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Nugget 5.10

Injectable methadone may better oral form for more severely affected heroin addicts

Findings The [first study](#) to randomise opiate addicts to injectable versus oral methadone maintenance has suggested that the injectable option may be preferable for addicts with relatively severe health and psychological problems.

Conducted at the Maudsley Hospital in London, the trial randomised 39 opiate-dependent injectors seeking maintenance treatment to either injectable or oral methadone. All had previous experience of maintenance. All were inducted on oral methadone to establish dose levels and apart from weekends, all drugs were taken under supervision at the clinic. A room was set aside for injecting. Doses were stabilised at an average 97mg injectable and 80mg oral methadone daily. Clients demonstrated a "striking" variation in knowledge about injecting and injecting techniques and at least four of the 19 on injectables injected in an obviously unsafe manner. The requirement to return empty ampoules from weekend take-home doses (to prevent diversion on to the illicit market) caused no problems. No patient in either group voluntarily stopped attending for treatment over the six months of the study.

Intake interviews were compared with the same measures taken six months later from 33 of the patients. Illegal use of drugs was substantially and significantly lower (heroin for example was used on a third of the number of days) as was the average number of days on which acquisitive crimes were committed and physical and psychological health improved. Though most outcomes were slightly better on injectables, the only significant difference was greater satisfaction with treatment. More clear cut differences emerged when intake problem severity was entered into the analysis. On most criteria, the more problematic patients tended to respond best to injectable methadone in terms of becoming abstinent from heroin, particularly noticeable (and statistically significant) for those with poor psychological or physical

health. A similar effect was generally not apparent after oral methadone, suggesting that high severity patients were differentially benefiting from the injectable regime.

The injectables regime cost nearly five times as much in drug and staff costs. Combined with outcomes, this meant that oral methadone was nearly four times as cost effective per heroin abstinent patient and six times cheaper for each patient no longer injecting illicit drugs.

In context The study was a pilot intended to test the feasibility of supervised injectable methadone in the context of an NHS dependency unit and to probe for criteria which might be used to select patients who would benefit most from this regime. It was not a test of injectable methadone as used in ways recommended in official guidelines or typical of today's clinical practice. In the mid-70s injectable methadone was the dominant drug prescribed for addiction in Britain. Now only about 10% of methadone patients in England and Wales are prescribed it in injectable form.¹ As this statistic suggests, and as the authors in study bb1 comment, injectable methadone is likely to be most useful for the minority of patients not attracted into treatment by oral methadone or who do not respond well to the oral formulation and continue to exhibit serious drug-related problems. However, that was not how the drug was prescribed in the study. Beyond certain minimal criteria, patients were allocated at random, reducing the potential for it to demonstrate any advantage with selected severely addicted and entrenched injectors. That nevertheless the results suggested such an advantage is all the more significant.

The patients were routinely attending a methadone clinic from which they might reasonably have expected to receive only oral medication. Addicts who would have been satisfied only with injectable methadone may have avoided both the clinic and the study. These are also the patients for whom the advantages of injectable prescribing might have been most apparent, as the alternative is no treatment at all. Randomisation did not allow allocation to injectables based on problem severity, continued risktaking despite oral methadone treatment, or ability to stop injecting, though in practice the decision to prescribe injectables is (and national guidelines say should be²) based on such considerations.^{3 4 5} Two features of the research protocol would have tended actively to eliminate many long-term frequent injectors, a group who might benefit most from injectables. For safety reasons, supervised injecting was allowed only into the arm. 11 (out of 55) patients for whom this was not feasible were eliminated from the trial. Resort to non-arm injecting is most common in longer term injectors at greater risk of overdose.⁶ At a clinic in Manchester under 30% of opiate addicts prescribed injectables (mainly methadone) injected into the arm and probably fewer injected there exclusively.⁷ The study also excluded anyone with serious medical or psychiatric illness though no one appears to have been excluded for this reason.

On the problem-related criteria, the study's test of whether more problematic and addicted clients benefited most from injectables would have divided the sample into two halves; the drug use criteria effectively asked whether daily users/injectors would do better on injectables, not a high hurdle for heroin users who commonly inject two or three times a day. If continued regular heroin injecting is considered the prime criterion for injectable drugs, then six-month results from NTORS suggest that a half and half split might be reasonable.⁸ However, in practice few believe that half of all maintenance seeking opiate addicts are suitable for injectable

prescribing and national guidelines speak of injectables having only a limited role in treatment.⁹ The fact that injectables are not licensed for the management of dependence would normally demand that the decision to prescribe is made on an individual basis taking into account the risks and expected benefits in each case.^{10 11} Nationally under 1 in 10 methadone prescriptions are in injectable form¹² and in the Manchester study just 5% of the caseload were prescribed injectables.¹³

