

## The Swiss studies on heroin-assisted treatment : a summary

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With the increase of replacement therapies (especially methadone maintenance treatment), the number of patients who continued heroin injecting while being on methadone, increased as well, and the idea of providing those patients with the 'original drug' invited new experimentation with heroin prescribing. Research projects started 1994 in Switzerland, 1995 in the Netherlands, 2002 in Germany and Spain, 2005 in Canada. The UK started reconsidering the former practice and set up a similarly controlled and psychosocially assisted type of heroin prescribing as in continental Europe. In all these projects, the target population were heroin addicts for whom other treatments had failed previously.

The final design of the Swiss project, the first in this series, was a prospective observational cohort study. It allowed to test the feasibility, safety and effects of the treatment programme as a whole, but was not able to identify the role of Diamorphine for those effects, because the original design – a randomised controlled study of injectable heroin versus injectable methadone versus injectable morphine met major recruitment problems (due to heavy side effects in the methadone and morphine groups) and had to be discontinued.

In addition, it was advisable to look at the possible consequences of heroin-assisted treatment on the treatment system as a whole, and to enquire in the value of such an approach for reducing the opiate-related problems in the country and at what costs.

The cohort study included 1'035 out-patients with complete admission data, out of 1'151 admissions (difference due to incomplete data), and 16 in-patients in a prison-based unit. For criminological analysis, police record of 604 patients and criminal registers of 561 patients could be used and compared to self-report data for corroboration of those.

Additional sub-studies included

- a randomised controlled trial of heroin-assisted treatment versus any other treatment while staying on a waiting list for the heroin programme (Perneger et al 1998)
- a double blind randomised trial with cross-over design using injectable heroin versus injectable morphine (Hämmig 1997)
- a randomised trial testing injectable heroin versus injectable methadone and injectable morphine (Ladewig et al 1997)
- a study on injectable methadone (Uehlinger et al 1996)
- pharmacological studies : pharmacodynamics and –kinetics of diacetylmorphine including various application forms (injectable, smokable, inhalable, oral slow-release, suppositories) (Brenneisen et al 1997)
- toxicology of diacetylmorphine including side-effects (Hämmig 1997, Ladewig et al 1997, Schmied 1997, Uehlinger et al 1996)
- studies on the criminal involvement of patients in heroin-assisted treatment (Rabasa & Killias 1996, Killias et al 1999)
- economic study on costs and cost-benefit of heroin-assisted treatment (Rossier et al, Frei et al, in Gutzwiller & Steffen 2000).

*A sub-study with randomised design* with an experimental group (n=27) and a waiting-list control group (who received conventional treatment, mostly methadone maintenance, n=21) showed significant differences after 6 months in daily illicit heroin consumption, mental health, social functioning, illegal income and delinquency. There were no benefits in terms of somatic health, housing, work and use of other drugs. Unexpectedly, only 9 control subjects entered the heroin maintenance programme at follow-up (Perneger et al 1998).

The *cost-benefit study* calculated the costs per patient day on the basis of the total costs incurring during 12 months for the first patient cohort (entering treatment during 1994), and the benefits per patient day based on the tangible benefits resulting from the difference between costs during the last 12 months before entering and 12 months since entering the programme. Benefits were found to amount to the double of the treatment costs (Rossier et al, Frei et al, in Gutzwiller & Steffen 2000).

A special study on the *utilisation* of the heroin clinics and on the characteristics of all admissions and discharges between 1994 and 2001 (n=2'199) came to the following conclusions (Gschwend et al 2003):

- the number enrolled in heroin-assisted treatment increased almost constantly over the years
- 10% of patients entered the treatment more than once
- the average age of new admissions increased from 30 to 35 years, while the rate of female patients decreased from 33 to 25%
- patients remained in heroin-assisted treatment on average for 3.7 years (median 2.8 years)
- 1'233 patients were during these years discharged at least once (24% within the first 4 months, 46% remained between 4 months and 2 years, and 30% longer than 3 years). Early discharges decreased significantly over time.

The *long-term course* has been analysed on the basis of 6-year follow-up data, including the first cohort entering the programme between January 1994 and March 1995 (n=366). 80% were available for personal follow-up interviews, including those patients who had left the programme (54% of those still alive). The mean length of stay in treatment of those remaining in treatment was 6.1 years (SD 0.3 years) since admission, of those who had left the treatment 2.4 years (SD 1.8 years) (Güttinger et al 2003).

Main findings from follow-up studies :

All patients admitted to heroin-assisted treatment between January 1994 and December 2000 (n=2'166 cases, corresponding to 1'969 patients) were followed (Rehm et al 2001).

- By December 2000, a total of 1'071 patients was discharged, whereof 90 patients twice and 7 three times
- retention was found to be relatively high (86% for 3 months, 70% for 12 months, 50% for 2-5 years and 34% for 5 years and longer)
- 59% of discharged patients started another treatment after discharge (22% started drug-free treatment, 37% methadone maintenance)
- the proportion of those switching to drug-free treatment increased with the length of stay in a heroin-assisted programme (29% of discharges after 3 years)
- discharge due to lack of compliance happened in 15% of discharges, mostly during the first months after entering treatment.

A subgroup of patients admitted between January 1, 1994, and March 31, 1995 (n=237) was followed up by interview (Rehm et al 2001):

- the health status of patients improved rapidly during the first 6 months, with small further improvements at 12 and 18 months (severe somatic problems  $p<0.001$ , severe psychiatric problems  $p<0.0001$ , body mass index  $p<0.0001$ )
- the socio-economic status also improved significantly for the housing situation, reduction of unemployment and of illegal income (all  $p<0.0001$ )
- significant reduction in nearly daily consumption of illicit heroin and of cocaine (both  $p<0.0001$ ).

