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Original Article

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Fatal poisoning among drug users in Denmark in 2017

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ABSTRACT

INTRODUCTION: Knowledge of trends of illegal drug use is vital for planning initiatives to reduce accidents and deaths among drug users. The aim of this study was to describe the cause of death, abuse pattern and geographic differences in fatal poisonings among drug users in Denmark in 2017.

METHODS: All fatal poisonings among drug users examined at the three institutes of forensic medicine in Denmark in 2017 were included in the study.

RESULTS: Overall, fatal poisonings declined from a maximum of 226 in 2007 to 162 in 2017. Methadone (52%) was the most common cause of death, followed by heroin/morphine (25%). A marked increase in deaths was due to stimulants (13%), especially cocaine. The abuse pattern has changed since 2012. Methadone remained the most frequently detected drug, but clonazepam and cocaine surpassed heroin/morphine, diazepam and tetrahydrocannabinol as the second-most frequently detected drugs. Ketobemidone had disappeared, whereas buprenorphine, oxycodone, fentanyl, pregabalin and gabapentin had increased. Antidepressants/antipsychotics were detected in half (47%) of the cases. Cocaine was more frequent in the areas covered by Copenhagen and Aarhus, whereas heroin/morphine was most frequently detected in the area covered by Odense. Amphetamine was more frequent in the Aarhus area.

CONCLUSIONS: Methadone and heroin/morphine still account for most fatal poisonings. However, deaths due to stimulants, especially cocaine, have increased. The abuse pattern has changed and geographical differences have emerged.

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TRIAL REGISTRATION: not relevant.

This is the seventh report on fatal poisonings among drug users in Denmark; reports have been prepared every fifth year since 1984 [1-6]. Data from the present study and data from the previous reports were included in a common Nordic study [7].

The earlier studies conducted in 1984 and 1991 had as their target group the young drug users in their twenties and thirties [1, 2]. Over the years, the average age has increased steadily from 29 years in 1984 to 41 years in 2012 [1, 6]. One explanation for this increase may be the methadone treatment program in the sense that methadone saves lives [6]. However, prescription opioid methadone has now replaced heroin as the most frequent cause of death [1-6].

Many European countries have seen that prescription opioids used for opioid maintenance treatment (OMT) (methadone and buprenorphine) and pain relief (fentanyl, morphine, tramadol and oxycodone) play a bigger role than heroin in abuse [8]. North America has experienced epidemic use of synthetic opioids, particularly fentanyl analogues [8]. This has not been the case in Europe, although deaths from fentanyl analogues increased in Sweden in 2017 [7, 8].

Cocaine has also manifested itself in abuse. Since 1997, 15-19% of the fatally poisoned drug users have tested positive for cocaine, and deaths from cocaine have occurred in all Danish studies since 1997 [3-6]. This was substantiated by an increase in the number of individuals seeking first-time treatment for cocaine abuse in 2015-2017 [9].

The aim of this study was to update causes of death, abuse patterns and geographical differences in fatal poisonings among drug users in Denmark in 2017 and to compare these findings with those of preceding studies.

METHODS

The study included all fatal poisonings among drug users examined in 2017 at the three institutes of forensic medicine in Denmark: Copenhagen (Zealand, surrounding island and Bornholm), Aarhus (Jutland excluding Southern Jutland) and Odense (Funen, surrounding islands and Southern Jutland). The definition of a drug user from previous reports was used herein [7]: “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, 3,4-methylenedioxy-methamphetamine (MDMA), LSD, tetrahydrocannabinol (THC), etc.)”.

The recorded data included gender, number of fatal poisonings, age, main intoxicants and other drugs detected in blood. Fatal poisonings caused by two or more drugs were classified according to the drug considered to be the main intoxicant.

Heroin is rapidly metabolised to morphine and detected as such in the toxicological screens; therefore, cases where morphine was detected are listed as heroin/morphine. Toxicological evaluations were conducted according to the experience at the participating institutes and literature reports [10-14].

The occurrences of fatal poisonings were compared between the geographical areas by adjusting the number of fatal poisonings for the number of inhabitants aged 15-69 years, because just one drug user fell outside this interval.

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

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

Trial registration: not relevant.

