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Mortality among drug users after discharge from inpatient treatment: An 8-year prospective study

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ABSTRACT

Background: Drug users who are leaving/completing inpatient medication-free treatment may, like drug users released from prison, have an elevated risk of dying from fatal overdoses. This is mainly explained by their low drug tolerance.
Methods: Two hundred and seventy-six drug users who had been admitted to 11 inpatient facilities in Norway, were followed prospectively after discharge from treatment during an 8-year period (1998–2006). The following instruments were used: EuropASI, SCL-25 and MCMI II. Information on deaths and causes of death were obtained from the National Death Register.
Results: A total of 36 deaths were registered after discharge from treatment during the observation period, of which 24 were classified as overdose deaths. During the first 4 weeks after discharge six persons died, yielding an unadjusted excess mortality of 15.7 (rate ratio) in this period (CI 5.3–38.3). All were dropouts and all deaths were classified as opiate overdoses. There was no significant association between time in index treatment and mortality after discharge, nor did any background characteristics correlate significantly with elevated mortality shortly after discharge.
Conclusions: The elevated risk of dying from overdose within the first 4 weeks of leaving medication-free inpatient treatment is so dramatic that preventive measures should be taken. More studies from similar inpatient programmes are needed in order to obtain systematic knowledge about determinants of overdose deaths shortly after leaving treatment, and possible preventive measures.

1. Introduction

It is well documented that there is a high mortality rate among drug users, and that death by overdose is common cause of death in that group (Clausen et al., 2008; Darke et al., 2007; Davoli et al., 2007; Bargagli et al., 2006; Johnson et al., 2005; Gossop et al., 2002). Actually, deaths from opiate overdose comprise the vast majority of all drug-related deaths (Strang et al., 2008; Darke and Zador, 1996). One situation of the utmost importance in relation to overdose deaths, and where the prevalence of overdoses seems to be especially high, is in the period of time immediately after release from prison. Numerous studies from different countries and cultures show that drug users who leave prison and start using drugs again within 2–4 weeks after release, have a significantly higher mortality from primarily overdoses than the rest of the drug use population (Darke, 2007; Farell and Marsden, 2007; Ødegård et al., 2009). This is mainly explained by a reduction in their drug tolerance.

Substitution treatment for opiate users is now common in most western countries, but medication-free inpatient treatment (MFIT) and therapeutic communities (TCs) are also common alternatives in the same countries. TC is a well-established treatment modality internationally, aiming at abstinence and full rehabilitation (Broekaert et al., 1999). One main characteristic of the programmes is that they are long-term, i.e. they usually last for 1–2 years. Dropout rates have always been high (60–70%) in most of these programmes (Broekaert et al., 1999; Ravndal et al., 2005). One may therefore assume that clients who are dropouts and relapse shortly after leaving treatment may, like drug users released from prison, have a greater risk of taking fatal overdoses. However, even those who complete treatment are in much the same situation due to reduced tolerance. A 1 year follow-up study investigated opiate clients receiving detoxification as part of a 28 day inpatient treatment programme. The main finding showed a clustering of deaths from overdose in the group of patients characterized by loss of tolerance, who had successfully completed treatment (Strang et al., 2003). Most treatment studies show that the longer clients stay in

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treatment, the better the outcome (Simpson et al., 1997; Hser et al., 1988). There is therefore reason to believe that the longer clients stay in treatment, the lower the chances of relapse and death by overdose.

Some studies mention that dropping out of both MFIT/TCs and substitution treatment is a commonly observed antecedent of fatal opioid overdose. However, these studies have not analysed the length of time elapsed between leaving treatment and death (Quaglio et al., 2001; Preti et al., 2002). Except for one study by Davoli et al. (2007), hardly any research on MFIT/TCs has looked into this phenomenon. Davoli et al. (2007) show that retention in both in- and outpatient treatment for opiate users helps to protect against overdose mortality. They also demonstrate that the hazard ratio of overdose death was 26.6 during the month immediately following treatment, as against 7.3 in the subsequent period.

