▶ New heroin-assisted treatment: Recent evidence and current practices of supervised injectable heroin treatment in Europe and beyond.

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Prescribing oral methadone to heroin addicts divides opinions, but prescribing injectable heroin elevates the controversy to another level. Fortunately we now have six randomised clinical trials involving over 1500 patients to ground us in the evidence – and this European Union review to pull it all together.

Summary The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) established by the European Union aims to be the central source of comprehensive information on drugs and drug addiction in Europe. In the featured report freely available from its web site it collates all major contemporary studies on treatments based on prescribing pharmaceutical heroin ('diamorphine' or 'diacetylmorphine') to heroin addicts, addressing two key questions:
• Does the evidence support the use of supervised injectable heroin treatment for those who have failed to respond adequately to other approaches?
• And if so, what are the clinical management issues necessary to ensure this option can be delivered in a manner that avoids the associated risks?

The following account of this 170-page report is based on its executive summary with minor editorial changes and links where appropriate to Findings analyses or original studies.

Supervised injectable heroin treatment has emerged over the last 15 years as a potentially important intensive second-line treatment for entrenched heroin addicts for whom previous orthodox treatments have produced little benefit. We now have results from a series of well-designed randomised clinical trials from Europe and Canada which have been peer-reviewed and published in scientific journals, as well as accumulating clinical experience of the development and provision of this treatment. For this report all findings from randomised controlled trials published in academic papers and project reports have been examined to gauge the efficacy (against a range of outcomes) as well as the cost and cost utility of this form of treatment.

Context and history

Supervised injectable heroin treatment was developed and initially introduced in Switzerland during the 1990s after a century of prescribing heroin for the treatment of addiction without direct supervision, mostly in the United Kingdom. Since the 1990s the approach has been tested as a new clinical practice, sometimes in the context of randomised clinical trials, in several European countries and in Canada.

Two common features characterise the new approach to heroin treatment:
• It is not a first-line treatment, but an option for patients who have not responded to standard treatments such as oral methadone maintenance treatment or residential rehabilitation.
• All injectable doses (typically about 200mg of diamorphine per injection) are taken under direct medical or nursing supervision, ensuring compliance, monitoring, and safety, and preventing the medication being diverted to the illicit market; this requires clinics to be open for several sessions per day, every day of the year.

Scientific evidence base

Over the past 15 years, six randomised clinical trials have been conducted involving more than 1500 patients. They provide strong evidence, both individually and collectively, in support of the efficacy of treatment with fully supervised, self-administered injectable heroin, when compared with oral methadone, for long-term heroin-dependent individuals who have proved refractory to previous treatment. These trials have been conducted in six countries: Switzerland; the Netherlands, for which also see this Findings analysis; Spain, for which also see this Findings analysis; Germany, for which also see this Findings analysis; Canada, for which also see this Findings analysis; and England.

Across the trials, major reductions in the use of 'street' heroin occurred in those receiving heroin-based treatment compared with control group patients, who were usually being prescribed oral methadone. Reductions occasionally amounted to complete cessation; more often there was continued but reduced irregular use of street heroin, at least through the trial periods ranging from six to 12 months. Lesser reductions also occurred in the use of a range of other drugs such as cocaine and alcohol.

Patients receiving injectable heroin treatment achieved gains in physical and mental health and social functioning, though in different trials improvements were not consistently or significantly superior to those in the control groups, particularly in relation to psychosocial functioning. Reductions in criminal activity were also evident and substantially greater than those made by control group patients. Retention in treatment varied substantially across the trials.

This evidence suggests that for long-term, treatment-refractory opioid users, supervised injectable heroin treatment plus supplementary methadone does add value, a verdict corroborated in respect of several outcomes including retention and mortality by a systematic review conducted by the Cochrane Group. However, it is important to note that more serious adverse events have been reported to occur in patients receiving supervised injectable heroin than oral methadone. This suggests that heroin treatment may be less safe, and therefore require more resources and clinical attention in order to manage the risks.

Finally, countries that have conducted longer term (up to six years) follow-up studies have seen a high retention in supervised injectable heroin treatment (55% at two years and 40% at six years), with patients sustaining gains in reduced street heroin use and marked improvements in social functioning (eg, stable housing, drug-free social contacts, and employment).

Cost and economic evaluations

In the trials the reported cost per patient per year of a supervised injectable heroin maintenance programme was between €12,700 and €20,400. These costs were consistently and substantially higher than the cost of oral methadone maintenance at €3500 in Germany and €1600 in the Netherlands, partly due to the higher cost of pharmaceutical heroin, but largely due to more staff being required for the heroin-based treatment. At least two staff members must be present at all times and no 'take-home' injectable heroin doses are permitted, so clinics need to open daily and for extended hours.

This higher cost was compensated for by extra significant savings to society. In particular, a greater reduction in the costs of criminal procedures and imprisonment arising from criminal behaviour was seen with supervised injectable heroin than with oral methadone treatment.

It should be noted that the provision of a more standard treatment to a patient who derives little benefit cannot be cost-effective, no matter how cheaply it may be delivered.

