

INSTITUT FÜR SUCHTFORSCHUNG [seal] INSTITUT FÜR SOZIAL- UND

IN VERBINDUNG MIT DER UNIVERSITÄT ---- PRÄVENTIVMEDIZIN DER UNIVERSITÄT
ZÜRICH

**PROGRAMME FOR A MEDICAL PRESCRIPTION
OF NARCOTICS**

FINAL REPORT OF THE RESEARCH REPRESENTATIVES

Ambros Uchtenhagen, Felix Gutzwiller and Anja Dobler-Mikola (Eds.)

SUMMARY OF THE SYNTHESIS REPORT

Ambros Uchtenhagen

Summary of the synthesis report

The Medical Prescription of Narcotics Programme (PROVE) was designed according to scientific tenets and criteria. A detailed research protocol was drawn up to govern the three year collection of data for analysis. It also describes the methods and times of the data collection as well as the rules governing data transfer and data protection. Data collection began on 1 January 1994 and ended on 31 December 1996.

The objectives of the study concern the effects of the prescribed narcotics: the effects on the health, social integration and dependent behaviour of the research participants; the suitability of this treatment for heroin dependents whose previous therapy had been unsuccessful; and the effectiveness of this treatment compared with that of other therapies currently available.

The general conditions for the conduct of the programme are described in the programme's research plan of 1 November 1993, based on the Swiss government decree of 21 October 1992. They set out the admission criteria for patients, the modalities of treatment and safety regulations. The admission criteria stipulated a minimum age of 20 years, a history of heroin dependency of at least 2 years, and participation in other treatments had to have failed on several occasions. An indication of the adverse affects of drug use on health and/or social relations also had to be present. The injections of prescribed narcotics had to be given under supervision and injectable narcotics could not be taken home. The treatment had to involve the provision of psychosocial care as well as the prescription of narcotics.

In accordance with the government decree, the narcotics to be tested in the programme were morphine, methadone and heroin for intravenous and oral use. In addition, use of the cigarette form of heroin was examined, and a pilot study was conducted based on the use of cocaine cigarettes.

The research issues which were to be analysed, therefore, span a wide range of topics relating to the pharmacology and toxicology of the prescribed substances; the participants' state of health lifestyle and dependent behaviour; the practicability of the study and its economic viability.

Research plan and organisation

A research plan governing the distribution of the different narcotics amongst the patients was drawn up to deal with these issues. Two double blind studies (the prescribed substance is not known to either the patient or the therapist), three randomised studies (treatment is allocated by randomisation) and eleven studies with individual indications (treatment is allocated after discussion with the patient) were set up. The feasibility of each was tested on three occasions in a methadone outpatient clinic and once in a penal institution. One treatment centre was allocated the prescription of intravenous and oral methadone only. On the basis of initial treatment findings, the original plan for the distribution of treatment places was modified; this, however, did not necessitate any amendments to the research protocol itself. A second series of additional treatment centres was approved in order to increase the scope of the research issues.

A total of 18 treatment centres were approved; one was in a penal institution, the others were all outpatient clinics. They were located in Basel, Berne, Biel, Fribourg, Geneva, Horgen, Lucerne, Olten, St Gallen, Solothurn, Thun, Wetzikon, Winterthur, Zug and Zurich. One application was withdrawn, one refused, and one approved treatment centre was not, in the event, set up.

In view of the large number of treatment centres involved and the range of research issues to be addressed, a clear organisation of the research, including uniform rules about powers and responsibilities as well as the flow of data, was needed. A particularly rigorous audit of the programme's research procedures was also required. An independent research team were mandated the tasks of devising the research protocol, data collection procedure and analysis, and the write-up of reports. Even before the start of the study, the programme's research protocol and research plan had been submitted to the supraregional Ethics Committee of the Swiss Academy of Medical Sciences for approval. Similarly each individual treatment centre had obtained the prior approval for its project from a regional or local ethics committee. The Federal Data Protection Officer checked that the relevant provisions were observed. In addition, a national specialist group was established to oversee and

assess the activities of the research team. An additional specialist group (the Safety Assurance Group) was responsible for checking and analysing in detail any side-effects of the prescribed substances.

PAGE 3

At the request of the INCB (International Narcotics Control Board), an international specialist group was appointed by the World Health Organisation to appraise the overall research programme and results.

Overview of research studies and data sources

This summary report incorporates the results of a series of studies mentioned below.

The main study was primarily focused on the participants and their characteristics on admission, during and on leaving treatment or on switching to another treatment programme. The information was derived from periodic interviews with the patients, conducted by specially trained interviewers. It also includes the daily treatment data on all prescribed narcotics (recorded electronically at the treatment centres). In addition, the main study examines the organisation of the treatment centres, narcotics dispensation, the professional background of the staff and the problems which arose during treatment. This information was obtained from periodic interviews with project managers.

Special medical studies examined trials carried out according to specific methodological designs (double-blind and randomised studies); side effects of the prescribed substances; pregnancies which occurred during treatment; deaths, the pharmacological properties of the heroin injected and the trial of non-injectable heroin products. The data were collected and analysed according to the terms outlined in the relevant research protocols.

