

This entry is our account of a review or synthesis of research findings selected by Drug and Alcohol Findings as particularly relevant to improving outcomes from drug or alcohol interventions in the UK. Unless indicated otherwise, permission is given to distribute this entry or incorporate passages in other documents as long as the source is acknowledged including the web address <http://findings.org.uk>. The original review was not published by Findings; click on the [Title](#) to obtain copies. Links to source documents are in [blue](#). Hover mouse over [orange](#) text for explanatory notes. The Summary is intended to convey the findings and views expressed in the review. Below are some comments from Drug and Alcohol Findings.

Click [HERE](#) and enter e-mail address to be alerted to new studies and reviews

► [Heroin maintenance for chronic heroin-dependent individuals.](#)



DOWNLOAD PDF
for saving to
your computer

Ferri M., Davoli M., Perucci C.A.

Cochrane Database of Systematic Reviews: 2011, Issue 12,
Art. No. CD003410.

Update of the first authoritative review to combine results from all trials to date of long-term heroin prescribing for the management of heroin addiction finds important advantages for seemingly intractable patients previously failed by methadone, including reduced illegal drug use.

Summary In the light of comments received from researchers responsible for the original studies, reviewers have fine-tuned their analysis published in 2010 of the findings of trials of prescribing heroin for the treatment of heroin addiction. As in 2010, this updated review and [meta-analysis](#) from the Cochrane collaboration includes recent studies of the treatment from [England](#), [Spain](#) and [Canada](#), supplementing the earlier [British](#), [German](#), [Swiss](#) and two [Dutch](#) studies.

The aim was to integrate findings on maintenance treatments based on injectable, or in one case, smokable heroin compared to other treatments, without limiting the selection to trials which allocated patients at random. Though the analysts sought all relevant trials whatever the comparator, seven of the eight studies explicitly compared [heroin maintenance](#) against what today is the more conventional oral methadone option. Effectively the remaining study did so too, since all but a few of the [control group](#) patients who had to find other sources of help in fact enrolled in methadone programmes.

The reviewers assumed that all patients were chronic heroin addicts since only these patients would qualify for such treatments. Today heroin prescribing is generally seen as a 'rescue' option for patients who have not benefited sufficiently from methadone maintenance. In line with this role, studies typically recruited addicts from the locality of the clinic who had regularly used illicit heroin for several years but had not done well in previous non-heroin based treatments. All treatments included counselling or other forms of psychosocial support. Except for the first trial in the UK, patients were required to take

their heroin under medical supervision at the prescribing clinic. Findings were analysed on the assumption that there was no 'true' impact of the treatment which varied across studies simply by chance, but that impacts really do vary under different circumstances.

Main findings

In the Dutch studies heroin patients faced stricter disciplinary discharge rules than methadone patients, biasing the retention rates. Omitting these, over the periods of the remaining six relevant studies (generally a year), for every 100 patients retained in treatment on methadone, another 44 were retained when this was (effectively) supplemented or replaced by heroin, a statistically significant advantage unlikely to have happened by chance. Similar results were found when the analysis was restricted to studies in which heroin was injected under supervision at the clinic.

The previous version of the featured review had pooled data on relapse to illicit heroin use, concluding that for every 100 patients prescribed methadone who used illicit heroin, just 70 did so when prescribed heroin, nearly a statistically significant advantage. However, the current version considered such pooling inappropriate, as outcomes were measured in different ways across the studies, and sometimes without distinguishing between heroin and other illicit drugs. Instead the analysts described each study's findings. All found a greater reduction in illicit drug use (and when this **was reported**, in illicit heroin use) when patients were prescribed heroin rather than just methadone.

Across the five relevant studies, fewer patients died when prescribed heroin (8 of 781 versus 11 of 793) and the same was true to a slightly greater extent when the focus was restricted to studies of supervised heroin injecting (6 of 737 versus 10 of 740). Neither difference was statistically significant. However, significantly more non-fatal adverse medical events thought due in some way to the prescribed medications were recorded among the heroin patients.

Based on the patients' own accounts, all but two of the seven relevant studies found significantly greater reductions in criminal activity among heroin compared to methadone patients, and in another this was a non-significant trend. Just two studies recorded arrests or imprisonment; across these there were significantly fewer such events among patients prescribed heroin.

In the few studies reporting these outcomes, employment rates and improvements in family relationships generally did not significantly differ between heroin and non-heroin patients.

Six of the eight studies (all featuring supervised heroin prescribing) adopted composite assessments of how far and how widely a patient had to have improved to have responded well to treatment, generally reflecting illicit drug use and/or health and crime. In all six the heroin patients were more likely to meet these criteria, and generally the advantages conferred by heroin were statistically significant.

