland.

Cannabis abuse has been frequent and unchanged through the years in all countries (34–41%) and remains one of the most frequently used drugs (Table 2). The z-hypnotics (zolpidem and zopiclone) were detected in all countries. Zopiclone was detected most frequently in Sweden (14%) with fewer cases (2.5–10%) in the other countries. Only a few cases (1–3%) were positive for zolpidem.

Pregabalin and gabapentin were detected in all countries, especially pregabalin (8–42%). The highest percentage was seen in Finland (42%) followed by Sweden (30%). The frequency of cases with gabapentin varied from 4–14%, with the highest percentage seen in Finland (14%).

Antidepressants and antipsychotics (one or more per case) were detected frequently in all countries. The percentages varied between 16 and 53%. Citalopram and mirtazapine were the most commonly used antidepressants, while olanzapine and quetiapine were the most frequently detected antipsychotics.

3.5.2. Benzodiazepines

The percentage of cases in which benzodiazepines (one or more per case) were found varied from 73.5–88% in all countries. Benzodiazepines were therefore the most frequent drugs detected in fatal poisonings in all countries. Many different benzodiazepines were detected, especially in Sweden (Table 3).

Clonazepam and diazepam were among the three most frequently detected benzodiazepines in all countries except Iceland, where clonazepam was not detected (Table 3). The increase in clonazepam use seen since 2002 continued in all countries, but to a lesser extent in Norway and Sweden. In 2017, clonazepam was the most frequently detected benzodiazepine in Denmark and Norway. In Finland, clonazepam shared the first place with diazepam. Cases with clonazepam and

alprazolam doubled from 2012 to 2017 in Denmark. The increase in alprazolam use seen since 2002 continued in Denmark and Sweden but stopped in Finland and Norway. Alprazolam was the most frequently detected benzodiazepine in Sweden and Iceland and the third most used in Finland and Norway in 2017. In Denmark, nitrazepam (14%) was the third most used benzodiazepine shortly followed by alprazolam (13%).

Flunitrazepam, which was one of the most frequent benzodiazepines in Norway in 2002 and 2007 and in Sweden in 2002, has almost disappeared. Only 2% of the fatal poisonings were positive for flunitrazepam in Sweden in 2017.

A number of different NPS benzodiazepines were found, especially in Sweden (Table 3). Thirteen percent (53 cases) of the fatal poisonings in Sweden contained the NPS benzodiazepine norfludiazepam. Another NPS benzodiazepine, phenazepam, was detected in 10 cases in Finland and in three cases in Sweden and in one case in Iceland. Flubromazolam was detected in Denmark, Finland and Sweden in 1–2 cases. Etizolam was detected in 3–4 cases in Finland and Sweden.

4. Discussion

The definition used in this study for a drug addict was agreed upon by the Nordic working group in 1984 and has been used in all subsequent papers [8-13]. The purpose of this definition was to focus on the problem of drug abusers applying an illicit route of administration, such as injection, or abusing the drugs listed in the international conventions from 1961 and 1971 [8].

Compared to the 2012 situation, the death rate increased in Finland, Iceland and Sweden but decreased Denmark and Norway, which had shown the highest death rates in previous years. Overall, the differences between the Nordic countries have levelled off over the years.

Illicit drug abuse has changed over the years, but opioid overdose is still the main cause of death among fatally poisoned drug addicts. In 2017, a wide variety of fentanyl analogues were detected in most Nordic countries. Sweden experienced an epidemic of deaths due to fentanyl analogues, while the findings were more limited in Denmark, Finland and Norway, and no deaths occurred in Iceland. A report from the Swedish Police [14] described the course of the epidemic between 2015 and 2018 and emphasised the crucial role of the local Internet vendors that were few in number but indirectly caused hundreds of deaths. This is an example of how a part of the illicit market has moved from the street to the Internet. It also shows how fast the drug market can change and how few criminals are able to supply NPS drugs to a large group of abusers.

