A CRITICAL EVALUATION OF THE DUTCH HEROIN PROVISION EXPERIMENT

Paul H. Lemmens
Dept. Medical Sociology
University of Maastricht

ABSTRACT
In this paper, design and protocol is reviewed of the Dutch heroin experiment that has recently started. Several scientific, ethical and political aspects are considered. The Dutch heroin trial has been presented as a scientifically rigorous experiment, one that would leave little doubt as to the pure effects of the medical prescription of heroin. Choice of the design was therefore one of a regular randomized clinical trial. In the paper it is argued that this presentation as a purely medical experiment may be somewhat illusive, since it is not the effects of heroin which are tested but the effects of decriminalising the circumstances in which heroin is used. The point is raised whether the choice of the target population is a sensible one. It is feared that the sole inclusion of end-of-the-line patients (those with a long career of use and unsuccessful in other therapy) may limit the possible positive effects of such treatment. Since the size of research sample was a politically hot issue, a design alternative to the traditional randomized trial is considered which would require less subjects. Outcome criteria of the experiment seem vulnerable. Furthermore, it remains vague which potential courses are politically feasible after different possible outcomes of the experiment.

RESUMEN
En esta ponencia se revisa el diseño y el protocolo del experimento holandés sobre la heroína que ha comenzado recientemente. Varios aspectos científicos, éticos y políticos son considerados. El ensayo holandés sobre la heroína se ha presentado como un experimento rigurosamente científico, que dejaría pocas dudas acerca de los efectos de la prescripción médica de la heroína. En consecuencia la elección del diseño fue la de un ensayo clínico aleatorio habitual. En la ponencia se discute que esta presentación como un experimento puramente médico puede ser algo ilusa, ya que no son los efectos de la heroína los que se ponen a prueba sino los efectos de despenalizar las circunstancias en las que se usa la heroína. Se plantea la cuestión de si la elección de la población objetivo es adecuada. Se teme que la sola inclusión de pacientes terminales (aquellos con un gran historial de consumo y sin éxito en otra terapia) puede limitar los posibles efectos positivos de tal tratamiento. Ya que la magnitud de la muestra de investigación era un tema políticamente comprometedor, se considera un diseño alternativo al ensayo aleatorio tradicional que requeriría menos sujetos. Los criterios resultado del experimento parecen vulnerables. Más aún, sigue siendo una incógnita qué cursos potenciales de acción son políticamente viables tras diferentes posibles resultados del experimento.
HEROIN AS AN ANTIDOTE

It has been estimated that in 1863, 20 years after the discovery of the syringe, the percentage of morphine addicts in the USA was somewhere between 1 and 4% (Nyswander, 1956). If this percentage would be extrapolated to the current situation and population in the Netherlands, the country would be faced with more than 650,000 opiate addicts, a number about the same as the current estimates of alcohol abusers (De Zwart and Mensink, 1993). When comparing this with the factual 25,000 opiate addicts in the Netherlands, one is easily carried away by fantasies over the magnitude of the addiction problem in the USA at the turn of the century.

Not surprisingly, the US society responded to this with a large increase in treatment facilities, and many antidotes to morphine addiction were offered. One of these antidotes was heroin. Since at first it was thought that heroin was not addictive, heroin was substituted in many patent medicines. It took the society about 25 years, until 1910, to become aware of its large addictive potential, and it is not a revelation to us that therapies with heroin as a replacement for morphine were ineffective in repressing the “morphine epidemic”.

It is an interesting question as such why it has taken so long to discover the addictive properties of heroin. Snyder (Derks, 1990) suggests that it is typical of the “impact mental attitude and physical and social settings can have on whether an addictive drug is abused. Because heroin was introduced as a medicine to treat coughs, patients using it were not seeking or expecting psychoactive effects” (p.34). Additionally, people drank the cough medicine, preventing the rush or flash. Obviously, context, expectancies and motives, together with mode of admission are important conditions for the (negative) effects of heroin, and psychoactive substances in general.

Heroin as a medicine against morphine addiction was not a success at the turn of the century. Some decades later, exactly the opposite was proposed! In 1983 an experiment was started to treat heroin addicts with morphine (Derks, 1990). Because of the limited positive outcomes, the experiment was stopped in 1987. Recently, the Dutch Health council suggested a scientific experiment, a randomized controlled trial, to evaluate the effects of heroin provision treatment (Gezondheidsraad, 1995; Centrale Commissie Behandeling Heroinreverslaafden, 1997). One could easily become cynical: heroin against morphine, morphine against heroin, heroin as medicine against heroin abuse. Last year I was asked to take a look at the protocol of the heroin trial, as it has become known. This paper is a summary of that evaluation.

MAINTENANCE TREATMENT

Nyswander, (1956) describes the dramatic developments in New York City shortly after 1900, when, instigated by the federal authorities, over-the-counter sales of opiates were banned. Neither in state laws (Boylan Act), nor in federal laws (Harrison Act) were there provisions for treating the vast number of morphine addicts. Within two years from enactment, it became impossible for doctors to legally sell morphine to addicted users. Within a few years, addicts were converted into criminals, who had to provide themselves with morphine on a quickly establishing black market.

