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Mortality in heroin-assisted treatment in Switzerland 1994–2000

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Abstract

Background: A major goal of heroin-assisted treatment in Switzerland has been to reduce the drug-related mortality of heroin users. Therefore, a continuous monitoring of deaths under treatment is essential.
Aims: To assess mortality of participants in heroin-assisted treatment in Switzerland over a 7-year period from 1994 to 2000, and to compare this mortality to the general population and to other populations of opioid users, as reported in the literature.
Method: Estimation of person years under heroin-assisted treatment from the complete case registry of heroin-assisted treatment in Switzerland. Estimation of standardized mortality ratios comparing the population in treatment to the Swiss population (standardized to the year 2000).
Results: Over the 7-year period, the crude death rate of patients in heroin-assisted treatment, and including one month after discharge from treatment, was 1% per year. The standardized mortality ratio for the entire observation period was 9.7 (95% C.I. 7.3–12.8), with females having higher standardized mortality ratios (SMR 17.2) than males (SMR 8.4). There was no clear time trend.
Conclusion: Mortality in heroin-assisted treatment was low compared to the mortality rate of Swiss opioid users 1990s (estimated to be between 2.5 and 3%). It was also low compared to mortality rates of opioid users in other maintenance treatments in other countries as reported in the literature. The SMR was also lower than that reported in the only meta-analysis in the literature: 13.2 (95% C.I. 12.3–14.1). The low mortality rate is all the more noteworthy as heroin-assisted treatment in Switzerland included only refractory opioid addicts with existing severe somatic and/or mental problems.
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Keywords: Heroin; Heroin-assisted treatment; Mortality; Switzerland

1. Introduction

The problems associated with illicit heroin use increased dramatically in Switzerland from the 1980s to the early 1990s. These problems were partially related to open drug scenes and public perception (Klingemann, 1996); and partly due to the spread of HIV and its associated costs (Zeltner, 1996). The reaction by public health authorities was to improve the situation of heroin addicts by implementing different measures, and integrating and combining these into successive national programs (Swiss Federal Health Office, 1991). The goats of these programs can be summarized into four broad categories (Cattaneo et al., 1993):

(1) Reduce the number of new drug consumers/addicts.
(2) Increase the number of addicts who become abstinent.
(3) Reduce opiate-associated health consequences and the social discrimination and stigmatization of consumers and/or addicts.

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(4) Protect society against drug-related harm and fight against drug-related organized crime.

Reducing drug-related mortality was a major part of the third category. This goal has been achieved, with drug-related overdose deaths dropping from a 3-year moving average of 390.3 deaths in 1994 to 194.3 deaths in 2001 (calculated from data given by the Swiss Federal Office of Police, 2004). The overall number of opioid dependent people in Switzerland during this time was assumed to be stable at 30,000 (Rehm, 1995).

The overall framework of drug policy in Switzerland has since been based on four pillars (Schweizer Bundesrat, 1992): repression, prevention, therapy, and risk reduction measures. Within this framework, heroin-assisted treatment evolved as one measure touching the pillars of both therapy and risk reduction. Heroin-assisted treatment has been geared towards patients who could not be reached or sufficiently treated with the traditional means of abstinence-oriented and methadone maintenance treatment (Uchtenhagen et al., 1999).

Heroin-assisted treatment has proven successful in improving physical and mental health, reducing criminal behaviour and illicit drug use, and facilitating social integration (Rehm et al., 2001). As a result, this treatment was reaffirmed on a non-experimental basis in the decree of March 8, 1999 (BAG, 2002). The following goals were formulated:

(1) Sustained therapeutic integration of opioid addicts.
(2) Improvement of physical and mental health.
(3) Improvement of social integration.
(4) Sustained abstinence of any illegal opioid consumption (decree on the medical prescription of heroin March 8, 1999).

Reduction of mortality is one of the indicators for goal 2, and was consequently installed in the monitoring system of heroin-assisted treatment established following the decree.