In this study, Denmark and Norway showed a similar drug profile. Both countries had heroin/morphine, methadone and a CNS stimulant (cocaine in Denmark and amphetamine in Norway) among the three most prevalent drugs, besides THC and benzodiazepines. Finland differed from those, having buprenorphine, pregabalin and amphetamine as the three most prevalent drugs. Sweden showed similarities with Denmark and Norway but also with Finland, having heroin/morphine and pregabalin as the two most prevalent drugs, while amphetamine and buprenorphine shared third place. It seems as the abuse of amphetamines has changed from methamphetamine to amphetamine in Norway.

A recent study analysed the persistently high buprenorphine-related mortality in Finland [15]. The origins of buprenorphine abuse date back to the 1990s, when two general practitioners in Helsinki introduced buprenorphine unlawfully for the treatment of opioid addicts. Currently, most of the abused buprenorphine is illegally trafficked Subutex[®] tablets originating from France. Despite the presence of naloxone in Suboxone[®], this product is also abused to a lesser extent. The percentage of parenteral Suboxone[®] users in which the pathologist has implicated buprenorphine in the cause of death was similar to that for parenteral Subutex[®] users [15].

Cocaine was previously rare in deaths in the north of Europe, but it has now made its appearance as a cause of death in all Nordic countries, and was the second most frequently drug detected in Denmark. This is in line with the fact that cocaine seizures in the EU reached record highs in 2017, with increased purity at the retail level [3]. MDMA also appeared as a marked cause of death in all Nordic countries. Similarly, in England and Wales [16], heroin/morphine and methadone continued to be the principal drugs involved in fatal poisonings, but a big increase in cocaine deaths and a steady increase in MDMA deaths was also found. Wastewater-based epidemiology from five Nordic capitals in 2016 has shown that cocaine use was still low compared with cities in the southern and western part of Europe, while MDMA and cocaine showed clear variations between weekdays and weekends, indicating recreational use during weekends [17].

Pregabalin and gabapentin have manifested themselves among components of poly-drug abuse, and these drugs were detected in all Nordic countries. Pregabalin was among the most frequently detected drugs in Finland and Sweden in both 2012 and 2017, and deaths from pregabalin were observed in these countries in both studies [13]. Pregabalin is prescribed to treat neuropathic pain, epilepsy and generalised anxiety disorder. It has been previously considered a drug with low abuse potential but more recent reports have demonstrated abuse and development of dependence [18-20]. Pregabalin at high doses possesses sedative effects like benzodiazepines, and consequently it adds to the respiratory depression caused by opioids.

Antidepressants/antipsychotics were frequently detected in all countries except for Norway. Some illicit drugs can induce psychosis; however, individuals with psychiatric illnesses may use drugs as self-medication. The high prevalence of antidepressants/antipsychotics is also due to the fact that these drugs have considerable off-label use as hypnotics and anxiolytics in the treatment of addicts [13, 21].

A limitation of this study concerns the definition of the main intoxicant, since the following rule has been used in all studies: “if the cause of death cannot be ascribed to a single substance, the drug with the lowest group number is considered the main intoxicant”. This rule made sense in the earlier studies when heroin was the most widespread and problematic narcotic drug. However, as the drug situation has changed, this rule camouflages the influences of other drugs like buprenorphine as cause of death. This may affect the data presented in Table 1 and Figure 3. In future work, the groups may need to be reorganised for a better illustration of cause of death by including all opioids in Group I. Another issue concerns the target age group, which originally consisted of drug addicts that died at the age of 15–35 years [8]. The situation has changed, as drug addicts live longer; consequently, the age group in this study was extended to 14–70 years.

The series of the Nordic studies on fatal drug poisonings, commenced in 1984, is unique since the same definition for a drug addict has been used in all studies and by all Nordic countries. To our knowledge, no similar studies exist in the literature. The current data is easily compared with earlier data, as the results have been presented, with some minor modifications, in similar tables and figures [9-13]. During the present study period, the post-mortem toxicology rate among all deaths was approximately 12% in Finland, 7% in Iceland, 5% in Sweden and Norway and 2% in Denmark. However, the study material is assumed to be almost population based, since comprehensive toxicology is performed in suspected cases of fatal poisonings in all the Nordic countries. Even in Denmark, with the lowest autopsy rate, all drug related deaths are, by law, undergoing a medicolegal autopsy and toxicological analysis.

