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Mortality and Cause of Death—A 30-Year Follow-Up of Substance Misusers in Sweden

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ABSTRACT

Background: This article presents a 30-year follow-up study of a cohort of 1163 substance misusers who were in inpatient treatment in the early 1980s. Data was originally collected in the Swedish Drug Addict Treatment Evaluation (SWEDATE). *Objectives*: The aim is to examine the overall mortality and identify causes of death in different groups based on self-reported most dominant substance misuse among those who have died during January 1984–December 2013. *Methods*: SWEDATE-data was linked to the National Cause of Death Register. Five mutually exclusive study groups were created based on self-reported most dominant substance misuse for the last 12 months before intake to treatment: Alcohol, Cannabis, Stimulants, Opiates, and Other. The Standardized Mortality Ratio (SMR) was calculated. *Results*: During the follow-up, 40% died. SMR is 10.3 for women and 11.7 for men. The study groups differed regarding SMR; 13.1 in the Alcohol group, 9.2 in the Cannabis group, 9.6 in the Stimulants group, 16.7 in the Opiates group and 10.8 in the Other group. Drug related death was the most common cause of death (28% only underlying, 19% both underlying and contributing) followed by alcohol related reasons (17% vs. 9%). *Conclusions*: Alcohol misuse among substance abusers might have a negative impact on mortality rates. Methodological changes in how drug related deaths is registered affects the interpretation of the statistics of cause of death. Further analysis on the relation between drug related cause of death and drug misuse related death is needed.

Introduction

Mortality and cause of death have been the focus of several national as well as international long-term follow-ups of drug abusers (see, e.g., Andréasson & Allebäck, 1990; Bargagli et al., 2005; Bartu, Freeman, Gawthorne, Codde, & Holman, 2004; Nyhlén, Fridell, Hesse, & Krantz, 2011; Oppenheimer, Tobutt, Taylor, & Andrew, 1994; Stenbacka, Leifman, & Romensjö, 2010), and premature death is highest among young abusers (Ghodse, Oyefeso, & Kilpatrick, 1998; Ledberg, 2016; Nyhlén et al., 2011; Oppenheimer et al., 1994). Several studies report higher mortality rates for women (Bartu, Freeman, Gawthorne, Codde, & Holman, 2004; Bird et al., 2003; Degenhardt et al., 2010; Mathers et al., 2013; Stenbacka et al., 2010), although some studies find no gender differences in mortality rates (Oppenheimer et al., 1994).

A meta-analysis that specifically compared studies on mortality among users of heroin and other opiates draws attention to the heterogeneity of results in previous research, with the interpretation that mortality among opiate-dependent individuals varies among countries, between classes and also between when the studies were carried out (Degenhardt et al., 2010). A later systematic review on mortality among IV drug users revealed that crude mortality rates (CMR) were higher in low and middle-income country cohorts (Mathers et al., 2013).

In studies where subgroups of opiates and stimulants abusers have been compared, the opiate group tends to have higher mortality rates than the stimulant abusers (Adamsson Wahren, Brandt, & Allebeck, 1997; Bartu, Freeman, Gawthorne, Codde, & Holman, 2004). An exception is a Swedish longitudinal follow up study by Stenbacka et al. (2010), which found similar standardized rates when comparing mortality among opiate abusers and amphetamine abusers. The group with the highest standardized rate in Stenbacka et al.'s study was the group with both drug and alcohol abuse.

Previous research on the causes of death among substance abusers shows great variation (EMCDDA 2011), often due to missing information or unascertained causes of death (Bargagli et al., 2005). However, overdose seems to be the most common cause of death (Bartu, Freeman, Gawthorne, Codde, & Holman, 2004; Bauer et al., 2008; Mathers et al., 2013; Nyhlén et al., 2011;

Ravndal, Lauritzen, & Gossop, 2015) often followed by suicide and traumatic-related deaths (Degenhardt et al., 2010). Methadone patients seem to be an exception. Several studies reveal that HIV-related deaths are the most common cause of death among those patients (Davstad, Stenbacka, Leifman, & Romelsjö, 2009; Jimenez-Treviño et al., 2011; Rehm et al., 2005).

