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▶ Effectiveness of diacetylmorphine versus methadone for the treatment of opioid dependence in women.

Oviedo-Joekes E., Guh D., Brissette S. et al.

Drug and Alcohol Dependence: 2010, 111, p. 50–57.

Unable to obtain a copy by clicking title above? Try asking the author for a reprint (normally free of charge) by adapting this prepared e-mail or by writing to Dr Oviedo-Joekes at eugenia@mail.cheos.ubc.ca. You could also try this alternative source.

From Canada the first study to show that among long-term, severely opiate dependent patients who have not responded well to prior treatment, women as well as men benefit more from being prescribed injectable heroin than oral methadone.

Summary In Canada between 2005 and 2008 a trial randomly allocated 251 long-term, treatment-resistant opioid-dependent patients to be maintained for a year on oral methadone, or instead on either injectable heroin or hydromorphone. The featured report analysed data from that trial to establish whether men or women benefited most from injectable heroin.

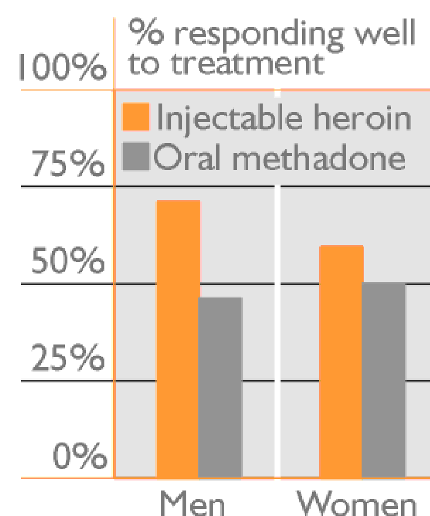
The parent study had allocated patients to the two forms of injectable opioids (heroin and hydromorphone) in a way intended to hide which drug they were being given. The 25 who were allocated to hydromorphone were omitted from the featured analysis, leaving 111 allocated to oral methadone and 115 to injected heroin. Of these 226 patients, 88 were women and 138 men. Most were insecurely housed, supported themselves through crime (and for 42% of the women, prostitution) rather than employment, were infected with hepatitis C, and regular cocaine as well as opioid use was common. Women had a worse overall profile including higher rates of reported sexual and physical abuse, HIV and hepatitis C infections, suicide attempts, sex work, and cocaine use, and less employment.

During the 12 months of the trial heroin-prescribed patients injected themselves up to three times daily at the clinics under staff supervision, but oral methadone was dispensed daily according to recommended practice in Canada. Patients allocated to injectables

could replace all or part of their prescription with oral methadone if patient and doctor agreed. After 12 months a further three months was allocated to transfer patients to other treatment modalities, primarily oral methadone.

Main findings

A year after starting treatment 65% of the women and 75% of the men were known to still be retained in some form of addiction treatment or to no longer be using opioid drugs. This lower retention rate for women was evident among patients prescribed injectable heroin (83% v. 90%) but more marked among those offered only oral methadone (48% v. 59%). However, none of the differences in retention between men and women were statistically significant, so may have been due to chance variations rather than a real difference in how they responded to treatment. What was statistically significant was that both were retained much better when they had been offered injectable heroin – an extra 36% of women and 32% of men. Almost all retained patients were still in the treatments offered by the study or in other methadone programmes; just three were known to be abstinent and none in other types of treatment.



As measured by the standard EuropASI interview schedule, a good clinical response to treatment was defined as an improvement of at least 20% in drug use/problems and/or crime and legal problems, and no greater than a 10% deterioration in all, or all but one, of the other domains, including family and economic situations, drinking, and physical and psychiatric health. On this yardstick, by the end of the 12 months of the study about the same proportions of women and men had done well (55% and 59% respectively), though fewer women than men (60% v. 71%) did well on injectable heroin. As with retention, none of the differences between men and women were statistically significant. Only among the men did significantly more patients respond well to injectable heroin than oral methadone (71% v. 46%). More women (60% v. 50%) also responded well to injectable heroin, but not to a statistically significant degree; ▶ chart.

The study also tested whether retention and response to treatment were related to sex once other variables had been taken in to account. Again there were no significant differences between men and women. There were also none related to (among other variables) housing status, age, previous methadone treatment, frequency of cocaine use, education, a measure reflecting reliance on criminal activity, sexual abuse, and sex work.