5. Conclusion

As in the previous years, abuse trends and patterns varied among the Nordic countries in 2017. Finland, in particular, had a different drug profile compared to the other countries. Opioids were still the main cause of death in all countries, but over the years the proportion of opioid deaths has decreased in all countries except Sweden. Instead, deaths from CNS stimulants like cocaine, amphetamine and MDMA have increased.

NPS were detected in all countries except Iceland. Fentanyl analogues appeared for the first time and were seen in all countries except Iceland. NPSs were most frequent in Sweden and changed from being the lowest cause of death in 2012 to the second highest cause of death in 2017. Abuse of pregabalin and gabapentin was established in all countries, with occasional death cases.

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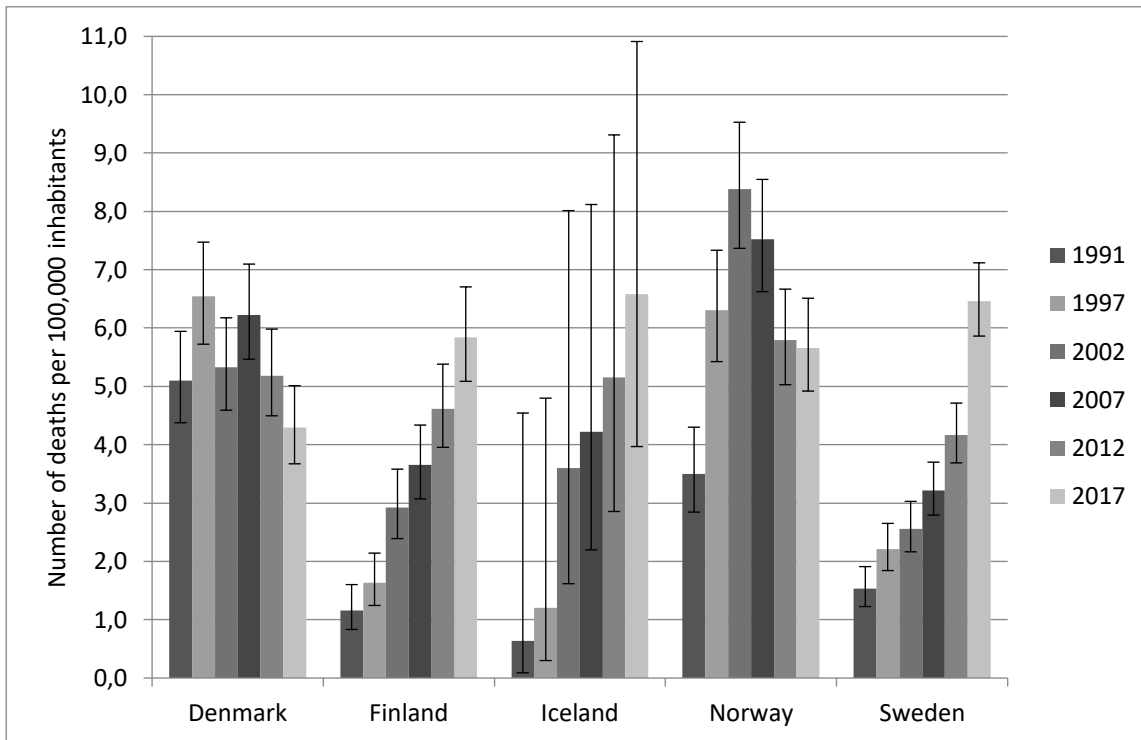


Figure1 Legend; Fatal poisonings among drug addicts in 1991, 1997, 2002, 2007 and 2017. Number of deaths per 100,000 inhabitants in 2017 was as follows: Denmark, 4.29; Finland, 5.84; Iceland, 6.58; Norway, 5.66; and Sweden, 6.46. The error bars in the figure are confidence intervals.