In the study by Stenbacka et al. (2010), the most common causes of death were suicide (definite and undetermined), cardiovascular disease and accidents. Almost half of all deaths were related to drug abuse, i.e., this being the main or contributing diagnosis. Comparisons show that among abusers of opiates and/or central stimulants cardiovascular disease and accidents were the most common cause of death, while the cannabis group died from alcohol abuse, tumors, accidents and definite suicide. Since overdoses rarely occur among those that have become opiate dependent through drugs for pain treatment, it is argued that lifestyle is a major influence factor (Ghodse et al., 1998). Additionally, previous research reveals that mortality is lower among methadone patients (Degenhardt et al., 2010; Fuglestad, Ågren, & Romelsjö, 1998).

Follow-up studies that have compared those who died with those who survived highlight protective and risk factors. These comparisons are summarized in a study from Austria as predictors of mortality, where the results show, for example, that people with higher lifetime hospitalization and bad economic situation were more likely to die, while social relations are described as protecting (Bauer et al., 2008). The importance of social relations is discussed by Hser, Hoffman, Grella, and Anglin (2001) in relation to gender differences regarding improved family relationships, and it is suggested that one reason for women's improvement could be related to their being of childbearing age or having had children. Another protective factor highlighted in several studies is treatment (Bartu, Freeman, Gawthorne, Codde, & Holman, 2004; Degenhardt et al., 2010). However, results also imply that treatment at a later point in the course of addiction and spending a greater part of life in treatment is not beneficial (Scott, Dennis, Laudet, Funk, & Simeone, 2011).

In general, previous research on mortality and causes of death have focused on either alcohol or drugs, assuming higher mortality risk among drug users. One exception is a Swedish prospective study of mortality up to eight years after starting treatment, where no differences regarding mortality risks were found between alcohol and drug dependent patients (Storbjörk & Ullman, 2012).

This article presents a 30-year follow-up study on the majority[1] of substance misusers treated in residential care for drug problems in Sweden during 1982–1983. Data were originally collected in a research project named Swedish Drug Addict Treatment Evaluation (SWEDATE), where Swedish inpatient care for substance misusers was studied (Berglund et al., 1991; Bergmark et al., 1994; Olsson, 1988). In all, 31 inpatient treatment units took part in the project.[2] The aim of this article is to (1) examine the overall mortality in different groups based on self-reported most dominant substance misuse reported in the SWEDATE data and (2) identify causes of death in different groups based on self-reported most dominant substance misuse among those who have died during the study period of January 1984–December 2013.

Material and Methods

The study is based on SWEDATE data linked to the National Cause of Death Register (NDR) held by the Swedish Board of Health and Welfare. The SWEDATE data were collected by personal interviews (usually but not always at time of intake) with 1163 of the 1656 substance misusers who were treated at 31 treatment units in Sweden in the period 1982–1983. All treatment units were focused on treatment for substance misuse, including poly drug misuse, often in combination with alcohol misuse. The dominating reason for not being interviewed was dropout from treatment before the interview. Therefore, the nonresponders are probably more marginalized as a group, which could imply higher mortality rates in this group. The interviews were carried out mainly during 1982–1983, although eight interviews were performed during 1981 and 1984, and six during 1985. Ten percent had entered treatment before 1982. Information on gender, age, sex, and type of self-reported most dominant substance misuse for the last 12 months before intake to treatment was retrieved from the SWEDATE questionnaire. The youngest were 15 years of age and the oldest 55 at the time of intake, with 69% males and 31% females. Overall evaluation of quality of the SWEDATE data, based on both validity and reliability testing, shows high quality (Olsson, 1988).

Date and cause of death were retrieved from the NDR. The cohort members were followed in NDR from the date of discharge until the end of 2013. The quality of the NDR is regarded as fairly high, and international comparisons with other countries that have committed to the International system of Classification of Diseases (ICD) is regarded as good. NDR covers all registered deaths in Sweden since 1961, whether the death occurred within or outside the country. The coding of causes of death follows the ICD (National Board of Health and Welfare, 2010). The registers were linked by use of the individually unique ten-digit personal id number (PIN) held by all

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[1] Estimated as 50% to 75% of the substance misusers in Sweden (Olsson, 1988).

[2] Including treatment units for young or adult misusers, substance misuse treatment wards within the penalty system and hospital wards for substance misuse treatment.