This paper will give an overview of mortality in the Swiss heroin-assisted treatment since its inception in 1994. Crude rates and causes of death will be presented as well as a comparison of the rates to standardized mortality rates in the general population (for SMR see Rothman and Greenland, 1998, pp. 234).

Before presenting the results, we will give a general overview of mortality in addicts of non-prescribed opioids (most of the results described had been based on heroin addicts but, especially for younger cohorts, other opioids have gained increased importance). The greatest risk for opioid dependent people is death from overdose or from health consequences due to the circumstances of consumption (Single et al., 1996). During the 1970s, before the HIV/AIDS epidemic, annual mortality rates for opioid dependent people documented in the USA, England, Scandinavia, Germany and Switzerland varied from 1.0 to 2.1% (see overview by Rehm, 1995). There are indications that mortality risks have since increased, at least in some jurisdictions. For instance, a five-fold increase in mortality rates from 1990 to 1998 was documented in Victoria, Australia (Gerostamoulos et al., 2001).

Specifically in Switzerland, for the 1990s, mortality rates for illegal drug users irrespective of treatment status were estimated to be 2.5–3% per year (Rehm, 1995; Estermann, 1996).

A range of variables influences mortality rates for opioid addicts: the methods used to assess these deaths (i.e., determining that it is the death of a drug user); estimation of the denominator (i.e., the number of opioid users in a given jurisdiction); prevalence rates of HIV and hepatitis infections; and dominant routes of administration. Additionally, the availability of emergency interventions and therapeutic services can also influence mortality rates. However, a detailed analysis of drug-related deaths for a very small group ($n = 28{,}1984$) in Zurich found no specific predictors (Voser, 1990).

The substitution of street heroin and other opioids by opioid agonists, in particular methadone, seems to meet the therapeutic objectives of reducing mortality risks. In the framework of comprehensive diagnostic and therapeutic programs, methadone maintenance treatment intends to minimize the risks of overdose, injection-related infections and suicide (Lepere et al., 2001; JAMA, 1998; BAG, 2002).

Studies have found evidence of reduced mortality rates during methadone maintenance treatment (Grönbladh et al., 1990; Caplehorn et al., 1996; Ward et al., 1999; Bell and Zador, 2000; Joseph et al., 2000). A review of studies in the USA concluded that the mortality risk (especially the risk of overdose) for those in methadone treatment is reduced by 70% compared to untreated addicts (Desmond and Maddux, 2000). Comparative cohort studies of dependent heroin users in methadone maintenance and out of treatment found an annual mortality rate of 2.2% in the HlV-seronegative users out of treatment group, and no cases of death in the HlV-seronegative methadone patients over 8 years. The fatalities in the HIV-seropositive persons were mostly due to infection (Fuglstad et al., 1997, 1998). A reduction of mortality was also documented in a methadone maintenance program where illegal substance use had been tolerated (Langendam et al., 2001).

Some Australian studies found an increased mortality risk in the initial phases of methadone maintenance which had been linked to dosing changes (Caplehorn, 1998; Caplehorn and Drummer, 1999; Bell and Zador, 2000; Zador and Sunjic, 2000). There is therefore reason to stress the importance of careful assessment and dosage when initiating methadone maintenance treatment.

After the onset of the HIV epidemic, infection-related death ranged high in the mortality figures regarding patients in methadone maintenance (Appel et al., 2000).

Another major contributing factor to mortality is the pharmaceutical interaction between methadone and other

psychoactive substances; the prevalence of such effects has increased over the years (Kohler et al., 1998). A systematic analysis of fatalities where postmortem examinations found traces of methadone also found evidence of other substances including alcohol; methadone alone was rarely found to be the main cause of death (Barrett et al., 1996). Fatalities in a clinic group of New York methadone patients aged 30 and up were mostly caused by a combination of different illegal substances and alcohol (Appel et al., 2000). Similar results were found in other New York methadone clinics (Kipnis et al., 2001). Other substances frequently identified in combined intoxications deaths are benzodiazepines (Sunjic and Zador, 1999; Oliver et al., 2001). Thus, finding traces of methadone during a postmortem examination cannot be interpreted as proof of a methadone-related death (Merrill and Garvey, 1996; Karch and Stephens, 2000).

