

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.

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► [Substitution treatment of injecting opioid users for prevention of HIV infection.](#)



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Gowing L., Farrell M., Bornemann R. et al.
Cochrane Database of Systematic Reviews: 2011, Issue 8, Art.
No.: CD004145.

Updated review conducted for the respected Cochrane collaboration finds that methadone maintenance and allied treatments for opioid dependence consistently and significantly reduce the risk of transmission of blood-borne viruses and curb the spread of HIV.

Summary Drug injectors are vulnerable to infection with HIV and other blood borne viruses due to the collective use of injecting equipment as well as sexual behaviour. This review aimed to assess the degree to which this risk is affected by the prescription of drugs such as methadone to be taken by mouth which substitute for the opiate-type drugs the patient is dependent. It assessed impacts on behaviours which place people at high risk of viral transmission and on actual rates of HIV infection. With one exception, it considered all sorts of studies, not just randomised trials, as long as the treatment and outcomes were relevant and participants were opioid dependent drug users, most of whom were currently or [recently](#) injecting. The exception was studies which required patients in treatment to at the same time recall their past risk behaviour before and after starting treatment. Non-English language studies were included. The studies were expected largely to relate to methadone, but evidence relating to other oral preparations (buprenorphine, LAAM, codeine and slow release morphine) was also considered.

A search discovered 38 studies involving about 12,400 participants. Just two randomly allocated patients to substitute prescribing versus other treatments. In the remaining studies, findings would have been complicated by influences other than substitution treatment resulting in potential bias. All but six were solely concerned with methadone treatment, 32 with treatment in a service specialising in addiction treatment, and 26 were set in the USA. Due to differences between the studies, no attempt was made to combine their findings in to an overall quantitative assessment of the impacts of the treatments. Instead the reviewers assessed whether effects were consistent across the studies and across different types of studies.

Main findings

Overall studies consistently find that after entering oral substitute prescribing treatment (generally involving methadone), patients move to being at substantially lower risk of HIV infection due to behaviours linked to their drug use, but less consistently in respect of their sexual behaviour.

Across 17 studies it was consistently found that starting oral substitution treatment was associated with significant falls in the proportion of patients who continued to inject and in the frequency of injecting. These reductions typically occurred in the first one to three months of treatment and were sustained for at least the first year. However, reductions were not necessarily sustained after treatment ended, particularly if termination had been involuntary.

Treatment was also consistently associated with a significant decrease in the sharing of injecting equipment, possibly due to reduced injecting. These benefits were sometimes sustained after treatment ended, though not in a study in which patients were forced to leave due to subsidised treatment no longer being available. In some studies similar reductions in sharing were achieved by other treatment modalities.

Like [another Cochrane review](#), the featured review also found that illicit opioid use (injected or not) significantly decreased after entering treatment and did so consistently across all relevant studies.

Since there were few studies, it was difficult to be conclusive, but the data also suggested that sex-related risks of viral transmission were also reduced due to fewer people having multiple partners or exchanging sex for drugs or money, though condom use was affected little if at all. In six of the seven studies to assess this, the overall drug-related risk of HIV infection assessed by composite scales was significantly reduced. The same was true of the seven studies which assessed risk due to drug use or sexual behaviour.

Four studies assessed relationships between the proportions of people who became HIV positive (seroconversion) and their participation in methadone treatment. All found that participation as such, or more extended or continuous participation, was associated with a lower rate of seroconversion. This suggests that reductions in risk behaviour do translate in to actual reductions in cases of HIV infection. Substitution treatment may also protect individuals already infected with HIV against further infection with other strains of HIV, or other blood-borne viruses.

The authors' conclusions

The reviewers concluded that oral substitution treatment for injecting opioid users reduces drug-related behaviours with a high risk of HIV transmission, but has less effect on sex-related risk behaviours. On this basis, provision of this treatment should be supported in countries with emerging HIV and injecting opioid use problems as well as those with established populations of injecting opioid users.

