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Fatal poisoning among patients with drug addiction

Kirsten Wiese Simonsen¹, Dorte J. Christoffersen², Jytte Banner³, Kristian Linnet¹ & Ljubica V. Andersen⁴

ABSTRACT

INTRODUCTION: Fatal poisonings among drug addicts in Denmark in 2012 were examined. Cause of death, abuse pattern and geographic differences are discussed and data are compared with previous studies.

METHODS: All fatal poisonings examined at the three institutes of forensic medicine in Denmark in 2012 were included in the study.

RESULTS: A total of 188 fatal intoxications were recorded. The median age increased from 37.5 in 2007 to 41.5 in 2012. The majority were men (77%). Methadone (59%) was the main intoxicant. The decrease in the frequency of heroin/morphine deaths since 1997 (71%) continued, declining to 44% in 2002, 33% in 2007 and finally to 27% in 2012. Few deaths from central stimulants (amphetamine and cocaine) occurred. Multiple drug use was common and consisted mainly of opioids, cocaine, amphetamine, cannabis, benzodiazepines and alcohol. Heroin/morphine use was most frequent on Funen and in South Jutland. Cocaine was most frequently detected in East Denmark, while amphetamine was more frequent in West Denmark.

CONCLUSIONS: The number of fatal poisonings among drug addicts has stabilised around 200. The increase in methadone deaths continued and, as in 2007, methadone was the main intoxicant. The increase in methadone deaths seems to be associated with use of methadone in substitution treatment. Nevertheless, methadone treatment also seems to save lives, as indicated by the increasing median age. Use of antidepressants and antipsychotics increased to a high level compared with 2007, indicating that a considerable number of drug addicts also have psychiatric illness.

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Despite national initiatives such as treatment programmes and heroin clinics, the number of drug addicts in Denmark remains at a high level. In 2010 the number of drug addicts in Denmark was estimated to 33,000, of whom 11,000 abused only cannabis [1]. It was estimated that 13,000 (40%) of the drug addicts injected their drugs [1].

Since 1991 the number of fatal poisonings among drug addicts in Denmark has remained stable at approximately 200 annual deaths [2-4]. However, through the years the abuse pattern has changed and the prescribed opioid, methadone has widely replaced heroin as the main cause of death in Denmark [2-4]. This trend has

also been observed in the rest of Europe where abuse of medicinal opioids (methadone, buprenorphine, fentanyl, etc.) has increased, while the abuse of heroin has diminished [5].

This paper presents a follow-up study on fatal poisonings among drug addicts in Denmark in 2012. The data will be compared between the different parts of the country as well as with similar studies from 1991, 1997, 2002 and 2007 [2-4, 6]. As in the former studies, the 2012 data were included in a common Nordic study on fatal poisonings among drug addicts [7].

METHODS

This study included all fatal poisonings among drug addicts examined at the three institutes of forensic medicine in Denmark: Copenhagen (Zealand, surrounding islands, and Bornholm), Aarhus (Jutland, excluding Southern Jutland) and Odense (Funen, surrounding islands and Southern Jutland) in 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 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, LSD, etc.)."

Data on sex, number of fatal poisonings, age, main intoxicants and other drugs detected in the blood were recorded. Fatal poisonings caused by two or more drugs were recorded according to the drug considered to be the main intoxicant. Heroin is rapidly metabolised to 6-monoacetyl-morphine and further to morphine. Thus, in this study, heroin/morphine is stated in cases where morphine was detected. The toxicological evaluations of the detected drug concentrations were performed according to the experience at the participating institutes [8, 9] and in line with reports from the literature [10-13].

Trial registration: not relevant.