RESULTS

Cause of fatal intoxication

Fatal poisoning was the cause of death in 162 drug users in 2017. The manner of death was accident in 85%. Four

percent (4%) was suicide and the manner of rest of the deaths was unknown (11%). The highest number of fatal poisonings (226) occurred in 2007 and the number has tended to decrease since then (Table 1) although an annual fluctuation cannot be excluded. In all study years, most fatal poisonings occurred in the area covered by Copenhagen. However, the number of fatal poisonings per 100,000 inhabitants in the age group from 15 to 69 years of age in 2017 was highest in the area covered by Odense (5.6), followed by Aarhus (4.4) and then Copenhagen (3.9). Women constituted 15% of the cases. The median age was 41 years (age range: 16-70 years) and remained unchanged compared with 2012.

TABLE 1 Fatal poisonings among drug addicts related to the institutes of forensic medicine in Denmark. The values are n (%).

Institute	1991	1997	2002	2007	2012	2017
Copenhagen ^a	110 (67)	121 (56)	90 (52)	101 (44)	99 (53)	74 (46)
Odense ^b	21 (13)	40 (19)	18 (10)	40 (18)	31 (16)	36 (22)
Aarhus ^c	33 (20)	55 (25)	67 (38)	85 (38)	58 (31)	52 (32)
Total	164 (100)	216 (100)	175 (100)	226 (100)	188 (100)	162 (100)

a) Zealand, surrounding islands and Copenhagen (1.87 mil inhabitants^d in the age group 15-69 yrs in 2017).

b) Funen, surrounding islands and southern part of Jutland (0.64 mil inhabitants^d in the age group 15-69 yrs in 2017).

c) The remaining part of Jutland (1.19 mil inhabitants^d in the age group 15-69 yrs in 2017).

d) Cf. Denmark Statistics.

Methadone poisoning was still the most frequent cause of death in 2017 (Table 2), but the increase in fatal methadone poisonings observed since 1997 has been replaced by a decline. The decrease in fatal heroin/morphine poisonings observed since 2002 has continued, although heroin/morphine remained the second most frequent cause of death. Fatal methadone poisonings were more frequent in the eastern part of Denmark (Table 3). In the areas covered by Copenhagen and Aarhus, three times as many deaths were caused by methadone as by heroin/morphine, whereas this proportion was equal in the area covered by Odense (Table 3). However, Copenhagen experienced a decrease in fatal methadone poisonings, whereas these poisonings remained unchanged in Aarhus compared with 2012. In contrast, the number of fatal methadone poisonings increased in Odense. The frequency of fatal heroin/morphine poisonings decreased in both Aarhus and Odense, whereas it remained almost unchanged in Copenhagen compared with 2012 (Table 3).

TABLE 2 Main intoxicant in fatally intoxicated drug addicts in Denmark in 2017 in comparison with previous study years. The values are n (%).

Main intoxicant	1991	1997	2002	2007	2012	2017
Heroin/morphine	94 (57.3)	153 (70.8)	76 (43.4)	75 (33.2)	51 (27.1)	40 (24.7)
Methadone	51 (31.1)	46 (21.3)	72 (41.1)	116 (51.3)	111 (59.0)	85 (52.5)
Buprenorphine	-	-	0	1 (0.4)	0	2 (1.2)
Ketobemidone	8 (4.9)	12 (5.6)	9 (5.1)	5 (2.2)	1 (0.5)	0
Fentanyl	-	-	-	0	0	2 (1.2)
Oxycodone	-	-	0	3 (1.3)	0	1 (0.6)
Tramadol	-	-	5 (2.9)	2 (0.9)	1 (0.5)	1 (0.6)
Cocaine	0	1 (0.5)	1 (0.6)	6 (2.7)	4 (2.1)	15 (9.3)
Amphetamine	1 (0.6)	1 (0.5)	2 (1.1)	6 (2.7)	2 (1.1)	2 (1.2)
MDMA	0	0	1 (0.6)	1 (0.4)	2 (1.1)	4 (2.5)
Other	10 (6.1)	3 (1.4)	9 (5.1)	11 (4.9)	16 (8.5)	10 (6.2)
Total	164 (100)	216 (100)	175 (100)	226 (100)	188 (100)	162 (100)

MDMA = 3,4-methylenedioxy-methamphetamine.

TABLE 3 Fatal heroin/morphine and methadone intoxications among drug addicts in Denmark related to the institutes of forensic medicine. The values are n (%).