Norway is one of the countries in Europe with the highest overdose-related mortality rate. From 1991 to 2001, there was a steady increase in overdose and unnatural deaths among drug users in Norway (Rusmidler i Norge/Alcohol and Drugs in Norway, 2008). The peak year was in 2001 with 405 registered deaths, followed by a drop in 2003 (255 deaths) and a stable situation until 2006 (251 deaths).[1] Substitution treatment, which was introduced nationally under rather strict rules in Norway in 1998, and other measures to establish low thresholds do not seem to have reduced mortality sufficiently. Effective, new prevention strategies for reducing overdose deaths should be based on studies that investigate special settings and/or periods of time featuring a particularly high risk of mortality.

We wanted to study whether the elevated mortality risk following release from prison also occurs when drug users leave MFIT/TCs. A prospective study was conducted on 276 drug users who had been admitted to 11 MFIT/TCs in Norway, with a mean observation period of 8 years. Our main questions for investigation were:

(1) What was the mortality rate during the 8-year period following discharge from MFIT/TC?
(2) Was there an increased risk of overdose death/unnatural death shortly after leaving treatment?
(3) What were the main causes of death?
(4) Do the length of time spent in index treatment or the dropout rate correlates with the risk of overdose death/unnatural death?
(5) Are client characteristics associated with increased risk of death by overdose?

2. Materials

The study is a prospective, naturalistic study of 300 subjects who consecutively entered 11 MFIT/TCs in Oslo and surrounding counties between January 1998 and August 1999. None of the treatment programmes were administered through a prison setting. Participation in the study was voluntary. Twelve clients left treatment before the interview took place, and 12 were unwilling to take part in the study. These clients did not differ significantly from the rest ($n = 276$) in terms of background characteristics. The modalities consist of two hierarchical (HTC) and nine democratic therapeutic communities (DTC). All modalities had abstinence and full rehabilitation as their primary goal and different forms of aftercare were included. While in treatment any use of drugs was not tolerated. However, no clients were forced to quit treatment involuntary because of drug use as long as they tried again to adhere to the treatment rules. Except for the two HTCs, and one DTC for women only that was based on the 12-step model (AA), treatment in the other facilities was based on no specific ideology or philosophy.

[1] The WHO ICD coding system versions 9 (code 304) and 10 (a combination of F, X and T codes were used in accordance with the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) standard protocol for unintentional death) defined these figures.

3. Methods

All clients were examined during the first 2 weeks of treatment. They were personally interviewed and rated using the European Addiction Severity Index (EuropASI) (Kokkevi and Hartgers, 1994). At the same time, they completed two self-report questionnaires: The Millon Clinical Multiaxial Inventory II (MCMI II) (Millon, 1987) and the Symptom Checklist 25 (SCL-25) (Derogatis et al., 1974).

3.1. The European Addiction Severity Index (EuropASI)

The EuropASI is a personal, structured interview that is designed for clinical as well as research purposes. It covers seven areas: medical status, employment and support status, drug and alcohol use, legal status, family history, family and social relationships and psychiatric status. The reliability and validity of EuropASI is well documented (Hodgins and El-Guebaly, 1992; Leonhard et al., 2000). Two people from the project group interviewed half the sample. Six staff members from different treatment facilities interviewed the other half. All interviewers were trained at an authorised EuropASI course before interviewing the clients.

3.2. The Symptom Checklist 25 (SCL-25)

The SCL-25 is a 25-point self-report inventory that assesses symptoms of depression and anxiety. The mean overall score is called the General Symptom Index (GSI), and it is used as a measure of a person's total symptoms the week prior to the interview. Clients with scores of 1.0 and above are considered 'cases'. The analyses used the depression and anxiety scales, as well as the GSI index.

3.3. The Millon Clinical Multiaxial Inventory II (MCMI II)

The MCMI II is a self-report instrument with 175 true/false items measuring 13 personality profiles and nine clinical syndromes according to the DSM-III-R system. Scores on the MCMI are reported as base rate (BR) scores that are transformed raw scores adjusted for gender differences. According to international practice, clients who score 85 or above are considered to have a personality disorder (PD). This study only used the personality profiles and the PD diagnosis in the analyses.

3.4. National Death Register

Information on deaths and causes of death (ICD coded) were obtained from the National Death Register kept by Statistics Norway. Inclusion of deaths in the 'overdose' category is based on ICD codes F11 and X42 with opioid use as the main cause of death.

3.5. Leaving treatment

Leaving treatment was defined as either voluntary dropout or completion of treatment. Dropout and completion of treatment were defined according to criteria set by the treatment staff in collaboration with the research group. The main criteria for successful completion of treatment were completion of all phases of the programme, full abstinence from substances and active involvement in some kind of psychosocial rehabilitation.