Impact, clinical practice and challenges

At the time of writing there are about 1000 injectable heroin patients in the European Union and a further 1400 in Switzerland. In the United Kingdom heroin has been used in clinical practice since it was first synthesised, both for the relief of terminal pain and (rarely recently) for the treatment of opioid dependence. In recent years, four other countries (Denmark, Germany, the Netherlands and Switzerland) have granted approval for diamorphine to be used as a medicinal product for treatment-refractory heroin addicts. In these countries, injectable heroin clinics are now integrated into local addiction service networks, and appear to successfully deliver important benefits to a small number of severely affected chronic heroin addicts. For these addicts, this new treatment delivers tangible benefits, for themselves, for their families and for society.

One Spanish clinic continues to provide treatment to participants enrolled in their trial, now operating under legal exemption, and Canada has approved diamorphine for research trials only.

Conclusions

Supervised injectable heroin has developed in to a useful addition to the treatment toolbox for opiate addicts, but seems unlikely to become the solution to the heroin problem. The objective to provide a second-line intervention for hard-to-reach and highly problematic heroin users is reflected in the small number of patients – in 2011 across Europe, about 2500 or ½% of all patients in substitution treatment. Where the heroin treatment is already well established, proportions were stable at between 5% and 8%.

Across countries, almost uniformly supervised injectable heroin treatments are strongly structured, with the patient having to attend the clinic to take all injected doses under medical supervision. The treatment is also embedded within wider psychosocial support and rehabilitation, with attention to family reunion, criminal charges and debt, etc, as well as to outstanding health and psychological disorders. Patients themselves see the prescribed heroin as one perhaps important part of their treatment, but just one part nevertheless, and the wider therapeutic engagement and rehabilitative effort is considered equally important.

Clinical precautions remain vital since, though rare (one in every 6000 injections), life-threatening and often unpredictable adverse events are seen – in particular overdoses, often for reasons not immediately apparent and sometimes very hard to predict, even with a carefully applied testing procedures. This means it is important for clinical teams to be appropriately trained and resourced to deal with such emergencies and for clinical protocols, training and facilities to be established in advance.

The high costs of this treatment and the potentially controversial status of the medication may limit its implementation. However, it must be remembered that diamorphine is a medicinal product prepared by the pharmaceutical industry in accordance with all the usual quality and safety controls. Also, the costs have to be compared with the gains; notwithstanding their relative cheapness, oral opiate substitution treatments can never be cost-effective for this selected group of heroin addicts if they do not derive the expected benefits.

Another challenge will be to make this form of treatment available to severely affected heroin addicts in such a way that it does not inadvertently undermine the commitment of other patients to more orthodox forms of opiate addiction treatment.

FINDINGS As the body of report makes clear, the Cochrane review which it cited found fewer deaths among heroin than methadone patients or (more broadly) other comparison patients, but these statistically insignificant findings might have been due to chance fluctuations, and the randomised trials covered by the review were it said "not appropriate for measuring this outcome". Also, for methodological reasons the calculations excluded two studies where neither heroin nor comparison patients died. Had these been able to be included, the gap in the death rate would have been less. Given these considerations, it remains probable, but far from conclusive, that prescribing heroin to the types of patients recruited to the trials does help keep them alive.

On the other side of the equation is the greater incidence among heroin patients of serious and potentially fatal adverse events. That more of these (and especially more that were related to prescribed medications) were recorded among the heroin patients was almost certainly largely due to the fact much of their injecting – and any resultant immediate complications – was observed at the clinics, while any injecting by methadone patients would have taken place elsewhere. That for the patients in the trials it was in fact safer to prescribe heroin is suggested by the difference in the death rate.

In line with the featured report, UK national clinical guidelines and guidance issued by England's National Treatment Agency for Substance Misuse recommend 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. Later (in 2009) an expert group of clinicians, service users, commissioners from England agreed that a "sustained attempt" at optimised oral prescribing programmes should precede injectable treatment. Only if this proved unsuccessful should injectables be considered, and they should continue to be prescribed only if in fact they gained greater benefits than the oral programme. Though for new patients "total supervision of injectables was the ideal", the group stopped short of recommending this be mandatory. They also recommended that patients doing well in the traditional non-supervised British model should be allowed to continue.

Apart from the issues of cost and controversy mentioned by the featured report, there is 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 and which was also implemented in all three clinics in the English trial. If supervision is primarily to prevent prescribed injectable drugs being diverted to the illicit market, insisting instead on the return of used ampoules may be a less intrusive and less expensive way to achieve this objective – a tactic used with seeming success at a clinic in London which did not routinely require ongoing supervised injecting.

English trial

The English trial's finding that (in patients previously failed by oral methadone) injectable heroin suppressed illegal heroin use much more effectively than oral methadone, was in September 2013 supplemented by a cost-effectiveness analysis. Though in itself heroin prescribing was the most expensive option, taking all costs in to account (of which the most decisive was the cost of crime committed by the patients), over the first six months of treatment it and the prescribing of injectable methadone registered lower costs overall than oral methadone. Since all three treatments led to roughly the same improvements in the health-related quality of life of the patients, the injectable options (and especially injectable methadone) were calculated to be the most cost-effective.

Results of the English trial helped secure a future for supervised injectable treatment as a supplement to the traditional less structured injectable prescribing practices in UK addiction clinics. In 2012 the Department of Health issued a £5.5 million competitive tender for services to "develop a cost-effective model" for supervised injectable opioid treatment. The contract was awarded to the groups running the trial clinics in south London, Darlington and Brighton, which had been continuing their treatments after the trial ended. A network of 'micro-sites' is intended to help cover the London area.

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. The Findings analysis of the Cochrane review cited by the featured report also includes an extended commentary.

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