Special social science studies considered the changes in criminal behaviour, the incidence of offences and of convictions. For this, information from police records and the central criminal register were extracted and compared with information obtained from the patient. Another special study examined the prison-based heroin-by-prescription project.

Special economic studies were commissioned to determine, firstly, the costs arising from treatment and, secondly, the economic benefit of treatment. Additional data were collected for these studies.

PAGE 4

Comparison of treatment results are based on systematically recorded reference data from abstinence-based in-patient treatment institutions in Switzerland and from methadone substitution treatments in the canton of Zurich. This has enabled a comparative analysis of the findings after at least one year's treatment. The randomised study in Geneva provides the additional data needed to compare the participants' treatment results with those from other treatment programmes. In addition, a comparative study is being carried out for patients who have recently entered selected methadone maintenance clinics.

Samples

The analysis of the overall programme is based on the data of the 1,146 patients admitted to the programme who effectively started treatment. For such cases where all admission data were recorded (n=1,035), 2 cohorts were formed (A admitted before the extension and 8 admitted after the extension of the study) in order to determine any differences between the two. By the end of 1996, 350 patients had dropped out of the study. Electronically recorded data on 403,402 treatment days were included in the analysis. The in-treatment study was based on the changes observed during 6, 12 and 18 months of treatment. The permanence of such changes, however, can only be ascertained after a longer period of time.

For the special studies, the analysis was based on data drawn from various samples, the size of which varied according to the characteristics of the study (e.g. according to the observation period and the prescribed substance). The smallest-sized samples were the pharmacological pilot studies (in accordance with their governing guidelines).

The summary of results below refers to the substance-related, patient related and projectrelated research issues.

Substance-related results

Recruitment of patients, retention rate (the duration of continuing participation) and compliance (adherence to the treatment instructions) were better with the prescription of injectable heroin than with that of injectable morphine and methadone.

PAGE 5

- Of the injectable narcotics used, morphine and methadone proved to be of limited use; heroin was also more suitable in therapeutic terms because of its fewer side-effects.
- There are as yet no apparent absolute contra-indications to the prescription of heroin; particular caution is necessary in cases of pre-existing epilepsy.

€ Heroin cigarettes are relatively ineffective (up to 90% of the heroin is destroyed) and may be replaced by other non-injectable forms (for example, slow-release tablets).

Patient-related results

This summarises the extent to which the designated target group of heroin dependents could effectively be reached, what changes occurred in their state of health during treatment, how illicit drug use and social integration among patients in the programme developed, and what changes were observed in criminal behaviour.

Target group

- The programme was able, to a greater extent than other treatments, to reach its designated target group: those with chronic heroin dependency, a history of failed attempts with other forms of treatment and marked deficiencies in terms of health and social integration.
- Those patients admitted to the project who had previously been following methadone substitution treatment had continued to use illicit heroin to a large extent during their methadone treatment.

Development of the state of health

- The improvements in physical health which occurred during treatment with heroin also proved to be stable over the course of one and a half years and in some cases continued to increase (in physical terms, this relates especially to general and nutritional status and injection-related skin diseases).

PAGE 6

- In the psychiatric area, depressive states in particular continued to regress, as well as anxiety states and delusional disorders.
- Pre-existing HIV infections were referred for suitable medical treatment in the majority of cases; the same applied to other clinically apparent infectious diseases.
- Three new HIV infections, 4 hepatitis B infections and 5 hepatitis C infections occurred during the study (in a total of 11 people). This was very probably related to cocaine injected outside the programme.
- The pregnancies and births which occurred during treatment were adequately supervised and progressed normally (with the exception of one spontaneous miscarriage during heroin withdrawal); there were no indications of developmental defects in the neonates.

Dependent behaviour

- Illicit heroin and cocaine use rapidly and markedly regressed, whereas benzodiazepine use decreased only slowly and alcohol and cannabis consumption hardly declined at all.
- In a minority of patients, the continued regular use of cocaine (5%) and benzodiazepines (9%) even after 18 months of treatment constituted a difficult therapeutic problem to manage.

Social integration

- The participants' housing situation rapidly improved and stabilised (in particular, there were no longer any homeless).
- Fitness for work improved considerably; those with permanent employment more than doubled (from 14% to 32%), and the number of unemployed fell by more than a half (from 44% to 20%); the remainder lived on benefits or irregular employment or were engaged in housework.
- Debts during the treatment period were constantly and substantially reduced.

PAGE 7

- A third of patients who, on admission, were dependent on welfare required no further support; on the other hand, others turned to welfare support (as a result of the loss of illicit income).
- Contact with drug dependents and the drug scene declined massively, but was not adequately replaced by new social contacts during the observation period.

Criminal activity

- Income from illegal and semi-legal activities decreased dramatically: 10% as opposed to 69% originally.
- Both the number of offenders and the number of criminal offences decreased by about 60% during the first six months of treatment (according to information obtained directly from the patients' and from police records).
- Court convictions also decreased significantly (according to the central criminal register).