The reviewers' conclusions

Compared to oral methadone only, studies have found statistically significant positive effects from also prescribing heroin in terms of retention in treatment, reduction of illicit drug use, and criminality and imprisonment. Across these studies too, fewer heroin patients died, though this difference was not statistically significant. Despite its benefits,

reports highlighted also the risks of adverse events associated with the treatment, suggesting it should be limited to patients clearly failed by methadone and to centres equipped to respond to emergencies.

However, what counts as 'failure' in this context remains to be clearly defined. Disadvantages such as poverty, lack of family support, and psychiatric problems are associated with poor compliance and response to many kinds of medical treatments. Since resources are limited, the open question is whether to allocate patients to more expensive medications like heroin rather than trying more effectively to address the health and social causes of non-compliance and relapse which prevent methadone working as well as it might.

Given the higher rate of serious adverse events, the risk-benefit balance of heroin prescription should carefully be evaluated before the treatment is implemented, as should the capacity of addiction services and whether the treatment can be afforded in the long term.

FINDINGS As the analysts make clear, the verdicts in this analysis relate primarily to treatments in which the self-injection of prescribed heroin is medically supervised daily at the prescribing clinic, rather than the traditional British practice of patients picking up their heroin at pharmacies and injecting it generally beyond medical supervision. Unlike original British practice too, patients were generally those considered not to have responded well to oral methadone.

As clear as the advantages of heroin were, given the patients' histories of methadone failures, it is equally striking that the advantages were not more clear cut, and that many patients improved on oral methadone alone, a testament it is thought to the intensified support and more adequate doses provided in some of the studies. Given the implication that even for many of these patients, oral methadone can be made more effective, it sharpens the dilemma posed by the reviewers about whether finite resources are best spent on this, rather than relatively expensive heroin prescribing.

The issue posed by the review of what constitutes a failure of methadone sufficient to justify heroin prescribing was addressed in a [review](#) conducted by a researcher involved in the major UK trial. His conclusion was that if it is to be used in this way, heroin treatment should only be available for patients who have not responded to a **significant period** of conventional treatment delivered under **optimal conditions**. 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** could be returned to conventional treatment, freeing up expensive heroin treatment places.

A few seemingly counter-intuitive or not obviously positive results in the featured review warrant comment. That more adverse effects were recorded among the heroin patients was almost certainly largely due to the fact their injecting – and any resultant immediate complications – were observed at the clinics, while continued injecting by methadone patients was not. That for these patients it was in fact safer to prescribe heroin is suggested by the difference in the death rate. As the analysts speculate (and sometimes patients have commented), employment and family life may not have improved to the same degree as other outcomes partly because of the disruption arising from the need to attend the clinic to take heroin two or three times a day. Longer stays in treatment are in the UK no longer seen as self-evidently a 'good thing', but in respect of prescribing substitutes for illicit heroin, it remains the case that research suggests these treatments **tend to be** like an on-off switch; while patients remain in treatment they quickly improve and most do relatively well, but a

rapid reversion to regular illicit heroin use with all its consequences is common if they drop out or are forced out of treatment.

For Britain the [RIOTT](#) trial conducted at clinics in London, Darlington, and Brighton between 2005 and 2008 is the vital study. The questions it posed 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 injectable 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 cutting crime (which fell greatly across the board) and improving health and quality of life. Because they demand frequent attendance, heroin prescribing clinics have the potential to aggravate drug-related nuisance and distress caused to the local community, but in fact around the London clinic no such effect [was noticed](#) by local informants and police records for the area revealed no increase in crime, while clinic patients recorded among street drinkers causing some nuisance at the start of the study relatively rapidly [disappeared from the records](#).

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. 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.

For more on substitute prescribing for heroin addiction see this Findings [hot topic](#). For heroin prescribing studies in particular run [this search](#) on the Findings site, and especially see this [Findings review](#) and a [later review](#) which paid careful attention to the context of the studies and the details of the treatments.

Last revised 12 June 2012

► [Comment on this entry](#) ► [Give us your feedback on the site \(one-minute survey\)](#)

Top 10 most closely related documents on this site. For more try a [subject or free text search](#)

[Prescription of heroin for the management of heroin dependence: current status](#) REVIEW 2009

[The Drug Treatment Outcomes Research Study \(DTORS\): final outcomes report](#) STUDY 2009

[The Andalusian trial on heroin-assisted treatment: a 2 year follow-up](#) STUDY 2010

[Naltrexone implants compared to methadone: outcomes six months after prison release](#) STUDY 2010

[Is heroin-assisted treatment effective for patients with no previous maintenance treatment? Results from a German randomised controlled trial](#) STUDY 2010

[Oral naltrexone maintenance treatment for opioid dependence](#) REVIEW 2011

[The SUMMIT Trial: a field comparison of buprenorphine versus methadone maintenance treatment](#) STUDY 2010

[Naltrexone implants after in-patient treatment for opioid dependence: randomised controlled trial](#) ABSTRACT 2009

[Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK](#) STUDY 2010

[Long-term outcomes of office-based buprenorphine/naloxone maintenance therapy](#) STUDY 2010