About three-quarters of patients at clinics in Manchester¹⁴ and west London¹⁵ prescribed injectable opiate-type drugs were abstinent from heroin, compared to under half in the featured study. In Manchester just four out of 125 were using heroin daily.¹⁶ However, these studies involved a highly selected set of patients with persistent problems despite oral methadone treatment and their outcomes may reflect the tendency documented in the featured study for more problematic clients to do better on injectable methadone. As in the featured study, the west London study (with on-site dispensing but not consumption) seems to have found few problems in persuading patients to comply with anti-diversion and other disciplinary rules.¹⁷

Only about half the patients potentially eligible for the trial attended the enrolment interview; outcomes with this self-selected group may not be replicated across the full caseload of that or of other clinics. Some who did enrol and were allocated to injectable methadone were initially apprehensive about having to inject in front of staff in the clinic (something they are said to have soon overcome); more may have turned down the offer of the trial for the same reason. After the study the clinic changed from supervised on-site injection five times a week to just once a fortnight, a regime which may attract a broader range of clients who respond differently to the treatment. If this is the case then the results of the study may not be replicated today even at the clinic featured in the study.

The post-trial reduction in supervision frequency was presumably an indication that diversion on to the illicit market was considered unlikely even in this less stringent regime. However, some residual supervision seems warranted in view of the scope the trial demonstrated for improving injecting technique, a potential benefit of prescribing injectables unavailable in oral regimes. Over two thirds of the patients prescribed oral methadone continued to inject illicit drugs without the benefits of such close supervision. Fortnightly supervision would also reduce costs to about three times as much as oral methadone and improve cost-effectiveness.¹⁸ Assuming the figures in the featured study, per patient abstinent from heroin it would cost 2.4 times as much as an oral methadone regime and per patient free of crime for a day, less than twice as much.¹⁹ Such ratios based on the full sample suggest that for the more problematic patients injectable prescribing could prove as cost-effective as oral methadone.

The baseline interview was conducted by the clinic staff and the follow up by researchers. The effect may have been to exaggerate the decline in illegal drug use as new patients have an interest in persuading clinical staff that they use more than they do.²⁰ This would not have affected the relative performance of oral and injectable prescribing but might have obscured the analysis of whether the heavier users benefited more from injectables.

In west London²¹ and Manchester²² about a third of patients considered eligible for injectable prescribing expressed a preference for methadone rather than heroin and few on injectables of either kind seem to have suffered persistent and severe injecting-related problems. However, in the Swiss trial of heroin prescribing a minority of patients allocated to injectable methadone dropped out due to reactions at the injection site.²³ This might have been due to also injecting oral methadone. Highly concentrated injectable methadone is also associated with severe reactions at the injecting site.²⁴

Practice implications For the authors the main implications of their study are that on-site supervision of injectable methadone prescribing is feasible in Britain, acceptable to patients, and may prove most effective for those with the greatest health and drug problems.

Whilst it may be desirable in the first stages of treatment, daily supervision of injecting is costly and unnecessary for stabilised patients who conform to safety and anti-diversion rules such as returning used ampoules. Less frequent supervision could profitably be used to identify and rectify particularly risky injecting practices. Even this regime is three times as costly as oral methadone. Cost and the established benefits of oral methadone would normally dictate that only the failure of oral regimes would precipitate consideration of prescribing injectables, along with other criteria related to problem severity, degree of addiction, and whether the alternative is continued injection of illegal drugs – see [Additional reading](#). Used in this way for a minority of patients, injectable prescribing is likely to gain the greatest benefits without unduly absorbing resources which could have been used to fund three times as many oral methadone slots.

The main therapeutic risk is the perpetuation of injecting with the heightened probability of overdose, infection and physical damage. However, the probability that these will occur is even greater if the alternative is injection of impure illegal heroin two or three times a day rather than pharmaceutical methadone once a day under specialist medical care. Less acute mood swings and fewer injections make injectable methadone preferable to injectable heroin for patients who can forgo heroin's greater psychoactive impact. In this sense injectable methadone is an intermediate option between oral drugs and drug-of-choice prescribing of heroin.

Featured studies Strang J., *et al.* “[Randomized trial of supervised injectable versus oral methadone maintenance: report of feasibility and 6-month outcome.](#)” *Addiction*: 2000, 95(11), p. 1631–1645. Copies: apply DrugScope.

Additional reading Sarfraz A., *et al.* “[Injectable methadone prescribing in the United Kingdom – current practice and future policy guidelines.](#)” *Substance Use & Misuse*: 1999, 34(12), p. 1709–1721.

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Links [Nuggets 5.9 4.6 3.2 2.3 1.5 Role reversal](#), issue 9.