3.6. Definition of the time window

The only study we found that examines the risk of premature deaths shortly after leaving treatment used a 4-week window (Davoli et al., 2007). In the prison literature, the time window for a high risk of death varies between studies, ranging from 1 to 4 weeks or even longer (Ødegård et al., 2009). In this study, we chose a time window of the first 4 weeks after dropping out or completing treatment, in accordance with the study of Davoli et al. (2007).

3.7. Statistical analyses

The number of deaths divided by the number of 100 person-years at risk (mortality rate) is specified, with confidence intervals in parentheses. The excess risk immediately after discharge from treatment was estimated by looking at the crude rate ratio for the first 4-week period compared with the rest of the follow-up period. Proportional hazard (Cox) regression was used to analyse the correlation between time to death and factors hypothesised to be associated with the risk of death. The proportionality assumptions were tested. Then the crude rate ratio for the 4-week period compared with the rest of the follow-up period was adjusted using Mantel–Haenszel methodology (Clayton and Hills, 1998). The adjustment was carried out bivariately for factors assumed to affect mortality or showing significant effects in the Cox regression.

4. Results

4.1. Sample characteristics

Seventy percent of the sample was male and the mean age at intake to index treatment was 31 years (SD = 6.4; range: 17–49

Table 1
Deaths by time after discharge from inpatient treatment, risk per 100 person-years ($n = 36$).

Time after discharge	Deaths	Years at risk	Risk of death	CI (95%)
4 weeks	6	20.1	29.9	13.4–66.5
From 5 weeks to ½ year	2	113.8	1.7	0.4–7.0
From ½ year to 1 year	2	133.5	1.5	0.4–6.0
Second year	7	263.4	2.7	1.3–5.6
Third year	5	256.3	2.0	0.8–4.7
Fourth year	7	250.6	2.8	1.3–5.9
Fifth year	5	226.8	2.2	0.9–5.3
Sixth year or more	2	329.0	0.6	0.2–2.4
Total	36	1594.1	2.1	1.5–3.0

Table 3
Unadjusted effects of background and treatment variables on risk of death after discharge from inpatient treatment ($N = 276$).

	Hazard ratio	CI (95%)
Age (years)	0.99	0.94–1.05
Alcohol abuse >5 years (yes–no)	1.77	0.92–3.41
Use of heroin (yes–no)	2.31	0.71–7.55
Use of syringes (yes–no)	1.64	0.39–6.81
Overdoses (yes–no)	2.25	0.98–5.13
Suicide attempts (yes–no)	1.30	0.68–2.50
In prison >12 months (yes–no)	2.75	1.43–5.30
Treatment model (DTC vs. HTC)	1.07	0.54–2.11
Number of months in treatment	0.81	0.63–1.05
Dropout (yes–no)	1.54	0.75–3.13

years). During the last 30 days before intake to treatment, 73% had used heroin, 36% amphetamines, 54% benzodiazepines and 81% had used syringes. The mean number of self-reported overdoses before entering index treatment was 4.8 (SD = 10.9, range: 0–99), and 59% reported one or more suicide attempts. Forty-eight percent were cases on GSI as measured by SCL-25, and 75% had a personality disorder (MCMI). Fifty-nine percent had previously been in inpatient treatment one or more times, and 30% had been in prison for a total of more than 1 year.

Altogether males had spent significantly more time in prison than females (17.6 months vs. 4.3 months, $p < 0.000$). They also had significantly higher scores on the MCMI antisocial ($p < 0.01$), while females had significantly more suicide attempts ($p < 0.05$), had used significantly more benzodiazepines ($p < 0.05$) and had significantly higher scores on the MCMI histrionic ($p < 0.01$). There were no gender differences in the depression or anxiety scores as measured by SCL-25.

4.2. Time in treatment and dropping out

Mean time in index treatment for all clients was 54 weeks (SD = 46.2; range: 0–172 weeks). Forty-one percent completed the programme and 59% were dropouts. There were no significant gender differences in dropout from treatment.

4.3. Deceased clients and mortality

Of the 276 clients in the study, a total of 36 deaths were registered during the 8-year period after discharge from treatment. Only three of these were women. This represents a mortality rate of 2.1 (CI 1.5–3.0) per 100 person-years, 3.1 for males (CI 2.2–4.3) and 0.6 for females (CI 0.2–1.8) (Table 1).

