The cost-effectiveness of buprenorphine maintenance therapy for opiate addiction in the United States

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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.

Health technology
The use of buprenorphine (BUP) maintenance therapy for opiate addiction among injection drug users (IDUs). The doses were not reported.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 1,000,000 IDUs.

Setting
The setting was not explicitly stated and it was unclear from the context of the original paper. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness data were partly derived from studies published between 1999 and 2001. No dates were reported for the resources used. The price year was 1998.

Source of effectiveness data
The effectiveness evidence was derived from published studies, augmented by the authors’ assumptions.

Modelling
A dynamic model was constructed to estimate the effect of treatment with BUP on the human immunodeficiency virus (HIV) epidemic. The impact on sexual partners and needle-sharing contacts of those under treatment was also considered. The model had a time horizon of 10 years. The hypothetical study sample entered the model through maturation and left via maturation or death. Individuals were grouped into nine mutually exclusive conditions on the basis of their HIV status and drug use status. Transition across the health states was described through dynamic non-linear differential equations.

Two main scenarios were considered:

BUP adoption resulted in a 10% expansion in the number of IDUs in maintenance and had no effect on the number of IDUs in MET maintenance (scenario I);
BUP adoption resulted in a net 5% expansion in the number of IDUs in maintenance and a 5% decline in the number of MET-maintained IDUs (scenario II).

A further classification was performed between high- and low-prevalence communities (prevalence rate of 40% versus 5%).

**Outcomes assessed in the review**
The health outcomes assessed in the review were:

- the annual average number of injections;
- the percentage of shared injections;
- the annual number of new sex partners;
- the annual mortality rate from non-HIV causes;
- the annual "graduation rate" (i.e. the rate at which individuals terminate treatment and become abstinent);
- the efficacy of BUP over MET (estimated through the number of positive urinalyses and the risk of terminating treatment); and
- the quality adjustments.

**Study designs and other criteria for inclusion in the review**
The authors stated that the model inputs came from an extensive review of the literature, but the inclusion criteria were not reported. Data on BUP efficacy came from a meta-analysis of short-term randomised trials.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
Not reported.

**Methods of combining primary studies**
It appears that the primary studies have been combined using narrative methods.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The annual average number of injections was 200 in untreated IDUs, 40 under MET, and 53.3 under BUP with a low prevalence. The corresponding figures with a high prevalence were 225 (untreated IDUs), 45 (MET) and 59.9 (BUP).

Shared injections were 20% in untreated IDUs, 6% under MET, and 7.2% under BUP.

The annual number of new sex partners was 3.5%.

The annual mortality rates from non-HIV causes were 3% in untreated IDUs, 1.13% under MET, and 1.29% under BUP.

The annual "graduation rate" was 3.50% under MET and 2.78% under BUP.

In terms of treatment efficacy, patients who received BUP had 8.3% more positive urinalyses than MET patients and a 26% higher risk of terminating the treatment.

The quality adjustments were 0.9 for quality of life in maintenance treatment and 0.8 for quality of life of an IDU.

Methods used to derive estimates of effectiveness
The authors made some assumptions for the decision model.

Estimates of effectiveness and key assumptions
It was assumed that:

the sexual partners of IDUs were more likely themselves to be IDUs;

individuals with acquired immunodeficiency syndrome (AIDS) were less likely to have sexual and needle-sharing partners than asymptomatic HIV-infected individuals;

untreated IDUs were less likely than treated IDUs to have access to antiretroviral drugs, but more likely to use other health care services; and

the relative efficacy of BUP over MET was the same in the long term as was observed in the short term.

Measure of benefits used in the economic analysis
The summary benefit measure was the quality-adjusted life-years (QALYs). QALYs were obtained through the decision model and were discounted to the present value at a rate of 3%. The utility data came from a published study. The source of the survival data was not reported.

Direct costs
An annual 3% rate was used to discount the costs that were incurred over a 10-year time period (horizon of the decision model). The unit costs were not reported separately from the quantities of resources used. The health services included in the economic evaluation were MET, BUP, urinalyses, physician evaluation, psychosocial interventions and other health care interventions, such as the treatment of HIV and AIDS (antiretroviral therapies). The cost/resource boundary adopted in the study was that of the health care system. No price was established in the USA for the take-home formulation of BUP (BUP compounded with naloxone), thus the authors estimated a plausible range from $5 to $30. Three prices ($5, $15 and $30) were considered in the cost analysis. The cost of naloxone was not considered because it is a generic product and its incremental cost per dose was negligible. The source of the other costs was not reported. Resource use was mainly estimated from the authors' assumptions. The price year was 1998. All of the costs were inflated to 1998 values using the consumer price index.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

**Indirect Costs**
The indirect costs were not included in the economic analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
Univariate and two-way sensitivity analyses were conducted to investigate the impact of uncertain parameters used in the model on the cost-effectiveness estimates. The model inputs varied were BUP efficacy (the two dimensions considered in the analysis), use of BUP, and quality of life estimates.