Maintenance treatment did not disappear immediately. Municipal clinics were founded which provided morphine to those already addicted. However, as Nyswander writes, the bad results of a single New York clinic eventually led to the termination of medically prescribed morphine in the US by 1924. Inexperience of the staff and ignorance were the main reasons for the failure of the New York clinic. Nevertheless, the closure of the clinics outside NYC was politically motivated. Other clinics were better organized, and Nyswander gives several examples. One example, the situation in New Orleans showed that the clinic had success in that no novel cases of morphine addiction were registered and that crime connected to morphine trade declined.

The goals of the morphine maintenance of the New Orleans clinic had similar goals as the current Dutch experiment: to relieve the patient from suffering, to curb trafficking, to prevent the “epidemic” from spreading, and to prevent criminal conduct of addicted users. Paradoxically, the American situation at the turn of the century can be seen as quite the opposite of the situation in the Netherlands: most of the addicted users led a normal life, were employed and had a family, few could be characterized as marginals. Crime connected to drugs was low. Within a few years, the predicament of the user changed drastically from an addicted patient to a criminal offender. (It remains a bit unclear, though, what has happened to all those hundred of thousands of morphine addicts. Musto, (1973) suggests that their number may have been overestimated.

The general aim of opiate maintenance programs is to stabilize and normalize the medical and social status of the dependent person. As was the case in the USA, the initiative for such programs lies with the local health services. The difference with the current Dutch situation is the support from the central government (Drug policy in the Netherlands, 1995). In Holland, resistance against the experiment does not come from federal IRS, FBI or BATF institutions as was the case in the USA (I am aware that some institutions had different names at the time or were not yet existent), but from the political right wing and christian
parties. Their critique is mostly morally based, but wrapped in arguments against the design. This has led to a pre-experiment with a fraction (N=50) of the initial 750. From the discussions surrounding this decision, I discern a tension raised by the awkward position the Netherlands occupy in the EU as regards drug policy. What if the outcome of the experiment is positive? Should Holland be the first nation within the EU to start the dispensation of “free” heroin nationwide?

A DUTCH RANDOMIZED CLINICAL TRIAL

This political delicacy (in the press: “gratuit” heroin) has been the reason for the rigorous RCT design of the Dutch heroin experiment, as if it was a regular medicinal drug (i.e. against coughs). The image in the press is one of a trial in which only the pharmacological effects are researched (NRC Handelsblad, 1997) Netherlands, 1995 Report Dutch Government). However, it is hard to sustain that one is investigating the pharmacological effects of heroin, or the effects of treatment with heroin. Rather than the effects of the drug (well known to the users, of course), the Dutch experiment is an evaluation of the de-criminalisation of the circumstances in which the drugs are administered. These circumstances are very specific, and consist of a controlled supply of a single dose, three times daily, and use under strict supervision. Another reason for a scientifically rigorous design is the negative evaluation of the scientific value of the Swiss experiment has received (Farrell and Hall, 1998).

Main aim is an improvement in a stable medical and psychological condition. Apart from individual benefits, the Dutch experiment is expected to result in a reduction of public disorder, drug crime and health risks. The experiment specifically targets the most difficult, toughest subgroup of heroin users: those causing most problems, and who are resistant to other forms of therapy. The restriction to this marginal group of heroin users has led to protests from (the users, of course), the Dutch experiment is an evaluation of the de-criminalisation of the circumstances in which the drugs are administered. These circumstances are very specific, and consist of a controlled supply of a single dose, three times daily, and use under strict supervision. Another reason for a scientifically rigorous design is the negative evaluation of the scientific value of the Swiss experiment has received (Farrell and Hall, 1998).

Main aim is an improvement in a stable medical and psychological condition. Apart from individual benefits, the Dutch experiment is expected to result in a reduction of public disorder, drug crime and health risks. The experiment specifically targets the most difficult, toughest subgroup of heroin users: those causing most problems, and who are resistant to other forms of therapy. The restriction to this marginal group of heroin users has led to protests from (the association of) heroin users, who claim that a large group of those who have managed to maintain a reasonable standard of living, are being “punished” for their efforts. Many of those who can be regarded relatively successful and stable users remain dependent on an illegal supply (and remain “at risk” for the downsides thereof).

The researchers apply a long list of inclusion and exclusion criteria. This makes size of the target population unclear. It is smaller, but how much smaller, than the initial 8000 so-called non-integrated and problematic users in the Netherlands, their prime target. One such criterion is the use of methadon of at least 60mg daily for at least one month. This dose is quite high. In Amsterdam only 60% of the methadon users had a daily dose of 60 mg for an entire week.

