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▶ Prescription of heroin for the management of heroin dependence: current status.

Lintzeris N. Request reprint

CNS Drugs: 2009, 23(6), p. 463–476.

Should heroin prescribing be a mass treatment entry route or a niche option for the few who have not done well in optimised (but still cheaper) mainstream treatments? With nearly all the latest studies to hand, this review came down firmly on the 'niche' side of the debate.

Abstract This review analyses studies of the prescribing of injectable or smokable heroin to heroin addicts on a maintenance basis (usually indefinite, at doses which substitute for the effects of illegal heroin, and without requiring dose reduction). Generally patients qualified for these trials because they had not done well in more conventional opiate substitute prescribing programmes based usually on oral methadone or sublingual (absorbed under the tongue) buprenorphine. The review extends an earlier review of English, Dutch and Swiss randomised trials by including later trials in Germany and Spain (making six randomised trials in all involving over 1600 patients) and by considering non-randomised studies in Britain and Switzerland.

Placing heroin prescribing in context, the author explains that managed withdrawal programmes alone rarely result in long-term benefits and risk post-withdrawal overdose. It is difficult to ensure that patients transfer to effective follow-on care such as residential rehabilitation, and these treatments can be very costly. The limitations of these approaches has resulted in the broad expansion of substitute prescribing programmes based on methadone or buprenorphine in order to enable patients to stabilise their drug use, improve their health and social functioning, and to curb crime. Heroin prescribing has been developed to help patients who do not benefit from these mainstream approaches. Heroin-based treatment is now routinely available in the UK (where it has been for many decades), Switzerland, the Netherlands and Germany. Generally it has been trialled and implemented according to the 'continental' model which requires all

heroin doses to be self-administered (typically two or three times a day) under supervision at specialist clinics. Supervision prevents diversion of medication on to the illicit market and enhances patient safety, thereby allowing for higher and more effective doses.

The review analysed the randomised trials one by one, with special attention to dose and other influences which may have tipped the balance in favour of or against heroin prescribing. In Britain the first such trial may have been affected by low heroin doses, while in Switzerland more intense psychosocial services were offered to heroin than to other patients. In the two (injectable and smokable heroin) Dutch trials, better overall outcomes among patients prescribed heroin may have been due to a higher total opioid dose, rather than to the type of opioid or how it was administered. A study in Spain was the first to compare broadly equivalent medication doses in heroin-based and non-heroin based maintenance treatments. Heroin patients reported significantly less illicit heroin use (though this remained high in both groups) and were at less risk of HIV infection, but differences were not significant for other measures such as crime, social functioning and mental health, and equivocal for physical health. A large German trial also prescribed broadly equivalent doses and was the first to use biological tests (special urine screens) capable of distinguishing illicit from prescribed heroin use. After a year significantly more patients remained in the injectable heroin as opposed to the oral methadone treatments, particularly if the 29% of patients who did not start their methadone treatment (presumably disappointed at not being allocated to heroin) are included in the calculations. However, at 12 months the same proportions were in some kind of treatment. The study's criterion for a successful substance use outcome was substantial reduction in illicit heroin use with little or no increase in cocaine use. It was satisfied by 69% of patients on heroin and 55% on methadone, a statistically significant difference. The health of most patients improved substantially in both groups but significantly (if only slightly) more patients met this criterion in the heroin group. Improvements among heroin patients were sustained over the two years after treatment started when 82% of patients were still in the treatment; non-retained patients tended to be more problematic and socially unstable.

Summarising these and other results from the studies, the author concluded that:

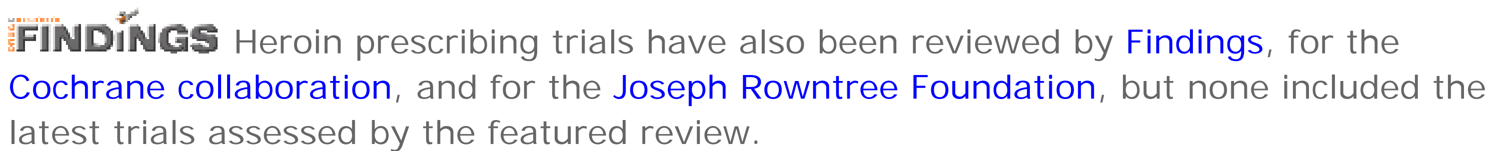
- Retention in treatment appears to be broadly comparable in heroin and methadone-only programmes.
- Compared to oral methadone, heroin-based treatment further reduces illicit heroin use, though in both treatments this is markedly reduced. Indeed, some oral methadone patients not only stop using heroin but also stop injecting, a major health-risk benefit. Heroin treatment is not a panacea which abolishes all illicit heroin or other drug use. Cocaine use in particular reduces to roughly the same degree in both types of treatments.
- Heroin-based treatment results in greater improvements in most other outcomes such as crime and psychosocial functioning; for every 100 patients, approximately 7–25 more will significantly improve than if offered conventional substitute prescribing. However, many patients benefit from oral methadone treatment, and heroin treatment has not been universally or substantially superior across all studies and all types of outcomes.
- Heroin treatment is considerably more expensive than conventional substitute prescribing, though this may be offset by savings for the criminal justice system and for the victims of crime. These results derive from the Dutch studies, which also found roughly equivalent gains in terms of years of life adjusted for quality of life, and no immediate healthcare savings. Since savings are in crime but costs are borne by health services, these services may be reluctant to fund the treatment.
- Randomised trials reported similar death rates among methadone and heroin patients. There are however several distinctive safety concerns with heroin treatment, including regular long-term injecting and a high incidence of serious incidents, particularly seizures and overdoses immediately after injection. The latter raises concerns about the long-term

effects of recurrent heroin-induced shortage of oxygen.