Other agonists or partial agonists used in substitution treatment have been found to create a similar risk situation. Mortality rates for maintenance treatment using dihydrocodeine are comparable to rates found in methadone maintenance (MacLeod et al., 1998). Prescription of buprenorphine, a partial agonist, largely used in France and estimated to be safer than other agonists because of antagonist properties, has also led to fatal intoxications when used in combination with other substances, especially benzodiazepines and alcohol (Tracqui et al., 1998a,b; Reynaud et al., 1998a,b; Ibrahim et al., 2000). To what extent this is due to intravenous application remains unclear (Byrne, 2001).

While mortality risks are reduced during methadone maintenance treatment, they may increase again if the user stops treatment and resumes illegal opioid use. In fact, some studies have found evidence of increased mortality rates after being discharged from methadone programs (Grönbladh et al., 1990; Zanis and Woody, 1998; Magura and Rosenblum, 2001). In one study in New York, the risk of mortality was higher for female patients than for male patients (Appel et al., 2000). In another US study, the mortality rate during the first year after discharge was found to be 8.2%, compared to the annual rate of 1% during treatment Zanis and Woody, 1998). When patients were removed from the program, the ensuing mortality risks were especially high (Grönbladh et al., 1990). The route of administration is also an important factor: returning to injecting illegal heroin results in higher mortality compared to sniffing or smoking (Langendam et al., 2001).

In sum, users of non-prescribed opioids have an increased risk of mortality compared to the general population. In Switzerland, for the 1990s, the mortality risk was estimated to be between 2.5 and 3% per year for the combined population of opioid users in and outside of treatment. This number corresponds well to reported mortality rates in other jurisdictions in established market economies. Overall, the mortality risks of opioid users in treatment are lower than outside of treatment.

2. Methods

2.1. Setting

Heroin-assisted treatment had been initiated in Switzerland in 1994 and this contribution examines all cases of deaths during treatment from this time period until the end of 2000.

Heroin is prescribed for opioid addiction in specialized centres 7 days a week, and taken under direct observation with limits to dose increases (see Gschwend et al., 2004, for details on dosage). No take home doses are allowed. Patients attend daily and inject 2–3 times under medical supervision. Methadone can be co-prescribed, often in the evening sessions or for periods, when the patients plan to be away from the centre (e.g. for a weekend travel or vacation).

Given the high frequency of treatment interactions, the costs of heroin-assisted treatment in Switzerland is relatively high. In 1995, costs have been estimated at about 50 CHF per patient per day (corresponds to about 32 Euros), i.e., the yearly average costs of one patient are between 10,000 and 11,000 Euros (Frei et al., 2000). However, the same analysis revealed that the cost savings incurred by lower criminality, lower health care and housing costs, more than offset these costs, resulting in a net benefit of about 45 CHF (about 29 Euros).

2.2. Data sources and inclusion criteria

Two main sources were used to analyze death in heroin-assisted patients between 1994 and 2000. The first source was two doctoral dissertations (Gacond, 2004; Ryser, 1999). The second source was records monitoring the efforts of heroin-assisted treatment. As this article examined mortality in treatment, deaths were included that occurred during the entire time being in treatment, i.e., from admission to discharge, plus including a timeframe of 30 days post heroin-assisted treatment. The 30-day-time period after treatment was included to be sure, that these patients had indeed left treatment. For people, who left treatment against medical advice and without informing the staff, the formal discharge was set at the day when they last received medication. The 30-days-time period after treatment was also added to include deaths which might be treatment-related but occurred in close temporal proximity after discharge from treatment. Finally, the procedures and guidelines of heroin-assisted treatment in Switzerland at that time were defined in a way that the treatment agencies and the Federal Health Office had to be informed of all deaths within the 30-day period. It should be noted, that this definition including 30 days post treatment makes the comparison between rates of different treatment unfavourable for heroin-assisted treatment, as most other articles with reported death rates in treatment included only the time between admission and discharge.