During the first 4 weeks after discharge from MFIT/TC, six persons died (two women), yielding an unadjusted excess mortality (rate ratio) of 15.7 (CI 5.3–38.3) in this period. They were all dropouts. These six deaths occurred during the first 3 weeks and were classified as opiate overdoses. Altogether, there were 24 overdose deaths, 7 violent deaths (including traffic accidents), and 5 from causes unknown.

Among the 36 deceased persons, 29 (69%) had taken overdoses and 19 (53%) had been in prison longer than 1 year before index treatment. Altogether, 13 (36%) had been in TC and 23 (64%) in DTC. Of the 36 persons, 25 (69%) were dropouts. The only significant difference in mortality was for those who had stayed a total of more than 1 year in prison (4.2 per 100 person-years) (CI 2.7–6.6) compared with those who had shorter or no stays (1.5 per 100 person-years) (CI 0.9–2.4). As to psychopathology as measured by MCMI and SCL-25, there was no difference in mortality between the deceased and the other subjects.

The association between time in index treatment and mortality after discharge showed no significant pattern. It is of interest, however, that no deaths occurred among the 22 subjects who stayed in treatment continuously for more than 2 years (Table 2).

4.4. Unadjusted effects of client characteristics on death after discharge

Using Cox regression, very few of the client characteristics before entering MFIT/TC were associated with mortality upon discharge from treatment (Table 3). Having spent more than 12 months in prison altogether was the only significant predictor. Gender could not be included in the Cox regressions because of the small number (3) of deceased females (just one of the women died after the 4-week period), and the variable did not meet the assumption of proportional hazards.

4.5. Adjusted associations of client background and treatment variables with excess mortality during the 4-week period after discharge

We used the Mantel–Haenszel method to adjust for possible correlations of background and treatment variables with excess mortality during the first 4 weeks after discharge from treatment compared with the rest of the period after discharge. None of the variables, i.e. age, time in index treatment, time spent in prison, number of self-reported overdoses or alcohol abuse, had any significant association with excess mortality during the first 4 weeks after discharge from treatment.

5. Discussion

The main finding of the study was the significantly higher risk of dying from overdose during the first 4 weeks after leaving treatment, as compared with the rest of the 8-year observation period. This concurs with the study made by Davoli et al. (2007), which

Table 2
Deaths after discharge by time in inpatient treatment, risk per 100 person-years ($N = 276$, $n = 36$).

Time in treatment	Number of persons	Deaths	Years at risk after discharge	Risk of death	CI (95%)
Up to ½ year	169	25	1161.2	2.4	1.6–3.5
From ½ year to 1 year	31	5	176.6	2.8	1.2–6.8
From 1 year to 1½ year	20	3	97.2	3.1	1.0–9.6
From 1½ year to 2 years	34	3	157.4	1.9	0.6–5.9
More than 2 years	22	0	101.7	(0)	–

also used a 4-week window to assess the risk of excess mortality shortly after leaving treatment. The association between time in index treatment and mortality after discharge showed no significant pattern. No deaths, however, occurred among the 22 subjects who stayed in index treatment continuously for more than 2 years. There was no significant difference in risk of death for dropouts and completers.

Thirty-six drug users died during the 8-year observation period, representing a mortality rate of 2.1 per 100 person-years. Only three of the deceased were females. This harmonises with other studies, showing that males have a significantly higher risk of death (Darke et al., 2007; Gossop et al., 2002; Ødegård et al., 2007; Clausen et al., 2008).

There was no significant association between treatment length and risk of death after discharge from inpatient treatment. However, there was a tendency for people with longer stays to have a lower risk of death. This question is of great clinical importance and needs to be investigated further in studies based on larger samples.

There was no significant difference in mortality between dropouts and completers. This clearly indicates that successful completion of treatment at one point in time does not prevent subsequent relapse and possible death later on (Strang et al., 2003). However, all deaths in the 4-week period after discharge were among the dropouts. The lack of opiate tolerance, probably in combination with resignation caused by dropping out of treatment makes this situation very risky. Dropouts from inpatient treatment should therefore be a special target group for special interventions, which should be planned in advance.

