Buprenorphine versus methadone maintenance: a cost-effectiveness analysis

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
Heroin patients were given buprenorphine at a clinic specialising in the treatment of opioid dependence. The comparator treatment was to give the patients methadone.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised heroin patients with a diagnosis conforming to criteria of the American Psychiatric Association (Diagnostic and Statistical Manual of Mental Disorders, 4th ed. 1994). The patients had to be older than 18 years, live within commuting distance of the clinic, appear mentally competent to give informed consent, and sign an informed consent form. Patients were excluded if they were pregnant or seemed likely to become pregnant. They were also excluded if they were suffering from an acute medical condition which would make participation difficult, were using anti-convulsant or anti-psychotic medications, or were currently in opioid treatment therapy. Also excluded were patients who were unable to attend the clinic on a daily basis, and those who had already been in a buprenorphine study.

Setting
The setting was community care. The economic study was carried out in Australia.

Dates to which data relate

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same patients who provided the effectiveness data, but it was only calculated for every second patient.

Study sample
No power calculations were reported in this paper. Full details of the effectiveness evidence were reported elsewhere (see Other Publications of Related Interest). All patients attending three government clinics were included in the study if they met the inclusion criteria, thus there was no sample selection. Of the 405 patients included, 205 were...
randomised to the methadone group and 200 to the buprenorphine group.

**Study design**
The first stage (weeks 1 to 13) of the trial was a double-blind randomised controlled trial (RCT). During the second stage (weeks 14 to 26), patients and researchers knew the medication they had been receiving. In stage 3 (week 27 to 104), patients could continue with the medication they had been allocated, or move to either buprenorphine or methadone. In total, 44% of the methadone group and 36% of the buprenorphine group completed the treatment, and 34% of the methadone group and 30% of the buprenorphine group were able to be followed up.

**Analysis of effectiveness**
The analysis of effectiveness was conducted on an intention to treat basis. The primary health outcome used was the change in heroin-free days between the month prior to treatment and 6 months after treatment. At baseline the two groups were comparable in terms of severity of dependence, age of first use, duration of use, craving, or the global severity of the drug problem as assessed by the patient and the research staff.

**Effectiveness results**
The average number of heroin-free days went from 2.59 (standard deviation, SD=5.66) to 22.57 (SD=7.92) in the methadone group and from 3.23 (SD=6.26) to 21.88 (SD=8.52) in the buprenorphine group.

When data for patients who were not available for follow-up were imputed, the estimated heroin-free days went to 9.43 (SD=11.36) in the methadone group and to 8.51 (SD=11.03) in the buprenorphine group.

Using the imputed figures, there was no significant difference between the groups (Mann-Whitney non-parametric test: z = -1.38, p=0.168).

**Clinical conclusions**
The authors stated that methadone was more effective as it resulted in a greater increase in heroin-free days, although the difference was not statistically significant.

**Measure of benefits used in the economic analysis**
The measure of benefit was the increase in heroin-free days.

**Direct costs**
No discounting was carried out since the costs were incurred during less than two years. The costs measured were staff time, diagnostic procedures, medication and overhead costs. These were derived from actual data obtained by examination of the clinical records of every second patient. The data were obtained from patient clinical records, actual staff salaries, and standard government charges for diagnostic procedures. The price of methadone was obtained from the government’s purchasing price, while the price of buprenorphine came from Medi Media Australia Pty Ltd. (2001). The overhead costs were obtained from the financial records of the clinics, while construction costs for each city were obtained from Rawlingsons Construction Consultants and Quantity Surveyors (1999). Prices were not given separately from the quantities. The price year was 1998-99.

**Statistical analysis of costs**
No statistical analysis of the costs was carried out.

**Indirect Costs**
No indirect costs were calculated.
Currency
Australian dollars (Aus$).

Sensitivity analysis
A sensitivity analysis was carried out on the effects of:

reducing the dosing time required to administer buprenorphine;
reducing the cost of buprenorphine by 30%;
reducing the amount of staff time spent with buprenorphine patients in clinic 3, as it was much higher than that in the other two clinics; and

doing all the above three simultaneously.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The mean cost over the 6 months was Aus$1,415 in the methadone group and Aus$1,729 in the buprenorphine group.

Both cost distributions were found to be skewed and a Mann-Whitney non-parametric test showed that the differences between the groups were not statistically significant.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (ICER) was estimated. Bootstrapping used to estimate 95% confidence intervals.

The point estimate for the ICER was -Aus$201, indicating that methadone dominates. However, the confidence intervals were estimated to be -Aus$2,068.91 to Aus$1,808.69, indicating that the difference in cost-effectiveness was not statistically significant.

Reducing its dosage time reduced the buprenorphine costs to Aus$1,596, reducing its price reduced the costs to Aus$1,599, and reducing the mean staff cost reduced the costs to Aus$1,724.

When all three reductions were conducted simultaneously, the cost went to Aus$1,460. The authors pointed out that there is then hardly any difference between the costs of the two medications.

Authors' conclusions
The authors speculated that the cost of administering buprenorphine is likely to come down in the future relative to methadone, as its price is likely to decrease and the time necessary to administer it also decreases as staff become more proficient. Even without these assumptions, the difference in cost-effectiveness between the two treatments was not found to be statistically significant. Thus, the authors concluded that buprenorphine should be considered a viable alternative to methadone.

CRD COMMENTARY - Selection of comparators
The justification for the comparator (methadone) was that it is widely used and has been well researched. You should decide if it is widely used in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness data were derived from a single study. The study design, an RCT, was appropriate for the study question. The study sample was representative of the study population, but the exclusion criteria meant that the results cannot be applied to all heroin addicts. It was reported that the results in the earlier paper (see Other Publications of Related Interest) showed that the patients in the two groups were comparable at baseline. The analysis of effectiveness was handled credibly, but it was unclear how the imputed heroin-free days had been calculated.

Validity of estimate of measure of benefit
The measure of health benefit was proxied directly by a single effectiveness estimate.

Validity of estimate of costs
From the cost perspective adopted, all the relevant categories of cost were included. However, as the authors noted, if a patient dropped out of the study and sought treatment elsewhere, this was not captured in the study. The costs were not reported separately from the quantities, which limits the generalisability of the results. The resource use quantities were taken from a single study. A sensitivity analysis was carried out on the resources used in dosing and treating the buprenorphine patients, and the authors presented a plausible case for their choice of variation in inputs. No other sources were used for the resource quantities. No other analysis of the quantities was carried out. The prices were taken from the authors' setting and from published sources. No statistical analysis of the prices was performed. A sensitivity analysis in which the price of buprenorphine was varied was appropriately carried out. No other sources were used for prices and no other analysis of the prices was conducted. The price year was reported.

Other issues
The authors made appropriate comparisons of their results with the findings from other studies. The issue of generalisability to other settings was addressed. The authors did not present their results selectively and were aware of several shortcomings in the study. For example, the use of retrospective data, only collecting cost data for every second patient, using a questionnaire to calculate staff time, and using self-reporting to determine the number of heroin-free days. A further shortcoming was the method of imputation used for patients missing from the follow-up. However, the authors did not draw attention to the fact that all of the sensitivity analyses were performed in a favourable approach regarding buprenorphine.

Implications of the study
The authors concluded that their study shows that buprenorphine is a viable alternative to methadone in the treatment of opioid dependence. The implicit implication of the study is that any new research should aim to gather resource data prospectively on all the patients in the study.

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Other publications of related interest

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