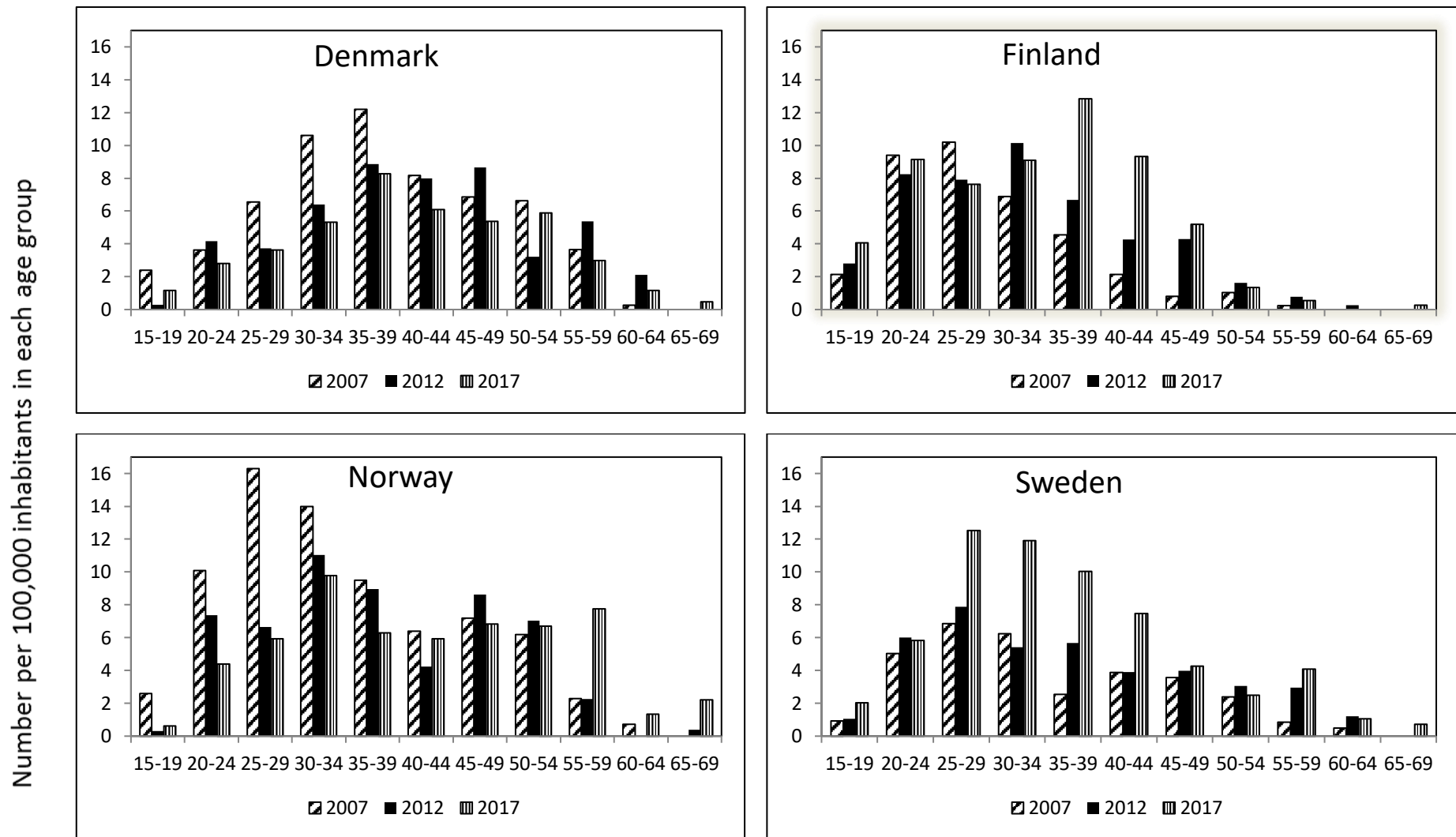


Figure 2 legend;

Age distribution in medico-legally examined fatal poisonings among drug addict deaths in the Nordic countries in 2007, 2012 and 2017.

