DRUG & ALCOHOL FINDINGS *Research analysis*

This entry is our analysis of a study added to the Effectiveness Bank. The original study was not published by Findings; click Title to order a copy. Free reprints may be available from the authors – click prepared e-mail. The summary conveys the findings and views expressed in the study. Below is a commentary from Drug and Alcohol Findings.

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▶ Outcome of long-term heroin-assisted treatment offered to chronic, treatment-resistant heroin addicts in the Netherlands.

Blanken P., Hendriks V.M., van Ree J.M. et al.

Addiction: 2010, 105(2), p. 300–308.

Unable to obtain a copy by clicking title? Try asking the author for a reprint by adapting this prepared e-mail or by writing to Dr Blanken at Peter.Blanken@Brijder.nl. You could also try this alternative source.

Unless there is a compelling medical or social contraindication, results of extended treatment in the Dutch heroin prescribing trials suggest treatment should be continued as long as possible for heroin-addicted patients who have been failed by methadone but benefit from being prescribed heroin.

SUMMARY The featured study documents the progress four years after they first started treatment of patients prescribed heroin in the Netherlands, focusing on those who, having done well, deteriorated when prescribing stopped at the end of the trials, and who as a result were offered resumed heroin prescribing.

Among several such trials in the UK and continental Europe, the Dutch trials of prescribing heroin to heroin addicts involved 549 patients treated in six cities between 1998 and 2001. All were long-term heroin users who used heroin daily or near daily and evidenced poor physical, mental, or social functioning, despite having been treated repeatedly with oral methadone at doses of at least 60mg (50mg for heroin smokers) and being currently enrolled in a methadone programme.

In separate studies for heroin injectors and smokers, patients were randomly allocated for six or 12 months to oral methadone only, versus to this plus a corresponding form of heroin (injected or smoked) consumed under supervision at a clinic three times a day. Doses were adjusted up to a maximum 1000mg heroin daily with a view to eliminating illicit heroin use. For the methadone-only group, oral methadone was prescribed daily up to 150mg. Patients who at the end of the trials were at least a 40% better in one of the areas where they had been doing badly at intake, without deterioration elsewhere, were considered to have responded well to treatment.

Key points

The featured study tracked for a further three years the progress of patients prescribed heroin (mostly in smokable form) as well as methadone in Dutch trials who responded well to the treatment and then deteriorated when it was stopped, leading to its reinstatement.

All the patients had previously not done well in methadone programmes; most were smoking heroin and were prescribed a corresponding form of the drug.

The analysis showed that most needed resumed heroin prescribing to regain and extend their initial improvements.

For the authors, the findings meant heroin prescribing should be continued as long as possible for treatment-resistant, heroin-addicted patients who benefit, unless there is a compelling medical or social contraindication.

Findings from elsewhere were seen as supporting this conclusion, justifying the extra cost and risk of heroin prescribing for the substantial minority of patients not attracted into or who do badly in optimised

programmes using orally administered drugs.

At the end of the trials, about half the patients allocated to heroin had responded well, 24% more than on oral methadone only. Improvements on heroin were evident across physical, mental, and social functioning but on methadone were much more limited.

Patients who had completed their initial six or 12 months on heroin were then transferred to oral methadone. Two months later over 80% who had responded well to heroin had seriously deteriorated, on average to their poor pre-treatment levels of functioning. These 149 patients – the subjects of the featured study – were offered reinstatement of heroin-assisted treatment. Nearly three quarters had been prescribed smokable heroin. They constituted just under half the 312 patients initially prescribed heroin.

Main findings

Two of the 149 did not resume heroin-based treatment and by the four-year follow-up, another 64 had left. Of these 66 patients, just 37 could be re-assessed by the researchers. In contrast, nearly all the patients still in treatment were re-assessed. The researchers tried several ways of accounting for patients who could not be reassessed, each leading to the same broad conclusions.

Few of the 44% of patients who either did not start or left their resumed heroin-assisted treatment did so on their own initiatives. Most were discharged because they were not sufficiently improving or had broken clinic rules, typically by trying to take heroin away from the centres. Leavers generally started methadone maintenance treatment; few opted for abstinence-orientated treatment. All but 9 of the 65 surviving (there was one death) leavers/non-starters were in some kind of addiction treatment (primarily substitute prescribing) at the four-year follow-up point.

According to the study's criterion of a 40% improvement in a domain where they were doing badly at intake, without deterioration elsewhere, at the four-year follow-up 68% of the 149 patients offered further heroin prescribing had responded well to resumed treatment. Whatever assumption was made about patients who could not be reassessed, patients who had remained in heroin-assisted treatment were significantly more likely to have responded well. For example, assuming non-assessed patients had continued as per their last assessments, 92% of retained patients were responding well but just 38% of those not retained in heroin-assisted treatment.

