

Original Article

Fatal poisoning among people who use drugs in Denmark in 2022

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Dan Med J 2025;72(11):A03250147. doi: 10.61409/A03250147

ABSTRACT

INTRODUCTION. The patterns of drug use and causes of fatal poisonings among persons who use drugs (PWUD) have been reported every fifth year since 1991 by the Danish Departments of Forensic Medicine. The present study aimed to describe these patterns in 2022.

METHODS. All fatal poisonings among PWUD undergoing legal autopsy at the three Departments of Forensic Medicine in Denmark in 2022 were included in the study.

RESULTS. The number of fatal poisonings among PWUD was 199. The median age was 42 years and 23% were female. Heroin/morphine and methadone were the most frequent main intoxicants, responsible for 22% and 37% of the poisonings, respectively. However, the proportion of deaths caused by other opioids and central stimulants has increased compared to previous years. Oxycodone deaths increased tenfold to 6% from 0.6% in 2017. Cocaine and amphetamine caused 11% and 4.5% of fatal poisonings, respectively. Methadone remained the most frequently detected drug, followed by cocaine, tetrahydrocannabinol, clonazepam and heroin/morphine, detected in 52%, 45%, 37%, 35% and 26% of cases, respectively. Tramadol and oxycodone were most frequently detected among PWUD aged 15-25 years.

CONCLUSIONS. Our findings indicate an increasing diversity of opioids causing fatal poisonings in PWUD and a rising detection rate and proportion of deaths linked to central stimulants.

FUNDING. None.

TRIAL REGISTRATION. Not relevant.

Since 1970, a legal autopsy and systematic toxicological analysis have been mandatory for all deaths suspected to involve narcotic drugs in Denmark [1]. This enables a comprehensive evaluation of the causes of death among people who use drugs (PWUD) based on data from the Danish Departments of Forensic Medicine. Toxicological analyses identify the primary intoxicants as well as other substances present in the deceased's blood. Consequently, surveys of fatal poisonings among Danish PWUD offer valuable insights into current trends and the risks associated with drug use. For this reason, Danish toxicological findings in PWUD have been reported every fifth year since 1991.

Overdose deaths from medicinal opioids increased in Europe in 2022, while deaths from synthetic fentanyl and nitazenes have been limited [2]. Overdose deaths from synthetic fentanyl surged in the USA in 2022, while deaths from prescription medicine remained at a high level [3].

Prescribed opioids, such as oxycodone and tramadol, have recently entered the illegal market in Denmark and are sold illegally from kiosks [4]. However, most young people who begin using opioids receive or buy them from friends/acquaintances. In 2023, Danish customs officials confiscated almost one million opioid tablets, representing a five-fold increase since 2021 [5]. This rising demand suggests a growing trend of medicinal opioid abuse, and this kind of abuse among young people has raised concerns among Danish authorities [6].

This study aimed to describe the main intoxicants and detected drugs among PWUD dying from drug poisoning in Denmark in 2022 and to compare these findings with previous studies.

Data from the present study and data from previous reports were included in a joint Nordic study [7].

METHODS

All fatal poisonings among PWUD who underwent legal autopsy at the three Danish Departments of Forensic Medicine - in Copenhagen, Aarhus and Odense, collectively covering the entire country - were included in the study.

The PWUD definition was consistent with that used in previous studies [8-13]: “a person who, according to information from the police and/or autopsy report, is known to have abused drugs intravenously and/or abused drugs listed in the Single Convention on Narcotic Drugs 1961, Schedule I (heroin, morphine, ketobemidone, cocaine, etc.), and/or the International Convention on Psychotropic Substances 1971, Schedules I and II (amphetamine, methamphetamine, MDMA (ecstasy), LSD, tetrahydrocannabinol (THC) etc.)”.

We recorded data from autopsy reports, including gender, age, main intoxicants and other drugs detected in blood. Fatal poisonings involving two or more drugs were categorised based on the drug deemed to have been the main intoxicant.

Heroin is rapidly metabolised to morphine and detected as such in toxicological screens; therefore, cases in which morphine was detected were listed as heroin/morphine cases.