If heroin-based treatment is to be a costly minority approach, a key question is who should be offered it. Increasingly, heroin treatment providers agree that it should not be a front-line treatment, but reserved for patients who do not respond well to conventional substitute prescribing. How 'failure to respond' should be defined is a matter for debate. It might mean:
• Heroin users who are not attracted to conventional treatment. However, treatment services in most countries are already overstretched.
• Heroin users who did poorly (eg, poor retention, continued drug use) in previous methadone treatments but are not currently in treatment. Heroin treatment may successfully engage these former patients, but so too may a new episode of conventional treatment. For these people heroin treatment is unnecessary, costly and possibly detrimental.
• Patients currently in methadone treatment but not doing well, indicated for example by frequent heroin use, high-risk injecting, and poor health and psychosocial functioning. However, such patients may not require heroin, but optimising adjustments to their current type of treatment and/or further psychosocial assistance. In particular, buprenorphine may be suitable for some unable or unwilling to tolerate high methadone doses.

According to this logic, heroin treatment should only be available for patients who have not responded to a significant period (for example, at least three months) of conventional treatment delivered under optimal conditions (high doses; psychosocial services; supervised dispensing; adequate medical care). Continued regular heroin use and related harms after this time may justify a trial period of heroin treatment. People who still do not do well (regular drug use; no significant improvement in health and social functioning) could be returned to conventional treatment, freeing up expensive heroin treatment places. Another key issue is whether heroin treatment is best seen as a long-term treatment in its own right or a transition to non-injecting treatment modalities.

At a policy level these clinical considerations suggest that diverting considerable resources to the perhaps 5–10% of patients who require heroin treatment should only be considered in jurisdictions which can already deliver optimal conventional approaches to all heroin users seeking treatment.


FINDINGS Heroin prescribing trials have also been reviewed by Findings, for the Cochrane collaboration, and for the Joseph Rowntree Foundation, but none included the latest trials assessed by the featured review.

For Britain a vital trial whose results came too late for all these reviews was the RIOTT trial conducted at clinics in London, Darlington, and Brighton between 2005 and 2008. The questions posed by the study were whether patients who remained wedded to street heroin despite extensive treatment were simply beyond available treatments, whether it was just that their current oral treatment programmes were sub-optimal, or whether they would only do well if prescribed injectable medications. Each of these three propositions was true for some of the patients. A third did seem beyond current treatments even as extended and optimised by the study. For a fifth, 'all' it took was to individualise and optimise dosing and perhaps also psychosocial support and treatment planning in a continuing oral methadone programme. But despite pulling out many stops

to make the most of oral methadone, nearly half the patients only did well if prescribed injectable medications, with heroin by far the better option than methadone at suppressing illegal heroin use. The upshot was that the most reliable option in terms of securing a divorce from regular illegal heroin injecting was to prescribe the same drug to be taken in the same way, but legally and under medical supervision. As defined by the study, two-thirds of these seemingly intractable patients responded well to this option. However, from a conference presentation it seems injectable medications and heroin in particular had a far less clear-cut advantage in respect of crime, health, and quality of life.

Conclusions similar to those reached by the featured review have been reflected in UK national clinical guidelines and in guidance issued by England's National Treatment Agency for Substance Misuse. In particular the latter is clear that injectable prescribing should be considered only for the minority of patients with persistently poor outcomes despite optimised oral programmes, and that the priority should be improving the effectiveness of oral maintenance treatment for the majority.

Apart from the obvious and serious issue of cost, there is in any event a major logistical problem in extending heroin prescribing programmes based as recommended on supervised consumption at the clinic. Studies in continental Europe and Britain have shown that requiring on-site injecting or smoking of heroin several times a day is feasible. However, this can only work for patients who can easily and quickly get to the clinic. Unless the network of heroin prescribing centres is greatly expanded, on-site consumption will leave large parts of Britain unserved, especially rural areas. There are other options (such as supervised consumption in a pharmacy, local surgery or drug service) but these will not be easy to organise and may be considered unsafe. The same problem arises even if on-site consumption is limited to the early stages of treatment, a precaution which may be considered necessary on patient safety grounds and one recommended by national guidelines. The inconvenience of on-site consumption can be tempered by allowing patients to skip visits and take oral medication instead, an opportunity most took advantage of in Swiss trials. Insisting instead on the return of used ampoules – a tactic used with seeming success in a study in London – may be a less intrusive and less expensive way to prevent diversion.

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