Institute	Year	Heroin/morphine	Methadone	Total
Copenhagen	1991	61 (55)	40 (36)	101 (92)
	1997	74 (61)	40 (33)	114 (94)
	2002	36 (40)	47 (52)	83 (92)
	2007	24 (24)	64 (63)	88 (87)
	2012	17 (17)	74 (75)	91 (92)
	2017	15 (20)	44 (59)	59 (79)
Odense	1991	17 (81)	1 (5)	18 (86)
	1997	38 (95)	0	38 (95)
	2002	13 (72)	4 (22)	17 (94)
	2007	18 (45)	20 (50)	38 (95)
	2012	17 (55)	10 (32)	27 (87)
	2017	16 (44)	16 (44)	32 (89)
Aarhus	1991	16 (48)	10 (30)	26 (78)
	1997	41 (75)	6 (11)	47 (85)
	2002	27 (40)	21 (31)	48 (71)
	2007	33 (39)	32 (38)	65 (76)
	2012	17 (29)	27 (47)	44 (76)
	2017	9 (17)	25 (48)	34 (65)

At the time of death, 44 (27%) addicts were reported to be in OMT with methadone, and one was in treatment with buprenorphine. Most of the subjects being treated with methadone (86%) died from a methadone overdose, either alone or in combination with other drugs. Buprenorphine poisoning was the cause of death in the one drug addict undergoing buprenorphine treatment.

Overall, 1-2 deaths were attributed to each of the opioids: buprenorphine (n = 2), fentanyl (n = 2), tramadol (n = 1) and oxycodone (n = 1). The new psychoactive substances (NPS) acryloylfentanyl and methoxyacetylfentanyl caused one death each.

Opioids were the main cause of death in 2017, as reported previously. However, the proportion of fatal opioid poisonings decreased to 82%, from 99% in 1997 and from 87% in 2012. Instead, poisonings with central stimulants (cocaine, amphetamine, MDMA) increased and accounted for 13% of the deaths compared to 1-6% of the deaths in the earlier studies. Cocaine was the main cause of this increase, as a three-fold increase occurred in fatal cocaine poisonings compared with 2007 and 2012 (Table 2). Nine fatal cocaine poisonings occurred in the area covered by Copenhagen and six in the Aarhus area. Fatal cocaine poisonings were not observed on Funen or in Southern Jutland.

The benzodiazepines alprazolam (n = 1) and clonazepam (n = 2) caused three fatal poisonings, and one fatal poisoning occurred due to the NPS benzodiazepine flubromazolam. Antipsychotics/antidepressants were the causes of death in three drug users.

Multiple poisonings occurred in 84 (52%) of the fatal poisoning cases. Many (63%) were combined poisonings from an opioid (i.e. methadone) and benzodiazepines and/or alcohol.

Abuse pattern

The median drug number (excluding ethanol) detected per case was five. Methadone (65%) was the most frequently detected drug followed by clonazepam (45%), cocaine (44%) and THC (41%) (Table 4). Compared with 2012 (19%), the frequency of positive cocaine cases has more than doubled. Only 35% of the deceased tested positive for heroin/morphine. Amphetamine was detected in 18 (11%) cases, and 5% were positive for MDMA. Benzodiazepines were the most frequently detected group of drugs (73%). One NPS benzodiazepine, flubromazolam, was detected.

TABLE 4 The results of the analytical screening programme for medical drugs, narcotic drugs and poisons in fatally intoxicated drug users related to the institutes of forensic medicine in Denmark in 2017. The values are n (%).

Detected drugs	Institute			Total
	Copenhagen	Odense	Aarhus	
<i>Group I^a</i>				
Heroin/morphine	22 (29.7)	16 (44.4)	18 (34.6)	56 (34.6)
Methadone	50 (67.6)	23 (63.9)	32 (61.5)	105 (64.8)
Buprenorphine	6 (8.1)	2 (5.6)	5 (9.6)	13 (8.0)
Oxycodone	2 (2.7)	0	5 (9.6)	7 (4.3)
Fentanyl ^b	1 (1.4)	2 (5.6)	7 (13.5)	10 (6.2)
Other opioids ^c	5 (6.8)	2 (5.6)	6 (11.5)	13 (8.0)
<i>Group II^a</i>				
Cocaine	37 (50.0)	8 (22.2)	26 (50.0)	71 (43.8)
Amphetamines ^d	7 (9.5)	1 (2.8)	11 (21.2)	19 (11.7)
MDMA	3 (4.1)	2 (5.6)	3 (5.8)	8 (4.9)
Methylphenidate	6 (8.1)	1 (2.8)	3 (5.8)	10 (6.2)
Tetrahydrocannabinol	32 (43.2)	13 (36.1)	22 (42.3)	67 (41.3)
<i>Group III^a</i>				
Benzodiazepines ^e	53 (71.6)	25 (69.4)	41 (78.8)	119 (73.4)
Zopiclone/zolpidem	4 (5.4)	0	2 (3.8)	6 (3.7)
Zopiclone/zolpidem	4 (5.4)	3 (8.3)	6 (11.5)	13 (8.0)
Gabapentin	3 (4.1)	1 (2.8)	3 (5.8)	7 (4.3)
Barbiturates	3 (4.1)	0	2 (3.8)	5 (3.1)
Antidepressants/antipsychotics	31 (41.9)	18 (50.0)	27 (51.9)	76 (46.9)
<i>Ethanol level</i>				
≥ 0.5 mg/g	11 (14.9)	3 (8.3)	3 (5.8)	17 (10.5)
< 0.5 mg/g	10 (13.5)	2 (5.6)	4 (7.7)	16 (9.9)
Total	74	36	52	162