This definition yielded a total of 49 deaths in more than 4600 person-years over the period between 1994 and 2000.

2.3. Definition of rates

Two mortality rates were calculated: crude rates, which denote the number of deaths per year, and the standardized mortality ratio, which compares the likelihood of dying in the cohort of opioid patients with the general population. For both kinds of rates, the denominator of the analyses had to be determined, i.e., person years in treatment. We undertook sex-specific analyses, based on the yearly records of heroin-assisted treatment from the monitoring projects funded by the Swiss Federal Health Office. Any patient who had received heroin-assisted treatment in a given year was included in the denominator based on his/her exact time at risk (in treatment as defined) during the respective year.

To calculate the standardized mortality ratio each annual cohort of heroin-assisted patients was divided by sex and age; 10-year age categories were used. Confidence intervals for SMRs were estimated assuming death to represent a Poisson distributed event (Rothman and Greenland, 1998). The comparator was the general population living in Switzerland as assessed by the Swiss Federal Office of Statistics (2004). Results were standardized to the year 2000.

2.4. Categories for causes of death

The following categories of death were used based on death certificates and coded according to ICD-10 (WHO, 1989):

- Infections
- Chronic disease
- Intentional injury
- Unintentional injury

For each death only one category was used. Ratings were undertaken by the two doctoral students and validated by the specific commission (Safety Assurance Group of the HegeBe) which was established to examine all deaths within heroin-assisted treatment.

3. Results

The number of patients in heroin-assisted treatment in Switzerland has increased between 1994 and 2000 (see Table 1). The increase was continuous with the exception of 1997 when there was an admission stop between the experimental prescription and the new decree. After 1998, treatment centres were allowed to admit new patients, and in 1999 and 2000, new centres were opened and others have been authorized to admit more patients. Overall, all admissions require the approval of the Swiss Federal Office of Public Health.

Table 2 gives an overview on the causes of death. The distribution of deaths reflects the causes of death cited in the literature: infections and injuries dominate.

Table 1
Annual number of patients receiving heroin-assisted treatment in Switzerland and person years under treatment between January 1, 1994 and December 31, 2000

Year	Number of treated patients			Person years under treatment		
	Total	Male	Female	Total	Male	Female
1994	377	243	134	137.2	87.7	49.5
1995	853	593	260	439.7	295.0	144.7
1996	995	700	295	782.3	547.1	235.2
1997	796	558	238	705.8	493.5	212.3
1998	956	684	272	715.3	508.6	206.7
1999	1109	807	302	886.8	645.3	241.5
2000	1195	887	308	956.0	700.0	256.0

A patient receiving a heroin dose at least during 1 day per year was counted prevalent for that year irrespective of his total time in treatment.

Table 2
Overview on causes of death for patients in heroin-assisted treatment

Cause of death	Number	Proportion (%)
AIDS or other outcomes associated to HIV	17	34.7
Other infections than HIV, liver cirrhosis	5	10.2
Cardiovascular disease	4	8.2
Cancer	2	4.1
Other chronic disease	4	8.2
Accidents	9	18.4
Thereof mixed intoxication and “overdose”	(5)	
Suicide	8	16.3
Thereof patients with HIV infection	(2)	
Total	49	100.0

The crude rates per person-years are given in the next Table (Table 3). Overall, these numbers are relatively low in comparison to the mortality rates of opioid users; including opioid users in treatment (see literature review above). There is no clear time trend, but the years 1998–2000 show lower mortality rates compared to the rates of the preceding years. At this point, it should be noted that the mean treatment cohort age has continuously increased between 1994 and 2000 (Gschwend et al., 2003) and therefore, increasing crude mortality rates would be expected.