RESULTS

Cause of fatal intoxication

Fatal poisoning was the main cause of death in 90% of all registered deceased drug addicts in Denmark. A total of 188 fatal poisonings among drug addicts were examined at the three institutes of forensic medicine in Den-

ORIGINAL ARTICLE

1) Section of Forensic Chemistry, Department of Forensic Medicine, Faculty of Health Sciences, University of Copenhagen

2) Institute of Forensic Medicine, Department of Forensic Toxicology, University of Southern Denmark

3) Section of Forensic Pathology, Department of Forensic Medicine, Faculty of Health Sciences, University of Copenhagen

4) Department of Forensic Medicine, Aarhus University and Department of Clinical Pharmacology, Aarhus University Hospital, Denmark

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TABLE 1

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

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

a) Zealand, surrounding islands and Copenhagen (2.3 m inhabitants).

b) Funen, surrounding islands and Southern Jutland (0.7 m inhabitants).

c) The remaining part of Jutland (2.2 m inhabitants).

mark in 2012 (**Table 1**). The frequency of fatal poisoning in the capital and suburbs was 33% and remained unchanged compared with 2007 [4]. The gradual decrease in the frequency of fatal poisoning in the capital and suburbs observed from 1991 (53%) to 2007 (31%) seems to have stopped [4]. Women constituted 23% of the deaths. The age distribution showed a maximum in the 45-49-year age group (see **Figure 1** for methadone deaths) (the median age was 41.5 years and the age range was 17-62 years). The median age has increased compared with 2007 (median: 37.5 years). The main intoxicant is listed in **Table 2**. Opioids were the dominant cause of death (87%) in 2012 as in previous studies conducted since 1991. Methadone was the main intoxicant in 2012 (59%) as in 2007 (51%), and the increase in methadone deaths observed since 2002 (41%) continued in 2012. The frequency of heroin/morphine intoxications showed a corresponding decrease in the same period from 71% in 1997 to 44% in 2002 and 27% in 2012 (**Table 2**). This trend was observed in the eastern and western parts of Denmark. However, in the area covered by Odense, the frequency of heroin/morphine deaths increased, and the frequency of methadone death decreased from 2007 to 2012 (**Table 3**). The frequency of methadone deaths (75%) was highest in the area covered by the institute in Copenhagen of which nearly half (47%) were recorded in the capital of Copenhagen (**Table 3**). At time of death, 52 of the drug addicts (28%) were in substitution treatment with methadone. This seems to be slightly higher than in earlier studies (17-23%) [4]. This should be considered a minimum number as information about methadone treatment was not available for all deaths. Methadone was the main intoxicant in nearly all (92%) of the drug addicts receiving methadone treatment.

Eight deaths were caused by central stimulants, amphetamine, 3,4-methylenedioxy-N-methamphetamine (MDMA/ecstasy) and cocaine (**Table 2**). This is a slight decrease compared with 2007. Furthermore, there was one death from gammahydroxybutyric acid (GHB).

Prescribed medicine other than methadone caused fatal intoxication in 16 (8.5%) of the drug addicts. The following medicinal drugs caused one death each: tramadol, ketobemidone, codeine, zolpidem, metformine and acetylsalicylic acid. Two deaths were caused by a combination of chlorthalidopoxide and ethanol. Anti-depressants and antipsychotics were the main cause of death in eight (4%) of the deceased drug addicts.

Two or more drugs were judged to have contributed significantly to 32% of the fatal poisonings of drug addicts in 2012. Multi-poisonings were most often (55%) caused by an opioid in combination with a benzodiazepine and/or alcohol.

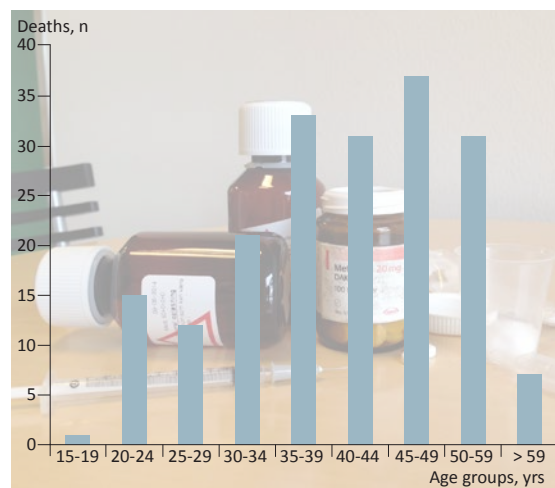
Abuse pattern

Table 4 presents all analytical findings in the poisoned drug addicts in 2012. On average, five drugs (median: four) excluding ethanol were detected per case. Ethanol was detected in 36% of the cases and ethanol was above 0.5 mg/g in half of the ethanol-positive cases.