The sum of fatal poisonings was compared across geographical areas by normalising it to the number of inhabitants aged 15-69 years. Only two PWUD fell outside this age range.

Information about opioid maintenance treatment was obtained from autopsy reports. The data presented are minimum figures, as the information was not always available.

Ethics

According to Section 14 of the Consolidation Act on Research Ethics Review of Health Research Projects, Consolidation Act number 1083 of 15 September 2017 [2], this project did not need approval from the Committees on Health Research Ethics. The study was registered at the University of Copenhagen, Aarhus University and the University of Southern Denmark. All data were handled in accordance with the General Data Protection Regulation (GDPR) and the Danish Data Protection Act.

Trial registration: not relevant.

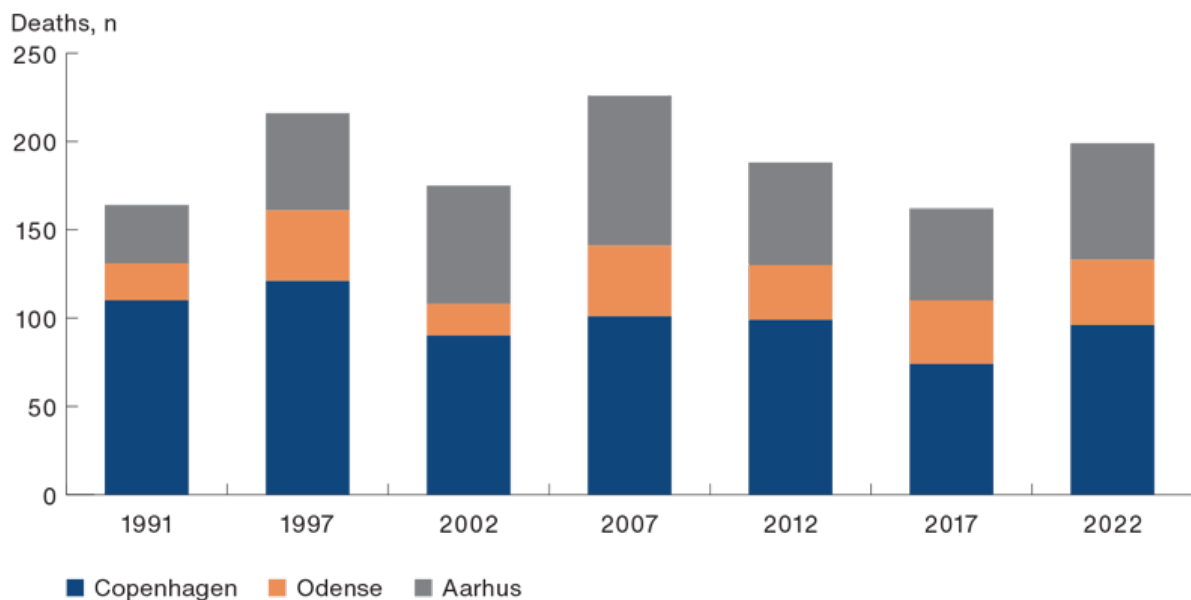
RESULTS

Number of deaths

The declining trend in the number of fatal poisonings among PWUD observed since 2012 was reversed in 2022,

with the number of deaths surpassing those recorded in 2017, primarily due to an increase in deaths in the Copenhagen and Aarhus areas (**Figure 1**). Although the absolute number of deaths was highest in Copenhagen, the number of deaths per 100,000 inhabitants in the 15-69-year age group was highest in the Odense area (5.8), followed by Copenhagen (5.0) and Aarhus (4.3).

FIGURE 1 Fatal poisonings among people who use drugs in the areas covered by the three departments of forensic medicine in Denmark, located in Copenhagen, Odense and Aarhus. The Copenhagen category covers Zealand, the surrounding islands and Copenhagen (2.02 mill. inhabitants in the age group 15-74 years in 2022). The Odense category covers Funen, the surrounding islands and the southern part of Jutland (0.69 mill. inhabitants in the age group 15-74 years in 2022). The Aarhus category covers the remaining part of Jutland (1.65 mill. inhabitants in the age group 15-74 years in 2022). Data on the number of inhabitants are from Statistics Denmark.