Finally, Table 4 depicts the annual SMRs separated by sex. As expected, the mortality of patients in heroin-assisted treatment is much higher than the general population. Again, no

Table 3
Person years and mortality in heroin-assisted treatment between 1 January 1994 and 31 December 2000

Year	Person-years in treatment	Deaths[a]	Crude rate
1994	137.2	1 (0)	0.0073
1995	439.7	12 (2)	0.0273
1996	782.3	8 (1)	0.0102
1997	705.8	10 (2)	0.0142
1998	715.3	6 (4)	0.0084
1999	886.8	6 (2)	0.0068
2000	956.0	6 (2)	0.0063
1994–2000	4623.1	49 (13)	0.0106

[a] Death during treatment or within first month after discharge (numbers in parentheses refer to females).

Table 4
SMR of patients in heroin-assisted treatment between 1 January 1994 and 31 December 2000

Year	Male	C.I.		Female	C.I.		Both	C.I.	
		High	Low		High	Low		High	Low
1994	9.6	68.2	1.4	No deaths	n.a.	n.a.	7.9	55.7	1.1
1995	27.9	51.8	15.0	28.3	113.3	7.1	28.0	49.2	15.9
1996	10.4	21.8	5.0	8.1	57.6	1.1	10.0	20.1	5.0
1997	12.5	25.0	6.3	16.8	67.3	4.2	13.2	24.5	7.1
1998	3.0	11.8	0.7	32.8	87.3	12.3	7.5	16.7	3.4
1999	4.6	12.3	1.7	14.0	56.0	3.5	5.9	13.2	2.7
2000	4.1	11.0	1.5	12.8	51.2	3.2	5.3	11.8	2.4
1994–2000	8.4	11.6	6.0	17.2	29.6	10.0	9.7	12.8	7.3

Standardized to mortality rates of Swiss population aged 15–59 during year 2000 according to death statistics of Federal Office of Statistics; confidence intervals assuming Poisson distribution.

clear time trend can be seen in our data. However, it should be noted that the numbers of deaths are quite small resulting in large confidence intervals for SMRs (particularly for females).

4. Discussion

With a crude rate of 1.1%, mortality in heroin-assisted treatment was low compared to the mortality rate of Swiss opioid users in the1990s which was estimated to be between 2.5 and 3%. It was also low compared to mortality rates of opioid users in other maintenance treatments from different countries as reported in the literature (see above).

The SMR in heroin-assisted treatment in Switzerland between 1994 and 2000 (SMR: 9.7; C.I. 7.3–12.8) was also lower than the SMR reported in the only meta-analysis reported in the literature (English et al., 1995: SMR: 13.2; 95% C.I. 12.3–14.1). The low mortality rate is all the more noteworthy, as heroin-assisted treatment in Switzerland included only refractory opioid addicts with existing severe somatic and/or mental problems.

There is no clear time trend in mortality of heroin-assisted patients in Switzerland between 1994 and 2000. The highest rates were between 1995 and 1997, and since then, rates have been substantially lower. The high rates between 1995 and 1997 may be related to the admission policy in the early years of heroin-assisted treatment. This policy was driven by the admission of many HIV-infected users, some of whom were already infected with fullblown AIDS. Fifteen of the 30 deaths between 1995 and 1997 were attributed to HIV or AIDS. The majority of HIV/AIDS related deaths occurred in the first few years. Non-systematic assessment of cause of death for ex-patients in heroin-assisted treatments also shows that HIV/AIDS had its peak for this group between 1995 and 1997 (Ryser, 1999). The gender ratio among all deaths resulting from HIV/AIDS was 11 to 6 (males to females). Overall, HIV/AIDS was the most prevalent cause of death for patients in heroin-assisted treatment. It should be noted that for all of the deaths, the HIV infection occurred before the treatment admission, i.e., all patients were already infected at the time of the treatment examination. The drop after 1997 may also be connected with more effective therapies for HIV introduced in 1996.