Swedish residents from birth (or date of immigration) to death.

Study groups

All the interviewed clients were in treatment and thus had a defined severe substance misuse at the time of the interview. For example, 80% said that they had injected drugs. Of those, 86% had injected a hundred times or more. Overall, the client group had a history of using a variety of substances. Five mutually exclusive study groups were created based on self-reported most dominant substance misuse for the last 12 months before intake to treatment. The response options were: Narcotics, Alcohol, Sedatives, and Solvents. The first study group consists of those who answered that Alcohol was their most dominant substance misuse ($n = 255$). About two thirds of the clients with alcohol as their most dominant substance misuse stated that they also had used narcotics once a week or more during their misuse. An additional three study groups were created out of those who answered that Narcotics or Sedatives were their most dominant substance misuse, depending on what they said was their dominating drug: Cannabis ($n = 239$), Stimulants ($n = 414$), and Opiates ($n = 182$). Approximately a quarter of the clients in these three study groups said that they also misused alcohol. The remaining individuals are included in the fifth study group called Other ($n = 73$). This group is heterogeneous and consists of: 7 individuals who answered that Solvents was their most dominant substance misuse, irrespective of what their dominating drug was; 45 individuals who answered that narcotics or sedatives were their most dominant substance misuse but did not provide an answer (or answered Other) on their dominating drug; 7 individuals who answered that narcotics was their most dominant substance misuse and that

cocaine (4 individuals) or hallucinogens (3 individuals) were their dominating drug; 2 individuals who did not provide an answer on most dominant substance misuse but answered that hallucinogens (1 individual) or other (1 individual) was their dominating drug; and finally, 12 individuals who did not provide an answer on either their most dominant substance misuse or dominating drug.

Statistical analysis

The observed mortality rates in the study population were compared with the mortality rates in the total Swedish population 1984–2013 using Standardized Mortality Ratio (SMR). SMR gives the ratio of observed number of deaths to the expected number of deaths, where rates above 1.0 indicate excess mortality in the study population. The expected number of deaths was calculated using age and gender specific mortality rates for the total Swedish population born 1941–1967 for the period of 1984–2013, based on life tables for 1984 and 2014 (Statistics Sweden, 2017). The choice of time period for the SMR calculation (1984–2013) follows the enrollment period, which stretched into 1983, and the study population was not complete until the end of 1983. In the study population, 12 individuals had died before 1984 and were therefor excluded from the SMR calculation, which is based on the population alive at the beginning of 1984. Furthermore, 15 persons born before 1941 (1927–1940) were also excluded from the SMR calculation due to sparse data. Thus, 1136 individuals were included in the SMR calculation, whereof 353 were women and 783 men (Table 2). Person-years at risk is calculated as the midpopulation times the length of the studied period (30 years).

The SMR is slightly underestimated, as the study population is also included in the death rates for the total

Table 1. Descriptive data of the study groups, based on self-reported most dominant substance misuse. Numbers (*n*) and percent (%).

	Study groups Alcohol		Cannabis		Stimulants		Opiates		Other		All	
	%	n	%	n	%	n	%	n	%	n	%	n
Sex												
Women	26.3	67	21.8	52	33.1	137	42.3	77	38.4	28	31.0	361
Men	73.7	188	78.2	187	66.9	277	57.7	105	61.6	45	69.0	802
Total	100.0	255	100.0	239	100.0	414	100.0	182	100.0	73	100.0	1163
Age at intake												
−19 yrs	11.8	30	26.4	63	19.6	81	8.3	15	13.7	10	17.1	199
20-29 yrs	56.1	143	56.1	134	52.9	219	68.1	124	58.9	43	57.0	663
30+ yrs	32.2	82	17.6	42	27.6	114	23.6	43	27.4	20	25.9	301
Total	100.0	255	100.0	239	100.0	414	100.0	182	100.0	73	100.0	1163

Note. Use of other substances during the last 12 month before intake:
Alcohol group; cannabis 40%, stimulants 33%, opiates 7% and other substances 10%.
Cannabis Group; alcohol 40%, stimulants 37%, opiates 3% and other substances 10%.
Stimulants group: alcohol 46%, cannabis 41%, opiates 5% and other substances 8%.
Opiates group: alcohol 38%, cannabis 25%, stimulants 19% and other substances 4%.
Other group: alcohol 30%, cannabis 7%, stimulants 7% and opiates 0%.