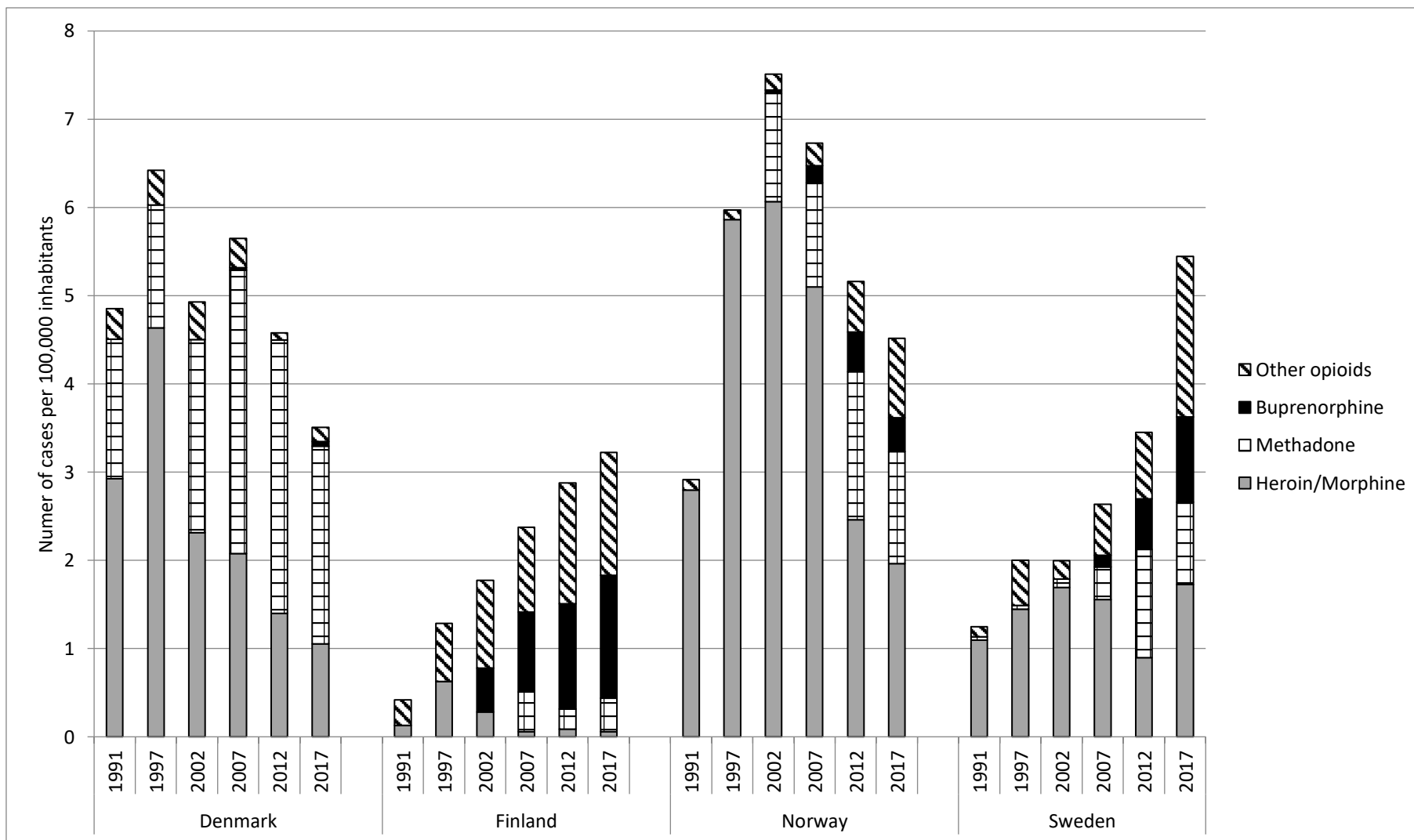


Figure 3 Legend:

Cause of death by opioids. Number of deaths per 100,000 inhabitants in 1991, 1997, 2002, 2007, 2012 and 2017. The years: 1991-2002 presents the age group 15-59 years and the years: 2007-2017 the age group 15-64 years.