MDMA = 3,4-methylenedioxy-methamphetamine.

a) For a description of the groups see [7].

b) Includes fentanyl and 1 finding of acryloylfentanyl and methoxyacetylfentanyl, respectively.

c) Includes ketomebidone, codeine, tramadol, and hydromorphone.

d) Includes 1 finding of methamphetamine.

e) Includes 1 finding of the illegal benzodiazepine flubroalprazolam.

CORRECTION PER 14 JANUARY 2021: See publication information below.

In all parts of Denmark, methadone was the most frequent drug, and the proportion of positive cases with methadone was similar in all areas. Fifty percent of the cases in the areas covered by Copenhagen and Aarhus involved cocaine, making cocaine the second-most commonly detected drug in these regions. The area covered by Odense differed by having heroin/morphine (44%) as the second-most frequently detected drug. Only 22% of the cases tested positive for cocaine in Odense. Clonazepam was also frequently encountered in all parts of Denmark. In the areas covered by Odense and Aarhus, clonazepam shared second place with heroin/morphine and cocaine, respectively, whereas it shared a third place with THC in the area covered by Copenhagen. Amphetamine was detected in 21% of the cases in the area covered by Aarhus as opposed to 8% and 3% of cases

covered by Copenhagen and Odense, respectively.

Buprenorphine was detected in 13 cases (8%) and in all regions. This is a doubling compared with 2012, when 4% of the cases were positive for buprenorphine. The number of cases that tested positive for fentanyl increased from one positive case in 2012 to eight (5%) positive fentanyl cases in 2017, and fentanyl was detected in all regions, but most frequently in Aarhus (10%). Pregabalin and gabapentin were detected in 13 (8%) and seven (4%) cases, respectively. This represents an increase, as only pregabalin was detected in 2012 and in 5% of the cases.

Methadone was more frequently found in older drug users above 45 years of age, whereas buprenorphine, fentanyl, tramadol and oxycodone were more frequent in young drug users aged 16-25 years. The frequencies of heroin/morphine, cocaine and THC were similar in both groups, whereas amphetamine and MDMA were more frequent in young drug users.

The frequency of cases found with antidepressants/antipsychotics increased from 25% in 2007 to 41% in 2012 and further to 47% in 2017.

DISCUSSION

The Danish authorities have adopted several strategies in their treatment of drug users, such as OMT, heroin-assisted treatment for hard-to-treat drug users, drug consumption rooms and take-home naloxone kits [9, 15]. The decline in the number of fatal poisonings indicates that all these initiatives work.

Almost all the drug users in methadone treatment in this study died from a methadone poisoning either alone or in combination with other drugs. A recent report on drug overdoses among patients in OMT indicated that patients were at risk of an overdose long after leaving the OMT [16]. The number of buprenorphine cases has been low or zero for the past ten years in Denmark [5, 6]. The prescribed medications: Subutex and Suboxone used for OMT in Denmark both contain buprenorphine. Suboxone also contains naloxone. Naloxone is an opioid antidote, which should reduce the risk of overdose. However, the number of buprenorphine deaths has been high and increasing for the past 10-15 years, especially in Finland [7]. Parenteral use of Suboxone and Subutex has been reported in many of the buprenorphine deaths in Finland [7]. Thus, even though the number of fatal buprenorphine cases in Denmark is low, we cannot exclude that more cases will emerge if the use of buprenorphine in OMT increases.