Table 2. Age and gender standardised mortality ratio (SMR) for the period of 1984–2013.

	Age at end of 1984	No: in study population 1984-01-01	Observed number of deaths	Percent deceased (CDR)	Expected number of deaths	Standard mortality rate (SMR)	95% CI Lower	Higher
Women	17-24 yrs	140	23	16.4	1.6	14.3	8.4	20.1
	25-34 yrs	181	49	27.1	4.5	10.9	7.8	13.9
	35-43 yrs	32	13	40.6	2.2	6.0	2.8	9.3
	All	353	85	24.1	8.3	10.3	8.1	12.4
Men	17-24 yrs	206	66	32.0	4.1	16.3	12.4	20.2
	25-34 yrs	441	205	46.5	15.6	13.1	11.3	14.9
	35-43 yrs	136	84	61.8	10.8	7.8	6.1	9.5
	All	783	355	45.3	30.4	11.7	10.5	12.9
By study group:								
Alcohol	Women	65	23	35.4	1.6	14.4	8.5	20.2
	Men	180	91	50.6	7.1	12.8	10.2	15.5
	All	245	114	46.5	8.7	13.1	10.7	15.5
Cannabis	Women	51	4	7.8	0.9	4.3	0.1	8.4
	Men	187	64	34.2	6.4	9.9	7.5	12.4
	All	238	68	28.6	7.4	9.2	7.0	11.4
Stimulants	Women	134	27	20.1	3.1	8.6	5.4	11.9
	Men	269	114	42.4	11.6	9.8	8.0	11.6
	All	403	141	35.0	14.7	9.6	8.0	11.1
Opiates	Women	75	23	30.7	1.7	13.5	8.0	19.1
	Men	103	66	64.1	3.6	18.3	13.8	22.7
	All	178	89	50.0	5.3	16.7	13.3	20.2
Other	Women	28	8	28.6	0.9	8.8	2.7	14.9
	Men	44	20	45.5	1.7	11.9	6.7	17.1
	All	72	28	38.9	2.6	10.8	6.8	14.8

Note. Expected number of death were calculated based on the life tables by sex and age for the general population 1984 & 2014. Study groups are based on self-reported most dominant substance misuse.

population. However, their small number in comparison with the total population (1136 out of 3.2 million in the entire population 1984) should make this underestimation insignificant.

Causes of death for deceased persons in the five study groups are investigated to examine to what extent misuse impacts on mortality. All 1163 individuals in the study population were included (Table 3). The NDR records both the underlying cause of death (the disease or injury assessed to have initiated the train of events leading directly to death, i.e., the primary reason for dying) and other substantial health conditions that may have unfavorably affected the course of a disease and thus contributed to the fatal outcome (i.e., contributing causes of death). For injuries, the external cause of injury is registered. The diagnoses in NDR follow the ICD (National Board of Health and Welfare, 2010).

The causes of death are divided into ten cause-groups (drug related, alcohol related, suicide, AIDS, poisoning, violence, injuries, lungs excl. tumor, circulation, tumor)[3]

according to standards put forward by the Swedish Board of Health and Welfare (National Board of Health and Welfare, 2017). The results are presented in two different ways, one that is based only on the underlying cause of death (given in column A in Table 3) and one where both underlying and contributing causes are taken into account (given in column B in Table 3).

Ethics

This research was scrutinized and approved by the Ethical Review Board in Stockholm, Sweden (2015/329-31/5, 2015/1205-32, 2016/542-32/5).

- ICD-10: E244, F10, G312, G621, G721, I426, K292, K70, K73-K746, K852, K860, O354, T51, Y901-Y909, Y911-Y919
- Suicide. ICD-8: 95. ICD-9: E95. ICD-10: X60-X84.
- AIDS. ICD-9: 2795-6. ICD-10: B20-B24.
- Poisoning
- ICD-8: 850-877; or 960-989 in chapter 17. ICD-9: E850-E869; or 960-989 in chapter 17.
- ICD-10: X400-X499; or T36-T65, T90-T98 in chapter 19.
- Violence . ICD-8: 960-978, 990-999. ICD-9: E960-E969, E990-E999. ICD-10: X85-Y099, Y35-Y369.
- Injury
- ICD-8: 80-89; or 800-959, 990-999 in chapter 17.
- ICD-9: E80-E89; or 800-959, 990-999 in chapter 17.
- ICD-10: V01-Y89; or S00-T35, T66-T78 in chapter 19.
- Lungs, excl tumour. ICD-8: 460-519. ICD-9: 460-519. ICD-10: J00-J99.
- Circulation incl heart attack and stroke. ICD-8: 390-458. ICD-9: 390-459, 7855. ICD-10: I00-I99.
- Tumour. ICD-8: 140-239. ICD-9: 140-239. ICD-10: C00-D48.