**Estimated benefits used in the economic analysis**
All of the results referred to the cohort of 1,000,000 IDUs. Under scenario I, the incremental change in QALYs with BUP over standard care was 274 in the low-prevalence community and 1,226 in the high-prevalence community. The corresponding values under scenario II were 123 (low-prevalence) and 561 (high-prevalence), respectively.

**Cost results**
Under scenario I, in the low-prevalence community, the incremental change in costs with BUP over standard care was $3.8 million with a BUP cost of $5, $7.1 million with a BUP cost of $15, and $12.1 million with a BUP cost of $30. The corresponding values in the high-prevalence community were $13.3 million (BUP $5), $25.1 million (BUP $15) and $42.9 million (BUP $30), respectively.

Under scenario II, in the low-prevalence community, the incremental change in costs with BUP over standard care was $2.2 million with a BUP cost of $5, $5.5 million with a BUP cost of $15, and $10.5 million with a BUP cost of $30. The corresponding values in the high-prevalence community were $7.9 million (BUP $5), $19.7 million (BUP $15) and $37.4 million (BUP $30), respectively.

**Synthesis of costs and benefits**
An incremental cost-effectiveness ratio was calculated to combine the costs and benefits of the two interventions under evaluation.

Under scenario I, in the low-prevalence community, the incremental cost per QALY with BUP over standard care was $14,000 with a BUP cost of $5, $26,000 with a BUP cost of $15, and $44,200 with a BUP cost of $30. The corresponding values in the high-prevalence community were $10,800 (BUP $5), $20,500 (BUP $15) and $35,000 (BUP $30), respectively.

Under scenario II, in the low-prevalence community, the incremental cost per QALY with BUP over standard care was $17,700 with a BUP cost of $5, $44,500 with a BUP cost of $15, and $84,700 with a BUP cost of $30. The corresponding values in the high-prevalence community were $14,000 (BUP $5), $35,100 (BUP $15) and $66,700 (BUP $30), respectively.

The variations investigated in the sensitivity analyses did not substantially alter the results obtained in the base-case.

**Authors’ conclusions**
The adoption of buprenorphine (BUP) was more cost-effective (below the threshold of $50,000 per quality-adjusted life-year) than methadone (MET) treatment under most of the scenarios considered in the analysis. The authors noted
that "factors other than cost-effectiveness considerations may influence those who decide whether to adopt substance abuse treatment innovations".

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear. MET was selected as the basic comparator because it represented the standard approach for maintenance therapy among IDUs. However, its use was forbidden in some states across the USA, thus it might not represent the most appropriate comparator in many settings. You should decide whether MET represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The authors stated that an extensive review of the literature was undertaken to derive the effectiveness estimates used in the decision model. However, the methods and conduct of the review were not reported. With the exception of one meta-analysis, the designs of the primary studies were not reported. It is likely though that some of the primary studies were randomised trials. It was unclear how many studies were included in the review, and details of the study samples and patient characteristics were not provided. In addition, the authors made some assumptions. The uncertainty around the estimates used in the decision model was investigated in the sensitivity analyses.

**Validity of estimate of measure of benefit**
QALYs were used as the summary benefit measure. This appears to have been appropriate to define the impact of the study intervention on the quantity and quality of life-years of IDUs. The 10-year time horizon for the decision model was used to avoid making assumptions about the future development of the HIV epidemic and available treatments. The source of the quality adjustments was reported, but it was unclear whether such estimates reflected the values associated with patients or individuals from the general public. The authors stated that the exclusion of cocaine injection practices may have overstated the benefits associated with BUP treatment.

**Validity of estimate of costs**
The perspective adopted in the study was explicitly reported. It appears that all the relevant cost components have been included in the analysis. The unit costs were not analysed separately from the quantities of resources used, and only the unit cost of BPU was reported. The costs were treated deterministically in the base-case, but three prices of BPU were considered in order to reflect the uncertainty around the economic cost of this cost component. Sensitivity analyses were not conducted on the other cost estimates. The source of the cost data was unclear. Appropriate discounting was performed. The price year was given, thus helping to facilitate reflation exercises in other settings. The authors noted that reduction in opiate use is likely to result in a reduction in the costs of social services agencies and the criminal justice system. However, such costs were not taken into account because the perspective adopted in the study was that of the health care service.

**Other issues**
The authors compared their findings with those of studies evaluating the cost-effectiveness of other medical care interventions delivered to opiate-addicted individuals. The issue of the generalisability of the study results to other settings was implicitly addressed by considering several scenarios and performing extensive sensitivity analyses, the results of which were reported clearly. However, it may be difficult to replicate the study in other settings due to the limited information on the cost data. The authors also stated that the model used to evaluate the cost-effectiveness of BUP in comparison with MET could be used in other countries by changing behavioural and economic parameters. The authors discussed some limitations of their analysis.

**Implications of the study**
The study results suggested that BUP maintenance therapy may represent a cost-effective strategy for IDUs, especially if the price per dose is $5.
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