As in 2007, methadone was the most frequently found drug and was detected in 134 (71%) cases [4]. This is an increase compared with previous studies, 2007 (61%), 2002 (33%) and 1997 (31%) [2-4]. Heroin/morphine was detected in 57 (30%) cases and remains among the most frequently found drugs even though there has been a continuing decrease compared with previous years, 2007 (40%), 2002 (48%) and 1997 (71%) [4]. Large regional differences were observed. Methadone was more frequent in the area covered by

FIGURE 1

The increase in methadone deaths seems to be associated with the use of methadone in substitution treatment. Nevertheless, methadone treatment also seems to save lives as indicated by the increasing median age over the time-period and by a maximum in the age group 45-49 years.



Copenhagen (84%) than in the areas covered by Aarhus (65%) and Odense (42%). Moreover heroin/morphine was more frequent in the area covered by Odense (55%) than in the area covered by Aarhus (33%) and Copenhagen (21%).

Other opioids, codeine (9%), tramadol (6%), buprenorphine (4%), ketobemidone (4%) and oxycodone (3%) appeared in a limited number of cases (Table 4). Except for an increase in buprenorphine-positive cases, there was no change compared with earlier years [2-4].

Cocaine was detected in 36 (19%) cases. This is a slight increase compared with previous years 1997-2007 (14-15 %) [2-4]. The frequency of amphetamine (10%) has not changed during the past ten years [2-4]. In the area covered by Copenhagen, 26% of the cases tested positive for cocaine. This is much higher than in Aarhus (14%) and Odense (6%). On the contrary, amphetamine appeared more frequently in Aarhus (17%) than in Odense (10%) and Copenhagen (6%). Similar to previous studies in 2007 and 2002, only few cases tested positive for new psychotropic drugs (NPS) (MDMA, methylenedioxypyrovalerone (MDPV) and para-methoxy-N-methylamphetamine (PMMA)). These NPS drugs were only detected in the area covered by Copenhagen.

Diazepam (35%) and tetrahydrocannabinol (34%) were the second most frequently detected drugs. In fact, benzodiazepines (71%) as a group occurred as frequently as methadone (Table 4). Methylphenidate (5%), pregabalin (5%) and GHB (1.6%) appeared for the first time and were only detected in the areas covered by the institutes in Copenhagen and Aarhus.

Cases with one or more antidepressants/antipsychotics increased from 25% in 2007 to 41% in 2012, and antidepressants/antipsychotics as a group were more frequent than heroin/morphine [4]. The frequency of antidepressants/antipsychotics was similar in all parts of Denmark.

DISCUSSION

As from 2009, the so-called hard-to-treat heroin abusers in Denmark have been eligible to receive prescribed heroin for injection at special heroin clinics [1]. Five heroin clinics existed nation-wide (Copenhagen, Aarhus, Odense, Hvidovre and Esbjerg) at the end of 2012. In total, 252 drug addicts have received heroin in these clinics from 2009 to 2012 [1]. Nearly 30% have left the treatment and most returned to substitution treatment [1]. The decrease in heroin/morphine deaths from 2007 to 2012 seems to be a continuing decrease initially observed in 2002, and any positive influence from the heroin clinics is uncertain. In Odense, the number of heroin/morphine deaths was unchanged from 2007 to 2012. Over the years, the number of fatal poisonings remained unchanged as the decrease in heroin/morphine deaths

has been replaced by a corresponding increase in methadone deaths. This trend, by which medicinal opioids have replaced heroin as the leading cause of death, has also been observed in the other Nordic countries and in rest of Europe and in the USA [5, 7, 14]. While methadone mostly replaced heroin as cause of death in Denmark, fatal poisonings from other opioids like buprenorphine and fentanyl increased markedly in Sweden and Finland in 2012 [7].