- The following diagnoses codes were used:
  - Drug related (Index by The National Board of Health and Welfare)
  - ICD-8: 292, 304, 6483, 6555, 9696, 9697, 9650; or 96500, 969, 9709, 971 in chapter 17.
  - ICD-9: 292, 304, 6483, 6555, 9696, 9697, 9650, 9685; or 9696, 9697, 9650, 9685 in chapter 17.
  - ICD-10: F11-F16, F18, F19, O355, T40, T436, Z503, Z715, Z722.
  - Alcohol related (Index by The National Board of Health and Welfare, incl. cirros)
  - ICD-8: 291, 303,5710, 860, 980; or 980 in chapter 17.
  - ICD-9: 291, 303, 3050, 3575, 4255, 5353, 571, E860, E980; or 980 in ch 17.

Table 3. Causes of death among deceased persons by study group. ICD8 – ICD10. Percent (%).

Study groups	Alcohol		Cannabis		Stimulants		Opiates		Other		All	
	A	B	A	B	A	B	A	B	A	B	A	B
Drug related	12.9	29.0	14.5	36.2	10.6	35.1	44.1	61.3	13.8	37.9	18.7	39.1
Alcohol related	14.5	45.2	5.8	29.0	8.6	27.2	3.2	18.3	10.3	31.0	8.8	30.7
Suicide	4.8	9.7	5.8	8.7	6.0	9.9	3.2	3.2	6.9	13.8	5.2	8.6
AIDS	2.4	4.0	1.4	1.4	3.3	4.6	12.9	19.4	3.4	3.4	4.7	6.9
Poisoning	14.5	21.8	20.3	30.4	13.2	24.5	9.7	28.0	31.0	55.2	15.0	27.3
Violence	0.0	0.8	4.4	7.2	2.0	2.6	1.1	6.4	0.0	6.9	1.5	3.9
Injuries	11.3	36.3	11.6	46.4	13.9	40.4	7.5	30.1	0.0	31.0	10.7	37.6
Lungs, excl tumor	4.0	4.0	1.4	1.4	2.6	2.6	4.3	4.3	3.4	3.4	3.2	3.2
Circulation incl heart attack and stroke	12.9	16.1	13.0	13.0	17.2	19.2	4.3	4.3	6.9	6.9	12.2	13.7
Tumour	8.1	8.9	11.6	13.0	10.6	11.3	4.3	4.3	6.9	6.9	8.6	9.2
Other	14.5	—	10.1	—	11.9	—	5.4	—	17.2	—	11.4	—
Total	100.0		100.0		100.0		100.0		100.0		100.0	
Total number (*n*)	124		69		151		93		29		466	

Note. A) Underlying cause of death. B) Underlying OR contributing cause of death. Study groups are based on self-reported most dominant substance misuse.

Results

A majority of the study population were men (69%) and most were in their twenties (57%). The most common misuse was stimulants, which one third said had been their dominating misuse for the last 12 months before intake to treatment (Table 1). The second most common dominant substance misuse was alcohol, according to the individuals themselves, even though everyone in the study population was in drug treatment. The gender distribution was most even in the Opiates group (58% men), while the Cannabis group had the most uneven distribution (78% men). The Cannabis group was the youngest, and the Alcohol group the oldest.

Mortality rates

From a total of 1163 individuals in the study population, 466 died during the follow-up period. That equals 47% of all the men and 26% of all the women in the study. The proportion of deceased is highest in the Opiate group during the major part of the follow up period, followed by the Alcohol group (Figure 1). However, compared with the Alcohol group, the increase in the Opiate group is steeper during the first ten years. Ten years after exit from treatment, the Opiates group has 4.7 times as high Crude Death Rate (CDR) as the Cannabis group. After twenty years, CDR is 2.6 times as high, and after thirty years it is 1.8 times as high. In general, Figure 1 shows that the differences between the study groups varies over time.