	Denmark, n				Finland, n				Norway, n				Sweden, n				Iceland, n		
	2002	2007	2012	2017	2002	2007	2012	2017	2002	2007	2012	2017	2002	2007	2012	2017	2007	2012	2017
Group I drugs sum ^a	163	209	169	146	43	52	60	70	210	206	156	155	107	151	176	292	8	7	9
Heroin/morphine	76	75	51	40	9	2	3	2	168	160	86	69	90	94	55	110	3	2	1
Methadone	72	116	111	85	0	16	8	13	34	37	56	46	5	22	75	59	3	0	1
Codeine	0	0	1	0	11	8	12	6	4	2	2	4	1	0	0	0	0	1	0
Cocaine	1	6	4	15	2	0	0	6	1	1	0	6	1	1	2	6	0	0	2
Fentanyl		0	0	2	3	7	12	3			3	7	0	10	27	16	2	0	2
Tramadol	5	2	1	1	9	14	18	16	0	2	4	6	2	12	8	21	0	3	0
Oxycodone	0	3	0	1	1	4	6	19	0	2	9	14	0	5	9	12	0	1	2
Group II drugs sum ^b	3	8	5	6	13	10	32	45	9	13	21	21	18	16	20	11	1	1	5
Amphetamine	2	6	2	2	12	8	13	14	9	9	4	7	16	11	8	3	0	0	1
Methamphetamine	0	0	0	0				8			10	7	1	0	1	1	0	0	1
MDMA	1	1	2	4	1	1	1	10			1	3	0	2	0	6	0	0	2
GHB		0	1	0		1	12	7		3	4	3	1	2	4	0	0	0	0
Methylphenidate		0	0	0		0	1	0		0	0	0		0	1	0	1	1	1
Group III drugs sum ^c	1	4	3	6	16	45	57	72	4	11	13	20	3	12	42	75	0	0	1
Buprenorphine		1	0	2	16	32	42	48	1	6	5	13		8	35	61			1
Pregabalin		0	0	0			10	9		0	0	1			3	3			0
Gabapentine		0	0	0			0	1		0	0	0		0	0	1			0
Group IV drugs sum ^d	8	5	11	4	22	22	13	16	9	7	3	7	8	15	17	30	1	3	0
Ethanol	0	1	1	0	7	13	7	6	2	3	1	1	0	1	8	4	0	1	
Total	175	226	188	162	94	129	162	202	232	236	194	203	136	194	255	408	10	11	15

2017 Comments: **Denmark:** ^aAcryloylfentanyl: 1, Methoxyacetylfentanyl: 1; ^cAlprazolam: 1, Clonazepam: 2, Flubromazolam: 1; ^dAntidepressant/antipsychotic: 3.

Finland: ^aCarfentanil: 2, Furanylfentanyl: 1, U-47700: 2; ^b3-MeO-PCP: 1, alpha-PVP: 3, THC: 2; ^cAlprazolam: 3, Clonazepam: 3, Oxazepam: 2, Diazepam: 1, Chlordiazepoxide: 1, Zolpidem: 1, zopiclone: 2; ^dAntidepressants/antipsychotics: 3.

Norway: ^aCarfentanil: 1, Mitragynine: 1, Ethylmorphine:1; ^b5-APB:1; ^cAlprazolam: 1, Clonazepam: 4, Diazepam: 1; ^d Antidepressants/antipsychotics: 4, Lighter gas:1, methanol: 1.

Sweden: ^aCyclopropylfentanyl: 52, Furanylfentanyl: 4, Acryloylfentanyl: 4, Methoxyacetylfentanyl: 3, Carfentanil: 2, 4F-isobutyrfentanyl: 1, Tetrahydrofuranfentanyl: 1, U-47700: 1; ^bEthylphenidate: 1; ^cAlprazolam: 3, Clonazepam: 1, Flunitrazepam: 1, Norfludiazepam: 3, Zolpidem: 2; ^dAntidepressants/antipsychotics: 7, Loperamide: 4.

Iceland: ^aKetobemidone.