- 1 Strang J., *et al.* "Randomized trial of supervised injectable versus oral methadone maintenance: report of feasibility and 6-month outcome." *Addiction*: 2000, 95(11), p. 1631–1645.
- 2 Department of Health, Scottish Office Department of Health, Welsh Office, Department of Health and Social Services Northern Ireland. *Drug misuse and dependence – guidelines on clinical management*. HMSO, 1999.
- 3 Sell L., *et al.* "One hundred and twenty-five patients prescribed injectable opiates in the North West of England." *Drug and Alcohol Review*: 2001, 20, p. 57–66.
- 4 Metrebian N., Shanahan W., Wells B., *et al.* "Feasibility of prescribing injectable heroin and methadone to opiate-dependent drug users: associated health gains and harm reductions." *Medical Journal of Australia*: 1998, 168(12), p. 596–600.
- 5 Ford C., *et al.* "Prescribing injectable methadone in general practice." *International Journal of Drug Policy*: 1999, 10, p. 39–45.
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- 8 Gossop M., Marsden J., Stewart D., *et al.* "The National Treatment Outcome Research Study in the United Kingdom: six month follow-up outcomes." *Psychology of Addictive Behaviours*: 1997, 11: (4), p. 324–337.
- 9 Department of Health, Scottish Office Department of Health, Welsh Office, Department of Health and Social Services Northern Ireland. *Drug misuse and dependence – guidelines on clinical management*. HMSO, 1999.
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- 11 Sarfraz A., *et al.* "Injectable methadone prescribing in the United Kingdom – current practice and future policy guidelines." *Substance Use & Misuse*: 1999, 34(12), p. 1709–1721.
- 12 Cited in: Strang J., *et al.* "Randomized trial of supervised injectable versus oral methadone maintenance: report of feasibility and 6-month outcome." *Addiction*: 2000, 95(11), p. 1631–1645.
- 13 Sell L., *et al.* "One hundred and twenty-five patients prescribed injectable opiates in the North West of England." *Drug and Alcohol Review*: 2001, 20, p. 57–66.
- 14 Sell L., *et al.* "One hundred and twenty-five patients prescribed injectable opiates in the North West of England." *Drug and Alcohol Review*: 2001, 20, p. 57–66.
- 15 Metrebian N., Shanahan W., Wells B., *et al.* "Feasibility of prescribing injectable heroin and methadone to opiate-dependent drug users: associated health gains and harm reductions." *Medical Journal of Australia*: 1998, 168(12), p. 596–600. Six month outcomes for retained patients.
- 16 Sell L., *et al.* "One hundred and twenty-five patients prescribed injectable opiates in the North West of England." *Drug and Alcohol Review*: 2001, 20, p. 57–66.
- 17 Metrebian N., Shanahan W., Wells B., *et al.* "Feasibility of prescribing injectable heroin and methadone to opiate-dependent drug users: associated health gains and harm reductions." *Medical Journal of Australia*: 1998, 168(12), p. 596–600. Six month outcomes for retained patients.
- 18 Costs of fortnightly supervised prescribing of injectable methadone

		Cost per time		Times per fortnight	Cost per fortnight	Cost per six months
		Drugs and equipme	Labour			
Fortnightly supervised injecting	Supervised injection	£5.54	£7.50	1	£13.04	
	Unsupervised injection	£5.34	£2.00	9	£66.06	
	Take-home	£5.34	£0.00	4	£21.36	
	Total cost per fortnight				£100.46	
	Cost per six months					£1305.98

19 Cost effectiveness of the three prescribing regimens

		Cost per six months	Per cent reduction	Cost adjusted for effectiveness
Fortnightly supervised injecting	Cost per six months	£1305.98		
	Outcomes	Heroin abstinence	44.4%	£2938
		Crime days		84.6%
Weekday supervised injecting	Cost per six months	£1973.00		
	Outcomes	Heroin abstinence	44.4%	£4439
		Crime days		84.6%
Oral	Cost per six months	£402.00		
	Outcomes	Heroin abstinence	33.3%	£1206
		Crime days		47.7%

20 Chermack S.T., *et al.* "Comparison of patient self-reports and urinalysis results obtained under naturalistic methadone treatment conditions." *Drug and Alcohol Dependence* 2000, 59, p. 43–49.

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22 Sell L., *et al.* "One hundred and twenty-five patients prescribed injectable opiates in the North West of England." *Drug and Alcohol Review*: 2001, 20, p. 57–66.

23 Uchtenhagen A., *et al.* *Prescription of narcotics for heroin addicts. Main results of the Swiss National Cohort Study.* Basel: Karger, 1999.

24 "Special amps leave trail of damage." *Juice* 1996, 1, p. 6.