Characteristics of cases

In 2022, 199 fatal poisonings occurred among PWUD. The manners of death were accidental (77%), suicide (5%) or unknown (18%). The proportion of women increased from 15% in 2017 to 23% in 2022 [13]. The median age was 42 (range: 16-73) years, which is similar to the median age recorded in 2017 [13]. Overall, 24% of PWUD were prescribed methadone and 4% were prescribed buprenorphine at the time of death. In 62% of the cases, the available information indicated that the individual was alone at the time of death.

Main intoxicants

Poisoning with multiple substances occurred in 42% of the cases. A combination of an opioid and a benzodiazepine was involved in 78% of these cases.

As previously reported, opioids caused the greatest number of deaths. However, the proportion of fatal poisonings mainly caused by opioids decreased to 73% in 2022 from 82% in 2017, 87% in 2012 and 99% in 1997. Among PWUD undergoing methadone treatment, methadone either alone or in combination with other substances was deemed the cause of 81% of the fatal poisonings. Buprenorphine contributed to the cause of death in 38% of those undergoing buprenorphine treatment.

Methadone has been the most frequent main intoxicant since 2007, a trend that persisted into 2022. However, the number of deaths caused mainly by methadone has decreased in all parts of Denmark since 2007 or 2012 (Figure 2 A). Heroin/morphine was the second most common main intoxicant in 2022, although the number of heroin/morphine deaths has shown a steady decrease since 1997 (Table 1), particularly in the area covered by Copenhagen (Figure 2 A).

FIGURE 2 A. Number of deaths with heroin/morphine and methadone, respectively, as main intoxicants from 1991 to 2022 in the areas covered by each department of forensic medicine. **B.** Proportion of fatal poisonings in people who use drugs in which the respective drugs or groups of drugs were detected by toxicological analysis in different age groups.