Table 1 Legend; Fatal poisoning in medico-legally-examined drug addict deaths in the Nordic countries in 2017 in comparison with 2002, 2007 and 2012 grouped according to the assumed main cause of death, n = number of fatal poisonings in the different groups.

	Denmark				Finland				Norway				Sweden				Iceland			
	2002	2007	2012	2017	2002	2007	2012	2017	2002	2007	2012	2017	2002	2007	2012	2017	2002	2007	2012	2017
Number of cases	175	226	188	162	94	129	162	202	232	236	194	203	136	194	255	408	6	10	11	15
	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%
Group I drugs																				
Heroin/morphine	48	40	30	35	35	3	6	5	78	71	45	37	69	49	29	32	50	30	27	20
Methadone	53	61	71	65	2	13	7	12	19	21	34	29	7	14	32	17	17	30	0	7
Codeine	15	8	9	4	27	17	15	9	6	6	8	11	9	2	2	1	17	20	27	20
Cocaine	15	15	19	44	2	1,5	0	6	2	8	5	5.9	4	3	5	10	33	10	0	33
Fentanyl			0.5	5		7	9	2		0	3	4.9		5	11	5		20	0	13
Tramadol	3	6	6	3	11	18	15	16	0	3	3	7.9	7	12	7	10	0	20	36	20
Oxycodone	0	2	3	4	1	8	6	15	0	2	5	9.9	0	3	5	8		0	9	20
Other Group I drugs ^a	17	5.8	5	2.5	12	1.5	2	4	2	0.8	0.5	2.5	11	6	0.4	18	17	0	0	7
Group II drugs																				
Amphetamine	9	10	10	11	23	25	22	32	30	15	13	25	29	32	14	23	33	40	18	60
Methamphetamine	0	0.4	0	0.6		5.5	9	20		23	35	20	4	6	2	1	0	0	0	27
MDMA	0.6	1.8	1.6	5	8	4	5	13	2	3	1.5	4.9	3	4	1	4	0	10	0	40
GHB		0	1.6	0		0.8	7	5		1	3	1.5		1.0	1.5	0		0	0	0
Methylphenidate		0	4.8	6		3	2	2		0	2	3.9		0	9	8		20	36	27
Tetrahydrocannabinol	36	26	34	41	37	36	38	40	24	21	31	39	21	22	25	34	17	0	36	13
Other Group II drugs ^b		0.4	2.0	1		0	15	11		0.4	8	0.5		0.5	10	4		0	9	0
Group III drugs																				
Benzodiazepines ^c	41	55	71	73.5	71	82	88	88	67	70	80	75	51	59	71	74	33	40	27	80
Zopiclone		3.5	4	2.5		6	4	6		6	7	9.9		8	16	14		9	7	
Zolpidem	0	0.4	1	1		0.8	0	3		0	2	1.0		2	2	2				0
Pregabalin		0	5	8		10	32	42		0.8	12	18			28	30			0	27
Gabapentin		0	0	4			1.2	14			0	7.4		0	3	6			0	13
Buprenorphine	0.6	2	4	8	19	40	54	54	2	6	7	21	2	10	24	23				13
Other Group III drugs ^d		0	0	0		0	0	0		3.2	0	0	9	3	0	0			0	7
Group IV drugs																				
Ethanol total	34	34	36	20	47	47	44	47	21	30	16	11	35	26	24	24	0	10	18	7
Ethanol >0.50 mg/g	25	29	18	11	40	41	34	30	16	22	11	8.9	23	20	16	15	0	10	18	7
Other Group IV drugs	41	45	65	70	50	68	66	49	52	32	40	43	68	47	47	52	33	70	73	47
Antidepressants/anti- psychotics			41	47			40	45			26	16			30	40			45	53