Polydrug use was widespread as in all studies since 1984 [1-6]. On average, 2.4 substances, excluding ethanol, were detected in the poisoned drug users in 1997, 3.6 in 2007 and five in 2017 [3, 5]. The increase in the number of drugs per case probably reflects a wider range of different drugs on the illicit market compared with earlier years. The high number of polydrug deaths shows how problematic polydrug use is. Young drug users in particular had a varied drug use, suggesting a need for educational initiatives in this age group.

Over the years, the drug abuse pattern has changed. In the eighties and nineties, heroin was the main intoxicant and the most frequently detected drug [1-3]. In 2002, the prescription opioid methadone surpassed heroin as the most frequently detected drug, and the number of methadone and heroin/morphine deaths was similar [4]. In 2012 and 2017, twice as many drug users died from methadone as from heroin/morphine, and methadone has been the most frequently detected drug since 2007 [4-6]. Ketobemidone, which previously (1991-2002) was a frequent cause of death, has disappeared from the abuse picture [2-4]. Instead, opioids like fentanyl, tramadol and oxycodone have appeared, and as causes of death as well. Two deaths even occurred from the NPS fentanyl analogues.

Fentanyl analogues are very potent opioids that can be purchased over the internet. North America and Canada

have experienced an epidemic use of synthetic opioids and especially fentanyl analogues [8]. This has not been the case in Europe, although Sweden experienced a considerable number of deaths from fentanyl analogues in 2017 [7]. Approx. 20% of the clients entering treatment for opioids in European countries report using synthetic opioids other than heroin. The abuse includes methadone, buprenorphine, fentanyl, morphine, tramadol and oxycodone [8]. Therefore, a concern exists that fentanyl analogues will enter the illicit market in Europe in the near future [8].

Opioids remained the main cause of death, but the proportion of central nervous system (CNS) stimulant deaths has increased. In particular, cocaine use has increased, as indicated by the large increase in cocaine deaths and cocaine-positive cases. The most prominent regional difference in abuse pattern in our study was the predominance of cocaine in the area covered by Copenhagen and Aarhus, whereas heroin/morphine was more frequent in Odense. These regional differences in drug use did not correlate well with drug seizures at street level in Denmark in 2017 [17]. The street drug study (excluding cannabis) revealed a predominant occurrence of cocaine in all parts of Denmark (65-90%) [17]. Amphetamine was the second most frequent drug in Odense and Southern Denmark (23%), and it was 2-3 times more frequent in this region than in Copenhagen (10%) and Aarhus (6%) [17]. Thus, cocaine is a major player on the illegal market in all areas of Denmark. We do not know why cocaine appears in fewer decedents in the area covered by Odense, but this may be related to regional differences in the use of cocaine among high-risk drug users.

The prescription drugs pregabalin and gabapentin appeared in the fatally poisoned drug users in Denmark and in all the other Nordic countries in 2017 [7]. Pregabalin was among the most frequently detected drugs in Finland and Sweden in 2012 and 2017 alike, and deaths from pregabalin were observed in these countries [7]. Pregabalin has been classified as having a low abuse potential, but recent reports have demonstrated abuse and development of dependence [18, 19]. The sedative effect of pregabalin increases the risk of an overdose and death, similar to the effects of benzodiazepines and alcohol.

The high prevalence of antidepressants and antipsychotics is in agreement with previous studies showing a considerable co-occurrence of psychiatric disease and drug abuse [5, 6, 20]. Attention should be given to drug users with these dual diagnoses as they die younger than drug users without a psychiatric disease [20].

CONCLUSIONS

Methadone remains the main cause of death, followed by heroin/morphine. However, the abuse pattern has changed. CNS stimulant drugs, and especially cocaine, now form a larger part of detected drugs and constitute the cause of death with increasing frequency.

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CORRECTION PER 14 JANUARY 2021: The original article had some errors in Table 4. The first three sections of the table were incorrectly named Medical drugs, Narcotic drugs and Poisons, respectively. Instead, the sections now are named Group I, Group II and Group III, followed by an explanation in a note. Consequently, the footnotes have been changed. Furthermore, one erroneous percentage of Other opioids in Odense has been changed. Unfortunately, these mistakes have been identified after the paper was published. Accordingly, these corrections have been made in Table 4, 14 January 2021.

CONFLICTS OF INTEREST: none. Disclosure forms provided by the authors are available with the full text of this article at Ugeskriftet.dk/dmj

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