Most of the studies in this review simply observed what happened after people started maintenance treatment, though some also recruited comparison groups of patients who did not enter, had left, or had less treatment, against which to benchmark the findings. Just two minimised possible bias by randomly allocating patients. This lack of data from

controlled studies leaves the findings open to bias and limits the strength of the evidence. However, these findings supplement stronger evidence from other reviews of the effectiveness of substitution treatment in retaining patients and reducing illicit drug use. Whether risk-reduction improvements persist after patients leave treatment is unclear; many relapse to illicit opioid use, but it is not clear whether they nevertheless continue to practice risk reduction strategies.

FINDINGS

Any review is limited by the studies available to it. In this case substantial methodological limitations meant results could not be combined to assess their strength and statistical significance, taking in to account sample sizes and other features of the studies. In particular, the review was unable to offer guidance on how to optimise risk reduction. The consistency of the results is reassuring, but is no substitute for rigorous studies. Nevertheless, the key findings of reduced injecting and probably associated with this, reduced sharing of injecting equipment, is both the intended and logical result of substituting an oral drug for an injected one; it 'makes sense', lending credence to the interpretation that the consistency of the findings reflects a real and consistent impact of making substitute prescribing programmes available.

In fact there are reasons to believe that the findings may be an underestimate of overall benefits across a local population of opioid injectors. Much of the data derives from treatments provided in the previous century, so may underestimate the impacts of improved procedures. Also, the review started at the point where injectors have entered substitute prescribing programmes, and asked what the impact was on their risk of becoming infected. But there is another major feature of these programmes which might be crucial to risk reduction – their ability to engage large numbers of opioid users in treatment. The risk-reduction benefits identified by the analysis may or may not be greater than those associated with other treatments, but they are likely to be extended to far greater numbers in areas with widely accessible substitute prescribing programmes. Across an entire population of opioid injectors, the result (identified for example [in Barcelona](#)) is likely to be reduced HIV-related mortality.

In 2005 the World Health Organization added methadone (and buprenorphine) to its List of Essential Medicines, [partly because](#) "The accumulated data demonstrate that methadone maintenance treatment is a major public health tool in ... HIV/AIDS prevention" – the effectiveness issue dealt with in the featured review – but also because it is capable of widespread implementation and the engagement of a large proportion of the at-risk population in treatment. This conclusion was boosted by [an analysis for the European Union](#) which found methadone maintenance cost-effectively prolongs and improves the lives of a population of opioid injectors by averting HIV infections, and that the cost of doing so is typically below the cost of treating the infections, creating health service savings. Such findings led [joint guidance](#) from Europe's drug and infection control agencies to itemise opioid substitution treatment among the seven key intervention components which should be applied and combined to achieve maximum prevention from infection.

Importantly, the mathematical model used in the analysis for the European Union showed that as the proportion of local drug users engaged in treatment increases, costs per averted infection dramatically decrease, and benefits across all drug users in or out of treatment escalate. This is because the treatment is capable of removing a large

proportion of drug users from networks of injecting equipment sharing, leading to a form of 'herd immunity'. This analysis and others find that benefits in respect of hepatitis C infection are much less convincing, and likely to be substantial at a population level only in very high quality programmes which reduce equipment sharing to very low levels and prevent relapse to injecting drug use.

To a lesser extent, these qualities have a similar influence on HIV prevention, spotlighting the importance of features of the programmes and the regulatory environment within which they operate which can undermine their infection-prevention potential. Among those [described for a US think-tank](#) are limited implementation, regulations restricting the import and supply of methadone, restrictions on the types of patients who can enter the programmes (eg, to those who have been failed by other treatments), under-dosing, and counterproductive rules and disciplinary procedures which deter patients and lead to high throw-out rates.

Another benefit not reflected in the analysis is the relatively stable platform substitute prescribing provides for engaging patients in the treatment of [HIV](#) or [hepatitis C](#) infection and for completing the therapy. By definition this cannot reduce the proportion HIV positive among these already infected patients (so its impact will not be reflected in the featured analysis), but it should help prolong their lives and reduce the risk that they will infect others.

For all Findings analyses related to the reduction of infection risk behaviour by methadone maintenance run [this search](#).

Thanks for their comments on an earlier version of this entry to Linda Gowing of the University of Adelaide, Australia and Roy Robertson of Edinburgh University. Commentators bear no responsibility for the text including the interpretations and any remaining errors.

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