The second most important cause of death was unintentional injury ($n = 9$ or 18%). The majority of deaths had some relation to the consumption of illicit drugs (five out of nine). The exact role of heroin intake in these cases is not clear, nor is the role of illicit heroin versus prescribed heroin. In general, drug-related deaths are ill defined and hard to distinguish (Raschke et al., 2000). The usual definition of "opioid-related overdose" entails a respiratory insufficiency following the consumption of opioids (Davidson et al., 2003). However, to determine this as the cause of death requires detailed biological analyses, which have not been routinely conducted. An expert evaluation of all cases by at least three renowned Swiss specialists ("Safety Assurance Group, subcommission on mortality")[1] came to the conclusion that, based on the available data, the prescribed heroin was not causally implicated in any of these deaths. For the most part, the time between the last intake of prescribed heroin and the occurrence of death was longer than 24 h.

The distinction between suicide and unintentional deaths is not always clear. To give but two real examples: a chronically paranoid person drowned while under the influence of alcohol in a lake with a water temperature of 16 °C. The patient had often spoken about suicide in the days before the incident. Another patient stole medication from an emergency room. Based on reports of another patient, the theft was undertaken with the intention of suicide. A mix of intoxicating substances caused the death in the hours following the theft (these stories are confusing and fragmented). Both cases could be classified as intentional or unintentional. The actual classification on the death certificate for the first case was suicide and for the second case, unintentional accident due to overdose from multiple intoxications. Other suicides were clearer; for example, a patient received help from a Swiss support organization aiding in the planning of suicides. Two of the suicides were undertaken by willingly taking a "hot shot", i.e., consciously injecting an amount which essentially guarantees overdose. Both these overdoses were completely

[1] Members between 1994–2000: W. Bar (chair), F., Gutzwiller, Th. Pasch.

unrelated to prescribed heroin. Finally, two individuals diagnosed with HIV/AIDS committed suicide and the illness was one of the reasons given for their suicide.

The overall mortality rates of patients in heroin-assisted treatment were low compared to mortality rates of other opioid users, both in and out of treatment. Even the liberal inclusion criteria of including the full treatment period plus 30 days post treatment did not change this fact. Overall, this result confirms the fact that heroin-assisted treatment is associated with considerable treatment success, even in comparison to methadone treatment (see Rehm et al., 2001; van den Brink et al., 2003).

With respect to the SMRs, three results are particularly interesting. First, even though heroin-assisted treatment can be labelled as an overall success, the mortality rates of patients are still markedly higher when compared to the general population. However, as indicated, the Swiss rates are substantially lower than rates for other opioid user populations reported in the literature (English et al., 1995; Frischer et al., 1997; Quaglio et al., 2001; Hickman et al., 2003). This is noteworthy as the Swiss trial intended to and succeeded in recruiting refractory opioid addicts with existing severe somatic and/or mental problems (Uchtenhagen et al., 1999). Finally, women displayed a higher standardized mortality rate compared to men, which is also consistent with the literature. This does not mean that opioid using women have higher mortality risks compared to men. In fact, the female crude rate (0.97) is even slightly lower than the respective rate for males (1.10), although this difference is not statistically significant. However, the mortality risk for women compared to men in the general population is lower, and thus the SMRs for women are higher.

Overall, the mortality for patients in heroin-assisted treatment in Switzerland is low in comparison to other treatment studies and opioid user cohorts. This corroborates other positive findings from the Swiss treatment trial and for high dose heroin-assisted treatment in general (Rehm et al., 2001; van den Brink et al., 2003).

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