Altogether, 1136 individuals were included in the SMR calculation, of whom 440 died during the 1984–2013 study period (for more details see Section "Statistical analysis").

In this study, *total* mortality among drug users is underestimated, as we do not follow this drug user population from the beginning of their misuse. In our study, 26% were 30 years or older at intake to treatment. Their peers who had already died from misuse are not included in this study for obvious reasons.

The age and gender standardized mortality rate (SMR) in the study population was 10.3 for women and 11.7 for men (Table 2); that is when we compare the observed number of deaths in the study population with the expected number of deaths calculated from the age and gender specific death rates in the general population for the period 1984–2013.

The SMR in the study groups was 13.1 in the Alcohol group, 9.2 in the Cannabis group, 9.6 in the Stimulants group, 16.7 in the Opiates group, and 10.8 in the Other group. Compared to the standard population, the excess mortality among the study population was higher
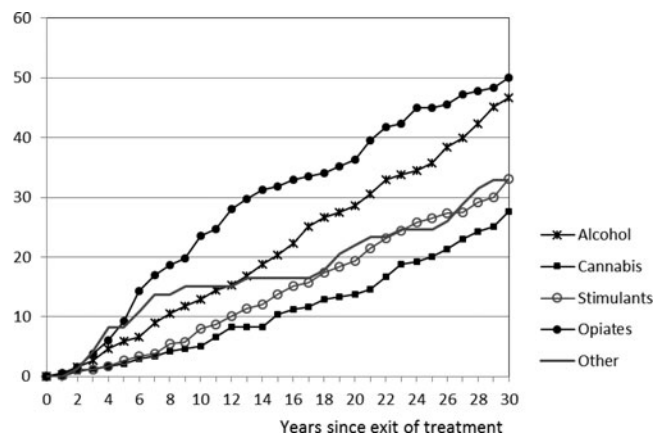
Figure 1. Proportion of deceased by study group and number of years since exit of treatment. Percent (%).

in younger birth cohorts than older birth cohorts; this applies for both men and women (Table 2). This is a known pattern, as many drug users die young and those who survive will become more experienced drug users as they get older. The oldest birth cohorts in this study had reached their forties at intake to treatment. When SMR is investigated by study group, the excess mortality stays higher among men, except in the Alcohol group, where women have higher SMR.

Causes of death

Drug and alcohol related death is most common in the group as a whole (Table 3), 19 respective 9% in total if only underlying causes are accounted for (column A) and 39 respective 31% if both underlying and contributing causes are considered (column B). Thus, there is quite a large increase in the proportion of deaths related to drug and alcohol when contributing causes of deaths are considered.

Drug related death is most common in the Opiates group, where 44% of death causes are drug related when *only* the underlying cause of death is taken into consideration compared to 61% when contributing causes of death are also considered. In the other study groups, the proportion of drug related deaths are two to three times as high when contributing causes of death are considered (29–38%) compared to underlying cause of death alone (11–14%). However, the biggest difference between only considering the underlying cause of death and also considering contributing causes of death is associated with alcohol related causes. The proportion increases by three to six times when contributing causes are also considered. Furthermore, the proportion of injuries increases three to four times when contributing causes are considered, and the proportion of deaths associated with suicide is doubled in the Alcohol group and the Other group.

Discussion

This article presents a 30-year follow-up study on a majority of substance misusers treated in residential care for drug problems in Sweden during 1982–1983, focusing on mortality rates and cause of death in the group.

Difficulties in comparing mortality rates between studies has been previously noted for reasons of variety among selected groups, time era, and geographical differences (Degenhardt et al., 2010). Additionally, great variation between studies on causes of death among substance misusers has been found (EMCDDA 2011). Thus, the results will be discussed mainly in relation to Scandinavian studies that are considered to be the most relevant comparison.