On the specific measures of welfare and functioning, both men and women generally improved between starting and ending the study treatments, including in their drug use,

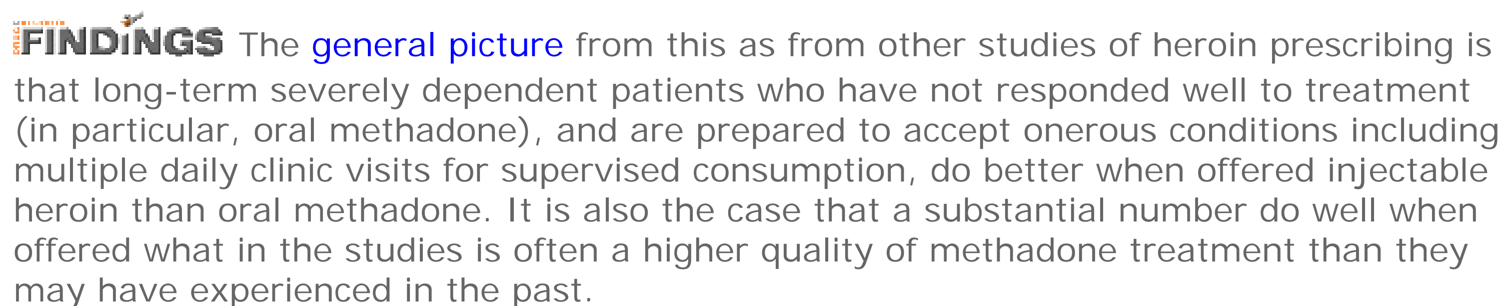
legal situations and health-related quality of life, and both improved significantly more on several domains if they had been prescribed injectable heroin. Where there were significant differences between the men and women, it was that men gained more from being prescribed injectable heroin, in particular in physical health, health-related quality of life, and family relationships.

One of the analyses in the featured report concerned patients prescribed hydromorphone, which another report had found responded almost identically to those prescribed heroin. With respect to these patients it was possible to confirm self-reports by urinalyses. Assuming missed tests were indicative of illegal heroin use, these showed that among both men and women illegal heroin was used significantly less often by patients allocated to hydromorphone than those offered only oral methadone.

The authors' conclusions

For the first time this report showed injectable heroin to be more effective than oral methadone for women as well as men. Although men more consistently benefited across the different outcomes, there were no significant differences between men and women in overall clinical response or retention a year after starting treatment. However, these findings emerged from a caseload of long-term opioid injectors with very poor housing, socioeconomic and medical conditions, and a broad history of addiction treatment, including oral methadone maintenance; they may not generalise to other types of patients.

Among other randomised trials of injectable heroin v. oral methadone, only the German trial [see this Findings analysis] has previously reported whether men or women benefit more. It found that men did better than women when prescribed injectable heroin but not when offered only oral methadone. Data from the non-randomised Swiss studies are also consistent with the featured study's finding that men benefited more than women from being prescribed injectables rather than oral methadone.



FINDINGS The general picture from this as from other studies of heroin prescribing is that long-term severely dependent patients who have not responded well to treatment (in particular, oral methadone), and are prepared to accept onerous conditions including multiple daily clinic visits for supervised consumption, do better when offered injectable heroin than oral methadone. It is also the case that a substantial number do well when offered what in the studies is often a higher quality of methadone treatment than they may have experienced in the past.

A previous report from the same study in Canada confirmed that substance use and a broad range of measures of welfare and functioning improved more among patients offered injectable heroin than oral methadone. As defined by the study (▶ above), 67% of heroin patients responded well versus 48% offered only oral methadone, and at 12 months the retention rate was 88% versus 54%. According to their own accounts, on average the heroin patients cut their illicit heroin use from 27 days a month to just five days, the methadone patients from 27 to 12 days, a steeper fall among the heroin patients. However, both continued to use cocaine at about the same rate as before starting treatment.

Another report from the study found that patients were unable to distinguish injectable

hydromorphone (a semi-synthetic opioid analgesic widely used for postoperative pain) from heroin, and that both drugs led to equally good retention and response to treatment and were equally safe.

A further report concerned satisfaction with treatment among patients prescribed injectable heroin or hydromorphone (these did not differ in patient satisfaction) versus those offered oral methadone only. It found the former more satisfied with their treatment and that whatever the treatment, satisfaction was related to being retained in treatment and responding well, including reduced substance use.

British trial

Britain too has trialled injectable heroin (and also injectable methadone) versus oral methadone in treatment regimens similar to those in Canada in the form of the RIOTT trial conducted at clinics in London, Darlington, and Brighton between 2005 and 2008. 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. Clinic patients among street drinkers observed to have been causing some nuisance at the start of the study relatively rapidly disappeared from the records.

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.

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