Both methadone and buprenorphine are used for substitution treatment of opioid dependence in Denmark. In 2011 about 6,200 drug addicts were in methadone treatment and 1,400 were in buprenorphine treatment [1]. The increase in methadone deaths is undoubtedly connected to the high number of clients in methadone treatment. This is supported by the fact that among the deceased addicts reported to be in methadone treatment, 92% died from a methadone overdose in 2012. On the other hand, the increase in median age indicates that treatment programmes also save lives. Substitution treatment of drug addicts has been found to be less restrictive in Copenhagen than in Odense and

TABLE 2

Main intoxicant in fatally intoxicated drug addicts in Denmark in 2012. The values are n (%).

Main intoxicant	1991	1997	2002	2007	2012
Heroin/morphine	94 (57.5)	153 (71)	76 (44)	75 (33)	51 (27)
Methadone	51 (31)	46 (21)	72 (41)	116 (51)	111 (59)
Cocaine	0 (0)	1 (0.5)	1 (0.5)	6 (3)	4 (2)
Amphetamine	1 (0.5)	1 (0.5)	2 (1)	6 (3)	2 (1)
Ketobemidone	8 (5)	12 (5.5)	9 (5)	5 (2)	1 (0.5)
Tramadol	NA	NA	5 (3)	2 (1)	1 (0.5)
Other	10 (6)	3 (1.5)	10 (5.5)	16 (7)	18 (10)
Total	164 (100)	216 (100)	175 (100)	226 (100)	188 (100)

NA = not analysed.

TABLE 3

Institute	Year	Heroin/morphine	Methadone	Fatal heroin/morphine and methadone intoxications among drug addicts in Denmark related to the three institutes of forensic medicine. The values are n (%).
Copenhagen	1997	74 (61)	40 (33)	
	2002	36 (40)	47 (52)	
	2007	24 (24)	64 (63)	
	2012	17 (17)	74 (75)	
Odense	1997	38 (95)	0 (0)	
	2002	13 (72)	4 (22)	
	2007	18 (45)	20 (50)	
	2012	17 (55)	10 (32)	
Aarhus	1997	41 (75)	6 (11)	
	2002	27 (40)	21 (31)	
	2007	33 (39)	32 (38)	
	2012	17 (29)	27 (47)	

 TABLE 4

The results from the analytical screening programme for medical drugs, narcotic drugs and poisons in fatally intoxicated drug addicts related to the three institutes of forensic medicine in Denmark in 2012. The values are n.

Detected drug	Copenhagen	Odense	Aarhus	Total
Heroin/morphine	21	17	19	57
Methadone	83	13	38	134
Proxyphene	0	0	0	0
Ketobemidone	3	0	5	8
Codeine	6	3	8	17
Tramadol	7	0	5	12
Oxycodone	3	0	3	6
Cocaine	26	2	8	36
Fentanyl	0	0	1	1
Hydrocodone	0	0	1	1
Amphetamine	6	3	10	19
Methamphetamine	0	0	0	0
Ecstasy (MDMA)	3	0	0	3
MDPV	1	NA	NA	1
PMMA	1	0	0	1
GHB	2	0	1	3
Methylphenidate	3	0	6	9
Tetrahydrocannabinol	31	7	26	64
Benzodiazepines	78	14	41	133
Zopiclone	5	0	2	7
Zolpidem	0	2	0	2
Buprenorphine	2	NA	5	7
Pregabalin	6	0	3	9
Barbiturates	1	2	1	4
Antidepressants/antipsychotics	42	13	22	77
<i>Ethanol concentration</i>				
> 0.5 mg/g	19	7	8	34
≤ 0.5 mg/g	21	8	4	33

GHB = gammahydroxybutyric acid; MDMA = 3,4-methylenedioxy-N-methamphetamine; MDPV = methylenedioxypropylvalerone; NA = not analysed; PMMA = para-methoxy-N-methylamphetamine.