Mortality rates

High mortality rates among substance misusers are found in several national as well as international studies (Bauer et al., 2008; Hser et al., 2001; Oppenheimer et al., 1994) and are also confirmed in this study. However, this study covers the majority of the clients treated for substance misuse in Sweden during recent years and contributes with a comparison of SMR between groups with differing main misuse, including alcohol misuse, which is seldom singled out in mortality studies on substance misuse. Additionally, few studies have previously investigated cannabis misuse and mortality.

The highest standardized mortality rate in this study occurs in the Opiate group, which is in line with several earlier studies comparing opiates and stimulants misusers (Adamsson Wahren et al., 1997; Bartu et al., 2004). An exception is a Swedish study by Stenbacka et al. (2010) showing similar SRR when comparing opiate misusers with amphetamine misusers. However, Stenbacka et al. note that their sample might include less severe addicts, as it is not collected from treatment facilities. Further, SRR is a less stable measure than SMR for small data materials, which might impact on Stenbacka et al.'s results.

A longitudinal Swedish study that in parts covers the same timespan but only part of the geographical area as this study, reports that when substances were detected post mortem in a 36-year follow-up, approximately 50% of those who had died did so from the same substance they misused at the first admission (Nyhlén et al., 2011). However, amphetamine use seldom causes drug related death but rather as a result of lifestyle (Degenhardt et al., 2009; Ericsson, Bradvik, & Håkansson, 2014). Thus, the high extent of drug related deaths in the group that reported stimulants as their most dominant substance misuse in this study implies that this group continued using other drugs.

The remarkably higher mortality rate in the Cannabis group compared with earlier studies on cannabis use and mortality also implies that the Cannabis group continued using other drugs, as previous studies state that cannabis is not associated with increased premature mortality (Nyhlén et al., 2011). A study of Swedish conscripts (Andréasson & Allebeck, 1990) reported three times higher risk of death for high consumers of cannabis compared with nonusers. In their study, the main cause of death was violent or accidental, including high levels of suicide and uncertain suicide, which in turn included overdose. In this study, these cases would in part be coded as drug related deaths. It is likely that the lower mortality rate in Andréasson's and Allebeck's study compared with our study refers to differences in the subjects. The fact that our subjects were all in treatment suggest that

their misuse was more severe than for the conscripts in Andréasson's and Allebeck's study, although they were also considered as having high levels of consumption (used cannabis >50 times). In another Swedish study where two cohorts of subgroups of patients diagnosed with substance misuse were followed, the SMR for the cannabis group was also lower than in our study (5.3 and 7.4, the differences between the two cohorts explained by age differences) (Adamsson Wahren et al., 1997). A Danish 5-year follow-up on individuals in treatment for illicit substance use reported an SMR of 4.9 for cannabis users (Arendt, Munk-Jørgensen, Sher, & Jensen, 2011; Arendt, Munk-Jørgensen, Sher, & Wallenstein Jensen, 2013). As Figure 1 implies, the length of the follow-up period affects the mortality rates, which complicates comparison between studies with differing follow-up periods.

Alcohol consumption is identified as a globally important attribute for mortality and disease (e.g., Rehm et al., 2009), and it is worth noting that the group with alcohol as self-reported most dominant substance misuse came up with the second highest standardized mortality rate in this study. Alcohol related death is also the most common cause of death in this study group, which is not the case in the other groups, suggesting that the Alcohol group, with a higher mortality rate than both the Cannabis and the Stimulants group, continued with alcohol as their dominant misuse. A follow-up study on mortality among Norwegian drug misusers after seeking treatment revealed that reported alcohol misuse before intake to treatment in the sample was a significant predictor of death (Ravndal et al., 2015). Further, in the follow up by Stenbacka et al. (2010), higher standardized mortality rates were found among those with both alcohol and drug misuse compared to those with drug misuse (opiates and/or central stimulants or cannabis). Additionally, the high CDR in the Alcohol group is in line with a previous Swedish study, where high mortality risks were found both among alcohol and drug users (Storbjörk & Ullman, 2012), implying the importance of including alcohol consumption in studies on mortality among drug users.

The majority of the clients in this study stating alcohol as their self-reported most dominant substance misuse were also using other substances. Further because the follow-up time in this study is relatively long, 30 years, many lifetime factors are involved during this time span, thus muddling the possibilities to interpret the connection between most dominant substance misuse at the base interview and cause of death. However, the results in this study indicate that alcohol misuse among drug misusers could play a significant role for mortality and should be further investigated.