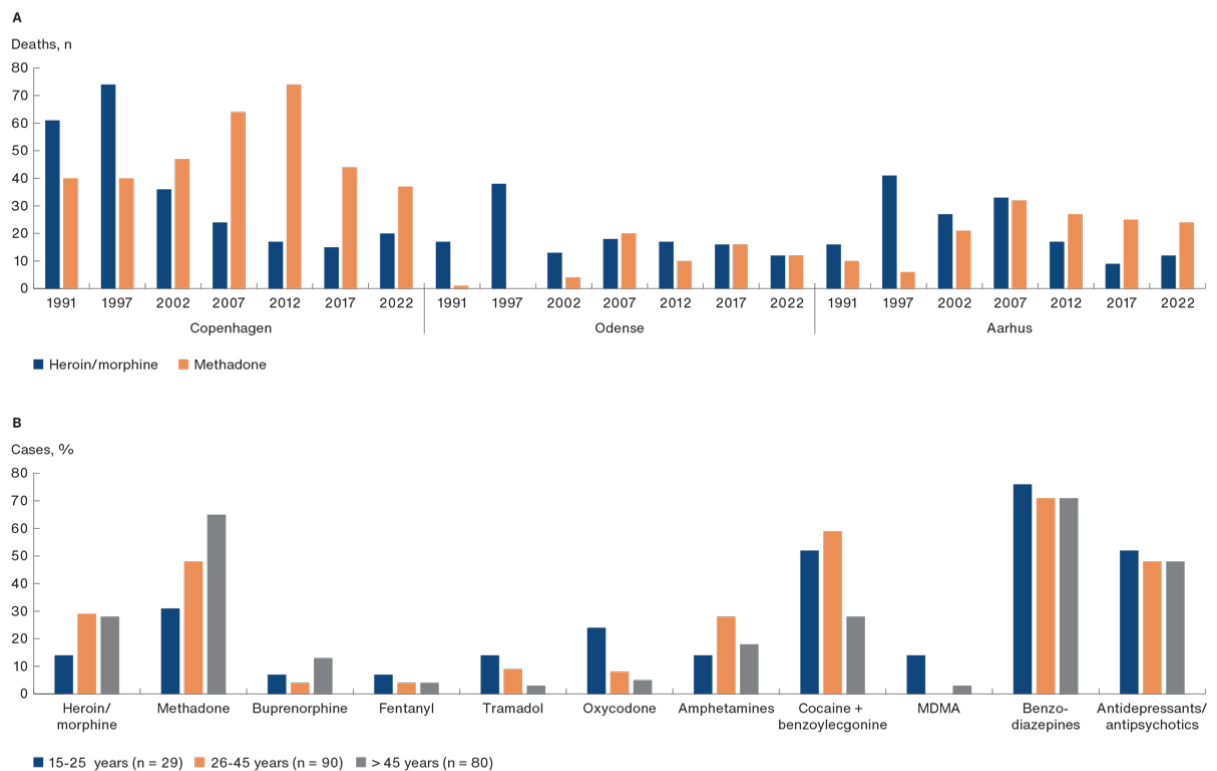


TABLE 1 Main intoxicant in fatally intoxicated drug addicts in Denmark in 2022 compared with previous study years. The values are n (%).

Main intoxicant	1991	1997	2002	2007	2012	2017	2022
Heroin/morphine	94 (57.5)	153 (71)	76 (44)	75 (33)	51 (27)	40 (25)	44 (22)
Methadone	51 (31)	46 (21)	72 (41)	116 (51)	111 (59)	85 (52)	73 (37)
Buprenorphine	-	-	0	1 (0.4)	0	2 (1)	7 (3.5)
Ketobemidone	8 (5)	12 (5.5)	9 (5)	5 (2)	1 (0.5)	0	0
Fentanyl	-	-	-	0	0	2 (1.2)	4 (2)
Oxycodone	-	-	0	3 (1.3)	0	1 (0.6)	12 (6)
Tramadol	-	-	5 (3)	2 (1)	1 (0.5)	1 (0.6)	3 (1.5)
Cocaine	0	1 (0.5)	1 (0.5)	6 (3)	4 (2)	15 (9)	21 (11)
Amphetamine	1 (0.5)	1 (0.5)	2 (1)	6 (3)	2 (1)	2 (1)	9 (4.5)
Ecstasy (MDMA)	0	0	1 (0.6)	1 (0.4)	2 (1)	4 (2.5)	3 (1.5)
Other	10 (6)	3 (1.5)	9 (5)	11 (5)	16 (9)	10 (6)	23 (12)*
Total	164 (100)	216 (100)	175 (100)	226 (100)	188 (100)	162 (100)	199 (100)

MDMA = 3, 4-methylenedioxy-N-methamphetamine.

a) Each of the following drugs had ≤ 3 (1.5%) observations: methamphetamine, gamma-hydroxybutyrate (GHB), pregabalin, chlordiazepoxide, 3-chloromethcatinone, metonitazen, butane (lighter gas) and nitrite; antidepressant/antipsychotics: 5 (2.5%); ethanol: 4 (2%).

Fatal poisonings with oxycodone and buprenorphine increased in 2022 compared to previous years, and

tramadol caused 1.5% of deaths (Table 1).

The proportion of deaths from the central stimulants: cocaine, amphetamine and MDMA increased from 1-6% in early studies to 13% in 2017 and then to 17% in 2022, with cocaine being responsible for most deaths (Table 1). The proportion of deaths caused by cocaine was 2-3 times higher in the area covered by Copenhagen (15%) than in the areas covered by Aarhus (7.6%) or Odense (5.4%).

A few deaths occurred due to methamphetamine, gamma-hydroxybutyrate (GHB), pregabalin, chlordiazepoxide, butane (lighter gas) and nitrite. The new psychoactive substances (NPS) 3-chlormethcatinone and metonitazene were responsible for 2% of the deaths. Antidepressants/antipsychotics and ethanol caused 2.5% and 2% of the deaths, respectively.

Pattern of detected drugs

The median number of detected drugs per case was five (excluding ethanol) and unchanged compared to 2017. The three most detected drugs (excluding THC) were methadone, cocaine and clonazepam, which were detected in 52%, 45% and 35% of the cases, respectively (Table 2).

TABLE 2 The results of the analytical screening programme for medical drugs, narcotic drugs and poisons in fatally intoxicated drug users related to the departments of forensic medicine in Denmark in 2022, registered as % positive.