Retention rate

In some cases, the improvement in the participants' health and social situation referred to above occurred soon after the beginning of treatment, but in others, not until after several months of treatment. The extent to which early discontinuation of treatment can be avoided therefore plays a major role. The retention rate in the study, 89% over a period of 6 months and 69% over a period of 18 months, proved to be above average compared with other treatment programmes for heroin dependents.

Drop outs

An analysis of the drop outs shows:

- More than half of the drop outs switched to another treatment.

PAGE 8

- By the end of 1996, a total of 83 people had decided to give up heroin and switch to abstinence therapy. The probability of this switch to abstinence therapy grows as the duration of individual treatment increases.
- The longer a patient remains in treatment, the more the rate of drop outs and exclusions from treatment decreases.
- Severe physical illness, particularly in conjunction with Aids, is over-represented among drop outs as it leads to hospitalisation.
- Improvements in the social situation which occurred in the course of treatment persisted for at least six months, whether or not follow-up treatment was administered.
- The use of illicit drugs increased somewhat after withdrawal but remained clearly below the initial level; the same applied to contacts with the drug scene and illicit income.
- Of the 1, 146 patients in the study, 36 had died by the end of 1996.
- 17 deaths are attributable to Aids and other infectious diseases., other causes of death include overdose of non prescribed narcotics, suicide and accidents. In the study itself there were no fatal overdoses.
- Despite a high toll on health, the annual mortality rate of 1% in the total cohort remains at the lower limit of what is known from other studies on treated heroin dependents (0.7 to 2.6% per year). The mortality of untreated patients is markedly higher.

Project-related results

As far as the organisation and operation of the treatment centres is concerned, the following remarks may be made:

Initially, the main problems lay in recruiting patients in some cases as well as in financing and in organisational problems in many.

PAGE 9

- The treatment centres in the second series, having benefited from the experience of the first series, had considerably fewer difficulties.
- No disturbance of note was caused to the local neighbourhoods, or if so only temporarily.
- Security problems (storage and control of narcotics, safeguarding against forced entries, etc.) were resolved satisfactorily.
- There remained a residual risk of overdosage among patients who were heavily consuming other drugs at the same time: the precautions which were taken helped prevent the occurrence of any fatal overdoses.

Heroin prescription in methadone outpatient clinics

In the eventuality of the possible continuation of heroin-assisted treatment, we examined to what extent this form of treatment could be given in the same institution providing methadone substitution treatment. The findings from three treatment centres showed that the accompanying problems could be overcome and that prescription-based heroin treatment is completely feasible in the context of polyvalent outpatient clinics.

Heroin prescription in prison

The pilot study of heroin prescription in a prison environment showed that this procedure required changes (in its operation and in the attitude of staff), but that the positive findings increasingly took precedence. Furthermore, it was noted that good collaboration with outpatient treatment centres could be readily established for the follow-up treatment of discharged inmates.

Costs and benefits

A detailed examination of the costs arising in the outpatient treatment centres showed average total costs per patient day of Fr. 51.--, compared with revenue of on average Fr. 35.-- per patient day (revenue includes contributions to costs by patients, and contributions from health insurance funds and the public purse).

PAGE 10

- The resultant deficits as a rule were borne by the public purse and exceptionally by private sponsors.
- The study of the overall economic evaluation of the programme in terms of a cost-benefit analysis according to detailed bases for assessment shows an overall economic benefit per patient day of Fr. 96.--- (the greater part relates to savings in criminal investigations and prison terms, followed by improvements in the state of health). After deduction of the costs mentioned, this yields a net economic benefit of Fr. 45.--- per patient day.

Conclusions

On the basis of these results, the report comes to the following conclusions and recommendations:

- Heroin-assisted treatment is useful for the designated target group and can be carried out with sufficient safety.
- As a result of above average retention rates, significant improvements can be obtained in terms of health and lifestyle and these persist even after the end of treatment of special interest is the striking decline of criminal activities.
- Such improvements are of great public interest too (prevention of dangerous infectious diseases, struggle against drug-related delinquency etc.).
- In view of the considerably impaired state of health of patients on admission to the programme, the mortality rate of 1% per year is relatively low.
- The economic benefit of heroin-assisted treatment is considerable, particularly due to the reduction in the costs of criminal procedures and imprisonment and in terms of disease treatment.
- These improvements were achieved subject to the prescription of heroin as part of a comprehensive programme of patient education and therapy.

PAGE 11

- The same can be said with regard to the general conditions governing the organisation and operation of the programme, the safety of participants and others can only be guaranteed by establishing appropriate supervisory measures

The continuation of heroin-assisted treatment can be recommended for the indications described in this research and as long as the general organisational and operational conditions set out in the research protocol are established

If the programme is continued, the unresolved questions and problems mentioned in the report should be further examined and elucidated through scientific research. The treatment itself should be appropriately monitored, documented and evaluated.

Final recommendation

It is apparent from these conclusions that a continuation of heroin assisted treatment can be recommended for the group targeted by this programme, provided that it is administered in suitably equipped and supervised outpatient clinics which meet the general conditions and criteria as described above.