A reduction of delinquency during the first 6 months in treatment could be seen from three data sets. Self-report data from a subgroup of patients entering heroin assisted treatment after April 1, 1995, of which the first follow-up interviews 6 months after entry could be achieved until May 31, 1996, were analysed in regard to involvement in criminal activities (n=248, Rabasa & Killias 1996). They showed significant reductions in thefts, robbery, burglary and drug trafficking within the first 6 months after entering treatment (all  $p < 0.0001$ ). An analysis of police records (n=604) showed also a significant reduction in incidence rates for robbery during the first 6 months after treatment entry (from 1.92 to 0.16, and victimisation rates for robbery during the first 6 months in treatment were reduced from 0.273 to 0.086 (Killias et al 1999).

The complete cohort entering heroin-assisted treatment between January 1, 1994, and March 1, 1995 (n=366) was followed up for 6 years (Güttinger et al 2003, Gschwend et al 2003). Those still on the programme were compared with those who had been discharged. Daily use of non-prescribed heroin, of cocaine and of benzodiazepines had decreased significantly in both groups; however, the rate of daily illicit heroin use at follow-up was lower in the treatment group than in the out-of-treatment group (3.8% versus 18.9%). The socio-economic status showed a significant reduction since entry to treatment for illegal incomes in both groups, and a significant increase in dependence on welfare and other sources in the treatment group, not in the group out-of-treatment

An analysis of mortality in heroin-assisted treatment over a 7-year period 1994-2000 included all fatalities during treatment and during one month after discharge (n=49) during more than 4'600 person-years. The crude death rate per year varies from 0.0273 (1995) to 0.0063 (2000). The standard mortality rate between 1994 and 2000 is 9.7 (95% CI 7.3-12.8) which is comparatively low. Cause of death, according to death certificates and coded according to ICD-10, included : 34.7% HIV-related, 10.2% other infections, 8.2% cardiovascular diseases, 4.1% cancer, 8.2% other chronic diseases, 18.4% accidents, 16.3% suicide. Prescribed heroin was not causally implicated in any of these deaths (Rehm et al 2005).

Side-effects of prescribed diamorphine were documented routinely in the HeGeBe Monitor, and a special study focused on patients' complaints in a random sample of programme participants (n= 127 out of 1061). The most frequently named immediate symptoms after injection concerned : skin itching (66.9%), profuse sweating (64.2%), reddening of skin at injection site (62.8%); among the less frequent complaints were nausea (29.3%), headache (22.0%), vomiting (18.5%). During the last 7 days, potentially more serious symptoms are memory problems (45.6%), problems with urinating (37.1%), pain in the cardiac region (21.0%), numbness in arms or legs (20.7%), epileptic seizures (5.9%). 5.9% reported epileptic seizures during the last 12 months. Other factors may have contributed to these symptoms (Dürsteler-McFarland et al 2005).

Two problems became obvious during the years : the high rate of *psychiatric comorbidity*, asking for an improved assessment and care for these patients, and a group unable to reduce their *cocaine use* during heroin-assisted treatment.

Screening of consecutive new admissions to 17 clinics with the SKID (n=85) showed a rate of 86% with a lifetime prevalence of at least one axis-I or axis-II disorder (personality disorders 58%, affective disorders 55%, anxiety disorders 26%, Frei & Rehm 2002a). This demonstrated higher comorbidity rates in comparison to a meta-analysis of 16 studies on the prevalence of co-occurring psychiatric disorders in opiate dependent persons (n=3'754, 78% lifetime prevalence of at least one disorder; personality disorders in 42%, affective disorders in 31% and anxiety disorders in 8%, Frei & Rehm 2002b).

In view of the cocaine problem, a review of the international literature on treatment approaches for cocaine dependence was made available on internet (Stohler et al 2006). Also, a randomised controlled study (Methylphenidate versus placebo, with or without

cognitive behavioural therapy in both groups, in addition to regular psychosocial care) was carried out which could not find outcome differences between methylphenidate and placebo, nor between CBT and regular psychosocial care (Dürsteler-McFarland et al 2006).

Studies on *treatment quality* included a detailed comparison of results from the 23 clinics, and also studies on patient satisfaction and quality of life.

The outcome of all new admissions from 1.1.2001 to 29.2.2004 (n=948) were compared in regard to type of treatment termination (favourable versus unwanted). The findings showed that treatment centres showed remarkable differences in the ratio of unwanted terminations, mainly due to diverse therapeutic strategies. The outcomes were similar to those in the original cohort study of 1994-1996; no diminution of positive findings when moving from the original scientific study to routine practice could be observed (Frick et al 2006a).

A study on patient satisfaction compared the subjective opinions of patients on injectable heroin with patients on oral heroin (immediate release and slow release tablets), using a list of 42 items on service, staff, therapeutic programme, and on satisfaction with results in the various health, social, substance use domains (all patients on injectable diamorphine of 2003, n=1'200; and all patients on oral diamorphine in 2004-05, n=365). The findings show on average a good satisfaction, with the exception of a wish for a more personal care, and dissatisfaction with bureaucracy, job opportunities and sex life. There were only marginal differences between application groups, except slightly better satisfaction with the oral preparations, and the satisfaction profile was stable over time (almost identical at entry, at 6 and 12 months, Frick et al 2006b).

As an instrument to observe the evolution of the programme after it became routine treatment, a double *monitoring system* was set up : a general one, documenting all new admissions and exits, and a specific one documenting dosages, drug combinations, all unexpected events including side-effects, with continuous reporting to an external safety assurance expert group.

References available from the author (<uchtenhagen.isgf.uzh.ch>).