Drug detected	Copenhagen (n = 96)	Odense (n = 37)	Aarhus (n = 66)	Total (N = 199)
<i>Group I</i>				
Heroin/morphine	26	35	21	26
Methadone	54	43	54.5	52
Buprenorphine	5.2	8.1	12.1	8
Oxycodone	5.2	11	14	9
Tramadol	8.3	5.4	6.1	7
Fentanyl	3.1	8.1	4.5	4.5
Other group I ^a	-	-	-	3
<i>Group II</i>				
Cocaine	43	32	56	45
Amphetamines ^b	15	19	33	22
Ecstasy (MDMA)	4.2	0	6.1	4.0
Methylphenidate	5.2	2.7	11	6.5
Tetrahydrocannabinol	29	43	45	37
Other group II ^c	4.2	0	4.5	3.5
<i>Group III</i>				
Benzodiazepines ^{d, e}	70	62	80	72
Zopiclone/zolpidem	5.2	5.4	4.5	5
Pregabalin	10	19	21	16
Gabapentin	7.3	8.1	9.1	8
Antidepressants/antipsychotics	48	35	56	48
Ethanol > 0.5 mg/g	16	16	14	15

MDMA = 3, 4-methylenedioxy-N-methamphetamine.

a) Includes findings of metonitazen (1.5%) etodesnitazen (< 1.5%), ketomebidone (< 1.5%), codeine (< 1.5%).

b) Includes findings of methamphetamine (1.5%).

c) Includes findings of gamma-hydroxybutyrate (GHB) (< 1.5%), ketamine (2.5%) and 3-chloromethcathinone (< 1.5%).

d) Includes 10 findings of the illegal benzodiazepines: etizolam (3.5%), flualprazolam, clonazolam, and bromazolam.

e) Clonazepam (35%), alprazolam (23%) and diazepam (14%) were the most frequently detected benzodiazepines.

The proportion of cases positive for methadone (52%) and heroin/morphine (26%) decreased across all areas from the 2017 values of 65% and 35%, respectively [13]. The proportion of cases positive for heroin/morphine was largest in the area covered by Odense, whereas methadone was more frequent in the areas covered by Copenhagen and Aarhus (Table 2).

The proportion of cases positive for oxycodone (9%) and tramadol (7%) increased compared to 2017, whereas that of buprenorphine remained unaltered [13]. Buprenorphine and oxycodone were most frequently detected in the western part of Denmark, whereas tramadol was slightly more frequent in the area covered by Copenhagen (Table 2).

The proportion of cases involving cocaine remained high, as 45% were positive for cocaine, as seen in 2017. The area covered by Odense had the lowest proportion of cocaine-positive cases (Table 2). However, the proportion increased from 22% in 2017 to 32% in 2022 [13]. The proportion of amphetamine-positive cases nearly doubled from 11% in 2017 to 20% in 2022 [13]. This increase was most pronounced in the area covered by Odense. Overall, cocaine and amphetamines were most frequently detected in the area covered by Aarhus (Table 2). The proportion of MDMA-positive cases remained unchanged compared to 2017, and MDMA was detected only in the areas covered by Copenhagen and Aarhus (Table 2).

The gabapentinoids pregabalin and gabapentin were found in twice as many cases as in 2017 [13]. This increase was observed in all parts of Denmark.

Clonazepam, alprazolam and diazepam were the most frequently detected benzodiazepines, detected in 35%, 23% and 14% of cases, respectively. Compared to 2017, the frequency of clonazepam and diazepam decreased from 45% and 29%, respectively, while the frequency of alprazolam increased from 13% [13].

NPS were detected in 7.5% of the cases. Nitazenes, metonitazene and etodesnitazene, which are opioids, appeared for the first time, but were only detected in less than 2% of cases. The stimulant NPS 3-chloromethcathinone was observed in less than 1.5% of the cases. Among the NPS benzodiazepines, etizolam was detected in 3.5% of cases, whereas bromazolam, clonazolam and flualprazolam were detected only sporadically.

Similar to 2017, nearly half (48%) of all cases were positive for one or more antidepressant or antipsychotic drugs [13]. Quetiapine and olanzapine were the most common antipsychotics, whereas mirtazapine and sertraline were the most frequently seen antidepressants.