No single characteristic was independently associated with elevated mortality shortly after discharge. However, there was a tendency for total time spent in prison before index treatment to be a predictor of death after discharge. One possible explanation may be that this group of males was more antisocial and prone to take risks, and both of these factors could lead to more crime and a more reckless lifestyle, including death by overdose. If this is the case, it is in line with another Norwegian study of drug users in treatment in which being a male, a case on the MCMI antisocial and having spent a long overall time in prison were all significant predictors of death 5 years later (Ravndal and Vaglum, 1998).

Our findings underline the need to introduce preventive measures among drug users leaving treatment in non-substitution programmes such as MFIT/TCs. As Darke (2007) underlines in a comment to the high risk of dying after release from prison: “If such high rates of death were occurring among young, ambulatory patients released from hospital there would be a scandal.”

However, there are not always easy solutions at hand. Successful preventive measures are not easy to implement in any population group. For a myriad of good reasons, the behaviour of heroin users is often quite difficult to change. A recent qualitative study of experiences with overdoses among Swedish heroin users is instructive. The participants were aware of many of the common risk factors for overdoses. In spite of this, most overdoses occurred as a result of conscious risk-taking behaviour. The search for the ‘ultimate rush’, as well as severe abstinence, anxiety and depression, feelings of indifference and dependency, and an unsafe, stressful environment were examples of factors that led to a decrease in considering risks (Richert and Svensson, 2008). The authors conclude that heroin overdoses cannot be fully understood simply by defining a variety of isolated factors. It is more important to better understand how heroin users understand and evaluate the risk they are taking, and what circumstances and which emotions and motives influence risk-taking that may lead to overdose.

Nonetheless, it is important for treatment providers and the healthcare authorities to seriously try to implement preventive strategies for clients in MFIT/TCs. As regards the drug users, different strategies are possible. First, it is important to ensure that clients in MFIT/TCs take part as early as in overdose prevention awareness programmes with particular emphasis on the nature of overdose risk in the event of leaving treatment prematurely. Studies show that drug users are an overlooked potential workforce, interested in and willing to attend preventive training courses and to apply such knowledge when necessary (Strang et al., 2008; Baca and Grant, 2007; Lagu et al., 2006).

Second, programmes to prevent fatal overdoses may be established and evaluated in the community, using resuscitation techniques as well as opioid antagonist medication such as naloxone (Strang et al., 2008; Piper et al., 2007; Galea et al., 2006). Since 1980s, naloxone has been available as an over-the-counter medication in Italy and distributed through low-threshold services in Berlin, Germany; Jersey, UK; and San Francisco, USA (Dettmer et al., 2001). Preliminary results indicate lifesaving events through peer administration of naloxone (Strang et al., 2008; Seal et al., 2005).

The above-mentioned research is still a young but promising field. Surely, a wide range of preventive strategies will have to be applied if overdose deaths are going to be reduced.

Preventive strategies must be planned and carried out in treatment and community settings alike, and in continuous cooperation between active users of heroin, clients in treatment, the families of heroin users, and healthcare and social service authorities. Only broad cooperation between all involved parties can help ensure that fewer heroin users, old and young alike, die from accidental or planned overdoses.

No final conclusions can be drawn concerning the lack of association between time in treatment and fatal overdose, or between client characteristics and premature death. There are some tendencies in the material, but the study needs to be repeated using a larger sample to be able to conclude whether these are just tendencies or can be stated as important findings. That being said, the strength of the study lies in the long observation time and the quality of the data.

6. Conclusion

In conclusion, the main finding of the study is the significantly higher risk of dying from overdose within the first 4 weeks of leaving medication-free inpatient treatment. This finding is in itself so dramatic that measures should be taken immediately to try to prevent this kind of overdose deaths. It strongly suggests a potential for structural intervention including, but not limited to, continuous surveillance and active use of various peers and networks. No particular client characteristics were associated with death after discharge, except that the majority was male. This may be due to our small study sample. Therefore more studies are needed from similar inpatient programmes in order to obtain more systematic knowledge about determinants of overdose deaths shortly after leaving treatment, and how preventive measures can best be implemented.

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Contributors

Edle Ravndal and Ellen Amundsen designed the study, executed the statistical analyses and wrote the manuscript. Edle Ravndal is the Principal Investigator of the study. Both authors have read and approved this final version of the manuscript.

Conflict of interest

There are no conflict of interest.

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