THERAPY-RESISTANT

Somewhat paradoxical is the condition that the subjects should be “methadon therapy resistant”, and without “psychosocial future perspectives”. As Dute and Bakker have noted (Dute and Bakker, 1995), this restriction excludes people who still have an outlook on a heroin-free existence. Exclusion of this group will bias the results of the experiment towards the null: it reduces the appraisal of the true potential of the treatment with people with a better prognosis. In the political evaluation of the experiment, detoxification and a drug-free state will be important issues for extension of the experiment to a larger group. Now there is a risk that the maintenance becomes limited to some sort of palliative care with only very limited chances of real progress in the patients. The recent Australian attempt, with a much wider target group of heroin users, and the subsequent flop in parliament shows, nevertheless, how difficult it is to find the right balance between political acceptability and scientific relevance.

Another essential weakness of the criterion of methadon-therapy resistance is the fact that the standard treatment in the control conditions (group II and III; see below), oral methadone, consists of a treatment that has already proven to be ineffective in this group of patients. For one third of the subjects in the RCT, this means that they have to wait for one year before they “progress” to the heroin condition. This may either cause many to drop out of the experiment, and those who remain may not answer to the criterion of being “therapy resistant”. One may also wonder whether a regular RCT should apply a standard treatment (i.e. oral methadone) that has never been formally evaluated.

The sample is randomly assigned to three conditions, each consisting of 250 subjects. Group I: 12 months of heroin + methadone; II: 6 months methadone + 6 months heroin + methadone; III: 12 months methadone treatment and 6 months heroin + methadone. The experimenters take into consideration an annual attrition rate of 6%, 14% and 20%, respectively. But experiences elsewhere report a usual drop-out rate of about 50% in natural (read: methadone) settings. For example, Hartnoll et al. (1980) report a loss of about 60%, part of which were abstinent. Once abstinent, one is probably not inclined to come back for a 6 months heroin treatment (II and III). (The results over the first few months indeed indicate a rather high drop-out rate).
RANDOMIZATION BEFORE OR AFTER INFORMED CONSENT

In designing the experiment, the researchers have chosen a traditional RCT, where randomization takes place after subjects have given their informed consent, over a design in which subjects are allocated to groups before they are informed about the experiment. In the latter case, only the heroin group would be informed and invited to participate. The advantages of the latter pre-randomization design are: (a) one avoids that people in the control group are aware of the fact that they will receive heroin after a certain period (it may affect their willingness to cooperate), (b) one avoids that addicts engage in a standard, control treatment which has been proven ineffective, and (c) a smaller group of people will receive the heroin treatment (a potential political delicacy). In this so-called Zelen design, the formal conditions are thus more realistic.

The advantages of a traditional randomization procedure are (a) the control group get a formal and uniform methadone treatment, and (b) one is able to get extensive baseline information. The choice for the latter has been the subject of a profound discussion in the Netherlands (Schellings, Kessels, Geurts, Sturmans 1995; Driessen and Smeets, 1995), a discussion which relevance extends beyond this specific heroin experiment (Schellings, Kessels, Riet ter, Sturmans forthcoming).

Disadvantages of the pre-randomized design are the problems with a baseline measurement, and uncertainty whether the two groups are completely comparable, since it is not known whether the control group would have engaged in a heroin experiment. This latter disadvantage is probably minimal, since the addicts prefer heroin over any other opiate (Farrell and Hall, 1998).

ENDPOINTS

A final point I would like to raise, concerns the endpoints, the evaluation criteria. Heroin provision is expected to result in an improvement in medical, social status, and a decrease in the use of illegal substances. The first will be assessed in a medical examination, the second mostly with the ASI-Europe instrument. A complex measure of change has been adopted, which would result in a classification of responders versus non-responders. Response is defined as a change of more than 20% in two out of the three target areas, given no deterioration of more than 10% in any other area, and no increase in use of other (illegal) substances. Combined, this responder/nonresponder evaluation is rather complex, and I have some doubts whether it is feasible to evaluate subjects in this respect (power of tests may easily become too low).

FINALLY

In summary, the Dutch heroin trial is designed to overcome the difficulties in interpretation that were encountered in other (read: Swiss) experiments. The presentation as a purely medical experiment may be somewhat misleading, however, since it is not the effects of heroin-as-such which are tested but the effects of decriminalising the circumstances in which heroin is used. Reasons for this presentation may lie in the politically sensitive nature of such an initiative. Political feasibility may also have inspired the restriction to extreme problematic heroin users, which leads to an inbuilt limitation of the potentially positive (and negative) effects of heroin provision on, for instance, abstinence, and also limiting generalization and assessment of a wider applicability to less extreme users.

It is not entirely clear which outcomes are crucial in the acceptance and continuation of heroin maintenance as part of the regular treatment in Holland. Politicians do not like to talk about hypothetical situations, and I am convinced that the outcome of the experiment is only one variable in the process of decision making. Following the political debate nationally and internationally, I think progress in this field, if possible, is made by taking small steps.

REFERENCES


Schellings R, Kessels AGH, Riet ter G, Sturmans F (forthcoming). The Zelen design may be the best choice for a heroin provision experiment. *Journal of Clinical Epidemiology.*