Pattern of detected drugs in different age groups

Heroin/morphine, methadone and buprenorphine were twice as frequent in PWUD above age 45 years as among those aged 15-25 years, whereas oxycodone and tramadol were 5-6 times more frequent in the 15-25-year age group than in the above 45-year age group (Figure 2 B). Cocaine was detected twice as often among 15- to 25-year-olds as in PWUD above 45 years of age, whereas amphetamine detection was slightly more frequent (1.2 times) in PWUD older than 45 years of age than in 15- to 25-year-olds (Figure 2 B).

DISCUSSION

The present study showed that while poisonings caused by the most common substances (e.g. methadone and heroin/morphine) seemingly decreased slightly, deaths from other opioids (e.g. oxycodone, tramadol, buprenorphine and fentanyl) and from cocaine and amphetamine have increased. The proportion of cases in which 'other drugs' were identified as the main intoxicant was also higher in 2022 than previously. Furthermore, NPS, including a nitazene, caused a few deaths. Some nitazene opioids have a potency comparable to or even higher than that of fentanyl [14]. Fentanyl is considered to be 100 times more potent than morphine and is responsible for numerous fatal poisonings in the USA [15]. Fortunately, no such trend has yet been observed in Denmark. Like fentanyl, nitazenes pose a significant risk of overdose, as even minimal amounts can cause lethal central nervous system inhibition and respiratory depression. New nitazenes continue to emerge in the European illicit drug market [15], and their appearance in the present study aligns with this trend. Overall, the 2022 results suggest a greater diversity of main intoxicants than observed previously. Furthermore, the demographics of PWUD may have changed, as we noted a higher proportion of women. This should be considered in future prophylactic strategies.

The pattern of detected drugs varied somewhat between regions, as heroin/morphine seems to be used more

frequently in the area covered by Odense, whereas cocaine and amphetamine seem more prevalent in the area covered by Aarhus. The use of the gabapentinoids gabapentin and pregabalin increased over time in this study and in general [16]. These drugs are currently not categorised as controlled substances in Denmark, and neither was tramadol until recently. In 2017, the Danish Medicines Agency introduced stricter reporting of adverse effects for medicines containing tramadol [17], confirming that tramadol addiction could occur even after treatment with therapeutic doses [17]. Furthermore, the Customs Agency seized increasing amounts of tramadol. In April 2022, tramadol changed status to a controlled substance in Denmark [18]. In the present study, tramadol was the main intoxicant in a limited number of deaths; however, the detection of tramadol in 7% of the poisoned PWUD overall, and in 14% of those aged 15-25 years, supports imposing opioid-type controls on tramadol.

According to a recent Danish questionnaire survey, 3.7% of persons aged 20-29 years had used medicinal opioids for recreational purposes [6]. The present study substantiates concerns raised in the survey regarding illicit use of medicinal opioid tablets among young individuals, as oxycodone and tramadol were most frequently detected among decedents aged 15-25 years. This concern is especially pertinent in light of a tenfold increase in oxycodone deaths. We recommend that adequate treatment be ensured for young people with opioid addiction to prevent this development.

The increasing frequency of cocaine and amphetamine as the main intoxicants and detected drugs is also in line with globally observed trends showing increased trafficking and seizures of these drugs [15]. In the questionnaire survey [6], 14% of the 20 to 29-year-old respondents had tried cocaine, and the increasing rate of deaths indicates that preventive measures targeting central stimulants should also be prioritised. Although we regard opioids as the most toxic drugs in terms of fatal poisonings, the increasingly frequent use of cocaine and amphetamines may result in more deaths if the trend continues.

CONCLUSIONS

Our results indicate an increasing diversity of opioids causing fatal poisonings in PWUD and a rising detection rate and proportion of deaths linked to central stimulants. Central to our concern is the rising incidence of fatalities among young individuals who use medicinal opioids, such as oxycodone and tramadol.

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Accepted 18 July 2025

Published 15 October 2025

Conflicts of interest none. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. These are available together with the article at ugeskriftet.dk/dmj

References can be found with the article at ugeskriftet.dk/dmj

Cite this as Dan Med J 2025;72(11):A03250147

doi 10.61409/A03250147

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