Aarhus [15]. Many drug addicts were not supervised while taking methadone in Copenhagen [15]. This could be the reason for the high number of methadone deaths in this area.

Buprenorphine deaths did not occur in Denmark in 2012, and there was only one buprenorphine death in 2007 [4]. Conversely, the development in buprenorphine deaths has been overwhelming in both Finland and Sweden. In 2012, 42 and 35 buprenorphine deaths were recorded in Finland and Sweden, respectively [7]. Suboxone – containing buprenorphine in combination with the opioid antagonist naloxone – is used for treatment of opioid dependence. The single buprenorphine death in Denmark was ascribed to this combination. Suboxone has long been used for treatment of drug addicts in Finland, and many deaths have occurred due to use of Suboxone [16]. Buprenorphine deaths in Finland are exclusively multi-poisonings, primary with benzodiazepines and alcohol [17]. As benzodiazepine and/or alcohol con-

tributed to more than half of the multi-poisonings in Denmark in 2012, side abuse should be taken seriously.

As previously, central stimulants (cocaine, amphetamine and MDMA) caused few deaths. The number of deaths from central stimulants was even lower in 2012 (n = 8) than in 2007 (n = 13) despite an increase in cocaine-positive findings [4]. More deaths from amphetamine and cocaine were to be expected due to a marked increase in non-fatal intoxications from amphetamine and cocaine from 2004 (n ≈ 125) to 2012 (n = 424) recorded by the hospitals in Denmark [1]. Countries like Spain and the United Kingdom have experienced a three-fold increase from 2000 to 2008 in the number of cocaine-intoxicated people admitted to hospitals [18]. Even so, cocaine deaths were rare in these countries [18].

Poly-drug use was widespread in all parts of the country. Opioids, cocaine, amphetamine, cannabis, benzodiazepines and alcohol were included in the abuse. The considerable regional differences in drug findings in this study were in agreement with the pattern of street drugs in Denmark reported in 2012 [19]. In that study, heroin was more frequently seized in the police districts of Odense and Esbjerg than in the police districts of Copenhagen, Aarhus and Aalborg [19]. Cocaine was more frequently seized in the Copenhagen police district, whereas amphetamine appeared more frequently in the western part of Denmark [19]. Heroin seems to play a smaller part in the abuse indicated by the decrease in heroin/morphine intoxications. Amphetamine and cocaine were seized 3-4 times more frequently than heroin in Denmark in 2012 [20]. But, still, 30% of the drug addicts tested positive for heroin/morphine.

Although the number of new NPS drugs has increased immensely in Europe [5], NPS drugs were seldom detected in the drug addicts.

The frequent use of antidepressants and anti-psychotics seen in all parts of Denmark was also observed in the other Nordic countries [7]. Even deaths from these medicinal drugs occurred. This indicates that a large number of drug addicts also have psychiatric illness. Treatment of such co-morbidity is highly recommended.

CONCLUSIONS

The number of fatal poisonings remains at a high level and has stabilised at approximately 200 annual deaths. Methadone was the main intoxicant. The decrease in heroin/morphine deaths, initially observed in 2002, continued and was, as in previous years, accompanied by an increase in methadone deaths. There seems to be a connection between the increase in methadone deaths and methadone treatment. Nevertheless, substitution treatment also saves lives. Large regional differences in abuse

patterns were demonstrated. Methadone was more frequent in the areas covered by Copenhagen and Aarhus, whereas heroin was most frequent in the area covered by Odense. Cocaine was most frequent in the eastern part of Denmark, whereas amphetamine was more frequent in western part of the country. Use of antidepressants and antipsychotics increased to a high level, indicating that a large number of drug addicts also have psychiatric illness. As the drug market is changing and different initiatives from the authorities influence the drug situation, further studies in this area are recommended.

CORRESPONDENCE: Kirsten Wiese Simonsen.

E-mail: kirsten.wiese@sund.ku.dk

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