Further analysis was made of the progress of the 83 patients retained continuously in heroin-assisted treatment since resuming it after the end of the trials. After major improvements during the year of the trials, they made little further progress in physical, mental and social welfare. However, there were significant further reductions in non-prescribed heroin use and in cocaine use, and the proportion extensively and completely recovered in their health and social welfare and substance use doubled from 12% to 25%.

The authors' conclusions

Having responded well to heroin assisted treatment in the first six or 12 months, but deteriorated when it was withdrawn, 56% of patients stayed in resumed treatment for at least another three years. During this extended treatment, on average they regained and sustained their previous improvements, or made further improvements in avoiding illegal heroin and cocaine use and in achieving overall good health and functioning and normalised substance use patterns. Even though most entered alternative treatments, on these measures patients who left heroin-assisted treatment were much less likely to have done well than retained patients. However, there remained a group of chronically treatment-resistant heroin addicts who neither responded well to methadone maintenance nor to heroin-assisted treatment, or who did not sustain long-term heroin-assisted treatment.

These findings suggest that heroin co-prescription should be continued as long as possible for treatment-resistant, heroin-addicted patients who benefit from the treatment, unless there are compelling medical or social contraindications.

FINDINGS COMMENTARY For the first time the Dutch trials showed what can happen when heroin maintenance is withdrawn from patients who have not done well on methadone yet are forced to revert to methadone. Heroin doses were tapered and (almost always) oral methadone simultaneously increased, and a personal treatment plan was developed to help patients manage without prescribed heroin. Nevertheless, relapse was the norm. This further analysis shows that resumption of heroin prescribing generally meant that the previous improvements too were reinstated. This was especially the case among the 56% of patients retained (apart from the enforced interlude on methadone after six or 12 months) continuously in treatment for four years.

With other findings, this constitutes strong evidence that the treatment received at the heroin clinics caused the initial and resumed/sustained improvements. Whether it was the heroin itself cannot be established. Counselling and other therapies were made equally available to all the patients, but the new staff and facilities at the specially established heroin clinics (methadone was prescribed by existing services) may have had an impact. However, this is unlikely to have been a major factor.

The studies were designed to test the possibility that a period on heroin – albeit one arbitrarily set without regard to the progress of the individual patient – would stabilise and improve patients to the point that they could then manage well without heroin. Generally for these severely addicted and hard-to-treat patients, this was not the case, and extended treatment was required to sustain initial gains.

The studies also exemplified a methodology for determining who needs heroin to supplement methadone by assessing their response to heroin-assisted treatment and how this changes when methadone-only treatment is tried. About half the patients offered it because of non-response to more usual treatments proved to need legal heroin to make and sustain substantial improvements. More will have benefited but not substantially enough to meet the study's criterion, or might have in other respects been doing well but fell foul of clinic rules, primarily those intended to prevent prescribed heroin leaking out of the clinics.

Lessons of the Dutch heroin trials

The authors of the featured study also co-authored a history and appraisal of the lessons of the Dutch heroin trials, taking in the results of the featured study. They concluded that supervised co-prescription of heroin to treatment-resistant patients dependent on heroin is more effective and more cost-effective than – and just as safe as – continued treatment with methadone alone, and that the extensive beneficial effects are linked to the continuation of treatment, meaning this should be continued as long as possible unless there is a compelling medical or social contraindication. Patients benefited generally without major problems for staff and without the clinics being associated with public nuisance.

The same article described the results of a study testing whether the benefits seen in the tightly controlled randomised trials would be replicated in the routine implementation of heroin-assisted treatment (using protocols similar to those in the trials) which followed the positive outcomes of the trials. Given the similarity in patient selection criteria and in treatment methods, plus regular regulatory oversight, the conclusion was that heroin-assisted treatment was just as safe and effective as in the trials, and should be made available to a large but strictly defined patient population of chronic, poor-functioning heroin dependents who have not benefited sufficiently from other substitution treatments.

The conclusions were similar when the authors took in the data available from trials and heroin prescribing experience to date in the UK, the rest of Europe, and Canada. As they read the evidence, all the studies indicated that for patients with a history of treatment failures in methadone or other treatments for heroin dependence, prescribing heroin is feasible, effective, and generally safe, but requires close monitoring and quality control to avoid and respond to adverse

events such as overdoses. Its role, they thought, was likely to be that of an exceptional last resort for patients not attracted into or effectively treated by other available interventions, including state-of-the-art oral maintenance programmes featuring adequate doses and supervision and a comprehensive offer of psychosocial treatment and support.

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