2017 comments: Denmark: ^aKetobemidone: 0.6%, Hydromorphone: 0.6%; Acryloylfentanyl: 0.6%, Methoxyacetylfentanyl: 0.6%; ^b Ketamine: 1%.; ^cFlubromazolam: 0.6%
Finland: ^a Dextromethorphan 0.5%, U-47700 1%, Carfentanil: 1%, Acetylfentanyl: 1%, Furanylfentanyl: 0.5%; ^b Alpha-PVP 6%, Ketamine: 2.5%;
2F-Methamphetamine: 0.5%, 5-MeO-MIPT: 0.5%, MDA: 0.5%, BZP: 0.5%, 2-CB 0.5%; ^cEtizolam: 1.5%, Flubromazolam: 1%
Norway: ^aAcetylfentanyl: 0.5%, Ethyl morphine: 1.0%, Carfentanil: 0.5%, Ketobemidone: 0.5%, Mitragynine: 0.5%, Tapentadol: 0.5%; ^b5-APB: 0.5%.
Sweden: ^aCyclopropylfentanyl: 13%, Furanylfentanyl: 1%, Acryloylfentanyl: 1%, Methoxyacetylfentanyl: 1%, Carfentanil: 0.5%, Tetrahydrofuranfentanyl: 0.5%;
U-47700: 0.5%, Ethylmorphine: 0.5%, 4F-Isobutyrfentanyl: 0.2%, Tetrahydrofuranfentanyl: 0.2%; ^bAlpha-PPP: 1%, Alpha-PiHP: 1%, N-isopropylnorhexedrone: 1%,
4F-N-Ethylpentedrone: 0.5%, 5CI-AB-PINACA: 0.2%, N-Ethyl-4methylnorpentedrone: 0.2%, Ethylphenidate: 0.2%, 4F-Ethylphenidate: 0.2%. ^cNorfludiazepam: 13%,
Etizolam: 1%, Phenazepam: 0.7%, Flubromazolam: 0.2%.
Iceland: ^aKetobemidone. ^dPhenobarbital.

Table 2 Legend; Analytical findings for drugs and poisons in medico-legally-examined fatal poisonings in drug addict deaths in the Nordic countries in 2017 in comparison with 2002, 2007 and 2012.

	Denmark				Finland				Norway				Sweden				Iceland			
	2002	2007	2012	2017	2002	2007	2012	2017	2002	2007	2012	2017	2002	2007	2012	2017	2002	2007	2012	2017
Number of cases	175	226	188	162	94	129	162	202	232	236	194	203	136	194	255	408	6	10	11	15
Diazepam (%)	35	26	34	29	50	63	54	47	30	35	33	28	25	35	25	20	17	20	9	7
Clonazepam (%)	3	12	22	45	1	5	37	47	13	20	50	53	4	15	27	28	0	0		0
Alprazolam (%)	4.5	4	7	13	15	24	36	31	3	12	19	19	4	18	39	45	0	10		40
Nitrazepam (%)	3	9	18	14	0	0		0	6	19	10	7.9	6	4	6	3	0	0		0
Bromazepam (%)	8	12	16	10	0	0		0					0	0	0.4	0.2				7
Flunitrazepam (%)*	1	7	6	0	0	0	0	0	48	27	6		21	4	4	3	0	0		0
Temazepam (%)	0	0	0	0	44	38	17	10					0	0	0	0				0
Oxazepam (%)	7	5	7	2	38	48	16	13	2	11	6	11	2	1.6	4	2	0	0	9	13
Chlordiazepoxid(%)	4	11	12	9	3	4		3.5					0	0	0	0	17	10	9	7
Midazolam (%)		0	2	0.6			4.3	5				1.5								0
Phenazepam (%)**		0	2.7	0			1.2	5		1	1		0	0	0.8	0.7				7
Lorazepam (%)		0.5	1.0	0	3	2		3.5					0.7	0	0	1				0
Triazolam (%)		0	0	0				0							0.4	0				0
Etizolam (%)			0	0				1.5			0.5				1	1				0
Flubromazolam (%)				0.6				1												0.2
Norfludiazepam (%)																13				

* 7-aminodesmethylflunitrazepam included, ** 3-OH-phenazepam included

Table 3 Legend; Frequency of benzodiazepines in medico-legally examined drug addict deaths in the Nordic countries in 2017 in comparison with 2002, 2007 and 2012.