The differences in SMR among males and females in the study is consistent with one Swedish study (Stenbacka et al., 2010) but not with another (Nyhlén et al., 2011). Earlier research on gender differences do not show a consistent picture. Thus, Nyhlén et al. (2011) suggest that when differences in gender appear, this might reflect subgroup differences rather than general gender differences.

Cause of death

For almost 56% of the deceased individuals, the cause of death was drug related and/or alcohol related. This is in line with the result from Stenbacka et al. (2010), where nearly half of the cases had either alcohol or drug dependence or misuse as contributory or main cause of death, although in their study alcohol composed the larger part, whereas drug related death was the most common in this study. It is also consistent with the study by Nyhlén et al. (2011), who found that drug-related death was the primary cause of death in 59% of the cases. When focusing only on underlying causes of death we end up with lower levels, however, it is unclear to what extent this is due to differences regarding sources of data.

When cause of death is investigated in this study, two principals are used (underlying and underlying together with contributing causes of death). When these principals are compared, differences are most apparent regarding alcohol related death, which is much lower if contributing causes are excluded. These differences illustrate the shortcomings with each principal. If only underlying causes of death are used, alcohol and/or drug related deaths might be underestimated. On the other hand, when underlying causes are accounted for, there is a risk of overestimating the number of drug or alcohol related mortality, as it might include cases where it is possible that the patient would have survived with the existing misuse if the contributing cause had not occurred. The difficulties of measuring and interpreting drug related cause of death are discussed in a report published by the Swedish National Board of Health and Welfare (NBHW) (National Board of Health and Welfare 2016). In this report, NBHW concludes that even though an actual increase cannot be ruled out, the reported increase of drug related deaths in Sweden since 2006 is mainly explained by methodological changes in the registration of drug related deaths. During the time span of the increase, the construction of the measurement of drug related death has changed and accuracy of death certificates has improved. Additionally, the authority in charge of analyzing the majority of drug related deaths has introduced new methods of analysis. The difference between drug related death and drug misuse related death is also important to note. Drug related deaths in the official National Cause of Death Register include, for example, suicide through an overdose of a

substance by individuals with no earlier drug misuse. Thus, it is a lot more delicate to measure drug misuse related deaths through the official death register (National Board of Health and Welfare 2016).

In total, 20 individuals in the sample died from AIDS, twelve of whom reported opiates as their most dominant substance misuse. This incidence of AIDS as a cause of death is low but higher than in the earlier referred to Swedish studies; Stenbacka et al. (2010) with a follow-up time of 37 years found no deaths from AIDS, and Nyhlén et al. (2011) found only three cases during a 36-year follow-up time. Suggested explanations for the low number of AIDS victims as a cause of death is the low prevalence in Sweden (Nyhlén et al., 2011) and the fact that patients with HIV/AIDS were given priority in methadone maintenance programs at the time (Fugelstad, Stenbacka, Leifman, Nylander, & Thiblin, 2006; Stenbacka et al., 2010). Further, the higher incidence in this study might be due to the earlier start date for the previous studies, 1967 versus 1970, which means that these cohorts were of a high age when the HIV/AIDS infection was peaking among Swedish substance users (Fugelstad et al., 2006). A Swedish study on cause of death among patients admitted to methadone treatment notes that 46% of the subjects died of HIV/AIDS related diagnoses (Davstad et al., 2009). According to Fugelstad et al. (2006), half of the participants in methadone programs in Sweden in 1988–89 were infected with HIV. In the year 2000, HIV infected subjects were down to less than 20%. Thus, it seems that HIV/AIDS will not continue to be a significant cause of death among drug users.

Conclusions

Alcohol misuse is included in the study, which is unusual in studies on substance misuse and mortality. The higher mortality rate in the Alcohol group compared with both the Cannabis and the Stimulants group might imply that alcohol misuse among substance misusers has a negative impact on mortality rates.

It is noted that methodological changes in how drug related deaths are registered has occurred during the measurement period, which affects interpretation of the statistics of cause of death. Thus, further and more thorough analysis is needed to investigate the relation between drug related cause of death and drug misuse related death in the data set. This distinction is needed for further conclusions in a prevention perspective.

Conflicts of interest

The authors report no conflicts of interest.

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