Cost-effectiveness of integrating methadone maintenance and antiretroviral treatment for HIV-positive drug users in Vietnam's injection-driven HIV epidemics

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study evaluated the cost-effectiveness of two strategies for adding methadone maintenance therapy to antiretroviral therapy (ART) for patients with HIV or AIDS, who were drug users, in Vietnam. The authors concluded that providing methadone with ART was cost-effective. The study was poorly reported and the paper was not well written, and so there can be little confidence in the results and in the authors’ conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
This study evaluated the cost-effectiveness of two strategies for adding methadone maintenance therapy to antiretroviral therapy (ART) for patients with HIV or AIDS, who were drug users.

Interventions
Three treatment programmes were evaluated: ART alone, ART with methadone administered at separate sites, and ART with methadone administered at the same facility. The first-line ART options were zidovudine or stavudine plus lamivudine plus nevirapine, or zidovudine or stavudine plus lamivudine plus efavirenz.

Location/setting
Vietnam/out-patient care.

Methods
Analytical approach:
The authors constructed a one-year decision tree that modelled the likelihood of virologic suppression, ART retention, injectable drug use, loss to follow-up, and death, with ART, based on the two methadone maintenance delivery options. Patients who became resistant to first-line ART were allowed to progress to second-line ART. Third-line ART was not modelled as it was not commonly available in Vietnam. The authors stated that a Vietnamese health services perspective was taken.

Effectiveness data:
The key effectiveness data were the odds ratios for having virologic suppression. The data for the baseline risk of virologic suppression with ART were from a Swiss study. Those for the two other interventions and for active injectable drug users, were from several non-Vietnamese, non-randomised studies. Other inputs were ART retention, mortality, drug use rates, and the rates of loss to follow-up or ART, for each strategy. For ART alone, these data were from the Vietnamese Ministry of Health. The same retention rate was used for all three options. The other clinical data were from Europe, USA, or Thailand. The model assumed that there was no difference in ongoing drug use between the same-site methadone and the separate-site methadone options.

Monetary benefit and utility valuations:
The utility values were estimated for each treatment, and for continued use of injectable drugs or for drug abstinence. These utilities were derived from some published Vietnamese studies.

Measure of benefit:
The primary measure of benefit was quality-adjusted life-years (QALYs), which were discounted at a 5% annual rate.

**Cost data:**
The costs included the drugs, personnel, management, laboratory tests, and site operation and maintenance. Site operation and maintenance costs were assumed to be identical for same-site and for separate-site therapy. The costs were from published Vietnamese sources and they were discounted at a 5% annual rate. The costs were converted from Vietnamese dong to US $ and inflated to 2009 prices.

**Analysis of uncertainty:**
The authors conducted a probabilistic sensitivity analysis, using Monte Carlo simulation. The results were presented as cost-effectiveness planes; in a cost-effectiveness acceptability curve; and in a table. Confidence ellipses and threshold lines were presented for a willingness-to-pay for a QALY that was derived from World Health Organization guidelines for cost-effectiveness in developing countries.

**Results**
Same-site ART and methadone was less costly and more effective than the next most effective treatment, which was separate-site ART and methadone. The cost-effectiveness plane for same-site versus separate-site therapy showed that there was high uncertainty in the cost-effectiveness, as a large proportion of simulations resulted in same-site therapy being more costly and less effective, than separate-site therapy.

Compared with ART alone, the incremental cost-effectiveness ratio for same-site therapy was $569 per QALY gained, which was below the strict cost-effectiveness threshold of the gross domestic product per capita of $1,113.4 per QALY gained. Same-site therapy was more cost-effective 87.1% of the time, at a willingness-to-pay threshold of three times the gross domestic product per capita ($3,340 per QALY gained).

**Authors' conclusions**
The authors concluded that providing methadone with ART for HIV-positive drug users in Vietnam was cost-effective.

**CRD commentary**

**Interventions:**
The first-line interventions were adequately described and appear to have been appropriate. The drugs included in the second-line ART were not reported.

**Effectiveness/benefits:**
The authors did not describe how they obtained the clinical effectiveness evidence, and the clinical studies that provided the evidence were not described. It is not clear that the best available evidence was used. The clinical effectiveness data were from various countries. The probability of virologic suppression with first-line ART was from a Swiss model and the inputs were not reported. The odds ratios for virologic suppression were from non-randomised US and French studies. The only effectiveness data that were from Vietnam were the probability of injectable drug use, during methadone maintenance therapy; the retention rates on ART; the mortality on ART; and the loss to follow-up on ART. These studies were small and non-randomised, with a risk of bias. It was not clear if the other inputs were generalisable to Vietnam. The QALYs were appropriately from Vietnamese HIV-positive drug users. As the model covered one year, the 5% annual discount rate was unnecessary. This short duration was correctly identified by the authors as a limitation to estimating the benefits of the interventions, as HIV, AIDS and heroin addiction are chronic conditions, with effects for longer than one year, and this would underestimate the benefits and costs.

**Costs:**
The costs were from an appropriate Vietnamese population and were described in detail. The price year was reported and the data were inflated using the consumer price index. Discounting of the costs was not necessary. The cost assumptions might have underestimated the savings with same-site therapy as the costs of site management and operation were assumed to be identical, based on trial funding rather than real-world application. The authors acknowledged that the costs of maintaining and staffing two sites, were likely to be more than that of one site, but alternative assumptions were not tested. They acknowledged that the one-year time horizon was a limitation for estimating the costs for the chronic conditions of HIV, AIDS and drug addiction.
Analysis and results:
There were many methodological problems with the analysis. The model was a decision tree, which could not adequately represent chronic conditions, with recurring events. A decision tree might have been selected because of the short time horizon, but this did not adequately capture the costs and health outcomes for addiction and HIV. Some of the inputs might have been inaccurate, as the probabilities of retention and loss to follow-up did not sum to one, and the probabilities differed between Table 1 and the model. The probabilistic sensitivity analysis seemed to contain distribution choice errors or was reported incorrectly. No cost-effectiveness acceptability curve was presented for the most relevant comparison between same-site and separate-site therapy, and this comparison was not quantified in the text. This makes it difficult to assess the uncertainty around the model results.

Concluding remarks:
While some appropriate sources were used for Vietnamese data, the study was poorly reported and the paper was not well written, and so there can be little confidence in the results and in the authors' conclusions.

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